REVIEW

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Barriers to HPV Vaccination in Brazil: A Systematic Review

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Abstract

Introduction: Cervical cancer is the third most common cancer worldwide. Expanding HPV (Human papillomavirus) vaccination coverage to 90% of all adolescent girls by 2030 is the World Health Organization's (WHO) primary vaccination strategy to eliminate cervical cancer by the end of the century. **Aim:** To identify the main challenges associated with HPV vaccination in Brazil. **Methods:** A systematic review in accordance with the PRISMA reporting guidelines was conducted using PubMed, EMBASE Lilacs, Cochrane Library, SCOPUS, and Web of Science databases, which included prospective and cross-sectional studies. Different term combinations were used: ((("HPV vaccination"[TITLE]) OR ("HPV vaccine"[TITLE]) OR ("HPV immunization"[TITLE]))) AND (Brazil); HPV vaccination AND Brazil; Barriers AND vaccination AND HPV AND Brazil; Barriers AND HPV vaccination AND Brazil. This study included published articles with no language or date restrictions. **Results:** A total of 179 articles were identified. After deleting 50 duplicates, 78 articles were excluded based on their title or abstract, while 28 were excluded after full reading, thus leaving only 23 articles. Seven studies were carried out in the southeast region, one in the southern region, one in the midwest region, and two in the north region. Knowledge was the biggest problem detected among parents and guardians, health caregivers, health students, and general users of the Brazilian Unified Health System (SUS). **Conclusion:** All studies indicated that knowledge is essential for adherence. For students and health professionals, a more comprehensive approach to the topic would be beneficial in advancing their knowledge.

Keywords: HPV- Papillomavirus Vaccines- Immunization programs- Vaccines- Patient Acceptance of Health Care

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Introduction

Cervical cancer is the third most common cancer globally, with high mortality when left untreated [1]. Human papillomavirus (HPV) is responsible for nearly all cases, therefore HPV vaccines have the potential to significantly reduce the incidence of cervical cancer [2]. In Brazil, 15.590 new cases are detected annually, representing an estimated incidence risk of 15.33/100.000 inhabitants. It is estimated that, of the confirmed cases, 5.160 resulted in deaths. Among the regions of the country, the North stands out for having the highest incidence of the pathology with 23.57 cases/100.000 women, followed by the Central-West and Northeast with 22.19/100,000 and 18.79/100.000, respectively, the South in fourth with a rate of 15.87/100.000, and the Southeast in fifth with a record of 10.15/100.000 women [3].

Access to HPV vaccines varies worldwide, with high-income countries having the highest coverage rates. Therefore, people living in the countries with the highest worldwide burdens of HPV-related diseases have the least access to vaccinations [4]. Many countries have started national HPV vaccination programs, with vaccine coverage ranging from 9% (Greece) to 32% (US) and 76% (UK) [2, 5]. Men living with HIV reported higher rates of HPV vaccination compared to their partners, potentially due to greater health care utilization or contacts with health care providers attuned to their health needs. However, HPV vaccination uptake is suboptimal given the high prevalence of high-risk HPV genotypes among this group [6].

In 2019, Mexico had a 97.5% immunization rate for females up the age of 15 years. Peru was another Latin American country, with 91% of its population vaccinated in 2019, and its National Immunization Program (NPI) featured a nonvalent vaccine (against HPV types 6,11, 16, 18, 31, 33, 45, 52, and 58) as well. Brazil is a country of continental dimensions with distinct social, cultural, and health characteristics in each region. This makes several tasks challenging, including immunization programs [7, 8]. In Brazil, insufficient access to health services and geographical difficulties make cervical cancer a public health concern. In 2014, the Brazilian Ministry of Health initiated a campaign of vaccination against HPV, and the goal was to vaccinate 80% of the population [9]. The HPV vaccine began to be offered, at no direct cost, in basic health units, public and private schools for girls aged 11 to 13 years [10]. In the first year of vaccination, 87% of

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the Brazilian municipalities had achieved the goal target of 80% coverage for the first dose among eligible girls; this number dropped to 32% of the cities for the second dose [11]. Over the second vaccination cycle, there was a noticeable drop in vaccine compliance, to less than 38%. Following the initial dose, eight patients experienced headache, vertigo, and limb numbness. The media made public the fact that three teenagers were hospitalized due to paralyzed legs. Based on the information at hand, none of these incidents was connected to the immunization [9].

The majority of developing nations face significant challenges in maintaining HPV vaccine coverage, and Brazil is no exception [11]. According to national immunization program data from 2014 to 2017, the cumulative vaccine coverage for the two-dose course in girls was 45.1%, and 72.4% of the targeted female population received at least one dose. The coverage for at least one dose in boys is disappointingly low at 20.2% [2].

Brazil was the first country in South America to administer the vaccine to boys as part of national immunization efforts and provide cross-protection for females against HPV-related malignancies of other affected systems [7,10]. Glehn et al. [12] analyzed the National Immunization Program data and demonstrated that vaccination coverage for males was lower than for females in all states and for both doses, leading to the conclusion that this could be due to the lack of knowledge of families on the negative impact of HPV on males., nonetheless there is no data available for a definitive conclusion.

In 2018, the World Health Organization (WHO) issued a global call to act on the elimination of cervical cancer as a public health problem, setting targets for this elimination based on three pillars: vaccination, tracking, and treatment. Expanding HPV vaccination coverage to 90% of all adolescent girls by 2030 is the key strategy in the vaccination strategy [13].

Barriers to vaccination vary among countries because some countries are better able to develop strategies to deal with vaccine hesitancy and cultural and geographic differences in access [14, 15]. In Brazil, about 8% of the target population exhibits vaccine hesitancy, with ineffective policies bearing the majority of the burden"[14]. This review aimed to identify the main barriers to HPV vaccination in Brazil.

Materials and Methods

The review protocol was registered with the National Institutes of Health Research International Prospective Register of Systematic Reviews (PROSPERO) (registration number CRD42021284800).

Search strategy

A review of the literature was conducted to identify articles using the PubMed, EMBASE, Lilacs, Cochrane Library, SCOPUS, and Web of Science databases using the terms Barriers OR obstacles AND HPV vaccination OR HPV vaccine AND Brazil with no language or date restriction until January 2025. Because they may lead to bias, there were no language or date restrictions. Despite the fact that HPV vaccination first began in 2006, it is possible that there has been some prior research. Different term combinations were used: ((("HPV vaccination"[TITLE]) OR ("HPV vaccine"[TITLE]) OR ("HPV immunization"[TITLE]))) AND (Brazil); HPV vaccination AND Brazil; Barriers AND vaccination AND HPV AND Brazil; Barriers AND HPV vaccination AND Brazil. A search for grey literature was also carried out using the OpenGrey database (http://www.opengrey.eu/search), Google Scholar, and WorldCat.

This review was conducted in accordance with the "Preferred Reporting Items for Systematic Reviews and Meta-Analyses" (PRISMA) checklist [16].

Data was collected from September, 2021
Eligibility criteria

The main inclusion criterion was that the study was conducted in Brazil. Other eligibility criteria for inclusion were studies that discussed barriers to HPV vaccination, factors associated with a lower vaccination rate, and routine HPV vaccination interventions to increase uptake. Survey research studies, published as qualitative, cross-sectional, and cohort studies, were included. Case reports, case series, letters to editors, abstracts, reviews, duplicates, and studies unrelated to HPV vaccine barriers in Brazil were excluded. The search was carried out independently by two authors who extracted relevant data from eligible articles, including author, year of publication, aim, design, sample size, assessment and analytical method, and results. In cases of disagreement, the data were evaluated by a third author.

Data extraction

The quality of each selected study was evaluated as part of the data extraction process by reading the full text of each article identified for inclusion in the review. Quality analysis was performed related to selection, measurements, and outcomes. Two reviewers independently assessed the quality of eligible studies using the JBI Critical Appraisal Checklist for Analytical Cross-Sectional Studies, developed by the Joanna Briggs Institute, an international research organization dedicated to promoting evidence-based health care. Newcastle-Ottawa quality assessment scale, which evaluates the selection, measurement, and outcome. Data were extracted from the texts and entered into a Microsoft Excel extraction table. We did not contact any authors to obtain data. The study design, objectives, and methodologies were also analyzed. Multivariate analyses involving confounding factors were also performed. Analysis of the results was conducted among three groups: adolescents and guardians, health caregivers and healthcare students, and general SUS users.

Results

A total of 179 articles were identified. After deleting 50 duplicates, 78 articles were excluded based on their title or abstract, while 28 were excluded after full reading. The remaining 23 articles were included in this review. No additional work was found using OpenGrey, Google

Scholar, or WorldCat (Figure 1).

Among the analyzed studies, 21 were cross-sectional, 1 qualitative study and one was a prospective cohort study. For better individualization, reports were separated by group. Adolescents and their guardians represented the first group. (Table 1) The second group comprised health professionals and healthcare students. (Table 2) The third group consisted of users of the health system (SUS). In all groups, we sought to identify barriers to HPV vaccination (Table 3).

The systematic literature search described above yielded no results for intervention or clinical trials. In general, these studies were representative of the Brazilian regions. In the southeastern region, three studies were conducted in São Paulo and four in Minas Gerais. In the southern region, one study was conducted in Santa Catarina, Brazil. In the Midwest region, one study was carried out in Brasília and one in Mato Grosso do Sul, and in the North region, one study was carried out in Roraima, one in Acre and one in Pará. In the Northeast region, one study was conducted at Piauí. Five studies were more comprehensive: two of them evaluated all the capitals of the 27 federative units, one analyzed seven cities, including the five regions of Brazil, and one used Facebook data, and did not identify the regions.

In general, the study demonstrates strong methodological rigor and aligned well with JBI standards. One study was a qualitative study and did not aim to quantify associations or control for confounders [35]. One study did not apply statistical controls or stratified analysis to address potential confounders [34]. Five studies [8,27,29, 32, 38], partially fulfilled the item regarding the identification and management of confounding factors, while one study only [31] partially addressed the use of appropriate statistical analysis. Nonetheless, in all cases, these items were at least partially satisfied, and the studies maintained an overall acceptable methodological quality. (Table 4).

Lack of knowledge was assessed in studies based on false assumptions regarding HPV infection and vaccines.

Parents and guardians and adolescents

Knowledge was the biggest problem detected among parents and guardians [2, 17, 18, 23, 25, 26]. Thinking that vaccination could be harmful to health was observed in 42.8% of adolescents by Costa et al. [28] Santos et al. [25] showed that low knowledge is associated with a high immunization dropout rate among adolescent girls. Farias et al. [26] Observed that Limited knowledge about HPV and the HPV vaccine was correlated with lower compliance to vaccination (adjusted OR = 1.42; 95% CI: 1.01 to 2.76). The belief that boys are not at risk of acquiring HPV is reported as the main reason for not vaccinating them [2, 20].

Costa et al. showed that only 28.3% of adolescents knew that the vaccine can be given to those who had already had sexual intercourse and 32.1% knew that the vaccine cannot cause HPV infection [28]. Oliveira et al. [24] showed that participants who knew HPV was a causative factor in cervical cancer were 1.94 times more likely to have been vaccinated than those who did not (CI 1.18 a 3.18; p=0.009) and that participants who knew that the HPV vaccine is part of the immunization program for female adolescents were 2.84 times more likely to have been vaccinated than those who did not (CI 1.32 – 6.12; p=0.008) [24] Santos et al. [14] showed that 2.1% of adolescents knew HPV was a causative factor in cervical cancer and 9% of mothers/guardians [25]. Farias et al. [26] also demonstrated that the belief that the HPV vaccine is important for the daughter as a factor for compliance (adjusted OR = 0.62; 95% CI: 0.23 to 0.93). Furthermore, Silva et al. [21] found that unawareness about HPV vaccination was the most common reason for nonvaccination of schoolchildren. Still, lack of information and fear of vaccination is associated with refusal to be vaccinated [19]. Another issue with refusing the vaccine was the fear of adverse events. Mendes-Lobão observed the fear of reactions reported as the primary reason for refusing HPV vaccination by 51% of the parents, and as one of them by 61%. Farias et al. observed adverse effects of the HPV vaccine as a risk factor for non-compliance (adjusted OR = 1.66; 95% CI: 1.01 to 2.71) [2, 26] .

Health caregivers and healthcare students

All studies with caregivers and healthcare students focused on knowledge about HPV, related cancers, vaccines, and factors influencing delivery in public health. Costa et al. showed that more than 90% of students of both sexes have a preconceived idea that the vaccine can stimulate early sexual intercourse, with 90.3% men and 96% women of respondents [28]. Biselli-Monteiro et al. [29] comparing freshman and senior undergraduate students of medicine, pharmacy, speech therapy, nursing, and physical education students, observed more knowledge among medicine students, with less knowledge about the relationship between HPV and other cancers than cervix. Wanderley et al. [8] observed that, of the medical students who admitted unwillingness to be vaccinated, 81.3% were males. The main reasons cited were the feeling of being safe, lack of counseling, or low efficacy of the vaccine. Among those who wanted to be vaccinated, the main barrier was the high cost of the vaccine. Figueroa-Downing et al. [30] focused on vaccine delivery and perceived that doctors were less likely to check vaccination status than community health agents, and that knowing the correct dosing schedule was associated with this verification with adjusted prevalence ratio (aPR) 0.25 (95% CI 0.07–0.91) and knowledge about the correct dosing schedule was associated with always rather than never verifying vaccination status (aPR 2.46 (95% CI 1.06–5.7) [30]. Other issues were observed by Manuel et al. related to community health agents, that The main issues was the belief that HPV can be cured with antibiotics (70.2%), that HPV test is necessary to determine who will get the vaccine (50.3%), not knowing that the vaccine protects against most cervical cancers (37.1%), and the thought that men are not at risk (40.9%).

General users of the Brazilian Unified Health System (SUS)

The issue of knowledge was also presented to the

Table 1. Selected Studies with Author/Year of Publication, Seting, Collection Period Study, Design, Sample Size, Assesment Methods and Results

Author, year	Setting/ collection period	Aim	Design	Sample	Assessment and analytical methods	Results
Silva, 2024[17]	Brazil states	To analyze the distribution and factors associated with lack of knowledge.	Cross-sectional	17,805 students of aged 13-17 years	2019 National School Health Survey among students of public and private schools, Logistic regression model was used to calculate Odds Ratio (OR) and 95% confidence intervals (95%CI).	The lack of knowledge about the HPV vaccine was reported by 45.54% of Brazilian students. The lower chance of lack of knowledge were female gender (OR 0.41; 95% CI 0.35-0.48), higher maternal education (OR 0.62; 95% CI 0.50-0.77) self-rated health as Poor/very poor (OR 0.64; 95% CI 0.49-0.86) and receiving contraceptive counseling (OR 0.77; 95% CI 0.65-0.91).
Heimbecker, 2024[18]	Paraná	To assess the knowledge of parents/guardians on HPV infection and vaccine prophylaxis	Cross-sectional	388 parents	A self-answered questionnaire. with uestions assessing sociodemographic characteristics, knowledge, and attitudes toward HPV infection and vaccination	A total of 212 (61.8%) participants showed HDK. Participants who were male (OR=0.39; 95% CI=0.22, 0.70) and lived in larger households (OR=0.48; 95% CI=0.25, 0.95) were less likely to present higher degree of knowledge.
Rodrigues, 2023[19]	Small rural Brazilian municipality: Alterosa, in the state of Minas Gerais.	To examine the main reasons provided by parents or guardians of a target population that did not have the first dose of HPV vaccine, and to verify the factors associated with the reasons for non-vaccination.	Cross-sectional	182 parents or guardians	interviews based on the Health Belief Model (HBM), conducted with parents and guardians of unvaccinated children or adolescents.	Lack of information as the reason most frequently reported by parents (62%;), followed by fear (30%) and logistical reasons.
Ferreira, 2023[20]	Montese, (Pará-Brazil)	to investigate the acceptance of the HPV vaccine of parents or guardians of a peripheral community.	Cross-sectional	147 parents or guardians	The questionnaire “Knowledge and Acceptability of HPV and Its Vaccine” was used.	Approximately 34.6% of the children's parent or guardians did not accept the vaccine, which was associated with having a son, not knowing the number of necessary vaccine doses, and not knowing anyone vaccinated.
Silva, 2022[21]	All regions of Brazil	to analyze the prevalence of schoolchildren vaccinated against human papillomavirus (HPV) and the reasons related to non-vaccination.	Cross-sectional	160 adolescents 13-17 years	Survey questionnaire in Brazilian public and private schools.	As for the reasons for not receiving the vaccine, most adolescent students in the country answered “did not know they had to take” (46.8%; 95%CI 45.4;48.3), followed by the answers “other reason” (26.7%; 95%CI 25.4;27.9) and “fear of reaction to the vaccine
Galvão, 2022[22]	municipality of Teresina, state of Piauí, regarding human papillomavirus (HPV).	To analyze knowledge, attitudes, and practices of adolescent students from public schools	Cross-sectional	472 adolescents	knowledge, attitude, and practice (KAP) survey	The percentage of adolescents with insufficient knowledge about HPV was 72.7%, and 65.9% had negative attitudes towards infection prevention
Gomes, 2020[23]	Health unit of Sao Paulo University, Brazil, (2015 to 2016).	To evaluate factors related to knowledge about HPV, its vaccine, acceptability and divergences among Brazilian adolescents and parents/guardians.	Cross-sectional study	1047 individuals, including 776 adolescents and 271 parents/guardians.	Adolescents and their guardians/parents answered a survey. The level of "suitable" knowledge about HPV, the vaccine and its clinical repercussions was analyzed.	The biggest barriers encountered by adolescents were in relation to knowledge: 28.3% knew that the vaccine can be given to those who have already had sexual intercourse, 31.4% that the vaccine gives the chance of changes in the preventive, 32.1% knew that the vaccine cannot cause HPV infection and 42.8% thought the vaccine could be harmful to health.
Oliveira, 2020[24]	Basic Health Unit located in Cruzeiro do Sul, Acre (May - August 2017).	To analyze the level of knowledge about and the acceptability of the HPV vaccine among vaccinated and unvaccinated adolescents in the Western Amazon.	Cross-sectional study	190 adolescents aged 10 to 19 years.	A questionnaire with 27 questions addressing the knowledge about HPV, the vaccine, barriers to vaccination, vaccine acceptability, and personal history related to HPV infection.	Participants who knew HPV was a causative factor in cervical cancer were 1.94 times more likely to have been vaccinated than those who did not (CI 1.18 a 3.18; p=0.009). Moreover, participants who knew that the HPV vaccine is part of the immunization program for female adolescents were 2.84 times more likely to have been vaccinated than those who did not (CI 1.32 – 6.12; p=0.008).
Santos, 2020[25]	OuroPreto (march 2014-march 2016)	To assess the knowledge of adolescent girls and their mothers/guardians about HPV and HPV vaccine, identify the factors associated with this knowledge, and evaluate immunization dropout rate.	Cross-sectional study	666 adolescent girls and 623 mothers/ guardians.	Interviews composed by multiple-choice and open questions that addressed sociodemographic data, sexual and gynecological history, knowledge about HPV, HPV vaccine, and cervical cancer.	High knowledge was associated with higher educational level and higher household income. Low knowledge was associated with a high immunization dropout rate of HPV vaccination among adolescent girls.
Mendes Lobão, 2018[2]	Parents in seven major Brazilian cities (July, 2015 - October, 2016).	To assess coverage and parental acceptance of the HPV vaccine for adolescent daughters and sons in Brazil.	Cross-sectional study	826 parents.	Individual interview with a semistructured script as a source of evidence of data that approached the user regarding access to vaccination A priori, the interview script was pre-tested.	Parents were more likely to refuse HPV vaccination if they believed that HPV vaccine is not safe or can cause severe reactions, that girls age 9 to 13 years are too young to get HPV vaccine, and that HPV vaccination can cause girls to become sexually active earlier. Parents refusing HPV vaccine for boys were less likely to perceive their sons as being at risk of getting HPV infection.
Farias, 2016[26]	Parents or guardians of pre-adolescents girls who were students of middle schools in the capital city Boa Vista, Roraima (2014).	To evaluate the HPV vaccination coverage in Boa Vista, Roraima (Brazil) and to identify personal and socioeconomic factors related to non-compliance to HPV vaccination.	Cross-sectional study	797 female students in vaccine target age.	Semi Structured questionnaire addressed socioeconomic and demographic data, the compliance to HPV vaccination, the knowledge of the parents / guardians about HPV, cervical cancer and the HPV vaccine and the parents’ perception of the HPV vaccine. The questionnaire had been previously tested and validated with persons of different levels of education.	Respondents who were concerned about the adverse effects of the vaccine showed a 60 % higher rate of non-vaccination (OR=1.62, 95 % CI 1.04 to 2.51). Those concerned with the quality of the vaccine freely offered showed an 80 % higher likelihood of non-vaccination (24.4 % vs 14.7 %; p=0.003; OR=1.78, 95 % CI: 1.15 to 2.99) Private school students had increased rate of non compliance compared to public school students (43.7 % vs 15.9 %; p=0.003; OR=4.51, 95 % CI: 1.63 to 12.46).

Table 2. Selected Studies with Author/Year of Publication, Setting, Collection Period Study Design, Sample Size, Assessment Methods, Results, and Quality of the Studies in Health Caregivers and Healthcare Students

Author, year	Setting/ collection period	Aim	Design	Sample	Assessment and analytical methods	Results
Souza, 2023[27]	Santa Mônica rural settlement in Terenos, Mato Grosso do Sul.	To understand health professionals' perceptions about vaccination against human papillomavirus (HPV)	Cross-sectional	Of the 18 health unit workers, 12 (two men and ten women) made up the conversation circle, seven community health agents, one nurse, one doctor, one dentist, one dental assistant and one pharmacy attendant.	Quantitative and qualitative methodologies, consultations on vaccination cards, records of community health agents	Vaccination hesitation or refusal in the first year of vaccine administration may be related to the fact that adherence could stimulate sexual activity and contribute to the decrease in condom use and cervical cancer screening.
Costa, 2020[28]	University of São Paulo Medicine School (2016).	To analyze factors associated with knowledge gaps and acquisition about HPV and its vaccine among medical students.	Cross-sectional study	518 medical students.	A convenience sample of students completed a data collection instrument containing questions on knowledge about HPV and its vaccine, and vaccine acceptability.	Men respondent think the HPV vaccine will stimulate the onset of sexual activity at an earlier age more than women.The questions "should HPV vaccine be applied before first sexual intercourse?" And "does HPV vaccine reduce the chance of genital warts?" showed that both groups did not have a good level of knowledge and there was no knowledge acquisition during graduation.
Biselli-Monteiro, 2020[29]	Campinas State University (August-november 2017).	To evaluate the knowledge related to HPV and HPV vaccination, among freshman and senior undergraduate students of medicine, pharmacy, speech therapy, nursing and physical education	Cohort study.	First questionnaire: 492 students. Second questionnaire:233 students.	A questionnaire was applied concerning sociodemographic aspects, sexual background, and knowledge about HPV and its vaccine. Three months later, it was applied a second questionnaire concerning the new rate of vaccination.	Knowledge that HPV infection is most often asymptomatic, may become latent and cause genital, anal and oropharyngeal warts showed a large difference among courses (p-trend < 0.001). Only 32.6% of physical education students knew that HPV can be asymptomatic, compared with 77% of medicine students. Regarding the other cancers related to HPV infection, the percentage of right answers among all of the women was below 40%.
Wanderley, 2019[8]	Medical school year 1 to 6, in a medical school, Brasilia (2017)	To explore how medical students differ regarding the HPV vaccination status according to their demographics sexuality, medical school year and sources of information regarding the vaccine.	Cross-sectional study	379 students.	Individual interview with a semistructured script regarding access to vaccination; technical visits to vaccine rooms. A priori, the interview script was pre-tested.	The high cost of the vaccine was perceived as a barrier among those respondents who wished to be vaccinated. Among the 84 (81.3% male) students who admitted unwillingness to be vaccinated, approximately two-thirds cited the feeling to be safe, lack of counseling, or low efficacy of the vaccine as the reasons for their reluctance.
Figueroa-Downing, 2017[30]	Five public health posts in São Paulo (July 28 - August 8, 2014)	To assess the association between Brazilian healthcare providers' characteristics and their knowledge, perceptions, and practices regarding the HPV vaccine.	Cross-sectional study	212 healthcares.	Healthcare professionals directly involved in patient care were asked to complete a written survey. Factors associated with routine verification of HPV vaccination status were evaluated.	Doctors were significantlyless likely to report always asking than were community health agents Adjusted prevalence ratio(aPR) 0.25 (95% CI 0.07–0.91). Knowledge about the correct dosing schedule was rather than never verifying vaccination status (aPR 2.46 (95% CI 1.06–5.7). associated with always
Manoel, 2017[31]	City of Tubarão-SC (2014)	To evaluate the knowledge of Community Health Agents about HPV and its vaccination.	Cross-sectional study	124 Community Health Agents	Data were collected through an evaluation tool about HPV and its vaccination, validated for English language and translated and adapted into Portuguese.	37.1% do not know that the vaccine protects against most cervical cancers, 50.3% think that the HPV test is necessary to indicate who needs the vaccine and 70.2% think that HPV can be cured with antibiotics, 40.9% think that men do not can get HPV

Table 3. Selected Studies with Author/Year of Publication, Setting, Collection Period Study Design, Sample Size, Assessment Methods, Results, and Quality of the Studies in Users of the Brazilian Unified Health System

Author, year	Setting/ collection period	Aim	Design	Sample	Assessment and analytical methods
Wendland, [32]	119 public primary care units from all 27 federative units of Brazil (September 2016 - November 2017)	To evaluate differences in the HPV infection rate according to vaccination status in a nationwide sample of women aged 16 to 25 years who utilized the Public Health System in Brazil.	Cross-sectional, multicentric study	5,945 young adult women	Face to face interviews
Kops, [33]	Capitals of all 26 states and the Federal District - 119 primary care units in Brazil (2016 and 2017).	To evaluate knowledge about HPV and vaccination among men and women aged 16–25 years who use the public health system in Brazil.	Cross-sectional study	8,581 participants.	Interview with a semistructured script as a source of evidence of data that approached the user regarding access to vaccination. A priori, the interview script was pre-tested.
Pereira da Veiga, [34]	Between January and July 2018.	To evaluated the posts published by the Ministry of Health and posted comments, shares and reactions of the population related to the HPV vaccination on Facebook page.	Cross-sectional Sociological investigation for behavioral research	28 HPV vaccination posts published and their comments, reactions and shares.	This study was divided into three parts: (1) overview of published posts; (2) analysis of posted comments; and (3) subgroup analysis of posts and attached comments.
Duarte, [35]	Four microregions of health in the Western Extended Region of Minas Gerais. Between June 2016 - April 2017.	To understand the feelings, senses, perceptions and perspectives of users regarding access to vaccination in Primary Health Care.	Holistic-Qualitative Multiple Case Study, based on Comprehensive Sociology of Everyday Life	74 participants. 19 - 67 years-old.	Intensive individual interview with a semistructured script as a source of evidence of data that approached the user regarding access to vaccination. A priori, the interview script was pre-tested.
Abreu,[36]	City of Ipatinga, MG (2014)	To assess the knowledge of men and women about HPV in the city of Ipatinga, Minas Gerais, and evaluate socioeconomic factors and preventive measures associated with such knowledge	Cross-sectional study	591 participants.	Data collection was performed verbally, through structured forms, in public and/or private environments
Osis, [37]	Users of five primary health units and two polyclinics in Campinas, SP (2011)	To investigate knowledge of HPV and HPV vaccines in men and women, users of the Brazilian Unified Health System, and the intention to get themselves and their teenage children vaccinated	Cross-sectional study	538 users of the Brazilian Unified Health System, 286 women (18-49 years old) and 252 men (18-60 years old).	Structured questionnaire for identifying variables associated with knowledge of HPV and HPV vaccines, and participants vaccination intentions

Table 4. Critical Appraisal Summary of Included Analytical Cross-Sectional Studies

Article Title	Inclusion Criteria	Subjects & Setting	Valid Exposure Measurement	Standard Outcome Criteria	Confounders Identified	Confounding Strategies	Reliable Outcomes	Appropriate Analysis
Silva, [17]	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes
Heimbecker, [18]	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes
Rodrigues, [19]	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes
Souza, [27]	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Partially
Ferreira, [20]	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes
Silva, [17]	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes
Galvão, [22]	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes
Wendland, [32]	Yes	Yes	Yes	Yes	Partially	Partially	Yes	Yes
Gomes, [23]	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes
Oliveira, [24]	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes
Santos, [25]	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes
Costa et al., [28]	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes
Biselli-Monteiro, [29]	Yes	Yes	Yes	Yes	Yes	Partially	Yes	Yes
Wanderley et al., [8]	Yes	Yes	Yes	Yes	Yes	Partially	Yes	Yes
Kops, [33]	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes
Pereira da Veiga, [34]	Yes	Yes	Yes	Yes	Partially	No	Yes	Yes
Duarte, [35]	Yes	Yes	Yes	Yes	Not applicable	Not applicable	Yes	Not applicable
Mendes Lobão, [2]	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes
Abreu, [36]	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes
Figueroa, [30]	Yes	Yes	Yes	Yes	Yes	Partially	Yes	Yes
Manoel et al., [31]	Yes	Yes	Yes	Yes	Yes	Partially	Yes	Yes
Farias, [26]	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes
Osis, [37]	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes

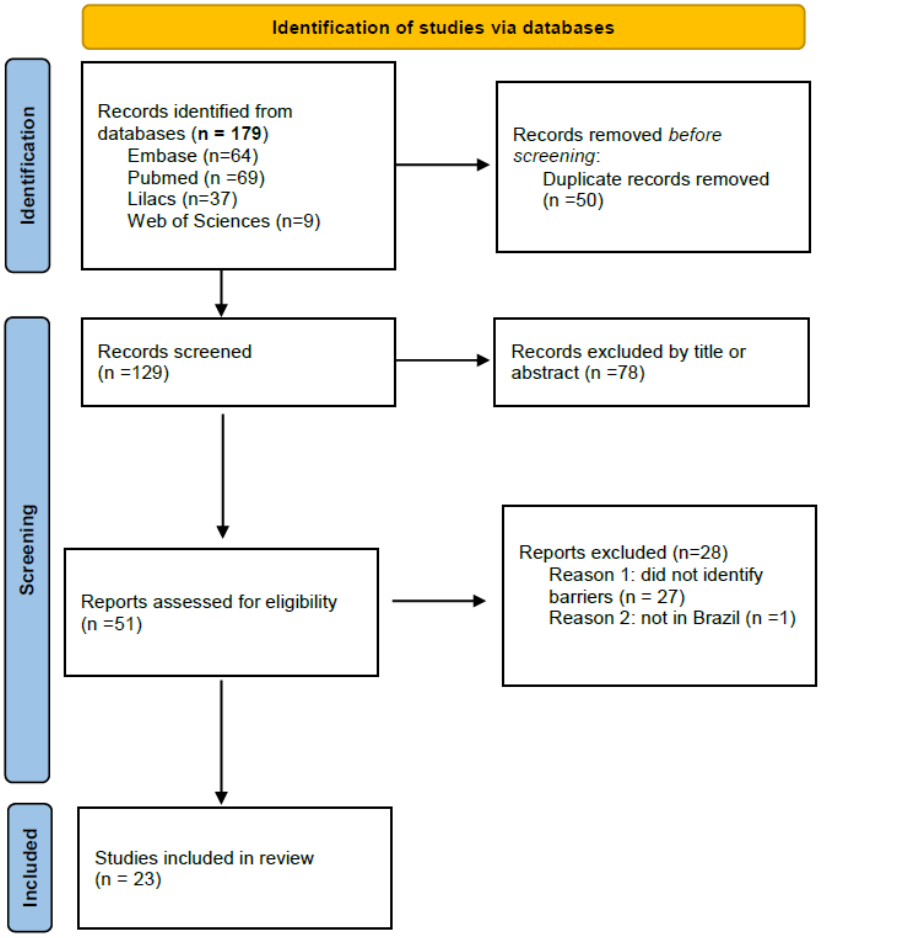

Figure 1. Barreiras Flow Diagram

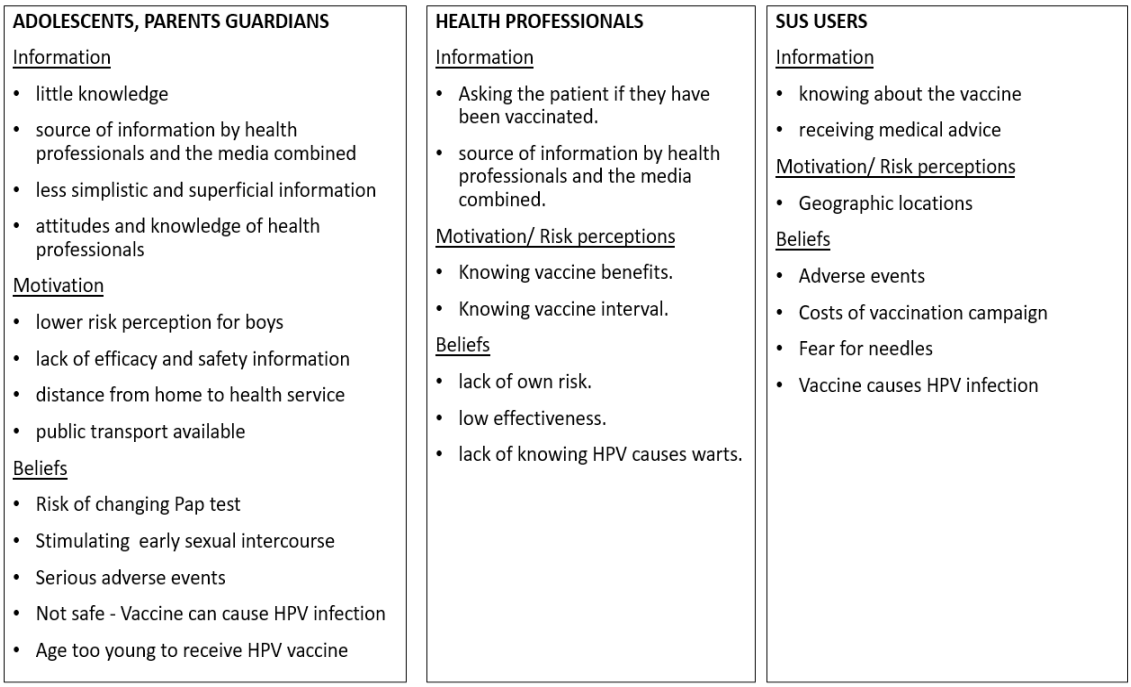

Figure 2. Information-Motivation-Behavioral (IMB) Barrier Model with Identified Factors of Adolescents, Parents and Guardians, Health Professionals and Students, and SUS Users in Selected Studies

group of general users of SUS. Osis et al. mentioned media as the greatest source of information, emphasizing that there is good receptivity to the vaccine by users, but little information is available. Similarly, Abreu et al. [36] mentioned television as the main source of information. Kops et al. [33] related greater knowledge about vaccines and HPV to older age and being in a relationship. Wendland et al. observed that rates of vaccination were related to low socioeconomic status, with vaccinated people being more likely to belong to social classes A-B (16.10%) than to classes C (11.68%) or D-E (10.63%), and geographical region, with the highest rate of vaccinated participants in Central-West region (14.57%), followed by the Southeast (13.47%), South (10.77%), Northeast (10.31), and North regions (9.24%) [32]. Duarte et al. [35] related low knowledge to difficult access, family fragility, fear of needles and fear of adverse effects and observed that scores for HPV knowledge among vaccinated subjects were significantly higher than those among nonvaccinated subjects [59.52% (95% CI 58.36-60.69) versus 51.17% (95% CI 50.0-51.65), respectively. Pereira da Veiga, analyzing he posts published by the Ministry of Health and posted comments and reactions of the showed negative posted comments involving concern over adverse vaccine events (84.0%), criticism of investments and the cost of the vaccination campaign (64.9%), vaccine availability (59.6%), and political issues (57.9%) [34]. Osis et al. observed that A little over 1/4 of participants reported having adequate information on HPV, and the variables associated in the bivariate analysis were: being female (37.2%), having a higher level of schooling (37.2% of those with nine or more years), belonging to socioeconomic strata A and B (35.7%) [37].

In the Information-Motivation-Behavioral (IMB) barrier model, we explain that the distance from home to the health facility, the availability of public transportation, and access issues can impact vaccine motivation. The IMB barrier model identifies factors that determined HPV vaccine nonadherence in selected studies (Figure 2).

Discussion

International studies have repeatedly identified several factors that hinder the acceptance of the HPV vaccine among adolescents. These factor include a lack of knowledge about HPV and the HPV vaccine, doubts about the safety and efficiency of the vaccine, a lack of time, a fear of pain, and previous negative experiences associated with vaccination [21]. Most studies on barriers to vaccination point to knowledge as an essential factor for adherence.

Several uniquely Brazilian contextual factors shape HPV vaccine hesitancy and uptake factors that go beyond general global trends and reflect the country's social, political, and healthcare landscape. Brazil's continental size and uneven distribution of healthcare infrastructure mean that populations in the North and Northeast regions often face greater logistical barriers to vaccination. These include long distances to health units, limited transportation, and fewer school-based vaccination programs. Such geographic inequalities are compounded by socioeconomic disparities, with lower-income and less-educated populations showing lower vaccination rates and knowledge levels [32].

While the quantitative synthesis of this systematic review offers valuable indicators regarding HPV vaccine awareness and uptake in Brazil, a thematic approach allows for a deeper understanding of the main barriers observed.

Knowledge gaps as a recurring barrier

Regarding knowledge about HPV in Brazilian studies, adolescents who were unaware of the association between HPV and cervical cancer were more likely to not be vaccinated [24, 25]. Beliefs that boys are not at risk have been highlighted in some studies. [2, 28]. Male vaccination has the potential to decrease the transmission of the virus to females, thereby reducing disease incidence beyond the effect of female-only vaccination [39]. Nonetheless, in many studies, male adolescents were less likely to receive HPV vaccination than female adolescents.

In addition, many SUS users are unaware of the asymptomatic nature of HPV infection [32, 33, 40]. Even more worrying, the same lack of knowledge has been demonstrated by health professionals, which may contribute to low adherence to vaccination [29,31].

Knowing that HPV can cause other types of cancer could be an additional factor in encouraging adherence; however, some studies have shown that many health professionals and students do not have this knowledge [29, 31]. Knowledge, or lack thereof, both for users and health professionals, seems to be a key factor in determining greater or lesser adherence to vaccination programs not only in Brazil.

In addition, limited awareness about vaccines is consistently reported in the literature. Many adolescents are unaware of the fact that it can be given to those who have had their first sexual intercourse [35], a fact that also occurs among medical students [28].

Structural and socioeconomic inequities

In Brazil, being black, belonging to lower socioeconomic classes, having less education, and not attending the basic health unit were associated with low levels of knowledge about the HPV vaccine, while older age and being in a relationship were associated with higher levels of knowledge [32, 33, 40]. After analyzing NPI data, Moura et al. observed that social inequality influences the spatial variability of vaccination coverage. This indicates that state administrators should develop individual strategies for each region. For example, despite being the first state in the North to administer the HPV vaccine in the public health network, Amazonas was noted for experiencing "relative difficulty" in achieving coverage [15]. A lower socioeconomic class was also associated with decreased vaccination rates by Wendland et al. [32] The cost of vaccines in age groups not covered by the vaccination program is also an important barrier [32, 33, 40].

Being female and having a higher level of education was an important factor positively associated with vaccination among adolescents [36, 37].

Fear and emotional hesitancy

The fear of adverse effects appears to be an important cause of non-acceptance of the vaccine for SUS users [34, 35, 41]. Some adolescents indicated that it was possible that the vaccine could cause infection as a reason for not being willing to vaccinate [23]. Among parents, the risk of stimulating early sexual activity was observed by Mendes-Lobão [2] and, even more worryingly, the same fear was shared by medical students in a study by Costa et al. [2, 28].

Information sources

Another distinctly Brazilian factor is the influence of media and public perception shaped by past events. The 2014 HPV vaccination campaign initially achieved high coverage, but media reports of adverse events, later found to be unrelated to the vaccine, sparked widespread fear and a sharp drop in adherence. This incident continues to influence public trust, particularly in communities where health literacy is low and misinformation spreads easily [9]. Silva et al., in a qualitative study, identified that the lack of clarification with a higher level of detail about HPV is due to how knowledge reaches the population, with information passed vertically, which does not lead to reflective thinking, causing people to doubt the subject. In addition, insufficient knowledge about the vaccine, identified in the speeches, has an impact on non-adherence to vaccination [42]. This observation shows that the education of professionals in universities does not lead students to change their own perceptions, which is dangerous as it perpetuates a mistaken idea. It is important that both the media and health professionals reinforce that the vaccine is a safe and effective option in preventing HPV infection and only increases protection, not having the effect of stimulating sexual intercourse. Many studies [43–45] point out that such decisions are not affected by the HPV vaccine.

The source of HPV information is important for attitudes. Being informed by friends was a risk factor for less knowledge about HPV and vaccines [33]. For Osis et al. [37] the media play a more important role in disseminating information about vaccination than their own health professionals. According to Kops et al., the source of information associated with the highest scores of knowledge about HPV was a combination of health professionals and the media [33]. This information is important to establish a strategy to increase user adherence. Because this is not a topic that is expressly discussed in the setting of adolescents, such as at school, it may be that adolescents lack the knowledge that has been discovered in this review.

In addition, social media is a popular place to discuss HPV vaccinations. Antivaccine messaging appeals to emotion and may trump the rational reasons a person would choose to get vaccinated, whereas pro-vaccine ads include factual information [46].

A significant current issue, "fake news" affects public health, as well as social and political issues. Despite concerns about vaccine safety dating back to earlier historical periods, the emergence of social media has magnified this tendency, allowing what UNICEF called a "real infection of misinformation" to spread. Information frequently circulates without being fully consumed in the modern environment when users' attention is contested by a massive amount of information on social networks [47].

Bringing together content creators from main platforms such as Instagram, Tik Tok, Facebook, YouTube, and Twitter, among others, with information about HPV, cancer prevention, and vaccine protection can

be an important tool to inform young people nowadays.

Healthcare professionals' role and limitations

Health professionals' attitudes and knowledge seem to stimulate the decision to vaccinate [40]. Therefore, physicians should be instructed to approach the topic of vaccination and their consultations in order to have a holistic view of the patient [30].

Issues that are not associated with knowledge have emerged in several studies. Wendland et al. pointed out geographic issues associated with lower adherence to vaccination, showing that the North and Northeast regions have poor adherence[32]. Some issues of an economic nature, such as concerns about vaccination campaign spending, emerged in a study that evaluated posts published by the Ministry of Health and comments posted [34].

In addition, we must observe the context of vaccination in Brazil, which has demonstrated that vaccine hesitancy has sharply increased. The role of the SUS also plays a unique part. The measles, mumps, and rubella vaccination rates have been steadily declining since 2013, which has sparked concerns about the potential for fresh outbreaks of vaccine-preventable diseases. It is important to understand the mechanics of Brazilian vaccine confidence in this situation. While SUS provides free access to vaccines, many users rely on it as their sole source of healthcare, making the quality of communication and trust in public health [48].

Government strategies

The preferred policies of the governing regimes have a significant impact on whether people accept or reject vaccines [49]. Government strategies may be important for increasing adherence to the vaccine. Kaul et al. found that schools that received both community-based education and on-site vaccination events had higher rates of adolescent HPV vaccination than schools that received only community-based education [50], demonstrating that certain public policies can help increase vaccine adherence.

Educational programs should focus on vaccine safety and on the importance of vaccinating boys. For adolescents, the focus should be on the information that the vaccine can be given to those who have already had sexual intercourse and also encourage studies on the effectiveness of the vaccine in people who have already started their sexual life. Reinforcing the idea that the vaccine does not cause HPV infection, in addition to the role of HPV as a causal agent of various types of cancer, is crucial. Training of health professionals should be encouraged, especially in family health programs, encouraging them to ask about vaccines, clarifying truths and myths, and informing them about the possibility that the vaccine brings to the elimination of cervical cancer of the uterus as a public health problem.

In addition, the repetition of successful strategies from the first dose of the 2014 campaign, such as availability in schools and targeted campaigns, may lead to the achievement of the WHO goal of eliminating cervical cancer as a public health problem.

Behavioral theories in practice

Using the IMB model to interpret the findings highlighted how inadequate information undermines motivation, consequently restricting action. Thematic analysis reinforces the IMB framework as a valuable foundation for guiding future interventions and the development of targeted campaigns in the Brazilian context.

This review has several limitations. The methodological approaches of the included studies varied considerably, which may affect the consistency of the findings. Notably, some studies did not adequately adjust for potential confounding factors, which could have influenced observed associations. Furthermore, the cross-sectional design common to all included studies limits the ability to draw causal inferences. Despite these limitations, a key strength of this review lies in its emphasis on context-specific analysis, incorporating cultural, socioeconomic, and geographic factors relevant to Brazil. Moreover, the included studies represent a broad spectrum of perspectives, encompassing adolescents, parents and guardians, health professionals, students, and general users of the public health system (SUS).

This research was able to reveal how the lack of knowledge about the disease and the vaccine impact on the refusal to vaccinate. With these results, we can show women's and children's health managers that information could change this scenario. Nonetheless, while education may inform people about the need to make changes, it may not effectively address motivation and accountability, implying that it is insufficient to change health behavior among the people. In this way, awareness campaigns in health units, schools and the media could be effective measures to reduce the barriers faced by vaccination.

Author Contribution Statement

All authors contributed equally in this study.

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Availability of data and material

articles using the PubMed, EMBASE, Lilacs, Cochrane Library, SCOPUS, and Web of Science databases using the terms Barriers OR obstacles AND HPV vaccination OR HPV vaccine AND Brazil with no language or date restriction until july 2022.

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Ethical Compliance

All procedures performed in this study involving human participants were in accordance with the ethical standards of the institutional and/or national research committee and with the 1964 Helsinki Declaration and its later amendments or comparable ethical standards.

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