



# Increasing Awareness of the Human Papillomavirus (HPV) Vaccine for Women 18–45 Years of Age

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**Abstract:** The human papillomavirus (HPV) vaccine prevents cancer and is highly effective; however, the uptake has been low in the United States of America (USA) and among the most vulnerable populations. A recent Center for Disease Control (CDC) report highlighted that approximately 13,000 new cases of cervical cancer are diagnosed each year in the USA. Although cervical cancer is considered treatable, especially when detected early, in the USA, approximately 4000 women die every year of cervical cancer. However, little is known about access and awareness among women in the USA. The objective of this article is to focus on the role played by clinical pharmacists in bringing awareness about the HPV vaccine. It offers recommendations to enhance the administration of the HPV vaccine. This rapid literature review revealed two significant themes: Disparities in healthcare access to the HPV vaccine among women and clinical roles in empowering women to access the HPV vaccine. This rapid review emphasizes the need for future research in enhancing awareness about HPV as a viable strategy for women. As an integral part of the healthcare team, pharmacists can significantly improve awareness and administer the HPV vaccine, yielding enhanced outcomes and cancer prevention.

**Keywords:** women; disparities; human papillomavirus (HPV); vulnerable population; USA



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## 1. Introduction

Human papillomavirus (HPV) is reported by the Center for Disease Control and Prevention (CDC) as the most common sexually transmitted infection in the United States of America (USA), with approximately 43 million infections reported in 2018 [1,2]. HPV infection is associated with the development of several different types of cancers, including cervical, oropharyngeal, vaginal, vulvar, and other mucosal cancers [1]. Cervical cancer is the most common HPV-related cancer, and HPV in women is associated with over 90% of cervical cancers, 75% of vaginal cancers, and 69% of vulvar cancers, leaving women disproportionately vulnerable to HPV-related cancers [1,3]. Adolescents and young adults are especially susceptible to HPV, with data showing almost half of the new HPV infections that occur annually do so in people aged 15–24 years [1,4].

As per a recent CDC report, approximately 13,000 new cases of cervical cancer are diagnosed each year in the USA [5]. Although cervical cancer is considered treatable, especially when detected early, in the USA, approximately 4000 women die of cervical cancer every year [5]. According to the CDC, the most important things that a woman in the USA can do to “help prevent cervical cancer are to get vaccinated against HPV, have regular screening tests, and go back to the doctor if your screening test results are not normal” [6]. Gardasil-9® (Merck Sharp & Dohme LLC, Rahway, NJ 07065, USA) has been shown to protect against many female-specific cancers, including cervical, vulvar, and vaginal cancers caused by HPV [3]. As the prevalence of cervical cancer continues to rise in developing countries and the USA, it is imperative that healthcare professionals proactively promote education on HPV infections and risks [7]. This reinforces the requirement to

enhance awareness about the HPV vaccine and establishes a need for stronger programs to empower this vulnerable population.

The HPV vaccine is a vital preventative tool to decrease HPV infection, and when used in addition to annual screening, it can potentially reduce cervical cancer rates and associated deaths [5]. As of December 2022, the World Health Organization (WHO) updated their vaccination schedule, recommending “a one or two-dose schedule for girls aged 9–14, a one or two-dose schedule for girls and women aged 15–20, and finally two doses with a 6-month interval for women older than 21” [8]. In the USA, the CDC recommends administering a two-dose regimen before reaching the age 15 [9]. A three-dose schedule is recommended for individuals who received the first dose after the age of 15 and those who are immunocompromised [9].

Six HPV vaccines are currently available throughout the world, all showing high efficacy for their indicated high-risk types of HPV [8]. These six vaccines include three bivalent vaccines (Cervarix<sup>®</sup> GlaxoSmithKline Biologicals Rixensart, Belgium, US License 1617, Cecolin<sup>®</sup> Xiamen Inovax Biotech Co. Ltd. China, and Walrinvax<sup>®</sup> Walvax Biotechnology Co., Ltd., Kunming, Yunnan, China, two quadrivalent vaccines (Gardasil<sup>®</sup> Merck Sharp & Dohme LLC Rahway, NJ 07065, USA and Cervavax<sup>®</sup> GlaxoSmithKline Biologicals Rixensart, Belgium, US License 1617), and one nonvalent vaccine (Gardasil 9<sup>®</sup> Merck Sharp & Dohme LLC Rahway, NJ 07065, USA) [10]. Thus, all six HPV vaccines are indicated for use in females aged nine years or older, up to either 26 or 45 years of age in the USA [10]. An overview of the scheduled doses and recommendations is presented in Table 1.

**Table 1.** An overview of the dosages and recommendations of the available HPV vaccines.

Vaccine Brand Name	Manufacturer, Country	Valency and VLP Types	Approved Ages (Females)	Number of Doses	Dose Schedule
Cecolin <sup>®</sup>	Inovax Biotechnology, China	Bivalent HPV-16, HPV-18	9–45 years	3	Dose 1: 0 mo Dose 2: 1 mo Dose 3: 6 mo
Cervarax <sup>®</sup>	Serum Institute of India, India	Quadrivalent HPV-6, HPV-11, HPV-16, HPV-18	9–45 years	3	Dose 1: 0 mo Dose 2: 1 mo Dose 3: 6 mo
Cervarix <sup>®</sup>	GlaxoSmithKline Biologicals, Belgium	Bivalent HPV-16, HPV-18	10–25 years	2 or 3	2 Dose Schedule: • Dose 1: 0 mo • Dose 2: 6–12 mo 3 Dose Schedule • Dose 1: 0 mo • Dose 2: 2 mo • Dose 3: 6 mo
Gardasil 9 <sup>®</sup>	Merck & Co, USA	Nonavalent HPV-6, HPV-11, HPV-16, HPV-18, HPV-31, HPV-33, HPV-45, HPV-52, HPV-58	9–45 years	2 or 3	2 Dose Schedule: • Dose 1: 0 mo • Dose 2: 6–12 mo 3 Dose Schedule: • Dose 1: 0 mo • Dose 2: 2 mo • Dose 3: 6 mo
Gardasil <sup>®</sup>	Merck & Co, USA	Quadrivalent HPV-6, HPV-11, HPV-16, HPV-18	9–26 years	2 or 3	2 Dose Schedule: • Dose 1: 0 mo • Dose 2: 6–12 mo 3 Dose Schedule • Dose 1: 0 mo • Dose 2: 2 mo • Dose 3: 6 mo
Walrinvax <sup>®</sup>	Walvax Biotechnology, China	Bivalent HPV-16, HPV-18	9–30 years	3	Dose 1: 0 mo Dose 2: 1 mo Dose 3: 6 mo

A large-scale study conducted by the CDC over a period of six years looked at tissue samples of over 10,000 women aged 18–39 years that were diagnosed with cervical precancers in the USA [11]. In this population of women, the percentage of precancers caused by HPV decreased from 55.2% to 33.3% among those women who underwent HPV vaccination [11]. This dramatic decrease in precancers caused by HPV due to HPV vaccination shows an urgency to recommend HPV vaccination to all eligible women.

Another important clinical trial that demonstrated the efficacy of the HPV vaccine is FUTURE II—a double-blind, randomized, placebo-controlled study that assigned 12,167 women between the ages of 15 and 26 years to receive three doses of the HPV vaccine versus a placebo [12]. FUTURE II showed an HPV vaccine efficacy of 98% for the prevention of cervical intraepithelial neoplasia grade 2 or 3, adenocarcinoma in situ, or cervical cancer related to HPV-16 or HPV-18 for three years after vaccination [12]. The quadrivalent HPV vaccine was also studied in a clinical trial for safety and efficacy in preventing the development of external genital lesions and anogenital HPV infection exclusively in boys and men [13]. In this trial, receiving the HPV vaccine reduced the incidence of external genital lesions related to certain HPV types by 90.4% [14]. These three specific trials strongly indicate the efficacy of the HPV vaccine in the prevention of HPV-related cancers affecting both genders [11–13].

An observational study evaluated the potential benefits of HPV vaccination [15]. Valasoulis et al. investigated the effects of HPV vaccination on HPV-related biomarkers' expression of oncogenic HPV genotypes HPV-16 and -18, as well as of the oncogenic HPV genotypes genetically related to HPV-16/18 in Greek women with low-grade (LG) cytology [15]. The study found that HPV vaccination reduced DNA positivity rates for genotypes 16, 18, and 31, which was statistically significant [15]. To conclude, this observational study reinforced the advantages of receiving the HPV vaccine and demonstrated “an earlier clearance of HPV infection” compared to those women who did not receive the HPV vaccine [15].

Furthermore, Sharpless et al. provided evidence-based recommendations for adjuvant HPV vaccination in patients undergoing treatment for cervical intraepithelial neoplasia grade 2 or worse (CIN2+) [16]. To ensure the guidelines follow appropriate evidence-based recommendations, the American Society for Colposcopy and Cervical Pathology (ASCCP) assigned a task force from their Practice Committee to review current CDC guidelines and previously published literature to recommend HPV vaccination in CIN2+ patients [16]. After examining the current guidelines for HPV vaccination, the dosing of the HPV vaccine, and the role of HPV vaccination in previously unvaccinated individuals, the ASCCP recommended that CIN2+ patients follow the existing CDC guidance for vaccination of patients aged 9–26 years and consider shared decision-making with a physician for unvaccinated patients aged 27–45 years [16]. The ASCCP recommended “considering the possible benefit of HPV vaccination pre- or post-surgical excision of CIN2+ in immunocompetent individuals” [16].

Despite similar HPV vaccination uptake among different races, mortality rates from HPV-related cancers differ among races [17]. Annual HPV-related cancer screening rates remain lower in certain populations, especially minority women [17]. According to the CDC, Hispanic women have the highest rates of cervical cancer, while Black women have the highest rates of dying from cervical cancer [5]. Data show that 14% of Hispanic women and 12% of African American women in the USA have never been screened for cervical cancer compared to only 6% of Caucasian women [7]. Geographical location has also been shown to impact HPV vaccination rates. Hirth et al. revealed that “from 2008–2010, adolescents in the South and Southwestern United states were less likely to initiate the HPV vaccine series compared to states in the rest of the US”, even though the southern states tend to have higher rates of cervical cancer [17].

Disparities in cervical cancer incidence and mortality rates by race persist in the USA, demonstrating a substantial need to empower all women to receive HPV vaccination [7]. Many social determinants of health can limit adolescent and young women from receiving

the vaccine, such as cost, access, and health literacy [7]. Insurance coverage plays a large role in determining a woman's level of access to care [7]. Hispanic women have the highest uninsured rates in the USA at 23% compared to 8% of Caucasian women and 12% of African American women [7]. A lack of insurance coverage could explain why rates of HPV-related screenings are lower in certain races. Nelson et al. showed that HPV vaccination rates in Minneapolis, Minnesota vary according to ZIP code [18]. Knowing that ZIP code plays a large role in the health of a community, this finding supports the idea that impoverished or medically underserved communities could have lower rates of vaccination compared to more affluent areas with adequate access to medical care [18]. Understanding the barriers that limit women from receiving the HPV vaccine is vital to empowering women to get vaccinated. For example, Afonso et al. identified barriers to HPV vaccination, including provider recommendation, education on effects of HPV, and parental choices regarding childhood vaccines [19]. With provider recommendation being strongly associated with HPV vaccination status, there is a substantial role and responsibility for healthcare providers to empower women to receive the vaccine [19].

This rapid literature review provides an overview of the present landscape of HPV access and awareness among women in the USA. Another objective of this manuscript was to focus on the role played by clinical pharmacists in bringing awareness about the HPV vaccine and offer recommendations to enhance administration of the HPV vaccine.

## 2. Methods

Due to the limited literature on women's usage of the HPV vaccine and the Medical Subject Headings (MESH) terminology to encompass the HPV vaccine, women, and the role played by clinical pharmacists in the USA, this study is a rapid literature review. Thus, it followed and adapted the Cochrane handbook for a rapid review [20]. The research team used the following broad key terms: 'HPV vaccine', 'Papillomavirus Vaccines', 'papillomavirus infection', 'papillomavirus vaccination empowerment', 'clinical pharmacist', and 'women' over a four-week period using three electronic databases (PubMed, CINAHL, and Embase). Additional key terms were used according to each specific subsection of this article. Because the HPV vaccine was approved in 2009 by the FDA, the inclusion criteria included articles in English after 2010 that were peer-reviewed and derived from clinical studies. Case reports and case series were evaluated and included based on the inclusion criteria. Although the inclusion criteria included studies published globally, this article focused on the underutilization of HPV by women in the USA.

## 3. Results

### 3.1. Disparities in Healthcare Access to the HPV Vaccine among Women in the USA

Although the Affordable Care Act (ACA) enhanced access to healthcare in minority populations, previous findings have reported that Latino individuals have lower insurance rates than their White peers [21,22]. To address this public health gap in minority women disproportionately affected by cervical cancer, Hopfer et al. explored preferences for receiving information about the HPV vaccines in Latina and Vietnamese women residing in California, USA [23]. The findings highlighted the varied resources used to obtain critical information about the HPV vaccine in this population, including social media, the Internet, and other female peers [23]. This study also emphasized the importance of receiving information from reliable resources and effectively conveying the appropriate message to engage Latina and Vietnamese women using various platforms [23].

Earlier research found that affordability can hinder adolescents' ability to obtain the HPV vaccine and might discourage parents from allowing vaccination [24]. This inequity in vaccine access can create a stigma against people in lower-income families and can further widen healthcare disparities [24]. Indeed, a publicly funded HPV vaccination program might have beneficial effects, including marketing HPV vaccination accessibility and increasing its coverage [24]. In contrast, not having a program financed by the government

might imply that HPV has a low health risk and that its vaccination is less of a priority than other vaccines [24].

Women from marginalized groups, such as many African American and Latina women, are most negatively impacted by HPV-associated diseases. Many factors may directly or indirectly impact HPV vaccine access and uptake by women, and these factors should be considered when working to enhance access [25]. A study conducted in eight planned parenthood clinics in three cities in the USA, Philadelphia, St Louis, and Chicago, aimed to find the short-term effects of a story-based intervention among unvaccinated women aged 18–26 years [26]. The study included 50% African American and 20% Latina women [26], highlighting that access is a crucial obstacle to HPV vaccination and is especially significant for minority women [26]. One solution to overcome this is by affiliating with planned parenthood clinics to provide the vaccine to uninsured patients at no cost [26]. This study also emphasized decreased levels of awareness about the HPV vaccine, attributed to the anti-vax movement [26].

Women have the highest rate of poverty in the USA, which is attributed to gender, wage and wealth gaps, segregation into low-paying jobs, inadequate or inaccessible public social assistance programs, socioeconomic resources, limited access to healthcare, and health insurance [27]. As a result, many women are underinsured, which may directly affect healthcare access and awareness about HPV access and accessibility to the vaccine in the post-Affordable Care Act era [28,29]. Compared to White women, African American and Latina women are more likely to become infected with HPV [30,31]. Earlier studies about racial and health disparities demonstrated that African American and Latina women are less likely than White women to complete the three-dose HPV vaccine [32,33]. Previous research investigated racial and ethnic disparities not only in the initiation of the HPV vaccine, but also in the completion of the HPV vaccine series [29]. The study showed that African American women presented comparable adjusted odds of initiating the HPV vaccine to White women [29]. However, African American women had significantly lower adjusted odds of completing the three HPV vaccine series compared to White women [29]. This study reinforced the racial and ethnic disparities pertaining to the initiation and completion of the HPV vaccine series [29]. For example, Latina women presented lower adjusted odds in the initiation and completion of the HPV vaccine series compared to White women [29].

### *3.2. Clinical Roles in Empowering Women to Access the HPV Vaccine in the USA*

Healthcare providers play an essential role in enhancing awareness of the HPV vaccine for women and reducing barriers to access and uptake, and should therefore be encouraged to provide key messages about the vaccine as a cancer prevention strategy. A systematic literature review focused on knowledge, willingness, behaviors, and perceived roles of dental providers in the USA concerning HPV-associated oropharyngeal cancer reported that although these providers knew of the HPV vaccine, they were unaware of vaccination recommendation, names of the vaccines, and billing [34]. The authors emphasized the importance of improving the communication between patients and dental providers to enhance HPV vaccine uptake [34]. Leung et al. highlighted the limited knowledge regarding HPV among healthcare professionals [35]. This systematic review acknowledged the beneficial role of enhancing educational interventions tailored toward healthcare providers' knowledge [35].

In an effort to address the awareness concerns regarding the HPV vaccine in future providers, medical students at a Midwestern USA medical school were surveyed to characterize their knowledge of and attitudes toward HPV vaccination [19]. The results showed that those medical students who received all three HPV vaccine regimens were more likely to recommend the HPV vaccine to friends and family compared to the non-vaccinated students [19]. This study reinforces the need for the development of strong counseling and communication skills in future healthcare providers to convince the public to enhance vaccination rates when practicing as physicians [19].



Strong collaboration between healthcare providers, including physicians and pharmacists, could be instrumental in enhancing the uptake of the HPV vaccine in communities. A qualitative study conducted interviews with an interprofessional healthcare team consisting of pharmacists, pharmacy technicians, physicians, and advanced practice registered nurses (APRNs) and found that developing a shared responsibility model between clinics and pharmacies might increase HPV vaccination rates [36]. A systematic literature review of pharmacists' perceived obstacles to HPV vaccination concluded that further qualitative studies are essential to uncover their perspectives on maximizing their efforts to enhance HPV vaccination rates in different pharmacy settings [37].

#### 4. Discussion

This rapid overview of the literature on HPV access and awareness in women in the USA provides a resource on studies confirming several factors that affect HPV vaccination. While both men and women are affected by HPV-related diseases, women are more likely to experience HPV-related cancer [9]. Women are more likely to live at or below the poverty line in the USA and have poor access to healthcare or healthcare insurance. Additionally, minority women are less likely to receive or complete the HPV vaccine series. Both Hispanic and Black women are at higher risk of developing or dying from cervical cancers [7].

Focusing on these disparities, such as lower socioeconomic status, being under- or uninsured, access barriers to healthcare, and costs, can help to identify methods of enhancing HPV disease and prevention awareness. Awareness campaigns that target racial groups could create increased vaccination rates in these groups and may involve the development of culturally appropriate intervention strategies that are specifically tailored [38]. When designing these interventions, including both cultural and community leaders may be required to understand the information and communication preferences of that racial or ethnic group [38–40].

Cost and access are significant barriers to HPV vaccination [41,42]. Strategies to address these barriers may include the promotion and identification of alternative locations for administration of the vaccine. Pharmacies in the USA are well-positioned, and studies have shown that 88.9% of the population live within five miles of a community pharmacy [43]. Most pharmacies provide vaccination services, including HPV vaccination [44]. While most private health insurance plans cover the cost of recommended vaccines, including the HPV vaccine, for those who are under- or uninsured, cost may be a barrier and the use of patient assistance programs may be helpful [45–47].

#### 5. Limitations

When reading this rapid literature review, some caveats should be considered. Firstly, this study is a rapid literature review that provides a snapshot of the literature in the USA with these foci. Second, the grey literature, such as non-peer-reviewed articles, conference abstracts, commentaries, and discussion articles, were excluded, which may have limited the breadth of our findings.

#### 6. Conclusions

The HPV vaccine is an effective option to prevent the development of several different types of cancers in women. This vaccine has been tested in several patient populations and has shown efficacy across the board. However, additional intervention studies are deemed necessary to advance its implementation in women to prevent various types of cancer. Given that the awareness of HPV among women is low, as well as the challenges posed by the COVID-19 pandemic and the division of vaccines, further research is needed to explore the facilitators for women to initiate HPV vaccination. As an integral part of the healthcare team, pharmacists can significantly improve awareness and administer the HPV vaccine, yielding enhanced outcomes and cancer prevention.

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