HPV vaccination: Reaching the catch-up population and beyond

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For more than a decade, human papillomavirus (HPV) vaccine has been part of routine vaccination recommendations for both males and females age 11 to 26 years as a primary prevention strategy against HPV-related diseases. More recently, the recommendation has been added to include adults age 18 to 26 years in what is called HPV vaccination catch-up. As of 2018, the US Food and Drug Administration has approved use of the vaccine in those up to age 45 years. This article provides insights into the critical need for catch-up HPV vaccination especially for individuals who are high-risk and underserved and strategies for nurse practitioners to reach them.

KEY WORDS: human papillomavirus, HPV, vaccine, catch-up, vulnerable populations, women's health

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Human papillomavirus (HPV) is associated with cervical, vulvar, vaginal, penile, anal, and oropharyngeal cancers.[1] Although more than 200 types of HPV have been identified, HPV-associated cancers are largely the result of infection by one of the oncogenic high-risk HPV subtypes 16, 18, 33, 45, 52, and 58.[1] HPV infection is one of the most common sexually transmitted infections and the vast majority of the population, even those infected with high-risk HPV subtypes, do not develop cancer.[1]

Cervical cancer has the potential to become a disease of the past. The incidence rate of this cancer decreased by more than 50% from the mid-1970s to the mid-2000s because of both increased screening, allowing for detection and treatment at early-stage disease, and primary prevention in the form of HPV vaccination of adolescents and young adults. However, annually over 14,000 women in the United States will still be diagnosed with cervical cancer and more than 4,000 will die from this largely preventable disease.[2]

Anal cancer follows the natural history of cervical cancer with persistent high-risk HPV infections found in 90% of cases.[3] Similar to the cervix, the anal canal has a transformation zone where columnar epithelial cells transition to squamous

epithelia. This zone is vulnerable to the development of precancerous lesions from HPV infection. Although anal cancer is relatively rare in the general population (~ 9,440 new cases per year), the rate of new anal cancer cases is higher in women than men (6,290 in women and 3,150 in men) and is steadily increasing in men and women.[4,5] Those who are living with human immunodeficiency virus (HIV) carry the heaviest burden and risk for anal cancer due to being immunocompromised.[5]

Oropharyngeal, or oral cancer, incidence is increasing and is expected to exceed that of cervical cancer.[6] It is estimated HPV is attributable to 40% of oral cancer cases. Currently, there are no formal screening recommendations for oral cancers, yet HPV vaccination has been shown to be associated with lower oral prevalence of HPV.[7]

Nurse practitioners (NPs) are key to improving HPV vaccination rates and decreasing rates of HPV-related cancers. This article provides insights into the critical need for catch-up HPV vaccination especially for individuals at increased risk for HPV infection and HPV-related cancers and strategies for NPs to reach them.

Benefits of HPV vaccination

The HPV vaccine is considered cancer prevention.[8,9] It has proven to be highly effective in preventing infection and preinvasive and invasive cervical, vulvovaginal, and anal disease caused by the HPV types in the vaccine prior to exposure.[8] The vaccine has been shown to lower oral HPV infections that lead to oropharyngeal cancer in young adults.[10] Many years of safety monitoring has shown that the HPV vaccine has no serious adverse effects after administration.[11,12]

A study published in 2020 revealed compelling health benefits of the HPV vaccination for women through age 26 and men through age 21.[13] The model predicts that the current US HPV vaccination program will reduce the number of diagnoses of anogenital warts and cervical intraepithelial neoplasia of grade 2 or 3 and cases of cervical cancer and noncervical HPV-associated cancer by 82%, 80%, 59%, and 39%, respectively, over 100 years and is cost saving (vs no vaccination).[13] When researchers extended HPV vaccination through age 45 in both men and women, they discovered it would further reduce these same outcomes by 0.4%, 0.4%, 0.2%, and 0.2%, respectively.[13] HPV vaccination has the potential to reduce the substantial economic burden due to loss of work productivity caused by HPV-attributed cancers.

HPV catch-up vaccination recommendations

Ideally, the HPV vaccine is given during adolescence before the onset of sexual intercourse to achieve maximum protection against HPV. However, the Advisory Committee on Immunization Practices (ACIP) estimates approximately 9.1 million women and 13.9 million men age 19 to 26 years are unvaccinated.[14] Thus, the CDC urges catch-up vaccination for adults up to age 26 who have not been previously vaccinated and remain vulnerable to developing preventable HPV-related cancers.[15]

A significant barrier to childhood HPV vaccination is parent refusal, so the catch-up population is an ideal target group who can now make autonomous decisions regarding their healthcare.[16] Healthcare providers' attitudes toward HPV vaccination are an important driver on the decision to be vaccinated. One study found that among insured women age 19 to 26 years, those who discussed the HPV vaccine with their physician and received a recommendation were overwhelmingly more likely to be vaccinated.[17]

Catch-up vaccination can be given to males and females up to the age of 26 years. For the catch-up population, or persons who are receiving the first vaccine on or after their 15th birthday, the three-dose schedule is recommended.[15] In a three-dose schedule, dose 2 is administered 1 to 2 months after the first dose. The third dose is administered 6 months after dose 1. There is no maximum interval between doses, thus if the subsequent doses are delayed or interrupted, the vaccine series does not need to be restarted. The second and third doses should be separated by an interval of at least 12 weeks. If the patient received one dose of the vaccine before their 15th birthday and the vaccination schedule was interrupted, the two-dose series is still adequate. The second dose should be administered as soon as possible. Patients should be advised the vaccine has no therapeutic benefit on existing HPV infection, anogenital warts, or HPV-related lesions. Yet, vaccination will provide some benefit against HPV types not already acquired.

Shared clinical decision-making counseling for those age 27–45 years

In 2018, the US Food and Drug Administration approved HPV vaccination up to age 45 years, which was followed by an updated recommendation from ACIP.[18] ACIP does not recommend catch-up vaccination for all adults age 27 through 45 years, but recognizes individuals who are not adequately vaccinated might be at risk for new HPV infection. As with the catch-up schedule,

vaccination in this age group can be beneficial for HPV types to which individuals have not yet been exposed and are susceptible. Unfortunately, there is no test to determine prior exposure to any HPV type. ACIP recommends shared clinical decision making for adults age 27 to 45 years for the public health benefit of HPV vaccination.[15]

NPs have the opportunity to provide education on the risk/benefit of receiving the HPV vaccine between age 27 and 45 years. The patient should be counseled the vaccine provides less benefit for those who are already sexually active and the risk of acquiring a new HPV infection while in a mutually monogamous partnership is low. At any age, the risk of acquiring a new HPV infection increases with a new sexual partner. It is important to counsel the patient that the vaccine is effective for prevention of new HPV infections only and is not therapeutic for clearance of an existing HPV infection, preventing progression of HPV-related lesions, or treating HPV-related genital warts. The NP should assess for factors that may increase the patient's risks of acquiring a new HPV infection such as smoking, new or multiple sexual partners, in a relationship with a partner with multiple sexual partners, or a weakened immune system.[1]

Populations at increased risk for HPV infection and HPV-related cancer

With catch-up recommendations and the age expansion for HPV vaccination, it is prudent to make concerted efforts to reach populations who are not likely to advocate for themselves, find relevant information about the vaccine, and utilize preventive services. Certain populations such as persons who are incarcerated, those with immune-compromising medical conditions, racial and ethnic minorities, and gender and sexual minorities are at an increased risk of HPV infection and HPV-related cancer.[19–22] Furthermore, these populations are at increased risk of underutilization of the HPV vaccine for reasons including lack of knowledge and awareness, missed opportunities for provider recommendations, or inability to access the vaccine.[20,23,24] Special consideration for populations vulnerable to poor HPV-related disease outcomes or underserved by existing HPV vaccine programs are imperative to ensure equitable benefits from HPV vaccination. These considerations may include increased surveillance, differing dose scheduling, targeted education and outreach programs, and resources.

Immunocompromised individuals

Patients who are immunocompromised from primary or secondary immunodeficiencies, including HIV, cancer, transplant recipient, or autoimmune inflammatory disease treated with immunosuppressive medications are at an increased risk for HPV-related cancers.[25] Immunosuppression plays a significant role in delayed clearance of HPV infections, resulting in an increased risk for HPV-related anogenital and oral disease and progression to cancer.[25] HPV vaccination is recommended through age 26 years for immunocompromised persons who have not been vaccinated previously or who have not completed a three-dose series. The three-dose series is recommended for all persons with immunocompromising conditions.[15] Special attention is warranted for patients living with HIV and with a CD4 count under 200 cells/mm^3, advanced Hodgkin disease patients, and hematopoietic stem cell transplant recipients who are among the most immunocompromised groups. Among people living with HIV, studies have found the HPV vaccine to be safe and immunogenic, but more research is needed to determine the efficacy of the vaccine between immunocompromised and immunocompetent individuals.[26]

Patients with immunocompromising conditions often receive care from a specialist rather than a primary care provider. For them, HPV vaccination may be missed if specialists assume vaccination is the responsibility of a general practitioner. Thus, a comprehensive patient assessment of immunocompromised patients should include vaccine history to capture missed opportunities for vaccination. Counseling immunocompromised patients on their increased risk of HPV disease and progression to cancer is an important first step in addressing the increased burden of HPV-related cancers. A recommendation for the HPV vaccine can further help reduce the personal and clinical costs associated with HPV disease among this high-risk population.

Racial and ethnic minority groups

Black and Hispanic women have an increased incidence in HPV infection as well as cervical cancer.[20,27] Black women have the highest mortality rate for cervical cancer.[27,28] HPV vaccine coverage is lower among Black and Hispanic women because, despite high rates of HPV vaccine initiation, they are less likely to complete the series—leaving them vulnerable to HPV infection.[29–31] Black and Hispanic women barriers to HPV vaccination include fear of vaccine safety, inaccessibility of the vaccine, and lack of awareness of the benefit of and recommendations for vaccination.[32–34] Trusted information on the high safety profile of the vaccine

and education on the benefit of the vaccine can help close the disparity gap among racial and ethnic minority groups.[35] NPs often work in healthcare settings that reach and serve racial and ethnic minority populations. They need effective approaches to help increase uptake and completion of the vaccine series. Further study into HPV vaccination strategies tailored to specific minority groups is warranted.[35]

Sexual and gender minority populations

There is limited research on HPV vaccination rates among sexual and gender minority populations. Among sexual minority women (SMW), defined as women who have sex with women and women who have sex with men and women, there is a higher prevalence of HPV infection.[22] Due to the paucity of research among SMW, the estimated prevalence of HPV infection is wide and ranges from 13% to 51%.[22] Perception of HPV risk among SMW has been reported as low, but in fact, they are at risk for HPV.[36] HPV infection can be transmitted between female or male sexual partners.

Transgender and gender diverse (TGD) populations represent approximately 1.4 million in the US. HPV vaccination rates are underreported due to lack of consistency in identifying this group.[37,38] Gender identity is independent of sexual identity. Specifically, cisgender individuals have a gender identity that is aligned with their assigned sex at birth, whereas TGD individuals have gender identities/expressions that do not align with their assigned sex at birth.[39] Many research or population-based studies do not make the distinction between sexual and gender identity, thus overlooking aggregated HPV vaccination rates and the facilitators and barriers that impact HPV vaccination among TGD populations. The few studies available suggest sexually active TGD individuals with a cervix have lower cervical cancer screening rates, delays in recommended screening intervals, and are less likely to receive initial HPV vaccination compared to cisgender women.[23,40,41]

Barriers to HPV vaccination among sexual and gender minorities (SGM) include low knowledge and awareness, lack of SGM competent providers, lower access or use of healthcare services, and healthcare stigmatization or previous discrimination in receiving healthcare.[19,42] It is important for NPs to make HPV vaccine recommendations to people of all genders and sexuality. It is critical for providers to engage in affirming, and culturally sensitive communication to create a safe environment where patients are comfortable to discuss sexual identity and sexual behaviors. A safe environment promotes retention of health information and promotion of positive health behaviors, such as HPV vaccination.

Individuals involved in the criminal-legal system

A particularly disproportionately affected group of women in the US, the one million US women involved in the criminal-legal system, has largely missed out on the benefits of health-promoting interventions, especially the HPV vaccine.[43–45] Women involved in the criminal-legal system are four to five times as likely to have cervical cancer when compared to the general population of women.[46] Social determinants and life circumstances associated with repeated, low-level criminal-legal system involvement for this population include high socioeconomic need, homelessness, substance use, frequent exposure to violence and abuse, and mental illness.[47,48] Many of these same factors are linked to infectious disease and other health risks.[49] Sexual health is especially challenging, because many incarcerated adults experience early sex initiation, multiple partners, histories of sex while high on drugs, commercial sexual exploitation, and sexual trauma.[50–53] These factors result in more exposure to high-risk HPV infections and the cancers they cause.[54,55] Inadequate or irregular access to high-quality healthcare may exacerbate poor cervical health and HPV cancer risk for many who are entangled with the criminal-legal system.[56,57] Interventions to get this population of women into cervical cancer screening and follow-up are needed, and catch-up HPV vaccination has been recognized as a priority.[58,59] NPs providing care in federally qualified health centers, departments of health, free clinics, and other community health centers are equipped to incorporate shared decision making for the HPV vaccine for this population.

Implications for clinical practice

Scientific evidence supports the HPV vaccine is beneficial in preventing mortality and morbidity from cervical and other HPV-related cancers. A clear understanding of the benefits, safety, efficacy, and cost-reducing strategies by NPs will aid in eliminating barriers to HPV vaccine uptake. The optimal timing for HPV vaccination is during adolescence. Catch-up vaccination is recommended for adults up to age 26 who have not been previously vaccinated. However, HPV vaccination catch-up is reasonable to consider for the adult population age 27 to 45 years. Common barriers to HPV vaccination among the catch-up population include lack of a provider recommendation, lack of knowledge or

awareness of the HPV vaccine, and lack of access to the vaccine.[60–62]

NPs are a trusted source of health information and often the sole source of screening and management of HPV-related disease, thus they have an impactful opportunity to counsel their patients in the catch-up age group about the importance of HPV vaccination as part of a comprehensive cancer prevention strategy. They are in an ideal position to provide optimal patient education and shared decision making with patients 27 to 45 years regarding the HPV vaccine. Trusted and reliable educational resources should be made available to increase awareness about the HPV vaccine and about the link between HPV and cancer. ■

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