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Improving Human Papillomavirus vaccination rates in the U.S.:

Recommendations for health professionals and policy makers

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Executive Summary

Human papillomavirus (HPV) is a common sexually transmitted infection that can cause high-risk cancer. Vaccination for HPV has been widely available since 2006. However, vaccination rates still remain far below optimal rates of coverage, especially among male-identifying individuals. There are disparities in vaccination rates among populations across many identity factors; including sexual and gender identity and race and ethnicity. Data indicate that lesbians may be less likely than heterosexual and bisexual women to have been vaccinated. Black and Latinx people are less likely than White non-Hispanic people to have been vaccinated. Gay and bisexual men, especially those living with HIV, are at elevated risk for HPV and should be vaccinated; however data indicate that men who have sex with men are also less likely to be vaccinated. There is limited data on gender identity and HPV vaccination. There are many identified barriers to vaccination, including but not limited to the politicization of vaccines, sex and gender-based stigma, medical mistrust, misinformation, and insufficient provider recommendation. Existing ACIP guidelines recommend routine vaccination of all adolescents aged 11-12. In 2019, these federal vaccine guidelines were expanded to recommend catch-up vaccinations for all adults through age 26 years and for high risk individuals age 27-45 years. Fortunately, we know what steps we can take to successfully promote utilization of the HPV vaccine. State and institutional vaccination programs, public-private partnerships, and tailored patient and provider education programs have been shown to increase HPV vaccination rates. Medical mistrust, stigma, and cost and structural barriers are proven barriers to HPV vaccinations and need to be addressed. Finally, research should continue to examine vaccine benefit maximization.

Acronyms

ACA	Affordable Care Act
ACIP	Advisory Committee on Immunization Practices
CDC	Centers for Disease Control and Prevention
FDA	Food and Drug Administration
FQHC	Federally Qualified Health Center
GBM	gay, bisexual, and other MSM
HepB	hepatitis B virus
HNSCC	head and neck squamous cell carcinoma
HPV	human papillomavirus
LGBT	lesbian, gay, bisexual, transgender individuals
MenACWY	meningococcal vaccination that protects against 4 strains of meningococcal bacteria
MSM	men who have sex with men
NIS	National Immunization Survey
OPC	oropharyngeal cancer
PCP	primary care provider
PWID	people who inject drugs
PLWH	people living with HIV
SGM	sexual and gender minority
STI	sexually transmitted infection
TDaP	tetanus-diphtheria-pertussis vaccination
UTD	up to date

Background

Human papillomavirus (HPV) is the most common sexually transmitted infection (STI) in the world. Some 79 million Americans, mostly in their teens and early 20s, are infected with HPV.[1] HPV causes genital warts, which affect about 1% of the sexually active population in America at any given time. HPV is implicated in several types of cancer.

The most well-known HPV-related cancer is cervical cancer, of which there are over 12,000 new U.S. cases annually.[2] Cases of cervical cancer are almost exclusively caused by HPV infection. HPV can also cause oropharyngeal and anogenital cancers. Oropharyngeal cancers, also referred to as head and neck squamous cell carcinomas (HNSCCs), are the most common HPV-related cancer in men. About 60% of all HNSCCs are caused by HPV.[3,4,5] HNSCC is on the rise in the U.S. and is predicted to continue to rise as the baby boomer generation ages.[6] Over 90% of anogenital cancers are attributed to HPV. Nearly 12,000 HPV-attributable anogenital cancer cases occur in the U.S. each year.[3] In 2019, 44,000 Americans were diagnosed with HPV-related cancers.[2]

Both oropharyngeal cancer and anal cancer are non-AIDS-defining cancers that are often found among people living with HIV (PLWH). Men who have sex with men (MSM) with HIV are at a particularly high risk of HPV and related cancers. HPV-related anal cancer is 80 times more prevalent among HIV-positive MSM than among the general United States population.[8] Studies have demonstrated high HPV prevalence among MSM which is associated with elevated anal cancer incidence.[9,10,11]

HPV-related anal cancer is 80 times more prevalent among HIV-positive MSM than among the general United States population.

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HPV-related cancer may be prevented through primary, secondary, and tertiary methods. Primary prevention occurs via the HPV vaccine, STI risk/behavioral education, and safer-sex practices including condom usage. The vaccine is only effective if it is administered before HPV transmission occurs. For that reason, the vaccine should be administered to youth before they become sexually active. The CDC recommends 2 doses for those who initiate vaccination at age 14 or younger and 3 doses for those who initiate at age 15 or older. The nonavalent vaccine can prevent over 90% of HPV-attributable cancers.[12] The vaccine also protects against genital warts.[13] Healthy behavior choices aid in the primary prevention of HPV and related cancers. Avoiding smoking and excessive alcohol consumption may protect against HPV-related adverse health outcomes. These behaviors can exacerbate the effects of HPV infection by weakening the immune system.[14,15,16] Additionally, the combined effect of smoking and excessive alcohol consumption with HPV positive status presents an increased risk for cervical and oropharyngeal cancers.[17,18,19,20,21]

Secondary prevention occurs via HPV testing and screening for HPV-associated cancers (e.g. cervical cytology/Pap testing, colposcopy, routine oral health examinations, and screening for anal cancer precursors). Forms of secondary prevention can be considered invasive for some, but are extremely important in early detection of precancerous lesions or cancer. The sensitivity of HPV testing via cervical self-swab is equivalent to testing via provider-obtained swab, which has positive ramifications for patients who prefer to avoid undergoing a provider exam.[22,23]

Treatment of pre-cancerous lesions and cancer serve as tertiary prevention. Pre-cancerous lesions of the cervix identified during a cervical screening may be removed via cryotherapy or loop electrosurgical excision procedure.[24] If pre-cancerous lesions develop into anogenital (anal, penile, or cervical) cancer or OPC, chemotherapy, surgery, or radiation may be used for treatment. The scientific community has called for continued research and funding towards immunotherapy drugs as a treatment for OPC and other HPV-related cancers, especially in patients who present with later-stage (i.e. more advanced) disease.[6]

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Age (years)	Gender	Dose 1 received before age 15?	Dosing Series
9–26	All	Yes	2-dose series
9–26	All	No	3-dose series
27–45	All	Not applicable	Shared clinical decision-making

On August 16, 2019 the U.S. Advisory Committee on Immunization Practices (ACIP) expanded recommendation for HPV vaccination for all young people at age 11-12 to include catch-up vaccinations for all adults through age 26 years and for high risk individuals age 27-45 years.[25] Vaccination recommendations for routine administration to adolescents have not changed. ACIP does not recommend catch-up vaccination for all adults age 27-45, but recognizes that "some persons who are not adequately vaccinated might be at risk for new HPV infection and might benefit from vaccination in this age range; therefore, ACIP recommends shared clinical decision-making regarding potential HPV vaccination for these persons." The scientific rationale for expansion comes from a clinical trial of women aged 27-45 that indicated that the HPV vaccine is safe and effective for adults in the tested age group.[26] Studies have shown that vaccination of MSM up to age 26 remains cost effective.[27,28] Although most sexually active adults have already been exposed to HPV, having a new sexual partner is a HPV infection risk factor for individuals at any age. The Gardasil HPV vaccination protects against 9 subtypes of HPV, so even if adults have already been exposed to 1 subtype, vaccination would protect them against the other 8.[29] Individuals who have an HPV infection should still receive HPV vaccination, as the vaccine may protect them against high-risk HPV subtypes they have not yet acquired.

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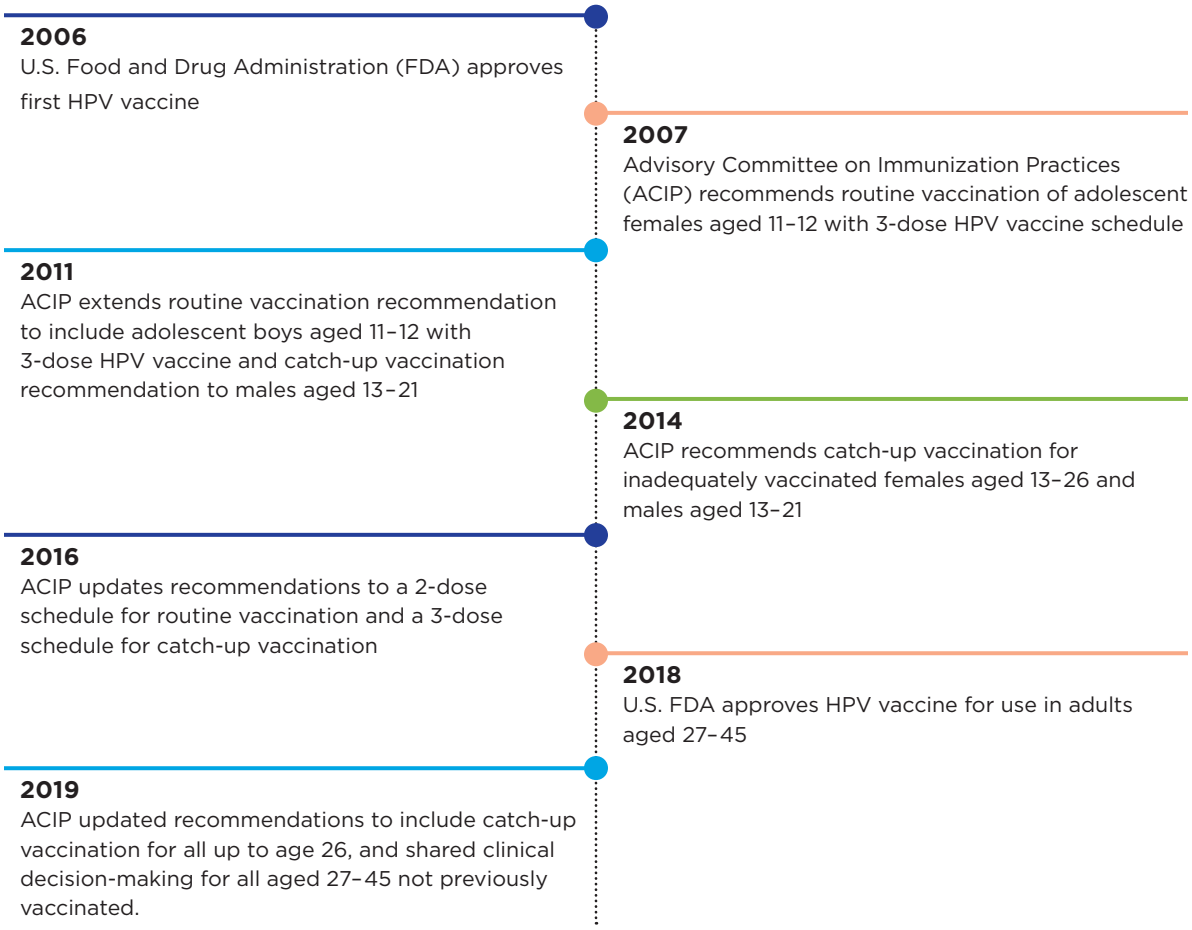
HPV Vaccination Guidelines Timeline



**The ACIP guidelines refer to individuals as females and males, with regard to assigned sex at birth. The ACIP guidelines do not reference transgender, non-binary, or other gender-diverse individuals in their recommendations.*

The Centers for Disease Control and Prevention (CDC) 2020 National Immunization Survey-Teen (NIS-T) reported that 58.6% of American adolescents aged 13-17 were up to date (UTD) with HPV vaccination recommendations, representing an increase from 54.2% UTD coverage in 2019.[30] Highest rates of coverage (>70% of adolescents) in this dataset are found in Rhode Island, Massachusetts, North Dakota, and the District of Columbia. Lowest rates of coverage were found in Mississippi (30.5%), Oklahoma (41.8%), Tennessee (43.0%), and Wyoming (41.5%). Seven years after the expansion of ACIP recommendations from all girls and young women aged 11-26 to include all boys and young men aged 11-26, there is still a significant gap in vaccination coverage between adolescent and young adult men and women. The NIS-T dataset reported that 61.4% of females and 56.0% of males were UTD nationwide in 2020. Many states have wider disparities, for example Indiana reported 60.0% of females and 47.1% of males UTD. The call for catch-up vaccination for all adults up to age 26 indicates the need to close existing gaps in coverage and to continue promotion of the HPV vaccine for all adolescents as well as all young adults.

61.4% of females and 56.0% of males were UTD nationwide in 2020.

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Vaccination and Sexual Orientation and Gender Identity[31]

Vaccination rates of adolescents by sex assigned at birth are well documented and collected by the CDC. However, the National Immunization Survey-Teen (NIS-T), which annually surveys 20,000 adolescents aged 13-17 years, does not currently quantify vaccination rates based on sexual orientation or gender identity (SOGI).

In recent years, a number of key studies have sought to examine relationships between sexual orientation and partner preference and HPV vaccination among U.S. adults. One study of young adult men and women who had received vaccine recommendation at some point in their lives found that adults "presumed to have mainly female partners—namely, lesbian women and heterosexual men—may be less likely to initiate and/or complete the HPV vaccine series relative to those presumed to have male sexual partners—namely, bisexual women and gay and bisexual men."[32] Research continues to point to lower HPV vaccination uptake and awareness among men overall compared to women. Even among a sample of adult men who had moderate HPV vaccination knowledge, the majority did not intend to receive the HPV vaccine.[33] Considering that men (aged 14-59) have a higher prevalence of high-risk HPV than women, this information is highly concerning. With respect to sexual orientation identity and sexual activity, there are further differences among populations.

A survey of lesbian and bisexual women in 2014 found that 45% of women studied had initiated the HPV vaccine, while 70% of these initiators had completed the series.[34] Another study, which examined sex of sexual partners and HPV vaccination, found that women who had only female past-year sexual partners had significantly lower odds of initiating HPV vaccination than women with only male past-year sexual partners.[35] Additionally, women with no past-year sexual partners had significantly lower odds of initiating HPV vaccination compared to women with male past-year sexual partners.[36] Intersectional analyses indicated that Black lesbian women had the lowest rates of vaccination initiation, followed by White lesbian women, Black heterosexual women, and White heterosexual women (in that order). This data suggests that sexual orientation identity and race may have a compounding effect among Black and White U.S. women and girls.[36]

A survey of lesbian and bisexual women in 2014 found that 45% of women studied had initiated the HPV vaccine

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In a 2016 study of gay and bisexual men and other MSM, 69.4% of participants had detected anal HPV while only 8.5% had exposure to the HPV vaccine.

Gay, bisexual, and other MSM (GBM) have a heightened risk for HPV infection compared to men who have sex with women.[37] In a 2016 study of GBM, 69.4% of participants had detected anal HPV while only 8.5% had exposure to the HPV vaccine.[38] One study of SGM individuals assigned male sex at birth, which included gay and bisexual men, other MSM, and transgender women, found vaccine coverage of 15% in the individuals studied.[39] Another found that 13% of the GBM studied had initiated the HPV vaccine series.[40] Among participants in this study who were vaccinated, provider recommendation to get vaccinated was the strongest correlate with vaccine initiation. Lack of vaccine coverage among GBM likely stems from the long history of women-centric health promotion strategies over the past decade and a half. In a qualitative study of GBM living with HIV, many participants associated HPV with cervical cancer and women, and cited the association as a reason for not getting vaccinated.[41] Multiple participants also reported that they had never received a vaccination recommendation from their PCP, and noted that a strong provider recommendation would be necessary for them to seek the vaccine. Overall, it is clear that providers should promote HPV vaccination among all people, regardless of sexual orientation and gender identity. Particular attention should be given to interventions focusing on GBM, who have low vaccination rates and high HPV risk.

Particular attention should be given to interventions focusing on gay and bisexual men and other MSM, who have low vaccination rates and high HPV risk.

Gender identity must be considered when quantifying HPV vaccination coverage. Recent research efforts have examined this relationship. One cross-sectional study of 660 individuals, 10% of which identified as transgender, found that "transgender respondents' HPV vaccination experience mirrored that of cisgender respondents with regard to sex assigned at birth."[42] Non-binary participants studied also indicated vaccination rates reflective of sex assigned at birth. These results indicate that providers may base vaccine recommendations on patients' sex assigned at birth, which may impact patients' vaccine coverage. The findings indicate the need for universal vaccine recommendations regardless of sexual or gender identity as well as training on LGBTQIA+ culturally responsive care. It should be noted that there is little research on vaccination rates of intersex individuals.

One study found that "transgender respondents' HPV vaccination experience mirrored that of cisgender respondents with regard to sex assigned at birth."

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Health Disparities and HPV

Disparate vaccination uptake and disease burden are clearly evidenced between females and males with respect to sex assigned at birth. Racial, ethnic, and geographic disparities are also evident and highly concerning. In multiple studies of young women, Black women were both least likely to be vaccinated and most likely to develop cervical cancer.[43,44] Vaccination rates among Hispanic women, particularly Mexican Americans, are significantly lower than those of White women.[45] CDC cancer data collected between 2012 and 2016 indicate disparate rates of HPV-related cancers among race and ethnicity groups. Black and Non-White Hispanic women had higher rates of cervical cancer than White women. Anal cancer rates were higher in White women compared with Black women, and lower in White men compared with Black men. HNSCCs were more prevalent among White men and women than Black and Non-white Hispanic men and women. Men had higher rates of HPV-associated HNSCCs than women across all race and ethnicity groups in the dataset.[46]

In multiple studies of young women, Black women were both least likely to be vaccinated and most likely to develop cervical cancer.

Data from the 2020 NIS-T indicates highly disparate vaccination uptake among urban and rural teens.[47] The survey, which includes teens aged 13 to 17, indicated that teens living in central-MSA counties (counties that are part of a metropolitan statistical area as designated by the U.S. Census Bureau) are much more likely to be vaccinated than teens living in non-MSA counties. On national average, 49.2% of non-MSA teens are fully vaccinated while 60.4% of central MSA teens are fully vaccinated.[47] This data indicates that rurality is likely to be a factor in teen vaccination uptake.

Teens living in rural areas are much less likely to be vaccinated.

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Contributing Factors to Low Vaccination Rates

There are many factors contributing to less than ideal vaccination uptake in the United States. Political agendas; sex, sexuality, and gender-based stigmas and fears; medical mistrust; false perceptions; disturbances due to the COVID-19 pandemic, and strength of provider recommendation all play a role in hindering the prevention potential of the HPV vaccine.

Politics and marketing

Politics appear to play a role on several fronts. It is clear that vaccination uptake varies greatly between states. States with conservative majority legislatures or governors have lower uptake on average. State legislatures have a role in the funding of vaccine programs. States with conservative majority legislatures are less likely to have expansive vaccination programs in place.[48] Additionally, historically HPV vaccine promotion and marketing focused primarily on cisgender women, which may contribute to continued inadequate uptake among male-identifying populations. Politics and marketing have limited HPV vaccination in the past and continue to impede progress today.

States with conservative majority legislatures or governors have lower uptake on average.

Sex, sexual identity, and gender identity-based stigma

Sex and gender-based stigma plays a role in vaccination trends. One study of trends in STI surveillance data indicated that young women are socially and medically encouraged to regularly test for HPV, while young men are rarely offered similar opportunities.[49] Sexually active women are more likely to be regarded as promiscuous than men who are just as sexually active. Meanwhile, men generally feel pressure to engage in sex with multiple partners to fulfill society's expectation of them.[50] These patterns are heteronormative and harmful in a public health context. Gender-based discrimination contributes to STI-associated stigma, especially in terms of seeking STI treatment and getting vaccinated.

Young women are socially and medically encouraged to regularly test for HPV, while young men are rarely offered similar opportunities.

Sexual and gender minority (SGM) patients face additional barriers to HPV vaccination. One qualitative study of SGM patients at a Boston community health center found several related barriers. Low HPV-related knowledge at both patient and provider levels posed a barrier. Study participants demonstrated lack of awareness about HPV and perceived risk, especially male-identifying individuals. Uncomfortable interactions between patient and provider about sexual health and HPV were described as invalidating and a barrier to vaccination. Participants described their PCP's HPV knowledge and SGM-affirming care as a facilitator for vaccination. At the systems level, SGM identity-affirming care settings were a vaccination facilitator. Experiences in healthcare systems that were non-affirming were described as "uncomfortable" and "negative". Increased vaccination was associated with providers with competence in SGM healthcare and SGM identity-affirming healthcare settings.[51]

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A study of behavioral intentions to initiate vaccination among young MSM revealed a number of barriers related to HPV vaccination for this cohort.[52] Perceived stigma, fear of judgement, and issues surrounding disclosure of sexual orientation were concerns for the studied individuals. Previous negative interactions with healthcare providers influenced some of the participants perceptions about overall competence among providers in caring for LGBTQIA+ patients. Some participants were most comfortable seeking vaccination from STI focused clinics (i.e. public health departments, Planned Parenthood health centers, or university medical services) due to the privacy and anonymity provided by these venues. There was concern about seeking sexual health services from a primary care provider, particularly when the provider was a family physician who may inadvertently or purposefully disclose sexual health information to parents. Some men expressed more comfort with female providers, who they perceived to be more comfortable with gay men than male providers. The participants discussed a need to know where their providers stood on issues related to sexuality for fear that the provider may be biased or incompetent in providing care. Fear of judgement, expectations about the attitude of providers, and perception of providers to be incompetent in LGBTQIA+ care were key concerns among the studied young MSM, and may impede patient intentions to get vaccinated.

A study of Pap test utilization among transgender men indicated that availability of competent care, distress about seeking sexual health care, and transgender affirming care settings were all factors in whether patients in the study were willing to get a Pap test.[53] The patient provider relationship was key, and participants stated that they would agree to a Pap test if their provider recommended it. In addition, participants who had received a Pap test said they were more likely to do so because they had a prior positive relationship with their provider. The factors identified in the Pap test study may have implications that relate to promoting increased vaccination among transgender men. A strong patient-provider relationship and an inclusive health care setting are facilitators of vaccine completion. In the Boston-based SGM study, fully vaccinated transgender men described that gender-affirming care resulted in high comfort levels and trust in their PCP, as facilitators of vaccination.[52] SGM-affirmative care and positive patient-provider relationships were facilitators across the studies, demonstrating that non-affirmative care settings and poor provider relationships can act as barriers to sexual health care access for transgender patients.

Gender-affirming care for trans masculine patients correlates with higher rates of HPV vaccination.

52. Wheldon, C. W., Daley, E. M., Walsh-Buhi, E. R., Baldwin, J. A., Nyitray, A. G., & Giuliano, A. R. (2018). An Integrative Theoretical Framework for HPV Vaccine Promotion Among Male Sexual Minorities. American Journal of Men's Health, 12(5), 1409–1420. doi: 10.1177/1557988316652937

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Medical mistrust

Medical mistrust is a particularly alarming barrier to healthcare utilization. Medical mistrust is recognized as a social determinant of health and health care disparities.[54] A systemic review of medical mistrust demonstrated that greater medical mistrust is associated with lower adherence to cancer screening guidelines, lower adherence to antiretroviral medication among PLWH, lower patient satisfaction with their patient-provider relationship, and more frequent engagement in risky behaviors.[55] Medical mistrust is defined as a tendency to distrust medical systems and personnel believed to represent the dominant culture in a given society.

Black, Hispanic and Native American populations have significantly higher rates of medical mistrust than White non-Hispanic populations.[56] In fact, Black communities have high levels of belief in HIV conspiracies such as "HIV is man-made", "there is a cure for AIDS that is being withheld from the poor" and "people who take antiretroviral treatment are human guinea pigs for the government".[57] These beliefs are rooted in knowledge and experiences of unethical medical practices and research experiments such as the US Public Health Service Syphilis Study at Tuskegee, a clinical study conducted between 1932 and 1972 to observe the course of untreated syphilis from infection to death. Black men over the age of 25 were recruited for the study and one cohort of men infected with syphilis were not offered treatment for the disease, even after penicillin became widely available.[58] Even those who are unaware of unethical medical experiments can harbor medical mistrust based on their own experiences of racial discrimination in health care settings. Research suggests that medical mistrust including conspiracy beliefs about HIV and other public health issues is related to health behaviors.[59,60] Black people are disproportionately burdened by HIV and some other health conditions, such as diabetes.[61] Black individuals are less likely to regularly utilize screenings and check-ups if they are distrustful of healthcare.[62,63] Medical mistrust interferes with both seeking medical care and adhering to medical recommendations.

Black, Hispanic and Native American populations have significantly higher rates of medical mistrust than White non-Hispanic populations.

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Black Americans are less likely to have health insurance and access to preventive health care than White Americans and Asian Pacific Islander Americans. Native Americans and Alaska Natives, and Hispanic people have even lower rates of health insurance coverage.[64] Lower rates of health insurance contribute to Black, Indigenous, and Hispanic people being less likely to access routine, preventive health care. This in turn probably also contributes to medical mistrust.

Higher rates of medical mistrust are also found among gay and bisexual men and MSM living with HIV.[65,66] Particularly among Black MSM, "medical mistrust is a barrier to HIV voluntary counseling and routine health care engagement"[67,68] An additional study found that race-based medical mistrust is a barrier to willingness to use pre-exposure prophylaxis (PrEP) among Black MSM.[69] This research highlights the intersection of stigmatized identities experienced by HIV-positive and HIV-negative Black MSM and calls attention to the dire need for interventions that will mitigate systemic racism in health care settings and ultimately improve patient trust in medical providers.

Medical mistrust has been indicated as a barrier to STI testing and preventative health services among transgender patients. A study investigating barriers to STI testing services for trans men found that medical mistrust is a barrier to accessing testing.[70] A cluster analysis investigating the relationship between medical mistrust and perceptions of PrEP among 56 trans women found that medical mistrust served as a barrier.[71] Both studies indicated that a trusted relationship with a provider and access to gender-affirming care facilitated reduced levels of medical mistrust.

Medical mistrust has been indicated as a barrier to STI testing and preventative health services among transgender patients.

In the context of HPV, it is known that provider recommendation is a key factor in vaccine completion. Additionally, trust in health providers is imperative concerning patient engagement in secondary prevention measures such as Pap tests and HPV testing, particularly for unvaccinated adults. Thus, medical mistrust is very concerning with regard to differential rates of vaccination and HPV infection across racial, ethnic, and sexual and gender identities.

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False perceptions

False perceptions about the vaccine are problematic. Perceived severity is not reflective of the dangers of HPV. ACIP recommends 3 vaccines for adolescents, meningococcal vaccination (MenACWY) which protects against meningococcal disease, tetanus-diphtheria-pertussis vaccination (Tdap) which protects against tetanus, diphtheria, and acellular pertussis, and HPV vaccination, which protects against human papillomavirus. Tdap and MenACWY vaccine coverage is above 80% nationally.[72,73] HPV vaccine coverage lags far behind. Yet, a person is 20 times more likely to die from HPV-related diseases than the other 4 diseases combined, for which vaccination rates are higher.[74]

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Having a general distrust of vaccines affects HPV. The anti-vaccination movement has generated a particularly strong opposition to the HPV vaccine.[75,76] At least 3 anti-vaccine documentaries have targeted the HPV vaccine and it has been a focus of anti-vax conferences.[77] The notion that HPV vaccination disinhibits adolescents adds fuel to the fire. Studies have consistently shown that HPV vaccination in adolescence is not linked to increased rates of sexual activity.[78,79,80] Misinformation contributes to distrust and negative perception of the HPV vaccine, which hinders widespread uptake across the United States.

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Provider competency in recommending that adolescents get vaccinated

Provider recommendation is pivotal in parental intent to vaccinate children. The top reasons parents cite for not vaccinating their kids are insufficient provider recommendation and safety concerns.[81,82] In a qualitative study, vaccine-hesitant parents noted that a firm, strong provider recommendation increased their willingness to vaccinate their children.[83] Other studies have noted the challenges providers face with HPV vaccination, particularly the struggles around recommending a vaccine to adolescents that protects against a sexually transmitted infection. In the past, many providers presumed that discussions around the HPV vaccine would be uncomfortable, or that parents would have a negative reaction.[84,85] This frame reinforces the notion that there is something strange about the HPV vaccine. Reframing the HPV vaccine for what it is – a cancer vaccine, is an important step that providers must take.

The impact of COVID-19

Reports show substantial declines in vaccine ordering through the early stages of the COVID-19 pandemic, indicating that HPV vaccine delivery has been disrupted.[86,87] Reductions in face-to-face visits, while clearly justified by the need for social distancing, have limited opportunities for providers to recommend and administer vaccines. New barriers to provider communication may be particularly detrimental to HPV vaccination, which has been already posed a challenge for providers due to perceived resistance from parents and the absence of widespread school entry requirements. The HPV vaccine in particular has been deprioritized to shift focus on to early childhood vaccination in pandemic recovery efforts.[88]

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Current policy

Several changes are facilitating uptake of HPV vaccination, including the most recent ACIP recommendations, vaccine coverage under the Affordable Care Act (ACA), and new anti-cancer vaccine marketing. The updated ACIP recommendations are an important step for improving national coverage of the HPV vaccine. The vaccine falls under preventive services covered by the ACA, meaning that all new private insurance plans are required to cover ACIP-recommended vaccines without cost-sharing in the next plan year that occurs one year after the date of the recommendation.[89] In multiple studies which assessed the impact of the ACA on HPV vaccination among women, prevalence of HPV vaccination initiation was significantly higher after implementation of the ACA[90,91] Furthermore, one study found that "unadjusted prevalence of HPV vaccination initiation was higher not only in U.S. women overall, but also in each sexual orientation identity group (i.e. heterosexual, bisexual, and lesbian)."[92]

Despite nearly universal insurance coverage and the ACIP recommendation of the vaccine, national HPV immunization has continued to represent a significant challenge in the United States. A nationwide vaccination mandate has been universally acknowledged as the most effective means of achieving widespread vaccination. School-based institutional mandates have been extremely successful in the past to implement vaccination protocols for diseases such as polio and measles.[93] School-based vaccination mandates require individuals to be vaccinated in order to attend school, unless the individual has a valid exemption. For HPV, major barriers continue to hinder the passage of a mandate in most U.S. states.

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Globally, some nations have experienced great success increasing vaccination coverage and decreasing HPV infections. Australia implemented a national free vaccination program in 2007 for adolescent females and then in 2013 for males.[94] Through the program, free HPV vaccination is offered to all students in Australian schools. As of 2018, 80% of females and 73% of males in Australia had completed the HPV vaccination protocol.[95] Since the vaccination program for females was enacted, the HPV infection rate among women under 24 has fallen to 1%.[96] It has been predicted that cervical cancer will be eliminated in Australia within the next two decades.[97]

It has been predicted that cervical cancer will be eliminated in Australia within the next two decades.

At present, 34 states, Puerto Rico, and the District of Columbia reference HPV vaccination in statute or regulation. Only five jurisdictions—Hawaii, Puerto Rico, Rhode Island, Virginia, and Washington D.C.—currently have vaccination mandates in place.[98] All are gender neutral except Virginia, which is specific to female students only. Four states (AZ, LA, SC, and WV) explicitly exclude HPV vaccination from their school vaccination requirements.

The Rhode Island Department of Health began requiring HPV vaccination for students entering 7th grade in 2015, and thus provides a good example to draw on. The requirement allows for medical and religious exemptions only. In the most recent national vaccination data, Rhode Island had the nation's highest vaccination rate of 83.0%.[99] Alongside the vaccination mandate, the RI Department of Health supplies the HPV vaccine to providers across the state, funds an immunization program providing vaccinations at no cost to RI middle and high school students, and supports a statewide promotion campaign.[100]

Other states have established strategies to promote HPV vaccination in school-aged children. Four states (AK, DE, WV, and WY) recommend HPV vaccination in law and 12 additional states require or recommend distribution of information to parents related to HPV vaccination. Two states (IA and TX) require HPV vaccination information to be incorporated in education curricula. Some states have laws that promote vaccination in non-educational settings. For example, youth camps and similar programs in Maine are required to assess HPV vaccination status of their campers. There are multiple states with laws that promote vaccine access, such as laws providing vaccination authority to pharmacists, allowing minors to give consent for the vaccination, and establishing mechanisms to cover, fund, or reimburse for HPV vaccination. Some states incorporate public health strategies into statutes, such as requiring their departments of health to collect HPV vaccination data or conduct public awareness activities.[101]

As of 2018, 80% of females and 73% of males in Australia had completed the HPV vaccination protocol.

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99. Australian Institute of Health and Welfare. (2018). HPV Immunisation Reports and Data. Australian Institute of Health and Welfare. Retrieved from https://www.aihw.gov.au/reports-data/indicators/healthy-community-indicators/national/all-australia/childyouth/children-youth?filter=IND0010|2|Per%20cent&filter=IND0010|4|2015%E2%80%9316&filter=IND0010|1|Boys%20who%20were%20fully%20immunised%20against%20HPV.
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101. Hall, M., Simms, K., Lew, J., Smith, M., Brotherton, J., Saville, M., Frazer, I., & Canfell, K. (2018). The projected timeframe until cervical cancer elimination in Australia: a modelling study. The Lancet: Public Health, 4(1), 19-27. doi:10.1016/S2468-2667(18)30183-X

State regulations are far from unified. In one cross-sectional analysis, coding questions were used to evaluate types of HPV-related statutes and regulations in U.S. states. The coding questions addressed vaccination mandates, education and promotion programs, access programs, and public health strategies. Of the 10 coding questions, eight had results from less than 6 states and no single question had results from more than one-third of jurisdictions.[102]

[102] National HPV Vaccination Roundtable. (2019). School Entry Requirements for HPV Vaccine. HPV Vaccination Roundtable. Retrieved from http://hpvroundtable.org/wp-content/uploads/2019/09/05_School_Entry_Requirements_for_HPV_Vaccination_WEB_updated.pdf

Learning from the Hepatitis B vaccine

It may be helpful for public health policy makers to learn from policy successes of past vaccines comparable to the HPV vaccine. Hepatitis B (HepB) is a virus affecting the liver with many similarities to HPV. Both infections are spread through sexual contact, can clear up on their own, and can cause cancer later in life. High risk groups for Hep B include gay and bisexual men and MSM, people who inject drugs (PWID), and individuals with multiple sexual partners. Childhood infections are particularly concerning as 90% of infected infants become chronically infected, compared to 2-6% of adults.[103]

In 1982, a vaccine for HepB was implemented. After minimal vaccination uptake throughout the duration of the 80s, ACIP recommended a comprehensive strategy to eliminate HepB transmission that focused on universal childhood vaccination, prevention of perinatal HepB transmission, and catch-up vaccinations for high-risk individuals.[104] The ACIP recommendations for HepB rolled out very similarly to those of HPV, beginning with recommendations for only high risk groups and eventually extending the recommendations to all children including catch-up vaccination for unvaccinated adolescents. From 1993 to 2000, the national coverage rate for the HepB vaccine among children under 3 years increased from 16% to 90%, and the coverage rate for U.S. adolescents increased from near zero to 67%.[102]

The HepB vaccine is now considered a routine childhood vaccination. Much of the success of these strategies is attributed to expanded funding for childhood vaccinations made available through the Vaccines for Children program which was enacted by Congress in 1994. Laws requiring HepB vaccination of school children have been enacted in 44 U.S. states.[102] The successful HepB programming and policies in the 1990s indicate that there is great potential for improvement of vaccination rates for HPV today.

[103] Walker, T., Elam-Evans, L., & Yankey, D. (2020). National, Regional, State, and Selected Local Area Vaccination Coverage Among Adolescents Aged 13-17 Years - United States, 2020. Morbidity and Mortality Weekly Report, 70(35), 1183-1190. doi:10.15585/mmwr.mm7035a1. Accessed April 7, 2022.

[104] Rhode Island Department of Health. n.d. HPV (Human Papillomavirus) Vaccine. State of Rhode Island. Retrieved from https://health.ri.gov/immunization/about/hpv/

Recommendations

1. **Public health officials and political leaders should take additional steps to promote broad utilization of the HPV vaccine.**

Optimal vaccine disbursement is to adolescents aged 11-13, prior to sexual debut. Primary promotion efforts should focus on adolescents and their parents, with an emphasis on increasing education and addressing misinformation about efficacy and safety of the HPV vaccine. A focus on male-identified adolescents is needed to close the gap between male and female vaccination rates, with regard to sex assigned at birth. Secondary promotion efforts should be focused on individuals up to age 26. Underutilization over the past decade has produced a young adult population with insufficient vaccination coverage. Promotion efforts among the young adult cohort are especially important as there is still opportunity to protect this age group from HPV-related diseases. These efforts should address people of all sexes assigned at birth, sexual orientations, and gender identities. Adults aged 27-45 who may be at risk for new HPV infection should engage in shared clinical decision-making as they might benefit from vaccination.

A focus on male-identified adolescents is needed to close the gap between male and female vaccination rates, with regard to sex assigned at birth.

2. **Vaccination promotion efforts must be reprioritized through the ongoing COVID-19 pandemic.**

The COVID-19 pandemic has presented an unprecedented disruption to routine vaccination and promotion programs. Efforts must be made to facilitate catch-up vaccines, support existing vaccination programs, and broaden promotion efforts. Vaccines for Children (VFC) is a well-established and impactful program that supplies publicly funded vaccines to eligible children. Efforts should be undertaken to ensure the children who have become VFC-eligible as a result of the COVID-19 pandemic are enrolled in the program.

3. **Vaccination programs should be supported and endorsed by state governments.**

State health departments should look to the success of the state program in Rhode Island to roll out programs in their states. A school-based mandate for adolescents, similar to current requirements for MenACWY and TDaP vaccination, should be implemented in all states nationwide. Military institutions and state and federally funded universities and community colleges could benefit from mandated vaccination. Programs in these types of institutions have potential to capture unvaccinated individuals in the young adult cohort. Vaccinations should also be offered and encouraged in juvenile justice and correctional facilities.

State health departments should look to the success of the state program in Rhode Island to roll out programs in their states.

4. Education of primary care providers should be prioritized.

Primary Care Providers (PCPs) are key endorsers of the HPV vaccine. They must be well-equipped to provide competent, culturally relevant, and comprehensive recommendations and clearly communicate the risks of HPV to their patients across the gender spectrum and the age continuum. Of particular note, healthcare personnel training should include more education on LGBTQIA+ health. Healthcare personnel must be supported in increasing their education about the unique health needs of sexual and gender minorities. In particular, providers must understand and recognize that gay and bisexual men are at high risk for HPV-related disease and maximize opportunities to recommend vaccination to individuals in this cohort. Partnerships between state health departments and professional clinical organizations may be of benefit to align priorities on increasing HPV vaccination uptake. It must be clear to providers that endorsing HPV vaccination will lead to lower rates of disease in the population and lower costs to the system.

5. Barriers to vaccination should be addressed through context-specific interventions.

a. **Priority populations should be targeted by educational campaigns.** Educational campaigns should target men, particularly gay and bisexual men and other MSM. Campaigns should also focus on transgender and nonbinary individuals, and lesbian and bisexual women. Evidence-based interventions that are adapted to the specific needs and experiences of multiply marginalized populations, such as Black lesbians, are needed. Information regarding the prevention of genital warts, anogenital cancers, and oral cancers should be widely available. STI clinics should be equipped with educational materials, and clinicians in these clinics should be equipped to provide evidence-informed recommendations pertaining to HPV vaccination. PLWH should be prioritized by healthcare providers.

b. **Educational campaigns should address stigma and fears about vaccination.** Stigma related to sex and gender should be addressed in targeted campaigns towards all gender cohorts. Campaigns to vaccinate adolescents should address fears among parents. Unfounded perceptions of the HPV vaccine as dangerous, ineffective, and morally hazardous should be dispelled. Safety and health benefits of the vaccine should be reiterated and emphasized. Male-specific campaigns should recognize the need for increased utilization among the male-identifying cohort. Because of lower rates of cervical cancer screening among sexual minority women and transgender men, public education campaigns should also encourage HPV vaccination among these populations. Vaccination is important for all individuals regardless of gender identity or sexual orientation.

c. **Remove structural barriers to vaccination.** Vaccine availability should be widespread. STI clinics and Federally Qualified Health Centers (FQHCs) should have ample vaccination supply as these clinics serve populations at high risk for HPV. No-cost vaccines should be supplied to school-based clinics to reach adolescents in middle and high schools. State health departments can take an active role in vaccine facilitation as has been successful in the Vaccinate Before You Graduate program in Rhode Island.[105]

d. **Remove cost barriers to vaccination.** HPV vaccines for U.S. children are ACIP recommended and therefore must be covered by insurance companies. Uninsured children are protected by the Vaccines for Children program. For adults, the ACA requires that all Marketplace plans and most private plans cover certain vaccines without charging a copayment when the vaccine is provided by an in-network provider. HPV vaccination coverage is an optional benefit for adult Medicaid beneficiaries that is decided on a state-by-state basis. There are gaps in coverage, especially for uninsured and underinsured adults and Medicaid beneficiaries in certain states. Coverage of the HPV vaccine for U.S. adults should be required for all insurers, both private and public. Federally funded programs should cover free vaccinations for the uninsured.

Coverage of the HPV vaccine for U.S. adults should be required for all insurers, both private and public. Federally funded programs should cover free vaccinations for the uninsured.

[105] Thompson, E.L., Daley, E.M., Washburn, T., Salisbury-Keith, K., Saslow, D., Fontenot, H.B., & Zimet, G.D. (2020). School-entry requirements for HPV vaccination: part of the patchwork for HPV-related cancer prevention. Human Vaccines & Immunotherapeutics, 1–5. https://doi.org/10.1080/21645515.2020.1851130

6. Medical mistrust among racial and ethnic minority populations and sexual and gender minorities should be addressed.

Medical mistrust in the context of preventative healthcare must be reduced. In this effort, medical mistrust among Black Americans must be recognized in the greater historical and contemporary context of racism. Increased provider education on culturally competent care and LGBTQIA+ health is critical to reducing medical mistrust among racial, ethnic, sexual, and gender minority groups. Addressing deeply-rooted medical mistrust additionally requires institutional, structural, and interpersonal interventions, such as increased representation of Black people and other people of color in healthcare professions, shared decision-making between patients and providers, and involvement of community-based groups and institutions. Attention must be brought to racism in healthcare, and resources should be dedicated to developing programs to reduce institutional racism. Future qualitative and quantitative research should focus on solutions to reduce health disparities, particularly in the context of preventative care. All efforts in this arena must consider the history of racism and mistreatment of marginalized groups in the United States.

Increased representation of Black people and other people of color in healthcare professions, shared decision-making between patients and providers, and involvement of community-based groups and institutions can reduce medical mistrust.

7. Continued research should examine vaccination benefits for high risk adult populations.

Recent studies have indicated that vaccination of all unvaccinated individuals aged 27-45 would produce limited population benefit compared to increased cost-effectiveness ratio. Future studies should investigate cost-effectiveness of vaccinating high-risk adults age 27-45, such as gay and bisexual men and other MSM, as well as people living with HIV (PLWH) and other immunocompromised populations. Recent ACIP recommendations endorsing vaccination of adults 27-45 on a case-by-case basis indicate that high-risk groups may benefit. Just how much they may benefit should be further explored.

Future studies should investigate cost-effectiveness of vaccinating high-risk adults age 27–45, such as gay and bisexual men and other MSM, as well as people living with HIV (PLWH) and other immunocompromised populations.

8. Continued research should examine therapeutic uses of the HPV vaccine.

Some clinical trials have indicated that vaccination of HPV-positive women may offer protection against genital warts or precancerous cervical lesions. Further exploration of therapeutic use is needed, particularly for male populations. Therapeutic use of the HPV vaccine to target oral cancers could be a topic of interest. HPV-related oral cancer is the most rapidly increasing HPV-related cancer. Examination of therapeutic vaccination for prevention of oral cancer could have potential to save lives.

Further exploration of therapeutic use is needed, particularly for male populations.

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