

# Issue Brief

VOLUME 16, NUMBER 1 JANUARY 2021

## HUMAN PAPILLOMAVIRUS: HPV-Related Cancers and Vaccination Coverage in Wisconsin

*Alexandria Cull Weatherer, MPH, Wisconsin Cancer Collaborative*

### Background

Human Papillomavirus (HPV) is an incredibly common infection that affects 80 percent of all men and women at some point in their lifetime.<sup>1</sup> HPV infection can occur regardless of sexual orientation, type of sexual contact, or number of sexual partners.

Most people with HPV do not develop symptoms and may not know they are infected. The US Centers for Disease Control and Prevention (CDC) estimates that 79 million Americans are currently infected with HPV, with 14 million people newly infected each year.<sup>1</sup>

Most HPV infections are cleared by the immune system in one to two years. In other cases, HPV infections cause serious health issues in both men and women. HPV causes almost all anal cancers, cervical cancers, and cervical cancer precursors, and the majority of oropharyngeal (back of the throat, base of the tongue, and tonsils) cancers, vaginal cancers, vulvar cancers, and penile cancers.<sup>2</sup> HPV also causes anogenital warts and recurrent respiratory papillomatosis in men and women.

No tests can determine whether an HPV infection will clear on its own or lead to health problems such as cancer. This is why it is recommended that everyone get the HPV vaccine.

### KEY POINTS

- **HPV is a common virus** that causes six kinds of cancer in men and women.
- **In Wisconsin**, the most common cancer caused by HPV is oropharyngeal cancer (areas of the mouth and throat), which is **twice as common in men**.
- **HPV vaccine** safely and effectively **prevents cancer**. The vaccine is **recommended for girls and boys**, ages 11-12.
- The majority of Wisconsin children are not getting the HPV vaccine. **Boys are especially at risk** of not getting vaccinated.
- **We can improve vaccination rates** by offering strong provider recommendations, educating parents about the importance of cancer prevention, and addressing barriers to access.



Since 2006, the HPV vaccine has been a safe and effective tool used to reduce the number of HPV infections and subsequent HPV-related cancers. The vaccine targets nine HPV types and is given in two or three doses based on patient age. The vaccine is currently recommended for boys and girls age 11-12, with some providers encouraging it as early as age 9, and a catch-up schedule for patients up to age 26.

Many public health initiatives, such as Healthy People 2020 and the Wisconsin Cancer Plan 2020-2030, promote the importance of the HPV vaccine in preventing cancer and offer strategies to increase vaccination rates across Wisconsin.<sup>3</sup> However, since the licensure of the first HPV vaccine in 2006, uptake has lagged far behind other adolescent vaccines in both the United States<sup>4</sup> and in Wisconsin, particularly among boys.<sup>5</sup>

To successfully increase HPV vaccine uptake and completion, we must address multiple barriers for patients, families, and health care providers, and we need to change the conversation around HPV vaccine benefits for males.

## Methods

National cancer incidence data come from the United States Cancer Statistics Data Visualizations Tool: 2012-2016, available from the combined resources of the US Department of Health and Human Services, CDC, and the National Cancer Institute (<https://gis.cdc.gov/Cancer/USCS/DataViz.html>).<sup>6</sup> National cancer mortality data for 2012-2016 are from SEER\*Stat public-use database with mortality data provided by National Center for Health Statistics (available at [www.seer.cancer.gov/nchs](http://www.seer.cancer.gov/nchs)).<sup>6</sup> (Note: State and national incidence and mortality rates for 2013-2017 were not available at the time of this writing. These rates were released shortly before publication, and the 2013-2017 data reflect similar trends.)

Wisconsin-specific HPV-associated cancer incidence and mortality data are from the Wisconsin Cancer Reporting System (WCRS), Office of Health Informatics, Division of Public Health, Department of Health Services. Cancer incidence and cancer mortality are expressed per 100,000 people and age-adjusted to the 2000 US standard population. Wisconsin vaccine coverage

data are from the Wisconsin Immunization Registry (WIR), a statewide, population-based immunization information system used to record and track immunization histories. Immunization data for children and adolescents are considered highly complete and accurate.<sup>7</sup> As of 2019, more than 3,794 health care providers and 2,368 schools and school districts are participating in the WIR.<sup>8</sup> Denominators used to calculate the vaccination rates are from the 2018 Wisconsin age- and gender-specific population estimates obtained from the Office of Health Informatics, Division of Public Health, Wisconsin Department of Health Services.

## How HPV-Related Cancers are Measured

Persistent HPV infection can progress to at least six types of pre-cancer or cancer. Unfortunately, cancer registries do not routinely collect whether HPV was present in cancer tissue at the time of diagnosis. Thus, incidence and mortality rates often capture HPV-associated cancers (*see Box 1*). *HPV-associated* is defined as a specific cellular type of cancer that occurs in parts of the body where HPV is often found.<sup>9</sup>

An *HPV-attributable* cancer is a cancer that is probably caused by HPV (*see Box 1*).<sup>9</sup> To determine the number of HPV-attributable cancers, we can multiply the number of HPV-associated cancers by the percentage of those cancers that are probably caused by HPV, according to CDC studies. Nationally, according to the CDC, HPV is the probable cause of 91 percent of cervical and anal cancers, 75 percent of vaginal cancers, 72 percent of male oropharyngeal cancers, 63 percent of female oropharyngeal cancers, 69 percent of vulvar cancers, and 63 percent of penile cancers.<sup>9,10</sup>

From 1999-2015, national HPV-associated cancers reflected the following trends: cervical and vaginal cancer rates have

### BOX 1

#### Associated vs. Attributable

**An HPV-associated cancer** is a cancer found in parts of the body where HPV is often found. These cancers may be caused by HPV or by other factors.

**An HPV-attributable cancer** is a cancer that is likely caused by HPV. These cancers are a subset of all HPV-associated cancers.



decreased; penile cancer rates have remained stable; and vulvar, anal, and oropharyngeal cancer rates have been on the rise.<sup>11</sup> Notably, oropharyngeal cancers are increasing more rapidly among men regardless of race or ethnicity<sup>12</sup>, and anal cancers are increasing more rapidly among white women and African American men (see Box 2).<sup>13</sup>

From 2012-2016, an average of 34,800 cancers were attributable to HPV in the United States each year. Of these cancers, 32,100 (92 percent) were attributable to the specific HPV types targeted by the current HPV vaccine.<sup>14</sup> This highlights the potential impact HPV vaccine can have on prevention.

## HPV-Related Cancers in Wisconsin

Cervical cancer is perhaps the most widely known HPV-associated cancer. It is also the most commonly diagnosed HPV-associated cancer among women, both in the US and in Wisconsin. From 2012-2016, the incidence rate of cervical cancer in Wisconsin was 6.6, which was slightly lower than the national rate of 7.6. The mortality rate for cervical cancer during this time was 1.6 in Wisconsin, and 2.4 in the United States. Data from 2013-2017 reflect similar numbers: the cervical cancer incidence in Wisconsin was 6.4, and the state's mortality rate was 1.6.

Significant health disparities exist within these numbers. In Wisconsin, cervical cancer incidence rates are notably high in the Black, Native American, and Asian/Pacific Islander communities, almost double the cancer incidence in white

### BOX 2

Per CDC guidance, anal and rectal squamous cell carcinomas are included in the case count for determining HPV-associated and attributable anal cancer. It is important to note that although anal cancer is fairly rare, incidence and deaths are rising in the United States. Possible causes include increases in HPV infection, HIV-related immunosuppression, smoking, and obesity, which are risk factors for anal cancer.<sup>13</sup>

populations. From 2012-2016, Black women had the highest incidence of cervical cancer both in Wisconsin and in the United States, at 11.9 per 100,000 in Wisconsin and 8.9 per 100,000 in the nation overall. Black women also experience the highest mortality rate, at 4 deaths per 100,000 people.

Unfortunately, many people mistakenly believe cervical cancer is the only cancer caused by HPV. This contributes to the widespread misconception that the HPV vaccine only protects women. In fact, oropharyngeal cancer affects far more men than women and is the most commonly diagnosed HPV-associated cancer in Wisconsin.

Oropharyngeal cancer (see Figure 1) is defined as cancer of the tongue, tonsil, oropharynx, or other oral cavity and pharynx sites (inclusive of all cell types). It is also known as oropharyngeal squamous cell carcinoma.

Of the six cancers that can be attributed to the HPV types targeted by the HPV vaccine, oropharyngeal cancer is the most common, as estimated in a 2019 CDC analysis of US

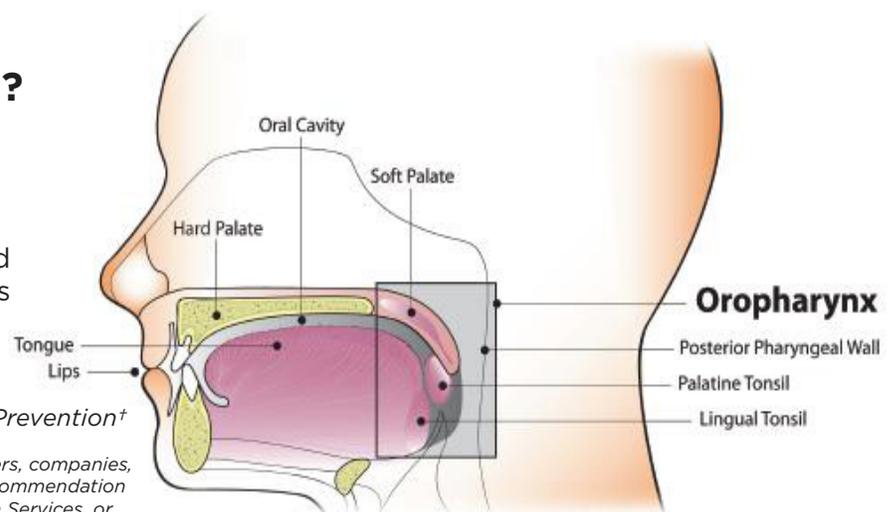
FIGURE 1

## What is “Oropharyngeal”?

Oropharyngeal describes the area of the throat at the back of the mouth. This includes the tongue, tonsils, oropharynx, and other oral cavity and pharynx sites. Oropharyngeal cancers are the most commonly diagnosed HPV-associated cancers.

Source: US Centers for Disease Control and Prevention†

†Reference to specific commercial products, manufacturers, companies, or trademarks does not constitute its endorsement or recommendation by the US Government, Department of Health and Human Services, or Centers for Disease Control and Prevention. The material is otherwise available on the agency website for no charge.



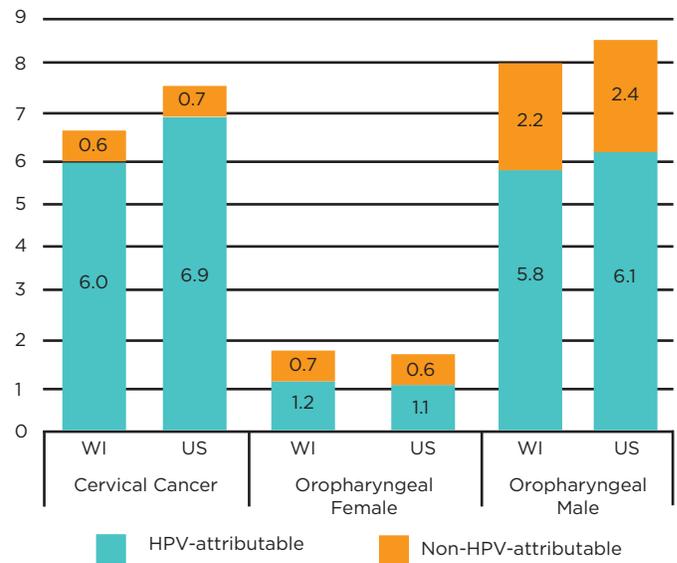
Cancer Statistics (USCS).<sup>14</sup> Oropharyngeal cancer is twice as common in men than in women, and national cases of oropharyngeal cancer attributed to HPV infection are on the rise.<sup>15</sup> In the past, most oropharyngeal cancers were caused by tobacco and alcohol, but recent studies suggest that about 70 percent of cancers of the oropharynx now may be linked to HPV. Many cancers of the oropharynx may be caused by a combination of tobacco, alcohol, and HPV, highlighting the need to further address the impact of multiple cancer risk factors.<sup>9,16</sup> (*How do Wisconsin's two most common HPV-associated cancers—oropharyngeal and cervical—compare to US rates? See Figure 2 to learn more.*)

Wisconsin's 2012-2016 incidence and mortality rates for HPV-associated oropharyngeal cancer were similar to national rates, with men experiencing significantly higher rates of diagnoses and higher rates of death than women. The 2012-2016 incidence rates for oropharyngeal cancer were 8.0 and 8.5 for WI and US men respectively, and 1.9 and 1.7 for WI and US women respectively. The 2012-2016 mortality rates for oropharyngeal cancer were 2.3 and 2.5 for WI and US men, and 0.7 and 0.8 for WI and US women.

Utilizing CDC methods,<sup>9</sup> an estimated 3,017 new cancer diagnoses in Wisconsin between 2012-2016 were attributable to HPV infection: 865 cervical cancer cases; 1,030 male oropharyngeal cancer cases; 221 female oropharyngeal cancer cases; 490 anal/rectum cancer cases; 278 vulvar cancer cases; 50 vaginal cancer cases; and 83 penile cancer cases (*see Figure 3 for annual averages*). In this same time period, at least 748 Wisconsin cancer deaths were attributable to HPV infection: an estimated 272 oropharyngeal cancer deaths among men and 88 oropharyngeal cancer deaths among women; 255 cervical

FIGURE 2

### Age-Adjusted Incidence Rates for Major HPV-Associated Cancers by Gender, in Wisconsin and the United States, 2012-2016



cancer deaths; 90 vulvar cancer deaths; 24 vaginal cancer deaths; and 19 penile cancer deaths (data for HPV-associated anal cancer deaths for this time period are not publicly available). From 2012-2016, Wisconsin's HPV-related incidence and mortality rates for cervical cancer

FIGURE 3

### HPV-Attributable Cancers in Wisconsin: Annual Average Cases, 2012-2016

Cancer Types	Wisconsin	United States
Oropharyngeal cancer (mouth and throat)	249	13,500
Cervical cancer	173	10,900
Anal cancer	98	6,200
Vulvar/vaginal cancer	66	3,400
Penile cancer	17	800

were lower than national rates, while the incidence and mortality rates for oropharyngeal cancer in Wisconsin were similar to national rates.

## HPV Vaccine

Since 2006, three HPV vaccines have been used to reduce the number of HPV infections and subsequent HPV-related cancers. Presently, Gardasil 9 (9vHPV) has been in use in the United States since 2014. It protects against nine HPV types, including seven types that cause cancer (16, 18, 31, 33, 45, 52, and 58) and two types that cause genital warts (6 and 11).<sup>14,17</sup>

Previous iterations of the HPV vaccine protected against fewer HPV types. The first vaccine (2vHPV, Cervarix) only protected against types 16 and 18, the two types of HPV that are responsible for approximately 70 percent of all cervical cancers.<sup>17</sup> The second vaccine (4vHPV, Gardasil) added protection against genital warts (types 6 and 11). The most recent vaccine (9vHPV, Gardasil) adds protection against an additional five high-risk cancer-causing types. The first two vaccines remain licensed in the United States but are not currently distributed or used.

Initiation of HPV vaccination is routinely recommended for both males and females beginning at 11 to 12 years of age (see Box 3).<sup>18</sup> HPV vaccination is also recommended via a catch-up schedule for males and females ages 13-26 who have not yet been vaccinated. Until 2016, HPV vaccine was administered via three doses, regardless of age. Since 2016, a two-dose schedule (0, 6-12 month schedule) is recommended for young adolescents ages 9-14.<sup>18</sup> The traditional three-dose schedule (0, 1-2, 6 month schedule) is recommended for males and females who

initiate the vaccination series at ages 15-26 years and for immunocompromised persons.<sup>18</sup>

Vaccine recommendations have evolved since 2006, beyond changes to the dose schedule, dependent on age of vaccine initiation and risk factors. In 2006, the first HPV vaccine was marketed as a cervical cancer prevention vaccine, offering only indirect benefit for males, and the Advisory Committee on Immunization Practices (ACIP) only recommended vaccination for girls ages 11-12.<sup>18,20</sup> Male HPV vaccination for the prevention of genital warts was not approved by the US Food and Drug Administration (FDA) until 2009,<sup>21</sup> and male vaccination for cancer prevention wasn't approved by the FDA or recommended by ACIP until 2011.<sup>22</sup> Although most research addresses the vaccination impact on female health outcomes, optimizing HPV vaccine efficacy and preventing cancer also applies to males. (See Box 4 to learn how COVID-19 has affected HPV vaccination.)

Recommendations were updated again in 2019 regarding individuals ages 27-45. Certain individuals in this age range may benefit from vaccination (and would receive the three-dose schedule). However, public health benefit of HPV vaccination in this age range often is minimal, as many have already been infected with HPV.<sup>23</sup> Therefore, routine catch-up schedules for this age range are not currently recommended. An individual's decision to be vaccinated should be individually based, using shared decision-making and clinical judgment with consideration of the possibility of acquiring a new HPV infection.<sup>23</sup> Many insurance companies have updated their coverage to reflect this recommendation. In Wisconsin, HPV vaccination for adults ages 27-45 is covered by more than 90 percent of commercial insurance plans and by BadgerCare.

### BOX 3

#### Why the HPV Vaccine is Recommended for Children Ages 11-12

- Antibody response in 9- to 14-year-olds is greater than older adolescents or young adults.<sup>19</sup>
- The vaccine has greater impact if given universally before any sexual activity.
- Younger vaccine initiation age means only two shots, instead of three given to older adolescents (because of the greater immune response among younger adolescents<sup>19</sup>). This increases the likelihood of vaccine completion.
- Adolescents are already scheduled for an immunization visit at age 11-12 years, minimizing burdens on parents and health systems.
- Cancer prevention should begin at an early age.



**BOX 4****The Impact of COVID-19 on HPV Vaccination**

The COVID-19 pandemic has caused substantial declines in HPV vaccine delivery across the United States.<sup>24</sup>

Delays in routine appointments early in the pandemic caused many children to miss important vaccinations. For example, available data suggests HPV vaccinations dropped by more than 70 percent in March 2020.<sup>24</sup>

As health care systems work to get immunizations back on track, many systems are prioritizing catch-up for infants and young children from birth to 24 months. As a result, some early childhood vaccinations appear to be returning to pre-pandemic levels, while HPV vaccination among adolescents remains low.<sup>24</sup>



Young adults also may be at risk of reduced access to the HPV vaccine during the pandemic. As in-person routine medical appointments have declined, adults may be more likely to access vaccinations via retail pharmacies. However, the HPV vaccine may be less available in pharmacy settings than in medical clinics, especially for adults over age 26.

Ongoing challenges related to the pandemic could prolong the negative impact on HPV vaccination. Fear of coronavirus exposure may persist for some time, prompting some parents to continue limiting in-person preventative medical appointments for their children. And some parents may experience increased overall vaccine hesitancy triggered by concerns over COVID-19 vaccination.<sup>24</sup>

Despite these challenges, routine vaccination remains an essential preventive care service that should not be delayed or missed because of the COVID-19 pandemic. Recommendations to ensure continued HPV vaccination include:<sup>25, 26</sup>

- **Strategies to spatially separate sick patients from well patients:**
  - Lower the number of patients on site at any one time. Such as closing a waiting room or registration area and have patients check in by phone from the parking lot.
  - Schedule well visits in the morning and sick visits in the afternoon.
  - Collaborate with other providers in the community to identify separate locations for well visits for children.
- **Minimize missed opportunities (when an adolescent goes to a provider visit and is due for HPV vaccine but it was not administered):**
  - Every time an adolescent comes in, assess for vaccination status.
  - Strongly recommend HPV vaccination for all eligible adolescents.
  - Health systems should make HPV vaccination a high, measurable priority.
- **Other recommendations:**
  - Vaccinate during sick visits for minor illnesses such as ear infections.
  - Examine patients and give vaccines by car visit, when possible.
  - Assess the vaccination status of all patients at each visit, and utilize appropriate catch-up schedules.
  - Promote clinic safety measures to parents, and remind parents of the importance of the HPV vaccine as cancer prevention.

## HPV Vaccine as Cancer Prevention

The HPV vaccine is a cancer prevention tool that reduces cancer incidence, pain and suffering, and the medical costs related to cancer diagnosis and treatment. The only other cancer prevention vaccine is the hepatitis B vaccine, which has been highly successful in decreasing global disease burden.

Studies have consistently shown that HPV vaccines are highly immunogenic, well-tolerated, and effective in preventing HPV infections while maintaining excellent safety.<sup>20,27</sup> For example, the HPV vaccine has had a significant impact on reducing the HPV infections that can lead to head and neck cancers and has reduced oral HPV infections in men in the United States by 37 percent over the span of eight years.<sup>28</sup> The 9vHPV vaccine increases overall prevention of cervical cancer from approximately 70 percent to approximately 90 percent.<sup>17</sup> Routine vaccination campaigns of girls in Scotland have led to a dramatic decrease of preinvasive cervical disease in later life (approximately 90 percent) and provide evidence of herd protection among unvaccinated populations.<sup>29</sup> Furthermore, application of current cancer cost estimates demonstrates that catch-up HPV vaccination reduces the estimated cost per quality-adjusted life year (QALY) gained by about \$12,400, meaning that vaccination benefits economically, as well.<sup>30</sup>

## HPV Vaccination Coverage in Wisconsin

A majority of Wisconsin children are still at risk for HPV infection. Based on WIR data, male and female HPV vaccine coverage in Wisconsin is far less than coverage for other vaccines administered to adolescents (MCV4 and Tdap).

Most children are still not receiving the HPV vaccine at the recommended age of 11-12 (see Figure 4). As of 2018, only 14.02 percent of girls and 12.99 percent of boys had completed the HPV vaccination series. Notably, in 2018, only 7 of Wisconsin's 72 counties had a vaccination completion rate for 11- to 12-year-olds that was higher than 15 percent.

Among older children ages 13-17, we have made some progress. As of 2018, 45.00 percent of girls and 39.36 percent of boys have completed the HPV vaccination series. However, this means fewer than half of all Wisconsin teens are fully protected (see Figure 4).<sup>31</sup>

Though Wisconsin's HPV vaccination rates are slowly improving, Wisconsin has fallen dramatically short of the state's goal of 80 percent vaccination completion by age 13-15 by 2020. Efforts must continue to focus on universal strong provider recommendations and vaccinating both boys and girls at the recommended age of 11-12.

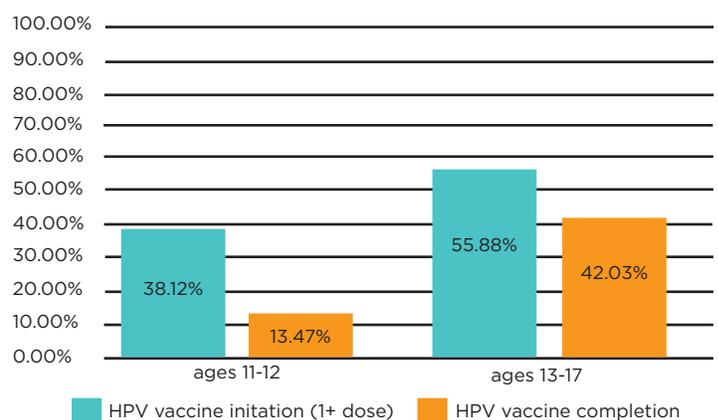
## Barriers to HPV Vaccination

Multiple barriers to HPV vaccination initiation and series completion exist among adolescents in the US and in Wisconsin. Some of these barriers were created by the rollout of the vaccine itself, which was suboptimal for many reasons. Early promotion of the vaccine focused on HPV's method of transmission (primarily through sexual activity) and lacked any focus on cancer prevention. The first vaccine was recommended only for females, was not required for school entry, was costly, and was targeted by vocal anti-vaccine movements. All of these factors have contributed to low HPV vaccine acceptance among parents and, therefore, low vaccination rates among youth.<sup>5</sup>

In general, parental concerns about adverse effects and safety of vaccines are a main reason for vaccine hesitancy. This is especially true for the HPV vaccine.<sup>32</sup> Common parental beliefs about the HPV vaccine include: lack of necessity, skepticism about effectiveness, concern that it encourages sexual promiscuity, and a belief that it is too new.<sup>33,34</sup> In addition, the gender- and age-based recommendations for the HPV vaccine have expanded over time, making guidelines more complicated and confusing for parents to follow.<sup>5</sup>

FIGURE 4

## HPV Initiation and Completion Rates in Wisconsin, 2018



Source: Wisconsin Immunization Registry<sup>31</sup>

Lack of knowledge about HPV creates a common barrier to HPV vaccination. Studies have shown that 70 percent of US adults do not know that HPV causes oral, anal and penile cancers<sup>34</sup> and 63.6 percent of US women do not know that HPV vaccine prevents cervical cancer.<sup>35</sup> A substantial proportion of US adults are uninformed about the HPV vaccine and have limited knowledge of the vaccine's effectiveness in cancer prevention, especially men.<sup>34</sup> This is significant, because HPV-related oral cancers in men have been on the rise in recent years and now outnumber cervical cancer cases, underscoring the importance of HPV vaccination for boys, as well as girls. Studies also suggest limited knowledge even among HPV-related cancer survivors, which is alarming.<sup>36</sup>

Parental attitudes, concerns, and gaps in knowledge can, in return, create barriers to strong medical provider recommendation.<sup>33</sup> Medical provider recommendation is a primary indicator of vaccination.<sup>33,37,38</sup> However, HPV knowledge and strong HPV vaccination recommendation among providers remains low.<sup>5,37</sup> Studies have identified barriers to provider recommendation, including lack of general HPV and vaccine knowledge, low self-confidence in counselling and addressing parental concerns, and discomfort in discussing sexual issues related to vaccination.<sup>37</sup>

Furthermore, important gender disparities exist in which patients receive a provider recommendation. Parents are less likely to vaccinate their adolescent boys than girls with the HPV vaccine<sup>37</sup> and they are twice as likely to report their main reason as a lack of provider recommendation.<sup>39</sup> This reinforces the misconception that boys do not directly benefit from vaccination, a commonly reported reason for not vaccinating sons.<sup>33</sup> Many providers identify a need to know more about oropharyngeal HPV. For example, Gnagi et al., reported that 53 percent of providers never discuss oropharyngeal cancer when counseling patients on HPV vaccine, and 95 percent of providers want more education.<sup>40</sup>

In many cases vaccine costs and the socio-political climate are main barriers to vaccine uptake and completion.<sup>20</sup> HPV vaccination on average costs \$212 per dose, including administration costs.<sup>30</sup> The HPV vaccine schedule may include two or three doses, increasing these costs.

Despite the fact that the vaccine's high efficacy and safety have been demonstrated for more than ten years, media and social network propagation of adverse effects can produce persistent insecurity among parents.<sup>20</sup> Moreover, anti-vaccine movements negatively influence vaccination rates

and vaccine confidence by using anecdotal and emotional appeals instead of facts and logic.<sup>20</sup>

Distrust of doctors and medical systems is another common barrier. Distrust rooted in personal and/or historical medical mistreatment is often higher among African Americans, which can decrease willingness to vaccinate.<sup>41</sup> Addressing this barrier with culturally appropriate interventions is an especially important priority given the higher rates of cervical cancer among African American and Hispanic women.<sup>41</sup>

## Policy and Program Implications

Medical providers need to be fully aware of the importance of vaccinating both male and female adolescents, and they need to increase their efforts to routinely recommend the HPV vaccine for all adolescent patients. Currently, a major challenge is the need to transform the inaccurate message that HPV vaccine is a female-only cervical cancer vaccine, and instead promote the fact that it is a universal childhood vaccine that benefits both boys and girls. Providers, patients, and parents of both sexes need more education about HPV and HPV vaccination. However, knowledge by itself is insufficient. Ongoing research and new study findings can help health officials focus on target populations with the vaccine and reevaluate their current policies and messaging. Interventions that address multiple factors and/or barriers are necessary to be successful.

The significant costs of HPV-related cancers and disease, combined with high vaccine effectiveness, ideally should encourage strong policies that encourage high vaccine uptake.<sup>5</sup> However, high cost is still a common barrier to HPV vaccination. Two mechanisms can help to mitigate costs for both providers and families. The Affordable Care Act (ACA) requires most private insurance plans to cover recommended preventive services and ACIP-recommended immunizations at no cost. HPV vaccine and pap tests are covered under the ACA, minimizing costs. However, vaccine administration fees and office visit costs may still situationally apply. Secondly, the federally financed Vaccines For Children (VFC) program pays for vaccines recommended by the ACIP for children ages 18 and under who are either Medicaid-eligible, uninsured, American Indian or Alaska Native, or underinsured. However, further funding mechanisms are needed to encourage high uptake, as costs remain a barrier.

Although strongly recommended by the ACIP, HPV vaccination is not required for school entry in most



states. This sends the unintended message that the HPV vaccine is unnecessary. Interestingly, while school entry requirements effectively improve uptake for other vaccines, some

jurisdictions with HPV vaccine mandates (Washington, DC, and Virginia) appear to have similar rates of HPV vaccination compared to states without mandates, possibly the result of less restrictive opt-outs or gendered school requirements.<sup>5,42</sup> Conversely, vaccine mandates can be highly controversial and unpopular with the public, leading other states to enact HPV education requirements instead of actual vaccination requirements.

For several years, Rhode Island was the only US state to enact school entry legislation requiring HPV vaccination for both boys and girls without allowing less restrictive opt-out provisions.<sup>42</sup> They were able to do so only after achieving high vaccination rates, broad public support, and a unique public health structure that allows them to make requirements without legislative approval. Hawaii and Puerto Rico have recently joined Rhode Island's ranks, enacting a new sex-neutral HPV vaccine school-entry requirement for 7th graders in Hawaii and for 11- to 12-year-olds in Puerto Rico, allowing only for medical or religious exemptions.<sup>43</sup>

Few other countries require HPV vaccination for school entry.<sup>42</sup> Countries with the highest rates of HPV vaccination (United Kingdom, Australia, and New Zealand) do not require HPV vaccination for school entry, but instead provide free vaccines in school-based clinics.<sup>44</sup> Thus, school-based clinics may be considered an effective alternative to school-entry requirements or vaccine mandates. School-based clinics have been successful in increasing vaccine rates in various settings<sup>45</sup> and would additionally address barriers of cost, missed opportunities for vaccination, time needed to go to the clinic, and low parental awareness of the vaccine. However, the upfront cost to purchase and store the vaccine<sup>33,45</sup> and inadequate reimbursement (primarily for students who are not

VFC-eligible) may deter school-based clinics. Issues of cost must be addressed in order for school-based clinics to be successful in the United States.

Growing evidence has found increased uptake may occur when HPV vaccine is initiated earlier, at age 9-10 instead of the recommended age of 11-12.<sup>38,46,47</sup> For example, a 2016 Minnesotan study found that adolescents who started the HPV vaccine series at age 9 or 10 were 22 times more likely to complete the two-dose series by age 15 than those who initiated the series at age 11 or 12.<sup>46</sup> Parents and providers may be more willing to initiate the vaccine at an earlier age when the HPV recommendation can be more easily disentangled from conversations about sex. Additionally, starting at an earlier age allows parents and providers more time to follow the recommendation and discuss the vaccine. Encouraging messages such as "HPV 9 at 9" (the HPV types in the currently available vaccine) may improve vaccination rates and reduce cancer deaths. However, a randomized controlled trial would be beneficial for determining whether younger age at vaccination alone accounts for improved rates or if other factors are contributing.

## Conclusion

HPV vaccination protects both males and females from future HPV-related cancers and other serious health issues. HPV vaccination is an essential and effective cancer prevention tool that is being significantly underutilized.<sup>14</sup> Parental education, improved HPV communication strategies and messaging, and an increase in strong physician recommendation are only part of what is needed to improve HPV vaccine coverage for males and females in Wisconsin (*see Box 5*). Further efforts are needed to reduce missed opportunities for HPV vaccination, address disparities in uptake, and address system-level barriers to vaccination.<sup>33</sup>



## BOX 5

**Take Action: Promote HPV Vaccination**

Improve HPV vaccination rates and prevent cancer in your community:

- ❑ Focus on the message that the **HPV vaccine is cancer prevention**.
- ❑ **Routinely monitor HPV immunization rates** from your clinic or community, and share with staff.
- ❑ Use the **“Same Way, Same Day”** strategy:
  - By offering all vaccines of the adolescent platform (HPV, meningitis, Tdap), parents are more likely to understand the importance for their child.
  - Providers using a more presumptive style instead of open-ended style achieve higher acceptance rates.<sup>40</sup>
  - An example of this is: “Now that your son is 11, he is due for vaccinations today to help protect him from meningitis, HPV cancers, and whooping cough. Do you have any questions?”<sup>43</sup>
- ❑ **Advocate for sex-neutral vaccination.** Girls and boys directly benefit from HPV vaccination.
- ❑ Consider using **“HPV 9 at 9”** messaging (see the *Policy and Program Implications* section for more information).
- ❑ Participate in **Immunization Quality Improvement for Providers** (IQIP) services from the Wisconsin Immunization Program:
  - These no-cost services are available to Vaccines for Children providers. This is the new and improved Assessment, Feedback, Incentive, and information eXchange (AFIX) quality improvement program.
- ❑ **Remove the stigma** and normalize the conversation:
  - Continued efforts are needed to ensure that health care professionals and parents understand the importance of vaccinating adolescents before they become sexually active<sup>28</sup>, and that HPV vaccination doesn’t encourage sexual activity.<sup>44</sup>
  - Consider non-traditional modes to raise awareness about the importance of HPV vaccination. For example, sports coaches providing HPV education for boys.
- ❑ **Engage dental health professionals** in HPV education and prevention activities. Dentists are a key stakeholder in oropharyngeal cancer education, prevention, and identification.
- ❑ Focus on **HPV vaccine policies** that promote voluntary uptake and **encourage strong provider recommendation**.<sup>37</sup>



## References

- Centers for Disease Control and Prevention. Sexually transmitted diseases (STDs)- genital HPV infection fact sheet. <https://www.cdc.gov/std/hpv/stdfact-hpv.htm>. Updated 2019. Accessed December 17, 2019.
- Saraiya M, Unger ER, Thompson TD, et al. US assessment of HPV types in cancers: Implications for current and 9-valent HPV vaccines. *J Natl Cancer Inst.* 2015;107(6):djv086. doi: 10.1093/jnci/djv086 [doi].
- University of Wisconsin Carbone Cancer Center. Wisconsin Comprehensive Cancer Control Plan 2015-2020. 2015.
- Han JJ, Beltran TH, Song JW, Klaric J, Choi YS. Prevalence of genital human papillomavirus infection and human papillomavirus vaccination rates among US adult men: National health and nutrition examination survey (NHANES) 2013-2014. *JAMA Oncology.* 2017;3(6):810-816.
- Hirth J. Disparities in HPV vaccination rates and HPV prevalence in the United States: A review of the literature. *Hum Vaccin Immunother.* 2019;15(1):146-155. doi: 10.1080/21645515.2018.1512453 [doi].
- US Cancer Statistics Working Group. US Cancer Statistics Data Visualizations Tool, based on November 2018 submission data (1999-2016); US Department of Health and Human Services, Centers for Disease Control and Prevention and National Cancer Institute; [www.cdc.gov/cancer/dataviz](http://www.cdc.gov/cancer/dataviz), June 2019.
- Koepke R, Petit AB, Ayele RA, et al. Completeness and accuracy of the Wisconsin immunization registry: An evaluation coinciding with the beginning of meaningful use. *J Public Health Manag Pract.* 2015;21(3):273-281. doi: 10.1097/PHH.0000000000000216 [doi].
- Wisconsin Department of Health Services. Presented at Wisconsin Immunization Registry user group meeting spring 2020. Madison, WI.
- Division of Cancer Prevention and Control, Centers for Disease Control and Prevention. How many cancers are linked with HPV each year? <https://www.cdc.gov/cancer/hpv/statistics/cases.htm>. Updated 2019.
- Centers for Disease Control and Prevention. HPV-associated cancer statistics. <https://www.cdc.gov/cancer/hpv/statistics/index.htm>. Updated 2019. Accessed December 23, 2019.
- Van Dyne EA, Henley SJ, Saraiya M, Thomas CC, Markowitz LE, Benard VB. Trends in human papillomavirus-associated cancers—United states, 1999–2015. *Morb Mortal Weekly Rep.* 2018;67(33):918.
- Faraji F, Rettig EM, Tsai HL, et al. The prevalence of human papillomavirus in oropharyngeal cancer is increasing regardless of sex or race, and the influence of sex and race on survival is modified by human papillomavirus tumor status. *Cancer.* 03 2019;125(5):761-769. doi:10.1002/cncr.31841.
- Deshmukh AA, Suk R, Shiels MS, et al. Recent trends in squamous cell carcinoma of the anus incidence and mortality in the United States, 2001-2015. *J Natl Cancer Inst.* 2019. doi: djz219 [pii].
- Senkomago V, Henley SJ, Thomas CC, Mix JM, Markowitz LE, Saraiya M. Human papillomavirus-attributable cancers—United states, 2012–2016. *Morb Mortal Weekly Rep.* 2019;68(33):724.
- Chaturvedi AK, Engels EA, Pfeiffer RM, et al. Human papillomavirus and rising oropharyngeal cancer incidence in the united states. *Journal of Clinical Oncology.* 2011;29(32):4294.
- Centers for Disease Control and Prevention. Cancers associated with human papillomavirus, united states—2012–2016. Centers for Disease Control and Prevention, US Department of Health and Human Services. 2019 (US Cancer Statistics data brief, No. 10.). <https://www.cdc.gov/cancer/uscs/pdf/USCS-DataBrief-No10-August2019-h.pdf>.
- Joura EA, Giuliano AR, Iversen OE, et al. A 9-valent HPV vaccine against infection and intraepithelial neoplasia in women. *N Engl J Med.* 2015;372(8):711-723. doi: 10.1056/NEJMoa1405044 [doi].
- Meites E, Kempe A, Markowitz LE. Use of a 2-dose schedule for human papillomavirus vaccination—updated recommendations of the advisory committee on immunization practices. *Am J Transplant.* 2017;17(3):834-837.
- Iversen O, Miranda MJ, Ulied A, et al. Immunogenicity of the 9-valent HPV vaccine using 2-dose regimens in girls and boys vs a 3-dose regimen in women. *JAMA.* 2016;316(22):2411-2421.
- de Oliveira CM, Fregnani, J H T G, Villa LL. HPV vaccine: Updates and highlights. *Acta Cytol.* 2019;63(2):159-168. doi: 10.1159/000497617 [doi].
- Centers for Disease Control and Prevention. FDA licensure of quadrivalent human papillomavirus vaccine (HPV4, gardasil) for use in males and guidance from the Advisory Committee on Immunization Practices (ACIP). *MMWR Morb Mortal Wkly Rep.* 2010;59(20):630-632. doi: mm5920a5 [pii].
- Centers for Disease Control and Prevention. Recommendations on the use of quadrivalent human papillomavirus vaccine in males--Advisory Committee on Immunization Practices (ACIP), 2011. *MMWR Morb Mortal Wkly Rep.* 2011;60(50):1705-1708. doi: mm6050a3 [pii].
- Meites E, Szilagyi PG, Chesson HW, Unger ER, Romero JR, Markowitz LE. Human papillomavirus vaccination for adults: Updated recommendations of the Advisory Committee on Immunization Practices. *MMWR Morb Mortal Wkly Rep.* 2019;68(32):698-702. doi: 10.15585/mmwr.mm6832a3 [doi].
- Gilkey MB, Bednarczyk RA, Gerend MA, et al. Getting human papillomavirus vaccination back on track: protecting our national investment in human papillomavirus vaccination in the COVID-19 era. *J Adolesc Health.* 11 2020;67(5):633-634. doi:10.1016/j.jadohealth.2020.08.01
- Centers for Disease Control and Prevention. Interim Guidance for Routine and Influenza Immunization Services During the COVID-19 Pandemic. <https://www.cdc.gov/vaccines/pandemic-guidance/index.html>
- National HPV Vaccination Roundtable. Back on Track. <https://hpvroundtable.org/get-involved/back-on-track/>
- Bonaldo G, Vaccheri A, D'Annibali O, Motola D. Safety profile of human papilloma virus vaccines: An analysis of the US vaccine adverse event reporting system from 2007 to 2017. *Br J Clin Pharmacol.* 2019;85(3):634-643.

28. Chaturvedi AK, Graubard BI, Broutian T, et al. Prevalence of oral HPV infection in unvaccinated men and women in the United States, 2009–2016. *JAMA*. 2019;322(10):977–979. doi: 10.1001/jama.2019.10508 [doi].
29. Palmer T, Wallace L, Pollock KG, et al. Prevalence of cervical disease at age 20 after immunisation with bivalent HPV vaccine at age 12–13 in Scotland: Retrospective population study. *BMJ*. 2019;365:l1161.
30. Chesson HW, Meites E, Ekwueme DU, Saraiya M, Markowitz LE. Updated medical care cost estimates for HPV-associated cancers: Implications for cost-effectiveness analyses of HPV vaccination in the United States. *Hum Vaccin Immunother*. 2019;15(7–8):1942–1948. doi: 10.1080/21645515.2019.1603562 [doi].
31. Wisconsin Department of Health Services. Wisconsin immunization rate data. Updated 2020. Accessed January 7, 2020.
32. Gidengil C, Chen C, Parker AM, Nowak S, Matthews L. Beliefs around childhood vaccines in the United States: A systematic review. *Vaccine*. 2019;37(45):6793–6802. doi: S0264-410X(19)31144-2 [pii].
33. Holman DM, Benard V, Roland KB, Watson M, Liddon N, Stokley S. Barriers to human papillomavirus vaccination among US adolescents: A systematic review of the literature. *JAMA Pediatr*. 2014;168(1):76–82. doi: 10.1001/jamapediatrics.2013.2752 [doi].
34. Suk R, Montealegre JR, Nemetlu GS, et al. Public knowledge of human papillomavirus and receipt of vaccination recommendations. *JAMA Pediatr*. 2019;173(11):1099–1102.
35. Fokom Domgue J, Chido-Amajuoyi OG, Yu RK, Shete S. Beliefs about HPV vaccine's success at cervical cancer prevention among adult US women. *JNCI Cancer Spectrum*. 2019;3(4):pkz064.
36. Shelal Z, Cho D, Urbauer DL, et al. Knowledge matters and empowers: HPV vaccine advocacy among HPV-related cancer survivors. *Support Care Cancer*. 2019. doi: 10.1007/s00520-019-05035-1 [doi].
37. Leung SOA, Akinwunmi B, Elias KM, Feldman S. Educating healthcare providers to increase human papillomavirus (HPV) vaccination rates: A qualitative systematic review. *Vaccine X*. 2019;3:100037. doi: 10.1016/j.jvacx.2019.100037 [doi].
38. Donahue KL, Hendrix KS, Sturm LA, Zimet GD. Human papillomavirus vaccine initiation among 9–13-year-olds in the United States. *Prev Med Rep*. 2015;2:892–898.
39. Beavis A, Krakow M, Levinson K, Rositch A. Gender differences in reasons for lack of HPV vaccination in 2015: Tailoring the cancer-prevention vaccine message. *Gynecologic Oncology*. 06/01 2018;149:143. doi:10.1016/j.ygyno.2018.04.327
40. Gnagi SH, Gnagi FT, Schraff SA, Hinni ML. Human papillomavirus vaccination counseling in pediatric training: Are we discussing otolaryngology-related manifestations? *Otolaryngol Head Neck Surg*. 2016;155(1):87–93. doi: 10.1177/0194599816639932 [doi].
41. Otanez S, Torr BM. Ethnic and racial disparities in HPV vaccination attitudes. *J Immigr Minor Health*. 2018;20(6):1476–1482. doi: 10.1007/s10903-017-0685-2 [doi].
42. Perkins RB, Lin M, Wallington SF, Hanchate AD. Impact of school-entry and education mandates by states on HPV vaccination coverage: Analysis of the 2009–2013 National Immunization Survey-Teen. *Hum Vaccin Immunother*. 2016;12(6):1615–1622.
43. State of Hawaii, Department of Health. 2020–2021 school health requirements. <https://health.hawaii.gov/docd/vaccines-immunizations/school-health-requirements/sy-20-21/>. Updated 2019. Accessed March 6, 2020.
44. Drolet M, Bénard É, Boily M, et al. Population-level impact and herd effects following human papillomavirus vaccination programmes: A systematic review and meta-analysis. *Lancet Infect Dis*. 2015;15(5):565–580.
45. Kempe A, Allison MA, Daley MF. Can school-located vaccination have a major impact on human papillomavirus vaccination rates in the United States? *Aca Pediatr*. 2018;18(2):S101–S105.
46. St Sauver JL, Rutten LJE, Ebbert JO, Jacobson DJ, McGree ME, Jacobson RM. Younger age at initiation of the human papillomavirus (HPV) vaccination series is associated with higher rates of on-time completion. *Prev Med*. 2016;89:327–333. doi: S0091-7435(16)30018-4 [pii].
47. Goleman MJ, Dolce M, Morack J. Quality improvement initiative to improve human papillomavirus vaccine initiation at 9 years of age. *Acad Pediatr*. 2018;18(7):769–775. doi: S1876-2859(18)30309-7 [pii].
48. Centers for Disease Control and Prevention. Answering parents' questions about HPV vaccine. <https://www.cdc.gov/hpv/hcp/answering-questions.html>. Updated 2019. Accessed December 20, 2019.
49. Brouwer AF, Delinger RL, Eisenberg MC, et al. HPV vaccination has not increased sexual activity or accelerated sexual debut in a college-aged cohort of men and women. *BMC Public Health*. 2019;19(1):821.

Special thanks to the Wisconsin Department of Health Services Immunization Program and the Wisconsin Cancer Reporting System for help with the data in this issue brief.

### Volume 16, Number 1; Published January 2021

**Editors:** Noelle LoConte, MD; Carrie Kilman, MFA; Sarah Kerch, MPH; Amy Johnson, JD; Chloe Weil

**For more information, contact:**  
Carrie Kilman, [cakilman@wisc.edu](mailto:cakilman@wisc.edu)



**Wisconsin  
Cancer  
Collaborative**  
REDUCING THE BURDEN TOGETHER