

# Conquering HPV Vaccine Hesitancy in Your Clinical Practice

## Overview of Vaccine Hesitancy

Vaccine hesitancy refers to the refusal or delayed acceptance of vaccines despite the availability of vaccination services and an overall recommendation for the vaccine.<sup>1</sup> Although we may think of vaccine hesitancy as a United States issue, it is not unique to the United States. The World Health Organization (WHO) reports vaccine hesitancy in more than 90% of the world's countries and has listed vaccine hesitancy as one of the top 10 threats to global health.<sup>2,3</sup> Vaccine refusal has been associated with many outbreaks of vaccine-preventable disease, including Hemophilus influenzae B, varicella, pneumococcal disease, measles, pertussis, and others. Measles, one of the most contagious viruses, can be prevented by vaccination. As a result, we often see measles pop up when vaccination rates decrease.

***Vaccine hesitancy is important because vaccination is one of our most cost-effective ways of avoiding disease. It is estimated that routine vaccination of children and adults currently prevents somewhere between 2-3 million deaths per year worldwide.***

***Up to 1.5 million more deaths could be avoided if global vaccination coverage improved.***

**--Rachel Caskey, MD, MAPP**

A 2014 study on the impact of routine childhood vaccinations in the United States estimated that the current routine vaccination program prevents approximately 20 million infections and 42,000 deaths annually. These vaccinations costs approximately \$7.5 billion per year but result in estimated direct and indirect cost savings greater than \$76 billion. This 10:1 benefit:cost ratio is far superior to any other routine preventive interventions, such as mammography and colon cancer screening. Thus, every \$1.00 spent on vaccination saves approximately \$10.00!

Vaccines are different from most other preventive interventions. For cancer screening, as an example, a neighbor's decision to get screening has little direct impact on your own health. In contrast, your neighbor's decision to be vaccinated can protect you by contributing to herd immunity. Herd immunity only occurs if a sufficient proportion of individuals in a community are immune to the disease. The level of vaccination needed to prevent the spread of contagious disease varies, but it typically ranges from 80% to 95%.

***Herd immunity is important to protect individuals who cannot be vaccinated or who have been vaccinated but may not have full protection.***

**--Rachel Caskey, MD, MAPP**

Vaccine hesitancy may seem to come from everywhere. Parents or families may not know whether vaccines are safe or have not really thought about vaccines and then find information about safety concerns. Some believe vaccines are toxic and that vaccinations are a conspiracy by pharmaceutical companies; some believe that children's immune systems are too immature and cannot handle multiple vaccines simultaneously. None of these ideas are supported by science as there has been a substantial amount of research over the years proving these theories to be false.

### **Impact of Human Papilloma Virus (HPV) Vaccination**

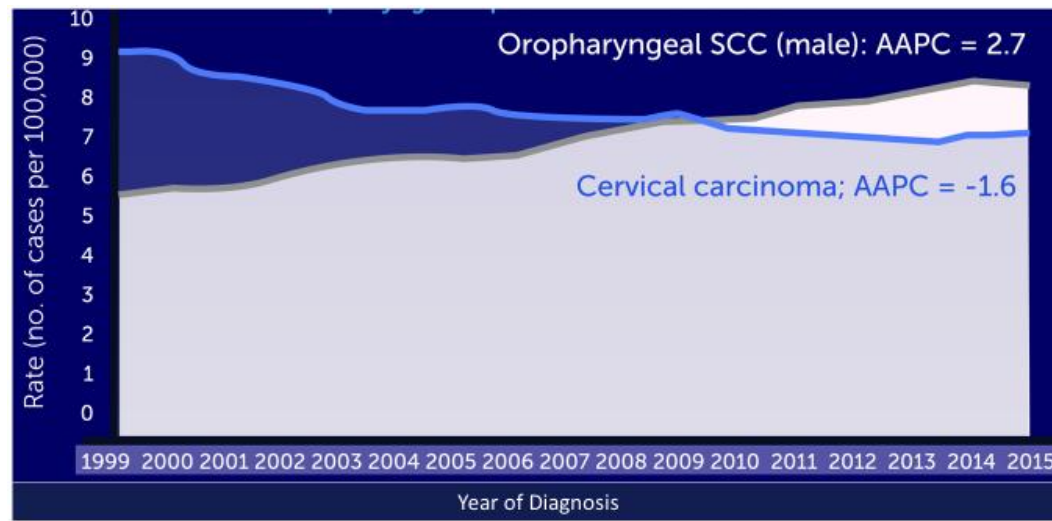
HPV is the most common sexually transmitted infection, both in the United States and worldwide. In the United States, more than 6,000,000 new genital HPV infections occur every year, mostly among adolescents and young adults.<sup>4,5</sup> Although HPV vaccination was originally intended for women, HPV infection is more common among males than among females. HPV is linked to several types of cancer beyond cervical cancers, including oropharyngeal, anal, vaginal, vulvar, and penile cancers (**Table 1**).<sup>6-8</sup>

Table 1: Cancers Caused by HPV in the United States<sup>8</sup>

<b>Cancer Type</b>	<b>Approximate % Caused by HPV</b>
Cervical cancers	>99
Oropharyngeal cancers	70+
Anal cancers	91
Vaginal cancers	75
Vulvar cancers	69
Penile cancers	63

It is important to understand that oropharyngeal cancer is strongly associated with HPV, which causes approximately 70% of cases. The incidence of HPV-related oropharyngeal cancers has been increasing steadily, particularly among men, and the rate of male HPV-related oropharyngeal cancers surpassed the incidence of cervical cancers in 2009-2010 (**Figure 1**).<sup>9</sup> This disproportionately high incidence results from the much higher rate of HPV infection in males than in females, particularly among men younger than 50 years of age.<sup>7,10</sup> This is not something parents and young adults understand when they are thinking about HPV vaccination.

Figure 1: Incidence of Cervical Cancer and Oropharyngeal Squamous Cell Carcinoma in the United States, 1999-2015<sup>9</sup>

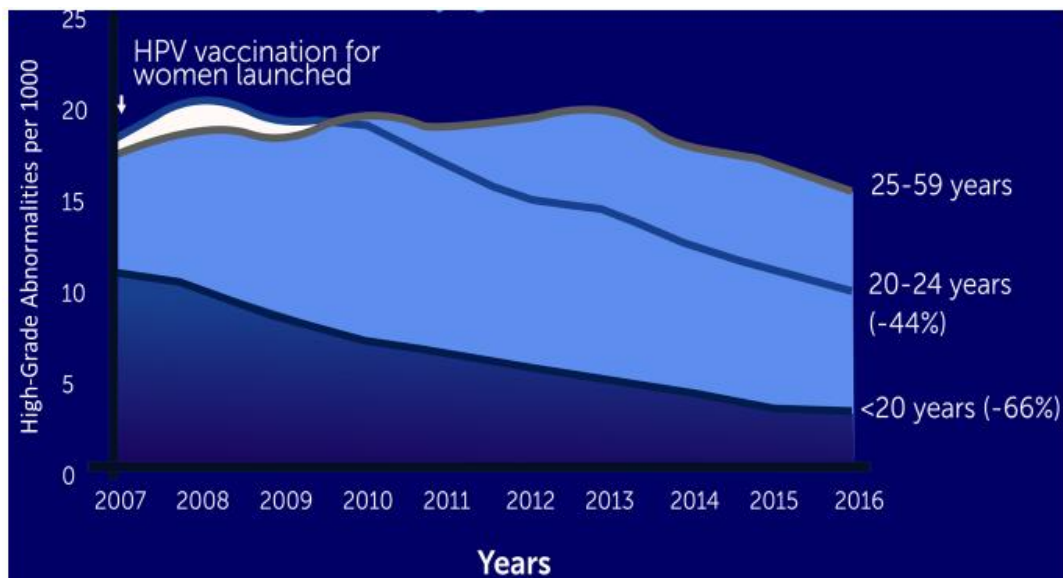


**Abbreviation: AAPC = average annual percent change; SCC = squamous cell carcinoma.**

One key question is whether the HPV vaccine is effective. Some of the best data available is from Australia, where the entire continent made a strong effort to vaccinate both females and males. By vaccinating through schools instead of the traditional health care system, Australia achieved a remarkable success rate: 80% of adolescent females were vaccinated within 2 years of vaccine approval by FDA. In Australia, women 20 years of age or younger, who were in the age group that was vaccinated in 2006-2008, saw the rate of high-grade cervical lesions decline by more than 65%. Women in older age ranges also saw declines: 44% among women 20 to 24 years old, who may or may not have been vaccinated, and a smaller decline among women 25 to 29 years old (**Figure 2**).

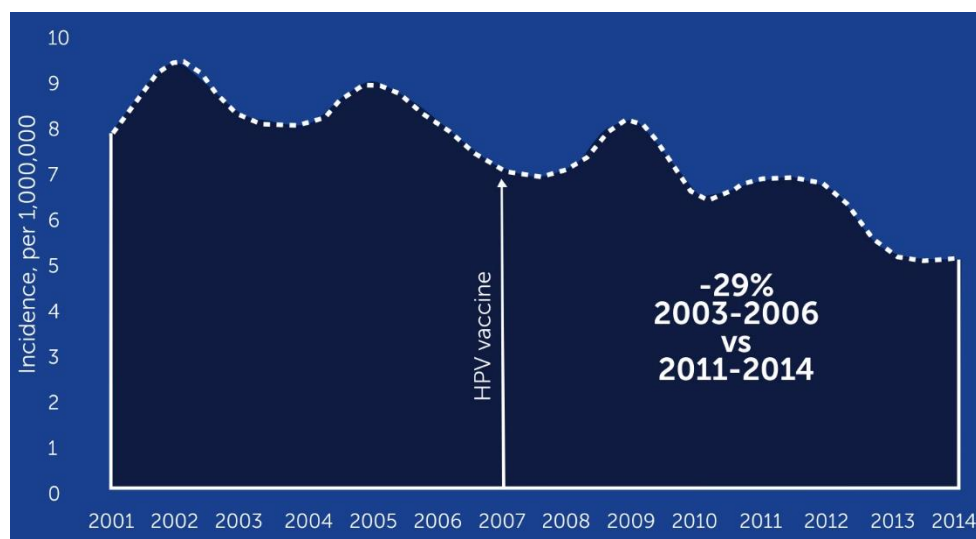
Trends for genital warts and other HPV-associated conditions have been similar.<sup>11</sup> Of note, women in the 25-to-29-year age group had not been vaccinated with the HPV vaccine, so their declining HPV infection rate is evidence for the importance of herd immunity.

Figure 2: Australian Trends in High-grade Cervical Abnormalities by Age Pre- and Post-Vaccination<sup>11</sup>



Although the United States has not reached the HPV vaccination rates achieved in Australia, we have seen a 30% decline from 2003 to 2006 in cervical cancer among 15 to 24 year olds (**Figure 3**). Because cancer develops slowly, we are likely to see more robust outcomes within the next 5 to 10 years.<sup>12</sup>

Figure 3: US Trends in Cervical Cancer Incidence Among 15- to 24-year-old Females<sup>12</sup>



In the United States, HPV vaccination is recommended for both males and females, with a target age range of 11 to 12 years of age, with two doses spaced at least 6 months apart for individuals who start before their 15<sup>th</sup> birthday. For individuals who start later, 3 doses are recommended, spaced 2 and 6 months apart. The indication has been expanded to men and women up to 45 years of age, so individuals in this age range can be considered for vaccination if they have not already been vaccinated.

Unfortunately, the United States has much lower HPV vaccination rates than many other countries, which across all adolescents averages 60% to 65% according to recent statistics for  $\geq 2$  doses. HPV vaccination rates are also low compared to other routine vaccines. For example, approximately 90% of males and females have received tetanus, diphtheria, acellular pertussis (Tdap) vaccination, and 85% have received meningitis vaccination. The high rates achieved with Tdap and meningitis vaccines imply that the lower HPV vaccination rates are **not** due to access issues. So the question is, *“Are we treating HPV vaccination differently from the other recommended vaccines?”* School mandates for entry into key grades (6<sup>th</sup> grade, 9<sup>th</sup> grade, and/or college) require vaccination for Tdap and meningococcus but not for HPV and may contribute to this difference.

### **Vaccine Hesitancy and Barriers to HPV Vaccination**

One important barrier to HPV vaccination is fear related to sexual activity and sexual behavior. However, there have been numerous research studies for ages ranging from early adolescence through college evaluating the impact of HPV vaccination on sexual activity. Multiple studies have found no difference in the age of sexual debut, number of sexual partners, risk of chlamydia, or risk of pregnancy comparing those vaccinated and those not vaccinated.

In order to increase the rates of HPV vaccination, we need to treat the HPV vaccine like all of the other universally recommended vaccines. If a patient or parent asks about whether the HPV vaccine is important or needed or if they want to delay the vaccination, focus the conversation on the reason for the vaccination: to prevent potentially lethal cancers. Normalizing all vaccines will help us succeed with vaccination.

***I propose that we simply normalize the HPV vaccine. I focus the conversation on why we have the vaccine. It is because HPV can cause lethal cancer.***

**--Rachel Caskey, MD, MAPP**

## References

1. MacDonald NE. Vaccine hesitancy: Definition, scope and determinants. *Vaccine*. 2015;33(34):4161-4164.
2. The Lancet Child Adolescent H. Vaccine hesitancy: a generation at risk. *Lancet Child Adolesc Health*. 2019;3(5):281.
3. World Health Organization. Ten threats to global health in 2019. 2019; <https://www.who.int/emergencies/ten-threats-to-global-health-in-2019>. Accessed November 24, 2019.
4. Ault KA. Epidemiology and natural history of human papillomavirus infections in the female genital tract. *Infectious Diseases in Obstetrics and Gynecology*. 2006;2006 Suppl:40470.
5. Dunne EF, Unger ER, Sternberg M, et al. Prevalence of HPV Infection Among Females in the United States. *JAMA*. 2007;297(8):813-819.
6. McQuillan G, Kruszon-Moran D, Markowitz LE, Unger ER, Paulose-Ram R. Prevalence of HPV in Adults Aged 18-69: United States, 2011-2014. *NCHS Data Brief*. 2017(280):1-8.
7. Shi R, Devarakonda S, Liu L, Taylor H, Mills G. Factors associated with genital human papillomavirus infection among adult females in the United States, NHANES 2007-2010. *BMC Research Notes*. 2014;7:544-544.
8. Bailey HH, Chuang LT, duPont NC, et al. American Society of Clinical Oncology Statement: Human Papillomavirus Vaccination for Cancer Prevention. *J Clin Oncol*. 2016;34(15):1803-1812.
9. Van Dyne EA, Henley SJ, Saraiya M, Thomas CC, Markowitz LE, Benard VB. Trends in Human Papillomavirus-Associated Cancers - United States, 1999-2015. *MMWR Morb Mortal Wkly Rep*. 2018;67(33):918-924.
10. Giuliano AR, Lazcano-Ponce E, Villa LL, et al. The human papillomavirus infection in men study: human papillomavirus prevalence and type distribution among men residing in Brazil, Mexico, and the United States. *Cancer Epidemiol Biomarkers Prev*. 2008;17(8):2036-2043.
11. The Kirby Institute for infection and immunity in society. HIV, viral hepatitis and sexually transmissible infections in Australia. Annual surveillance report 2018. 2018; [https://kirby.unsw.edu.au/sites/default/files/kirby/report/KI\\_Annual-Surveillance-Report-2018.pdf](https://kirby.unsw.edu.au/sites/default/files/kirby/report/KI_Annual-Surveillance-Report-2018.pdf). Accessed November 24, 2019.
12. Guo F, Cofie LE, Berenson AB. Cervical Cancer Incidence in Young U.S. Females After Human Papillomavirus Vaccine Introduction. *Am J Prev Med*. 2018;55(2):197-204.