

This book contains information to be used by representatives of Area Health Education Centers (AHECs) and other organizations in the planning, implementation and evaluation of activities to increase HPV vaccination rates locally.

HPV Vaccination Resource Book

For Area Health Education Centers and
other organizations

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NATIONAL AHEC ORGANIZATION

THE GEORGE
WASHINGTON
UNIVERSITY
WASHINGTON, DC



Cancer Center

Table of Contents

A NOTE TO AREA HEALTH EDUCATION CENTERS	ii
LIST OF ACRONYMS AND KEY TERMS	iii
INTRODUCTION TO HUMAN PAPILLOMAVIRUS (HPV)	1
Background on HPV	1
Epidemiology of HPV Infection and Risk Behaviors.....	1
PUBLIC HEALTH PROBLEM & SIGNIFICANCE.....	3
Background on HPV-Associated Cancers.....	3
Impact of HPV-Associated Cancers.....	3
Prevalence and Incidence	3
Mortality and Survival.....	4
Cost of Care.....	5
THE SOLUTION	6
Background on HPV Vaccines	6
Safety and Effectiveness	7
HPV Vaccine Uptake	8
Factors Impacting HPV Vaccination Uptake.....	9
Policies Impacting HPV Vaccination Uptake	13
Opposition & Threats.....	19
References	20

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A NOTE TO AREA HEALTH EDUCATION CENTERS

The HPV Vaccination Resource Book is a primer on human papillomaviruses (HPV) to help prepare you to facilitate professional education and provider outreach to help increase HPV vaccination rates in your area as part of a Centers for Disease Control and Prevention (CDC) funded cooperative agreement awarded to the National AHEC Organization (NAO). This is a five-year project with the goal of increasing HPV vaccination rates among eleven and twelve-year-old boys and girls as well as administering “catch-up” vaccinations to older adolescents and young adults.

This book provides a basic introduction to HPV and HPV-associated cancers with data on the number of cases, mortality rates and cost of care nationally. The book also provides a basic overview of risk factors that increase the chance of an individual becoming infected with HPV. It describes the safety and effectiveness of available HPV vaccines in the United States, provides data on HPV vaccination rates nationally as well as factors, including policies, that influence whether a patient receives the HPV vaccine. This book will be updated in each year of the project. Please send questions and update requests to info@ntc.nationalahec.org.

AHECs will be responsible for gathering additional regional data, including assessing the local policy landscape, identifying local vaccination providers and clinician networks, and determining other potential partners who are working on HPV issues in the area.

Please contact the Project Director with questions, concerns or comments about your role or activities related to this project:

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LIST OF ACRONYMS AND KEY TERMS

AAP	American Academy of Pediatrics
ACA	Patient Protection and Affordable Care Act
ACIP	The Advisory Committee on Immunization Practices (ACIP) is a group of medical and public health experts that develop recommendations on how to use vaccines to control diseases in the United States. Learn more.
ACS	American Cancer Society
AFIX	Assessment, Feedback, Incentives, and eXchange (AFIX) is a quality improvement program used by CDC awardees to raise immunization coverage levels, reduce missed opportunities to vaccinate, and improve standards of practices at the provider level. Learn more.
APA	Academic Pediatric Association
CDC	Centers for Disease Control and Prevention
CEU/CME	Continuing Education Unit / Continuing Medical Education
CMS	Centers for Medicare and Medicaid Services
Completion	HPV vaccination completion rate is the proportion of those who get one shot who then finish the series.
Coverage	Coverage is the percentage of the indicated population who receive a certain number of shots (one-shot coverage, two-shot coverage, three-shot coverage).
DCPC	CDC's Division of Cancer Prevention and Control
EHR/EMR	Electronic Health Record / Electronic Medical Record
FDA	Food and Drug Administration
HEDIS	The Healthcare Effectiveness Data and Information Set (HEDIS) is a tool used by more than 90% of America's health plans to measure performance on important dimensions of care and service. Learn more.
HIPAA	The Health Insurance Portability and Accountability Act (HIPAA) is a federal law enacted in 1996 requiring certain reforms to the healthcare industry in an attempt to reduce administrative costs, simplify administrative processes and burdens, help patients maintain continuity of coverage, and improve the privacy and security of patients' information. Learn more.
HPV	Human papillomavirus
HPV-associated cancer	A cancer that is diagnosed in a part of the body where HPV is often found. These parts of the body include the cervix, anus, penis, vagina, vulva, and oropharynx (back of the throat, including the base of the tongue and tonsils). Learn more.
HPV-attributable cancer	A cancer that is probably caused by HPV. CDC studies use population-based data from cancer tissue to estimate the percentage of cancers that are probably caused by HPV. Learn more.
Initiation	Starting the HPV vaccine series; Coverage with one-shot.

IIS	Immunization information systems (IIS) are confidential, population-based, computerized databases that record all immunization doses administered by participating providers to persons residing within a given geopolitical area. Learn more.
Incidence	A cancer incidence rate is the number of new cancers of a specific site/type occurring in a specified population during a year, usually expressed as the number of cancers per 100,000 population at risk. Learn more.
MenACWY	Meningococcal conjugate vaccine capsular polysaccharide of serogroup C, W135, and Y
MOC	Maintenance of Certification (for board-certified clinicians)
NACCHO	National Association of County and City Health Officials
NCI	National Cancer Institute
NCIRD	CDC’s National Center for Immunization and Respiratory Diseases
NIS-Teen	National Immunization Survey-Teen
NVAC	The National Vaccine Advisory Committee (NVAC) recommends ways to achieve optimal prevention of human infectious diseases through vaccine development, and provides direction to prevent adverse reactions to vaccines. Learn more.
SEER	The Surveillance, Epidemiology, and End Results (SEER) Program of the National Cancer Institute works to provide information on cancer statistics in an effort to reduce the burden of cancer among the U.S. population. Learn more.
STI/STD	Sexually Transmitted Infection / Sexually Transmitted Disease
PCP/PCC	Primary Care Provider (sometimes Physician) / Primary Care Clinician
PHI	Protected Health Information
“Big P” Policies	“Big P” policies are formal laws, rules, and regulations enacted by elected officials and official bodies.
“Little p” policies	“Little p” policies are less formal policies, usually related to administration or implementation, such as resolutions adopted by an organization or decisions about local implementation of a formal policy. Watch this YouTube video to learn more.
PPHF	Prevention and Public Health Fund
Prevalence	Prevalence is defined as the number or percent of people alive on a certain date in a population who previously had a diagnosis of the disease. Learn more.
Tdap	Tetanus, Diphtheria, Pertussis
VAERS	The Vaccine Adverse Event Reporting System (VAERS) is a post-marketing safety surveillance program, collecting information about adverse events (possible side effects) that occur after the administration of vaccines licensed for use in the United States. Learn more.
VFC	Vaccines for Children (VFC) is a federally-funded program that provides vaccines at no cost to children who might not otherwise be vaccinated because of inability to pay. Learn more.
YRBS	The Youth Risk Behavior Survey is a survey of the Youth Risk Behavior Surveillance System (YRBSS) that monitors six types of health-risk behaviors that contribute to the leading causes of death and disability among youth and adults. Learn more.

INTRODUCTION TO HUMAN PAPILLOMAVIRUS (HPV)

Background on HPV

Human papillomaviruses (HPV) are a class of more than 150 viruses that infect epithelial tissue, primarily in the genital and mouth/throat regions.¹ At least forty of the virus subtypes/strains are easily passed between individuals through skin-to-skin contact during vaginal, anal and oral sex.² There is no treatment for HPV infection; however in the case of most healthy adults, HPV infection goes away on its own without causing any health problems.² However, individuals who have weak immune systems, unprotected sex and sex with multiple partners are at greater risk for getting HPV.³ Anyone who is sexually active can get HPV, even individuals who have only had one sexual partner.⁴

For most men and women there are typically no signs or symptoms of HPV infection.² HPV types 6 and 11 cause 90% of all anal/genital warts.² HPV types 6 and 11 can also cause a condition known as respiratory papillomatosis, when small tumors grow in the air passages from the lungs to the nose and mouth.⁵ Genital warts and respiratory papillomatosis can be treated with prescription medication, excisional surgery, cryosurgery or laser surgery, but currently there is no treatment for the HPV infection itself.¹

Persistent infections with high-risk or oncogenic (cancer-causing) HPV subtypes can cause damage to cells that may lead to anogenital (cervical, anal, vaginal, vulvar, penile) or oropharyngeal (mouth and throat) cancers.^{1,2} The medical community generally diagnoses a persistent HPV infection when a woman tests positive for HPV in two consecutive visits at least four to six months apart;⁶ however the United States (U.S.) Food and Drug Administration (FDA) has not yet approved any tests to detect HPV in men.¹ The most common high-risk, cancer-causing subtypes include 16, 18, 31, 33, 45, 52 and 58.⁷ Persistent infection with HPV 16 and 18 is the most important risk factor for development of cervical, anal, mouth, throat, vaginal, vulvar and penile cancers.^{1-3,5} It is estimated that effectively all cases of cervical cancer, the most common HPV-associated cancer, are caused by persistent HPV infection where seven of ten cases can be directly linked to HPV subtypes 16 and 18.⁸ HPV vaccination is a safe and effective cancer prevention method that is best accomplished before an individual becomes sexually active and risk of HPV infection increases.^{1-3,5}

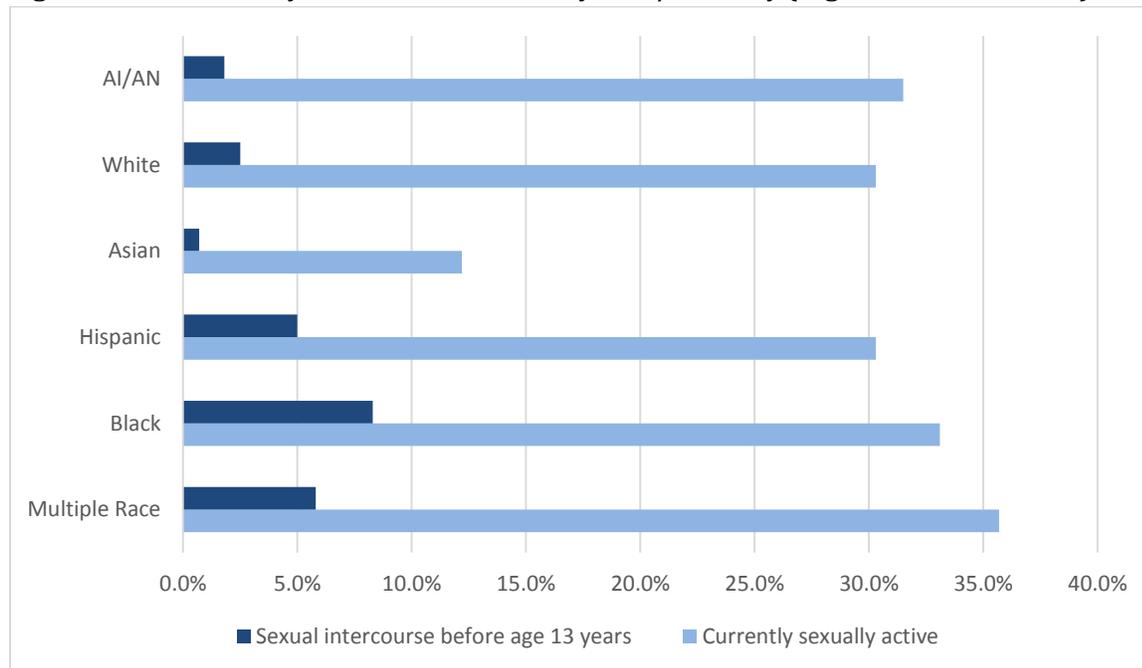
Epidemiology of HPV Infection and Risk Behaviors

HPV is the most common sexually transmitted infection in the U.S.;¹ almost every sexually active person will acquire it at some point in their life.⁹ In fact, approximately seventy-nine million people are currently infected with HPV in the U.S.³ In addition, an estimated fourteen million new HPV infections occur annually, half of which are acquired by individuals aged 15 to 24 years.³ Adolescents and young adults have the highest HPV prevalence and incidence rates compared to other individuals.³ Approximately 50% of new HPV infections occur among those who are between the ages of fifteen to twenty-four years.³ Because of the high infection rates among adolescents, it is suggested that young age (less than twenty-five years) is a risk factor for HPV infection.³

Age is not the single determining factor for an individual's risk for acquiring HPV. Sexual behavior including: sexual activity status, number of sex partners, unprotected sex, partners' sexual history and age at sexual initiation are also well-documented risk factors for HPV.³ The 2015 U.S. High School Youth Risk Behavior Survey (YRBS) provides the most recent data highlighting some of the populations that are at the greatest risk for acquiring the HPV infection. Survey data indicated high school-aged blacks, people of more than one race and Hispanics have the highest rates of two of the most significant HPV risk factors: having sexual intercourse at an early age and being currently sexually active.¹⁰ Specifically, 8.3% of blacks, 5.8% of people of more than one race and 5.0% of Hispanics had sexual intercourse before the age of thirteen compared to 2.5% of whites, 1.8% of American Indians/Alaska Natives (AI/AN) and 0.7% of Asians (Figure 1).¹⁰ Additionally, 35.7% of high school-aged people of more than one race, 33.1% of blacks, 31.5% American Indians/Alaska Natives, 30.3% of Hispanics, 30.3% of whites and 12.2% of Asians reported being sexually active (Figure 1).¹⁰ The responses to the 2015 YRBS also indicated 46% of 12th graders, 35.5% of 11th graders, 25.5% of 10th graders and 15.7% of 9th graders reported being currently sexually active.¹⁰

Survey data indicated blacks, people of more than one race and Hispanics have the highest rates for two of the most significant HPV risk factors.¹⁰

Figure 1. Sexual Activity Risk Factors for HPV by Race/Ethnicity (High School YRBS 2015)⁹



TAKE NOTE!

This resource book includes information on sexual activity and HPV infection as background information only. The CDC has found that discussing this type of data with parents or clinicians is counterproductive. Unfortunately, if

clinicians explain the link between sexual activity and HPV while recommending a child be immunized, parents are actually less likely to vaccinate the child. **In outreach and continuing education for physicians, the CDC recommends emphasizing that adolescents in the targeted age range of eleven to twelve years have the most robust immune response when vaccinated and that the HPV vaccine is cancer prevention.** The effects of physician recommendations on HPV vaccination acceptability among parents and other influential factors are described in greater detail on pages 11-12.

PUBLIC HEALTH PROBLEM & SIGNIFICANCE

Background on HPV-Associated Cancers

The role of HPV infection in the development of certain cancers has been well established. Persistent infection with HPV is associated with cervical, anal, oropharyngeal, vaginal, vulvar and penile cancers.^{1-3,5,11} According to a CDC study that tested for HPV in samples of cancer tissue, 91% of all cervical and anal cancers can be attributed to persistent HPV infection.¹¹ Data also indicated 63% to 75% of all oropharyngeal, vaginal, vulvar and penile cancers can be attributed to persistent HPV infections (Table 1).¹¹

Table 1. Estimated Percentages of Specific Cancers Attributed to Persistent HPV Infections (%)¹⁰

Cancer Site	Attributed to HPV
Anus	91%
Cervix Uteri	91%
Vagina	75%
Oropharynx /Oral Cavity	70%
Vulva	69%
Penis	63%

Impact of HPV-Associated Cancers

Prevalence and Incidence

The most prevalent HPV-associated cancer among women in the U.S. is cervical cancer, and the most prevalent among men are oropharyngeal/oral cavity cancers. Based on cancer registry data from 1975-2013, more than 248,900 women nationwide reported a history of cervical cancer diagnosis, and more than 200,250 men had a history of oropharyngeal/oral cavity cancer.¹² Data on incidence, or new cases, from 2008 to 2012 show approximately 38,000 HPV-associated cancers were reported in the U.S. each year; about 22,400 among females and more than 15,500 among males (Table 2).¹³

Table 2. HPV-Associated Cancer Annual Incidence in the United States (2008-2012)¹³

Site	Sex	Annual Incidence Count	Annual Incidence Count (Females)	Annual Incidence Count (Males)	Annual Incidence (per 100,000)
Oropharynx /Oral Cavity	Females	3,100	3,100		1.7
	Males	12,638		12,638	7.6
Anus	Females	3,260	3,260		1.8
	Males	1,750		1,750	1.1
Cervix Uteri		11,771	11,771		7.4
Vagina		802	802		0.4
Vulva		3,554	3,554		2.0
Penis		1,168		1,168	0.8
TOTAL		38,043	22,487	15,556	

Although cervical cancer is the most common among the HPV-associated cancers, new cases of other HPV-associated cancers are rising in some populations. Based on data from 2000 to 2011, the rates of newly reported cancers of the oropharynx/oral cavity have been increasing for men while anal cancers have been increasing for women.^{12,14,15} The rate of newly reported cervical cancer has continued to decrease since 1975, due primarily to preventive screening for pre-cancerous lesions with Pap tests, while the rates of vaginal, vulvar and penile cancers have stayed relatively constant.^{16,17,18} Newer data on incidence from 2009 to 2013 showed that cervical cancer still has the highest rate of new cases among women (7.5/100,000), and oropharyngeal/oral cavity cancer has the highest incidence rates among men (16.7/100,000).¹²

In the U.S. there are significant disparities with respect to HPV-associated cancer incidence. While cervical cancer incidence rates are much higher among some racial and ethnic minority groups, oropharyngeal cancer incidence rates are higher among whites. Data from 2008-2012 indicate cervical cancer incidence per 100,000 population was 9.7 for Hispanics, 9.2 for blacks, compared to 7.1 for whites, 6.3 for American Indians/Alaska Natives and 6.1 for Asian/Pacific Islanders.¹³ Oropharyngeal cancer incidence per 100,000 population was 4.7 for whites, 3.9 for blacks, 2.6 for American Indians/Alaska Natives, 1.2 for Asian/Pacific Islanders, and 2.4 for Hispanics.¹³

Cervical cancer incidence rates are highest among Hispanics and blacks.¹³

Mortality and Survival

Mortality and survival among adults diagnosed with HPV-associated cancers varies by cancer site and sex. During the period 2006 to 2012, the five-year relative survival rate for cervical cancer was 67.5% (Table 3).¹² This means that almost sixty-eight of every one hundred women diagnosed with cervical cancer were alive five years after diagnosis. This also means that thirty-two of every one hundred women diagnosed with cervical cancer were not alive five years later. For the most common HPV-

associated cancers in men, cancer in the oral cavity and pharynx, the overall survival rate was 63.0% and fell between 32.5-89.2%, depending on the specific cancer site.¹²

Although the five-year survival rates for some HPV-associated cancers are relatively high, there are still a substantial number of deaths. During the period of 2009 to 2013, the five-year mortality rate showed that oropharyngeal cancers cause the most deaths for men (3.8/100,000) while for women, cervical cancer death rates were highest (2.3/100,000), as shown in Table 3.¹²

Table 3. Annual U.S. Incidence, Mortality & Five-Year Relative Survival¹²

Site	Incidence Rate/100,000 (2009-2013)		Mortality Rate/100,000 (2009-2013)		5-year Relative Survival (%) (2006-2012)	
	Males	Females	Males	Females	Males	Females
Oral cavity and Pharynx	16.7	6.2	3.8	1.3	63.0	66.3
Anus, Anal Canal, and Anorectum	1.5	2.1	0.2	0.3	60.4	70.1
Cervix Uteri	-	7.5	-	2.3	-	67.5
Vagina	-	0.7	-	0.2	-	47.8
Vulva	-	2.4	-	0.5	-	71.9
Penis	0.9		0.2		69.1	

Cost of Care

In addition to their impact on health, HPV-associated cancers also carry a huge financial burden to cancer patients, their caregivers and society.¹⁹ HPV prevention and treatment cost the U.S. health system nearly \$8 billion per year in direct medical costs, which makes HPV the second most expensive sexually transmitted infection (STI) after the human immunodeficiency virus (HIV).²⁰ Of the total cost, approximately \$6.6 billion was for routine cervical cancer screening and follow-up, while \$1 billion was for cancer treatment (including \$400 million for cervical cancer and \$300 million for oropharyngeal cancer).¹⁹ Genital warts alone cost \$300 million and treatment of HPV-associated respiratory conditions cost \$200 million.¹⁹ In addition, losses in time and productivity due to cervical cancer deaths in the U.S. were valued at \$1.8 billion in 2005.²¹ A more recent 2012 study projected that the general cost of all cancer care at the state-level will increase between 34% and 115%, with the cost to states ranging from \$347 million to \$28.3 billion in the year 2020.²¹ Unfortunately, all cancer related direct medical expenditures and productivity costs are expected to increase as the quality of treatment advances, as the population ages and with

All cancer related direct medical expenditures and productivity costs are expected to increase as the quality of treatment advances, as the population ages and with improved survival following diagnosis.²²

improved survival following diagnosis.²² Reducing the financial burden on both the patient, their family and society is an important goal and benefit of HPV-associated cancer prevention efforts, including HPV vaccination.

THE SOLUTION

Background on HPV Vaccines

As of January 2017, there were three vaccines on the market in the U.S. that prevent HPV infection. Gardasil, produced by Merck and Co., was first licensed in 2006 for use among girls and women aged nine to twenty-six years (Table 4).^{23,24} In 2009, the FDA approved a second HPV vaccine called Cervarix, produced by GlaxoSmithKline, for use among women aged ten to twenty-five years.^{23,24} On December 10, 2014 the FDA announced approval of a third HPV vaccine, Gardasil 9.^{25,11} By May 2017, Gardasil 9 will be the only HPV vaccine available in the U.S.²⁶

Table 4. Summary of Human Papillomavirus (HPV) Vaccines Licensed in the U.S.^{23,24}

Vaccine Name	Manufacturer	HPV Strains	Target Population (Sex, Ages)	FDA Approval Year	Approximate Cost per Dose ²⁷
Gardasil®	Merck and Co.	6, 11, 16, 18	Males & Females 9-26 years	2006	\$160
Gardasil 9®	Merck and Co.	6, 11, 16, 18, 31, 33, 45, 52, 58	Males & Females 9-26 years*	2014	\$177

* The FDA originally approved Gardasil 9 for males aged 9-15, and on December 14, 2015, FDA extended the age indication by including males aged 16–26 years.

Gardasil is a quadrivalent vaccine that prevents infection by HPV types 6, 11, 16, and 18, protecting against cancer, genital warts and papillomatosis.²⁸ In addition to the four HPV strains included in the original Gardasil vaccine, Gardasil 9 also prevents infections with additional cancer-causing HPV types 31, 33, 45, 52 and 58 with 96.7% effectiveness,²⁹ adding protection against an additional 15% of cervical cancers not previously covered.^{2,23,25,11} According to the National Cancer Institute, “widespread vaccination has the potential to reduce cervical cancer deaths around the world by as much as two-thirds.”¹ Recent U.S. estimates also suggest 81% of new cases of cervical cancer could be prevented by HPV vaccination.¹¹

81% of new cases of cervical cancer could be prevented by HPV vaccination.¹¹

ACIP is the official body that makes evidence-based vaccination schedule recommendations in the U.S.; Table 5 details the current HPV recommendations. ACIP recommends routine administration of Gardasil for males and females at age eleven to twelve.³⁰ The reasoning for early vaccination is that the vaccine is effective in preventing, but not treating HPV infections, that are sexually transmitted.^{23,30} Moreover, the HPV vaccine has been found to prevent twice the amount of cervical pre-cancer among those who receive the vaccine by age fourteen compared to those who receive it after fifteen.³¹ Furthermore, ACIP recommends “catch-up” vaccination for those not previously vaccinated adequately.³⁰

TAKE NOTE!

On October 19, 2016 the Advisory Committee on Immunization Practices (ACIP) voted to recommend a two-dose HPV vaccine schedule for young adolescents.³² CDC now recommends two doses of HPV vaccine to be given at least six months apart at ages eleven and twelve years to protect against cancer-causing HPV infections.³³ Adolescents ages thirteen and fourteen are also able to receive the vaccination on the new two-dose schedule, while older adolescents and adults (fifteen to twenty-six) must stay on the previously recommended three-dose schedule.

Table 5. ACIP Recommended Number of Doses and Intervals for Human Papillomavirus (HPV) Vaccine, by Age at Series Initiation and Medical Conditions — United States, 2016³³

Population	Recommended number of HPV vaccine doses	Recommended interval between doses
Persons initiating HPV vaccination at ages 9 through 14 years,* except immunocompromised persons [†]	2	0, 6–12 months [§]
Persons initiating HPV vaccination at ages 15 through 26 years [¶] and immunocompromised persons [†] initiating HPV vaccination at ages 9 through 26 years	3	0, 1–2, 6 months**

*ACIP recommends routine HPV vaccination for adolescents at age 11 or 12 years; vaccination may be given starting at age nine years.

[†] Persons with primary or secondary immunocompromising conditions that might reduce cell-mediated or humoral immunity

[§] In a two-dose schedule of HPV vaccine, the minimum interval between the first and second doses is five months.

[¶] For persons who were not adequately vaccinated previously, ACIP recommends vaccination for females through age 26 years and for males through age 21 years; males ages 22 through 26 years may be vaccinated. Vaccination is recommended for some persons aged 22 through 26 years; [see Medical conditions and Special populations](#).

** In a three-dose schedule of HPV vaccine, the minimum intervals are four weeks between the first and second doses, 12 weeks between the second and third doses, and five months between the first and third doses.

Safety and Effectiveness

FDA licensure and ACIP recommendation of Gardasil and Gardasil 9 were based on several large scale clinical trials that proved the safety and effectiveness of the vaccine in females and males.^{24,25,34,35} The three-dose series of both vaccines causes the body to produce a strong immune response against the

specified HPV types and have outstanding safety records.^{30,34,35,36,37} Moreover, research has shown that the HPV vaccine has an even stronger immune response in preteens,⁹ and that protection against HPV can last at least eight to ten years or more without losing effectiveness.^{38,39} The new two-dose recommendation was based on studies suggesting high efficacy against HPV infection of the two-dose series^{40,41} or similar efficacy between the two- and three-dose series.⁴² In addition, the duration of protection of the two-dose series is expected to be similar to the three-dose series given the similarities between the two vaccines^{43,44} as well as having no evidence of waning protection of the three-dose series confirmed by ten years of follow-up from clinical trials.²³

Some individuals have questioned the safety of some of the ingredients in the vaccines, but there is no evidence indicating they are unsafe.⁴⁵ Each of the HPV vaccines contains aluminum and formaldehyde at levels that have been proven to be perfectly safe and non-toxic to the body.⁴⁶ As with other vaccines, a very small amount of aluminum is added to boost the body's immune response, which allows for lesser quantities of the vaccine and fewer doses.⁴⁶ In fact, infants consume greater levels of aluminum through breast milk or formula than from the HPV vaccine.⁴⁷ Formaldehyde is a naturally occurring organic compound used in vaccines to inactivate viruses and detoxify bacterial toxins so that they do not cause disease; there is more formaldehyde naturally occurring in the bloodstream than in a vaccine.⁴⁸

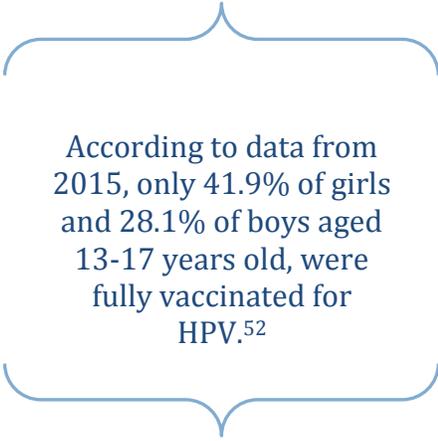
Globally, the highly effective Gardasil and Cervarix vaccines have been distributed in hundreds of millions of doses throughout more than sixty-four countries.^{36,49} During 2006 to 2016, almost ninety million doses of the HPV vaccines were administered in the U.S. alone, 87% of which were Gardasil.⁵⁰ Safety reports from the Vaccine Adverse Event Reporting System (VAERS) indicated that of the Gardasil doses distributed, approximately 33,945 resulted in adverse effects, 93% of which were non-serious (e.g. redness or soreness at the site of the injection, headache or fainting immediately following vaccination).⁵⁰

Of the reported adverse events among girls and women, 7% have been serious; including 117 reports of death with only 51 verified through medical records.⁵⁰ CDC investigations into the reported deaths found that these deaths could not be directly associated with the vaccine.⁴⁹

HPV Vaccine Uptake

Despite proven safety and effectiveness, HPV vaccine uptake rates remain far below the Healthy People 2020 goal of 80% and below those of other vaccines recommended for adolescents.^{24,51} Data from the 2015 National Immunization Survey-Teen (NIS-Teen) indicated vaccine coverage among adolescents aged thirteen to seventeen years was highest for >1 dose tetanus-diphtheria-acellular pertussis (Tdap) (86.4%), followed by >1 dose meningococcal conjugate vaccine (MenACWY) (81.3%), and lowest for >1 dose HPV (62.8% girls) and (49.8% boys).⁵² Moreover, when comparing HPV vaccine uptake, many studies indicated a person's gender, race, ethnicity and socioeconomic status (SES) influenced

vaccination completion^Φ rates.^{53,54} Also according to NIS-Teen data, only 41.9% of girls and 28.1% of boys aged thirteen to seventeen years old were fully vaccinated for HPV.⁵² In regards to race/ethnicity, American Indians/Alaska Native females were the most likely to start the HPV vaccine series (70.5%) while white females had the lowest initiation rate (59.2%). However, series completion rates were highest among Asian females (53.5%) and lowest among American Indians/Alaska Native females (38.7%).⁵² The 2015 NIS-Teen study also reported higher levels of vaccine series initiation and completion among females below the poverty level (70.0% and 44.4% respectively) when compared to girls at or above the poverty level (60.4% and 41.3% respectively).⁵²



According to data from 2015, only 41.9% of girls and 28.1% of boys aged 13-17 years old, were fully vaccinated for HPV.⁵²

Achieving the highest possible HPV vaccination coverage rates not only has the potential to decrease HPV incidence and associated cancer mortality rates but also has the potential to establish herd immunity. Herd immunity is “the resistance to a disease that develops in an entire community when a sufficient number of individuals are vaccinated.”^{55 (p 801)} This form of immunity can provide a measure of protection for those who are unable to receive the vaccine.⁵⁵ The greater the number of individuals in a community who are immune to HPV, the smaller the odds are for individuals who are not immune to acquire or come in contact with HPV. Though the coverage is currently lower for boys than girls, and male HPV vaccination is still controversial in some circles, a recent study suggested that an increased effort to vaccinate boys is likely to protect more people from HPV-associated diseases for the same price.⁵⁶

Factors Impacting HPV Vaccination Uptake

Parental Barriers and Facilitators of HPV Vaccination

As summarized in Table 6, several factors have been identified that may explain the low HPV vaccination rates. Because administering the vaccine to adolescents most commonly requires parental consent, some of the greatest challenges to HPV vaccine acceptance are parental knowledge, attitudes and beliefs.^{57,58} Many parents do not understand the urgency to target adolescents, but this is the most effective time to vaccinate them.^{9,58} Research has shown that most parents feel their child is too young and would not initiate sexual activity for many years to come.^{58,59,60} Furthermore, some parents feel vaccinating their child(ren) against an STI, sends a message to them that it is okay or expected that they become sexually active.⁵⁹

^Φ The HPV vaccination “completion” rate is the proportion of those who get one shot who then finish the vaccination series. Completion is not the same as coverage; “full coverage” is the percentage of the population who complete the vaccination series (e.g. 2014 data from NIS-Teen showed that nationally 39.7% of female adolescents had received the previously recommended three doses (coverage), 60.0% of females received at least one shot, and the completion rate was 69.3% for girls who had started the series).⁵²

Table 6. Summary of Barriers and Facilitators of HPV Vaccine Uptake among Adolescents

	Barriers to Vaccination of Child(ren)	Facilitators of Vaccination of Child(ren)
Parent	<ul style="list-style-type: none"> • Knowledge, attitudes, beliefs and perceptions <ul style="list-style-type: none"> ○ Lack of urgency • Acceptability <ul style="list-style-type: none"> ○ Fear of condoning promiscuity or early sex • Cost • Safety <ul style="list-style-type: none"> ○ Fear side effects ○ Distrust “newness” 	<ul style="list-style-type: none"> • Physician’s strong recommendation
	Barriers to HPV Vaccine Recommendation	Facilitators of HPV Vaccine Recommendation
Physician	<ul style="list-style-type: none"> • Younger adolescent • Anticipated parental disapproval • Discomfort discussing sex with young patients • Lack of time • Fear of religious and cultural sensitivities • Low perceived risk of sexual activity in patient • Cost <ul style="list-style-type: none"> ○ To purchase, store ○ Low reimbursement • Safety and efficacy <ul style="list-style-type: none"> ○ Desire more information/data 	<ul style="list-style-type: none"> • Younger doctor • Female doctor • Pediatrician

Physician Barriers and Facilitators of HPV Vaccine Recommendation

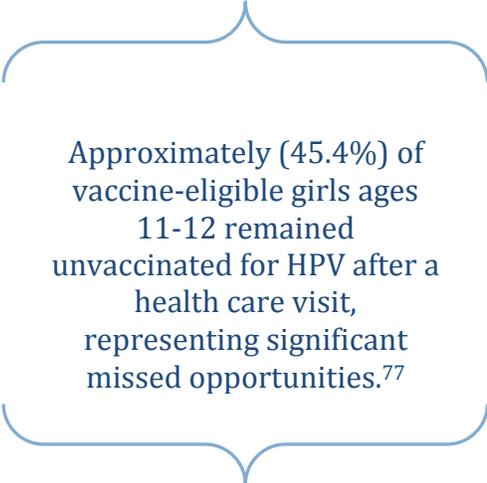
Parental perceptions’ play a key role in the decision making process; however, physician recommendations have an even greater influence on HPV vaccine acceptability.⁶¹ A health care provider’s strong recommendation is the most effective method of encouraging HPV vaccination among adolescents.^{62,63,64,65} According to the CDC a strong recommendation should be presented using a presumptive approach.^{62-65,66,67} Presumptive recommendation includes verbal dominance and emphasis of vaccine effectiveness.⁶²⁻⁶⁷ The presumptive approach calls for providers to “announce” that it is time for the HPV shot, as opposed to “asking” if the patient wants to get the vaccine.⁶⁷ This helps to assure the patient/parent of the providers’ trust in the vaccine’s safety and effectiveness. Personal belief in the importance of the vaccine can be highlighted by stressing cancer prevention and vaccine safety.⁶²⁻⁶⁷

A national study was conducted in 2014 assessing multiple aspects of physicians’ HPV vaccination recommendation quality. Recommendation quality was measured using four indicators: strength, timeliness, consistency and urgency.⁶⁸ Findings indicated that recommendation quality was higher among physicians that used the presumptive approach versus giving information or eliciting questions.⁶⁸ Visit the [CDC’s YOU ARE THE KEY](#) website and take a look at GW Cancer Center’s [HPV Vaccine Myth Busting for Health Care Providers Social Media Toolkit](#) and [archived webinar](#) for tips to help vaccine providers with making strong recommendations. Quantitative data suggested physician discussions and a strong physician recommendation together were “associated with a ninety-three-fold increase in the

odds of initiating the HPV vaccine series among a sample of women aged nineteen to twenty-six years.”^{62(p 621)}

According to a 2015 study assessing predictors of provider recommendation for the HPV vaccine, those who received a provider recommendation were thirty-five times more likely to receive >1 dose of the vaccine compared to those who did not receive a recommendation.⁶⁹ In addition, the CDC and ACIP have suggested that physicians bundle (co-administer) HPV vaccination recommendations and deliver with other routine vaccinations for adolescents such as the MenACWY and Tdap booster to achieve greater acceptability.^{25,70,71,72} Co-administration also offers convenience to both patients and providers, which can increase the likelihood of on-schedule vaccine uptake among adolescents.^{21,73,74} Providers should be trained to use a combination of the above approaches to convey to parents that the HPV vaccine is a normal and routine part of their child’s vaccination schedule.

Although encouraging the use of strong provider recommendations has proven effective in increasing HPV uptake, some physicians have expressed reservations and have been reluctant to recommend the vaccine to the intended population.⁷⁵ According to a recent study assessing physician communication regarding the HPV vaccine, 95% of physicians report recommending Tdap as highly important for patients aged eleven to twelve, 87% recommend MenACWY and only 73% recommend the HPV vaccine for the same group.⁷⁶ This study also indicated that 70% of physicians who had a preferred order for discussing adolescent vaccines preferred discussing the HPV vaccine last.⁷⁶ An analysis of data from a large health claims database (n=407,371) also indicated that 45.4% of vaccine-eligible girls aged eleven to twelve remained unvaccinated for HPV after a health care visit, representing significant missed opportunities.⁷⁷ The CDC defines a missed opportunity as a health care encounter occurring on or after the 11th birthday and on or after the publication date of ACIP’s HPV vaccination recommendation (March 23, 2007), during which they received at least one vaccine but did not receive the HPV vaccine.² A survey of health care professionals and the general population conducted by the Prevent Cancer Foundation in December 2015 found that physicians were least likely to recommend the HPV vaccine to younger adolescents.⁷⁸ Among health professionals’ reasons for not “always” recommending the HPV vaccine, 40% was attributed to patients being too young,⁷⁸ which demonstrates non-adherence with ACIP recommendations.⁶⁵ Evidence suggests that anticipated parental disapproval, discomfort discussing sexual matters with young people, insufficient time to discuss HPV vaccination with a parent and fear of religious and cultural sensitivities are all known barriers impacting a physician’s decision to recommend the vaccine.^{58,59,64,79} Furthermore, perceived risk of expediting initiation of sexual activity has also been identified as a major factor impacting a physician’s decision to recommend the HPV vaccine. In recent reports several providers described using an un-validated profiling method to assess their patients for perceived risk of sexual activity and in turn deciding when to recommend HPV vaccination.^{58,80}



Approximately (45.4%) of vaccine-eligible girls ages 11-12 remained unvaccinated for HPV after a health care visit, representing significant missed opportunities.⁷⁷

TAKE ACTION!

CDC is asking **health care professionals** to lead the conversation about the importance of HPV vaccine for cancer prevention with patients and their parents, practice staff, and colleagues in the community. See CDC [resources](#) to answer any questions parents may have.

Physician recommendations vary by physician characteristics, including gender, specialty and age. Studies have found younger physicians are more likely to recommend the vaccine, compared to older physicians “who are not as receptive to adopting new practice.”^{64 (p 81)} Research has also shown that of the three physician specialist types that typically provide preventive care for females aged nine to twenty-six, pediatricians have greater odds of recommending the HPV vaccine compared to family practitioners and obstetrician/gynecologists.^{65,81} This could be attributed to having a greater knowledge of the vaccine; a recent study found that approximately 64% of pediatricians reported being very knowledgeable of the HPV vaccine compared to 54% of general practitioners who consider themselves somewhat knowledgeable.⁷⁸ In addition, patients of female primary care providers (PCPs) are more likely to start the HPV vaccine series compared to male PCPs.⁸² The American College of Obstetricians and Gynecologists released a [resource](#) in 2016 to help their providers make stronger recommendations, including patient information sheets.

Cost

While parents and physicians have different motivations for vaccine hesitancy, both recognize cost and affordability as important barriers to provision and uptake. Costs for the complete HPV vaccine series can total \$160-177 per dose plus administrative fees (Table 4).²⁸ Currently, the price for the vaccine at retail pharmacies can reach up to \$235 per dose without insurance.⁸³ Furthermore, although there are federally funded vaccine programs like the Vaccines for Children (VFC) program, which provides vaccines to Medicaid-eligible and uninsured children for low or no cost, “females nineteen and older have limited access to vaccine-specific funding and they are also less likely to be insured.”^{82(p 520)} Research participants often report that HPV vaccines are too expensive without insurance coverage; especially for low-income families.⁸⁴ A systemic review of twenty-two studies focused on self-reported barriers and facilitators to HPV vaccination demonstrated that cost is often the most influential barrier to vaccine access.⁸¹ For providers, the amount of reimbursement received for a vaccine plays a large role in whether a physician administers the vaccine.^{79,85} In fact, one study revealed that providers are 55% less likely to recommend the HPV vaccine due to inadequate insurance reimbursements.⁵⁸ Lastly, up-front costs of ordering and stocking the vaccine have also been identified as barriers to physician recommendations and administration of the vaccine.⁸⁶

Misperceptions about Safety and Effectiveness

In addition to financial burdens, several research studies have been published implicating safety concerns and lack of knowledge as barriers to HPV vaccine acceptance among parents and providers.^{59,36,60,81,87} The literature suggests parents still fear the potential side effects and distrust the “newness” of the vaccine, despite ten years of safety and effectiveness data since original FDA licensure.^{37,57,88} In recent studies and studies published in the initial years following vaccine availability, many parents and physicians reported information deficit as an additional barrier to HPV vaccine

uptake. Many parents have expressed dissatisfaction with the information available to them and stressed the importance of receiving sufficient, clear and understandable information to enable them to make an informed decision.⁵⁹ Additional data from the 2015 Prevent Cancer Foundation survey indicated 92% of respondents believed that there is a need for more information specifically regarding the dangers of HPV.⁷⁸ Similarly, two studies published between 2008 and 2011 found that physicians want more information on safety and efficacy to feel comfortable administering the HPV vaccine.^{70,89}

Policies Impacting HPV Vaccination Uptake

Vaccine uptake is not only influenced by patients, parents and providers but several types of policies as well. Formal or “big P” policies that can impact HPV vaccination include laws, rules, and regulations enacted by elected officials and official bodies, such as U.S. Preventive Services Task Force and ACIP recommendations, school entry vaccination requirements enacted at the state level, funding for public education campaigns to increase immunization rates, mandates on insurance coverage of vaccines and required adherence to ACIP recommendations.^{90,91} “Little p” policies that can impact HPV vaccination include less formal policies such as Medicaid funding decisions, lack of statewide coordination and planning, a fragmented health system, professional association endorsement of the ACIP recommendations, provider-level decisions about administrative fees and weak oversight of exemption from school mandates.

ACIP Recommendations

As discussed previously, ACIP recommendations for HPV vaccines differ slightly by the target audience’s age, sex and risk status.³³ All ACIP recommendations are based on several large-scale clinical trials that proved the safety and effectiveness of vaccines in females and males.^{24,25,34,35} ACIP recommendations impact Medicaid policies, VFC programs, private insurance coverage and state-level school vaccination policies.

Mandates for Insurance Coverage & Financing Issues

With the 2010 enactment of the federal Patient Protection and Affordable Care Act (ACA), mandated insurance coverage for HPV vaccination was greatly expanded. ACA requires that the cost of the HPV vaccine be covered through both private and public insurers for the ages recommended by ACIP, with no cost-sharing (e.g. co-pay).⁹² Table 7 shows specific information on coverage and cost by insurer type and assistance program. Unfortunately, vaccines are regarded as an optional benefit for adults by Medicaid and it is at a state’s discretion whether to cover the HPV vaccine.⁹³ Also, providers can charge an “administrative fee,” even if the cost of the vaccine itself is fully covered. These rates are often negotiated between insurance companies and providers. The Centers for Medicare and Medicaid Services (CMS) sets maximum amounts for vaccine administration fees among participating providers, which vary by state; the 2016 range was between \$19-\$33.⁹⁴ Despite variations in state coverage and administrative fees, a 2015 Health Affairs study indicated that ACA provisions are associated with a 7.7% increase in HPV vaccine initiation and a 5.8% increase in completion rates among women aged nineteen to twenty-five.⁹⁵

Of most salience to this project, the VFC program, run by the CDC, requires coverage of all ACIP recommended vaccines.⁹⁶ Those eligible for the VFC program include children under nineteen years who are Medicaid-eligible, uninsured, underinsured or American Indians/Alaska Natives. According to the CDC:

“Underinsured means the child has health insurance, but it doesn't cover vaccines, doesn't cover certain vaccines, or covers vaccines but has a fixed dollar limit or cap for vaccines. Once that fixed dollar amount is reached, a child is then eligible. Underinsured children are eligible to receive vaccines only at Federally Qualified Health Centers or Rural Health Clinics.”⁹⁶

ACA provisions are associated with a 7.7% increase in HPV vaccine initiation and a 5.8% increase in completion rates among women aged nineteen to twenty-five.⁹⁵

Additionally, CDC states that

“There is no charge for any vaccines given by a VFC provider to eligible children. But there can be some other costs with a vaccination: Doctors can charge a set (or standard) fee to administer each shot. But if the family can't afford the fee per shot, the fee must be excused. A VFC-eligible child cannot be refused a vaccination due to the parent's or guardian's inability to pay for shot administration. There can be a fee for the office visit. There can be fees for non-vaccine services, like an eye exam or blood test.”⁹⁶

Through the VFC program, the CDC purchases discounted doses of vaccines from manufacturers and distributes directly to registered public and private health care providers.⁹⁶

Table 7. HPV Vaccine Coverage by Insurance Type

Insurance Type	Population Covered for HPV Vaccine	Coverage level
Employer-sponsored and Private Insurance	Covered as ACIP recommends	No cost-sharing (e.g. no co-pay, no co-insurance). Providers may charge an administrative fee, which may be partially covered by the insurer.
Medicaid	19-20 years, as ACIP recommends	No cost-sharing under Early Periodic Screening, Diagnosis, and Treatment (EPSDT) program. ⁹⁷
Medicaid	21+, as ACIP recommends	Coverage depends on the state and whether or not they expanded Medicaid after ACA implementation. In 2010, 9 states offered coverage with a co-pay and 28 offered coverage without a co-pay. ⁹⁸ Providers may charge an administrative fee, which may be partially covered by Medicaid – maximum varies by state (ranges from \$19-\$33). ⁹⁴
Vaccines for Children (VFC)	9-18 years and Medicaid-eligible Uninsured Underinsured American Indian or Alaska Native	No cost. Those who are underinsured must receive immunizations through a Federally Qualified Health Center or Rural Health Clinic. Providers may charge an administrative fee, which may be partially covered by Medicaid.
State Children’s Health Insurance Program (SCHIP)	9-18 years	No cost. SCHIP programs that are separate from state Medicaid must cover ACIP vaccines because children enrolled are ineligible for VFC coverage.
Section 317 of the Public Health Service Act (Immunization Grant Program)	May include children not eligible for VFC or SCHIP or uninsured or underinsured adults (e.g. undocumented immigrant children)	Utilization of 317 funding varies by state. ⁹⁹
Merck Vaccine Patient Assistance Program	Adults 19-26 years old, not covered by any of the means above.	Gardasil® & Gardasil®9 at no cost. ¹⁰⁰ http://www.merckhelps.com/Programs.aspx

School Vaccination Requirements & Exemptions

In the U.S., states have the authority and responsibility to regulate which vaccines, if any, are required for entry into public schools and daycare facilities. School vaccination requirements are typically determined by the state legislature or a regulatory body such as the health department. Often, states follow CDC recommendations, but the requirements differ by state.¹⁰¹ If a state chooses to make a vaccine mandatory, it must consider and address financing issues such as coverage under Medicaid,

State Children’s Health Insurance Program (SCHIP), VFC, coverage for children who may be uninsured, funding for public awareness and education campaigns and historically, and whether to require coverage by insurance providers.¹⁰²

The [Immunization Action Coalition](#) provides lists of required vaccinations by state. As of 2016, Virginia, Washington, D.C. and Rhode Island are the only three locations in the U.S. that have passed laws requiring the administration of the HPV vaccine for school entry, though the specifics differ. Virginia’s law went into effect in October 2008 with the requirement being that girls entering sixth grade must have at least had the first dose of the previously recommended three-dose HPV series. Washington, D.C.’s law went into effect in January 2009 and also requires girls entering sixth grade to have started the series. Rhode Island’s law went into effect in August 2015 and requires girls and boys to have one dose by seventh grade, two doses by eighth grade and to have completed the series by ninth grade.¹⁰¹ The CDC also has a detailed page with more information on [state school vaccination laws and exemptions](#).

With school entry requirements, an additional policy to consider is the exemption process. As with other vaccines, parents are afforded the right to refuse to follow the requirement. Typically these exemptions are based on medical restrictions or religious beliefs, but parents are allowed to opt out of vaccination requirements for philosophical reasons in many states.¹⁰³ For example, Virginia’s law states that upon reviewing educational materials from the Board of Health, the parent or guardian may choose for the child not to receive the HPV vaccine.¹⁰⁴ Washington, D.C. parents wishing to opt out simply fill out a form available on the Department of Health website declaring that the parent or legal guardian has been informed of the HPV vaccination requirement and has elected not to participate.¹⁰⁵ Rhode Island’s law includes exemptions for religious or medical reasons.¹⁰⁶

While more states are proposing school-entry requirements for HPV vaccination in the last decade, there are limited data on parents’ support of such mandates. One 2016 study that surveyed a national sample of 1,501 parents of 11- to 17-year old children found that only 21% of parents supported school-entry mandates for HPV vaccination.¹⁰⁷ However, the study observed that more parents supported these mandates (57%) if they included opt-out provisions.¹⁰⁷

Recent studies have shown that states and jurisdictions with school-entry and education mandates do not currently have higher HPV vaccination coverage than states without such legislation. This may be due to the exemptions allowed for the HPV vaccine that do not apply to other vaccines.¹⁰⁸ A 2016 study found that girls living in states and jurisdictions with education and school entry mandates did not have higher HPV vaccination series initiation or completion compared to those living in states that did not have similar mandates.¹⁰⁹ In a study that evaluated the uptake of HPV vaccine among girls seeking well-child care five years after the introduction of the statewide mandate in Virginia, findings showed no change in HPV vaccine uptake or distribution of uptake in the state.¹¹⁰ Another recent study targeting thirteen to seventeen year old girls reported HPV vaccination mandate in Virginia did not have a significant impact on vaccination or on provider recommendations. However, the study did find a strong link between provider recommendations and HPV vaccination, which is consistent with the literature.¹¹¹

According to a Kaiser Family Foundation analysis updated in September 2015, twenty-nine states lacked policies supporting HPV vaccination (school mandate, public funding for vaccine costs or publicly-funded education campaigns).¹¹²

Parental and Minor Consent Laws

Laws governing consent for delivery of health care services to minors also vary by state. As determined by various statutes and/or court decisions, parents or legal guardians are required to consent for most health care services provided to minors in every state.¹¹³ It is generally understood that parental consent is required for each dose of a vaccine series; however, in every state a minor may consent for a vaccination on their own based on two types of exceptions.¹¹³ The first exception allowing a minor to consent for health care services is based on status (e.g. emancipation, marriage, age and capacity, living apart from parents).¹⁰⁹ The second exception relates to the type of service (e.g. services for diagnosis and treatment of sexually transmitted and reportable diseases).¹¹³ Again, varying by state, some laws not only allow minors to consent for diagnosis and treatment of STIs, but for prevention of STIs as well, and thus could include vaccinations for HPV.¹¹³

Standing Orders

State medical practice laws govern medical practice and permits licensed physicians to delegate medical practice powers through the use of standing orders.¹⁰¹ “A standing order is a written protocol that outlines the circumstances under which a non-physician health professional can engage in medical practice under medical supervision.”¹⁰¹⁽ⁱⁱ⁾ Although physicians traditionally have the authority to delegate medical practice powers, some states allow specific classes of health professionals to conduct at least one of three elements of immunization practices (e.g., patient assessment, prescribing and administering) under their own license.¹⁰¹ In addition to registered nurses, advanced practice nurses and physician assistants, several states have also permitted immunization practice by local pharmacists.¹¹⁴ With state-specific limitations such as age and vaccine type (prescription and prescriber protocol), pharmacists have the authority to administer HPV vaccines in approximately forty-eight states and territories.¹¹⁵ These limitations however create a barrier for ease of access to the HPV vaccine.¹¹⁶ Given the large number of pharmacists who are trained and available to vaccinate, the American Pharmacist Association and the Immunization Action Coalition have advocated for advancing the President’s Cancer Panel’s call to action for states to implement policies and enact laws that allow pharmacists to administer vaccines to adolescents. Read the President’s Cancer Panel Annual Report (2012-2013): [Accelerating HPV Vaccine Uptake](#).¹¹⁶

Addressing Barriers

In conclusion, for all of the major challenges to HPV vaccine access, affordability and acceptability, preventive strategies ranging from policies to educational interventions have been proposed and implemented. It has been proven effective for providers to engage in continuing education programs that aim to increase knowledge, attitudes and beliefs regarding the HPV vaccine.¹¹⁷ Similar educational programs targeting patients and their parents are equally impactful.¹¹⁷ However, the Community Guide does not recommend using patient education alone as a strategy because of insufficient evidence that it will increase HPV vaccination coverage.¹¹⁸ Health care facilities adopting various procedural and

operational methods, such as standing orders and immunization information systems (IIS), have also increased adolescent HPV vaccination rates.^{117,119} Recent studies found that managed care-based mail and telephone reminder/recall increased adolescent immunizations and preventive visits.^{119,120} **Finally, one of the most important interventions and key take home messages of this resource book is encouraging providers to decrease missed opportunities and deliver strong HPV recommendations.**^{62,63,75} **CDC recommends that physicians be trained to administer the HPV vaccine routinely with the other adolescent vaccines and to emphasize that the vaccine is safe and has a more robust immune response in preteens.**^{8,61,70,74}

Figure 5. Social Ecological Model of Points of Potential HPV Vaccination Intervention

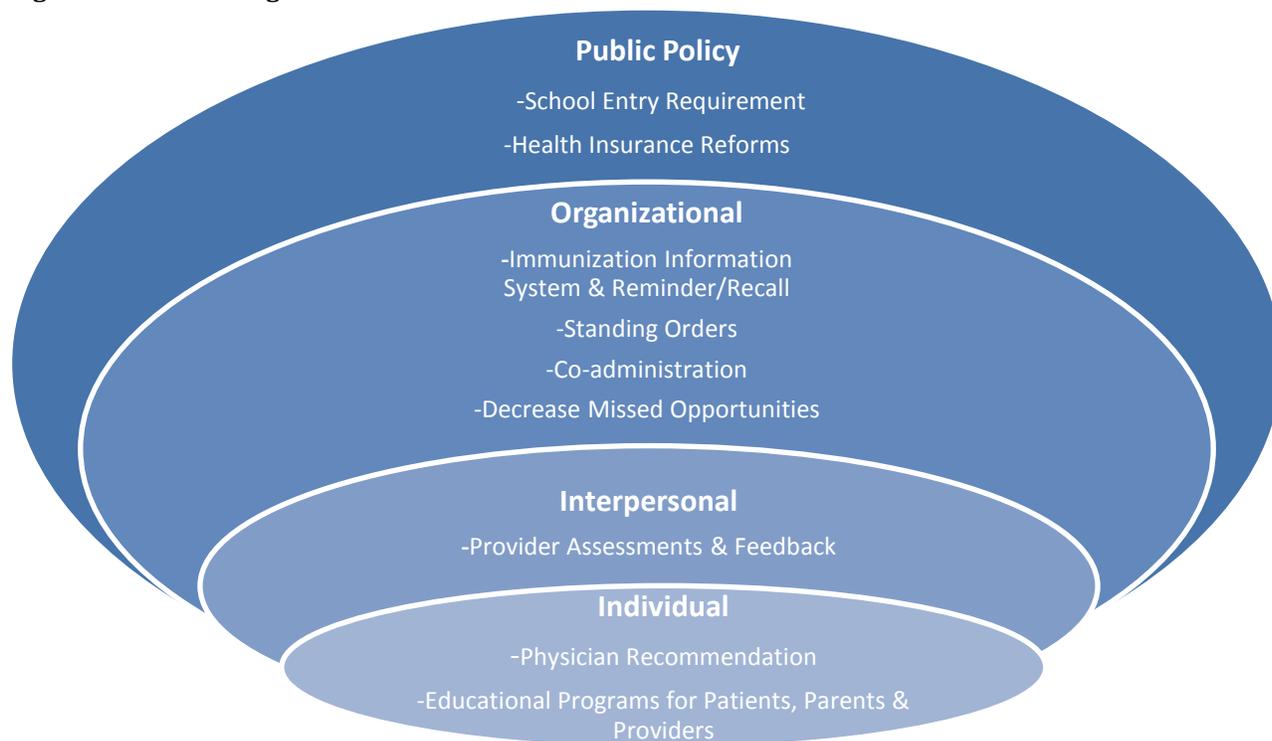


Figure 5 shows where each of these potential solutions falls in a social ecological model. It is important to consider the interrelationships among the various levels of impact when proposing prevention strategies.¹²¹ Future intervention efforts should address both the population-level and individual-level determinants of vaccine uptake. Using an ecological approach to improve HPV vaccination rates is likely to be more effective and improve sustainability over time.¹²¹ The [National HPV Vaccination Roundtable](#) was established by ACS and CDC in 2014 to coordinate leadership and strategic planning aimed at reducing HPV-associated cancer incidence and mortality in the U.S. The Roundtable hosts a SharePoint site with resources for different audiences including pharmacies, coalitions, insurers and more. The American Cancer Society’s [HPV Vaccination Resource Clearinghouse](#) includes “resources to support the implementation of strategies to increase HPV vaccination. The Clearinghouse features [Patient Education Tools](#) and [Provider Education Tools](#), including printable educational materials, vaccine information statements, toolkits, and multimedia to increase HPV vaccination awareness and uptake.” See also

CDC's [HPV toolkit](#), Preteen VaxScene [webinar series](#) and [resources](#) on vaccine information for providers with preteen and teen patients.

Opposition & Threats

Despite all of the evidence-based interventions and strategies, there is still a major barrier that stands in the way of HPV vaccinations. Opposition against vaccines dates as far back as 1869 and 1908 when the first anti-vaccination leagues were formed in the United Kingdom and the U.S., respectively.^{122,123} The anti-vaccine movement was built on several claims including belief that vaccines cause illness, reduce immunity, that adverse events are underreported and that policies are motivated by profit, among other claims.¹²⁴ Arguments against vaccination mandates include that they are an unacceptable infringement on personal liberty and violate the first and 14th Amendments to the U.S. Constitution, vaccines are inherently harmful, vaccines contradict religious beliefs and vaccines are unnatural, among others.¹²³ Specifically regarding the HPV vaccine and potential school mandates, opponents have used similar arguments. Anti-vaccine activists believe the school requirement for HPV vaccine is a clear demonstration of inappropriate governmental intrusion of parental rights, is not sufficient for public health justification because HPV is not spread by casual contact and promotes “sexual disinhibition” and thus it is inconsistent with family values and messages regarding abstinence.¹⁰¹

The efforts of the anti-vaccine movement have significantly threatened the effectiveness of the HPV and other vaccines. Over the past years, anti-vaccine advocacy has led to an increase in exemption policies, parental resistance, lower vaccination rates and delayed vaccination, effectively reducing herd immunity across the U.S.¹²⁵ Providers and parents may very well encounter webpages, social media and popular press materials with anti-vaccine messaging. This carries serious implications for public health efforts to increase HPV vaccination rates. For further reading to help better understand the opposition, see the [National Vaccine Information Center](#), [Vaccination Liberation](#), and [Natural News](#) websites and read some of the many popular press articles on the subject over the last months and years. Also familiarize yourself with national and local groups that are potential allies such as [Immunization Action Coalition](#), [Every Child by Two](#) and [Voices for Vaccines](#). Watch an [archived webinar](#) from GW Cancer Center on using immunization information systems to increase HPV vaccination uptake.

References

- ¹ HPV and cancer. National Cancer Institute Website. <http://www.cancer.gov/cancertopics/factsheet/Risk/HPV>. Updated February 19, 2015. Accessed December 29, 2016.
- ² Workowski K, Bolan G. Sexually transmitted diseases treatment guidelines, 2015. *Morbidity and Mortality Weekly Report*. 2015; 64(3):1-140.
- ³ Hamborsky J, Kroger A, Wolfe S. Epidemiology and prevention of vaccine-preventable diseases- human papillomavirus. Centers for Disease Control and Prevention Website. <http://www.cdc.gov/vaccines/pubs/pinkbook/hpv.html>. Updated August 5, 2015. Accessed December 29, 2016.
- ⁴ Genital HPV infection - fact sheet. Centers for Disease Control and Prevention Website. <https://www.cdc.gov/std/hpv/stdfact-hpv.htm>. Updated November 4, 2016. Accessed December 29, 2016.
- ⁵ National Institutes of Health Website. Recurrent respiratory papillomatosis or laryngeal papillomatosis. <http://www.nidcd.nih.gov/health/voice/pages/laryngeal.aspx>. Updated April 1, 2011. Accessed December 29, 2016.
- ⁶ Fernandes J, Galvao de Araujo J, Fernandes M. Biology and natural history of human papillomavirus infection. *Open Access Journal of Clinical Trials*. 2013; 5:1-12. doi:10.2147/OAJCT.S37741.
- ⁷ Clifford G, Smith J, Aguado T, Franceschi S. Comparison of HPV type distribution in high-grade cervical lesions and cervical cancer: a meta-analysis. *British Journal of Cancer*. 2003; 89:101-105. doi:10.1038/sj.bjc.6601024.
- ⁸ Other sexually transmitted diseases. Centers for Disease Control and Prevention Website. <https://www.cdc.gov/std/stats14/other.htm>. Updated November 17, 2015. Accessed February 10, 2016.
- ⁹ HPV also known as human papillomavirus. Centers for Disease Control and Prevention Website. <https://www.cdc.gov/vaccines/parents/diseases/teen/hpv-indepth-color.pdf>. Updated July 2015. Accessed December 29, 2016.
- ¹⁰ 2015 High School Youth Risk Behavior Survey Questionnaire. Centers for Disease Control and Prevention. <https://nccd.cdc.gov/youthonline/App/Results.aspx?LID=XX>. Accessed on September 28, 2016.
- ¹¹ Saraiya M, Unger E, Thompson T, et al. US assessment of HPV types in cancers: implications for current and 9-valent HPV vaccines. *Journal of National Cancer Institute*. 2015; 107(6):1-12.
- ¹² Howlader N, Noone AM, Krapcho M, et al. SEER Cancer Statistics Review, 1975-2013. National Cancer Institute. Bethesda, MD. http://seer.cancer.gov/csr/1975_2013/, based on November 2015 SEER data submission, posted to the SEER Website, April 2016. Accessed September 28, 2016.

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- ¹³ Viens LJ, Henley SJ, Watson M, et al. Human papillomavirus–associated cancers — United States, 2008–2012. *Morbidity and Mortality Weekly Report*. 2016; 65:661–666.
- ¹⁴ Fakhry C, Cohen E. The rise of HPV-positive oropharyngeal cancers in the United States. *Cancer Prevention Research*. 2014; 8(1):9-11.
- ¹⁵ Chaturvedi A, Engels E, Pfeiffer R, et al. Human papillomavirus and rising oropharyngeal cancer incidence in the United States. *Journal of Clinical Oncology*. 2011; 29(32):4294-301.
- ¹⁶ Sasieni P, Castanon A, Cuzick J. Effectiveness of cervical screening with age: population based case-control study of prospectively recorded data. *British Medical Journal*. 2009; 339(2968):1-7. doi: 10.1136/bmj.b2968
- ¹⁷ Sawaya G, McConnell K, Kulasingam S, Lawson HW, Kerlikowske K, Melnikow J, et al. Risk of cervical cancer associated with extending the interval between cervical-cancer screenings. *New England Journal of Medicine*. 2003; 349(16):1501-1509. doi: 10.1056/NEJMoa035419
- ¹⁸ United States Cancer Statistics: 1999 - 2011 Incidence, WONDER Online Database. United States Department of Health and Human Services, Centers for Disease Control and Prevention and National Cancer Institute; 2014. <http://wonder.cdc.gov/cancer-v2011.html>. Accessed March 8, 2015.
- ¹⁹ Mariotto A, Yabroff K, Shao Y, Feuer E, Brown M. Projections of the cost of cancer care in the United States: 2010-2020. *Journal of National Cancer Institute*. 2011; 103(8):117-128.
- ²⁰ Chesson H, Ekwueme D, Saraiya M, et al. Estimates of the annual direct medical costs of the prevention and treatment of diseases associated with human papillomavirus in the United States. *Vaccine*. 2012; 30(42):6016-6019.
- ²¹ Trogdon J, Tangka F, Ekwueme D, Guy GP, Nwaise I, Orenstein D. State level projections of cancer related medical care costs; 2010 to 2020. *American Journal of Managed Care*. 2012; 18(9):525-532.
- ²² Yabroff K, Lund J, Kepka D, Mariotto A. Economic burden of cancer in the US: estimates, projections and future research. *Cancer Epidemiology Biomarkers & Prevention*. 2011; 20(10):2006-2014. doi: 10.1158/1055-9965.EPI-11-0650.
- ²³ Markowitz LE, Dunne EF, Saraiya M, Chesson HW, Curtis CR, Gee J, et al. Human papillomavirus vaccination: recommendations of the Advisory Committee on Immunization Practices (ACIP). *Morbidity and Mortality Weekly Report*. 2014; 63(5):1-30.
- ²⁴ Isidean S, Tota J, Gagnon J, Franco E. Human papillomavirus vaccines: key factors in planning cost effective vaccination programs. *Expert Review Vaccines*. 2014:1-15. doi: 10.1586/14760584.2015.964213.
- ²⁵ FDA approves Gardasil 9 for prevention of certain cancers caused by five additional HPV types. U.S. Food and Drug Administration Website.

<http://www.fda.gov/NewsEvents/Newsroom/PressAnnouncements/ucm426485.htm>. Published December 10, 2014. Updated December 11, 2014. Accessed December 29, 2016.

²⁶ HPV (Human papillomavirus) VIS. Centers for Disease Control and Prevention Website. Published <http://www.cdc.gov/vaccines/hcp/vis/vis-statements/hpv.html>. Published February 2, 2016. Accessed December 29, 2016.

²⁷ Vaccines for Children (VFC). Centers for Disease Control and Prevention Website. <http://www.cdc.gov/vaccines/programs/vfc/awardees/vaccine-management/price-list/>. Updated February 1, 2016. Accessed October 24, 2016.

²⁸ Al Moustafa AE, Al-Awadhi R, Missaoui N, Adam I, Durusoy R, Ghabreau L, et al. Human papillomaviruses-related cancers presence and prevention strategies in the Middle East and North African regions. *Human Vaccines & Immunotherapeutic*. 2014; 10(7):1812-1821.

²⁹ Joura EA, Giuliano AR, Iversen O, Bouchard C, Mao C, Jesper M, et al. A 9-valent HPV vaccine against infection and intraepithelial neoplasia in women. *New England Journal of Medicine*. 2015; 372(8):711-723. doi: 10.1056/NEJMoa1405044.

³⁰ Petrosky E, Bocchini J, Hariri S, et al. Use of 9-valent human papillomavirus (HPV) vaccine: updated HPV vaccination recommendations of the Advisory Committee on Immunization Practices. *Morbidity and Mortality Weekly Report*. 2015; 64(11):300-304.

³¹ Gertig D, Brotherton J, Budd A, et al. Impact of a population –based HPV vaccination program on cervical abnormalities: a data linkage study. *BioMed Central Medicine*. 2013; 11(227):1-12. doi: 10.1186/1741-7015-11-227.

³² CDC recommends only two HPV shots for younger adolescents. Centers for Disease Control and Prevention Media Relations. <http://www.cdc.gov/media/releases/2016/p1020-hpv-shots.html>. Published October 19, 2016. Accessed October 24, 2016.

³³ 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. *Morbidity and Mortality Weekly Report*. 2016; 65:1405–1408. doi: 10.15585/mmwr.mm6549a5.

³⁴ Bonanni P, Cohey C, Kjaer, S, et al. A summary of the post-licensure surveillance initiatives for GARDASIL/SILGARD. *Vaccine*. 2010; 28(30):4719-4730.

³⁵ Ribeiro-Muller L, Muller M. Prophylactic Papillomavirus vaccines. *Clinics in Dermatology*. 2014; 34(2): 235-247. doi: 10.1016/j.clindermatol.2013.08.008.

³⁶ Brotherton J. Human papillomavirus vaccination: Where are we now? *Journal of Pediatrics and Child Health*. 2014; 50(12):959-965. doi: 10.1111/jpc.12627.

-
- ³⁷ Klein N, Hansen J, Chao C, Velicer C, et al. Safety of quadrivalent human papillomavirus vaccine administered routinely to females. *Archives of Pediatrics & Adolescent Medicine*. 2012; 166(12):1140-1148. doi: 10.1001/archpediatrics.2012.1451.
- ³⁸ Human papillomavirus vaccine: questions and answers. Centers for Disease Control and Prevention Website. <http://www.cdc.gov/hpv/parents/questions-answers.html>. Updated December 28, 2015. Accessed September 18, 2016.
- ³⁹ Human papillomavirus vaccines: World Health Organization position paper. *Weekly Epidemiological Record*. 2014; 89(43):465-492.
- ⁴⁰ Kreimer AR, Struyf F, Del Rosario-Raymundo MR, Hildesheim A, Skinner SR, Wacholder S, et al. Efficacy of fewer than three doses of an HPV-16/18 AS04-adjuvanted vaccine: combined analysis of data from the Costa Rica Vaccine and PATRICIA trials. *The Lancet Oncology*. 2015; 16:775-86. doi: 10.1016/S1470-2045(15)00047-9
- ⁴¹ Kreimer AR, Rodriguez AC, Hildesheim A, Herrero R, Porras C, Schiffman M, et al. CVT Vaccine Group. Proof-of-principle evaluation of the efficacy of fewer than three doses of a bivalent HPV16/18 vaccine. *Journal of the National Cancer Institute*. 2011; 103(19):1444-51. doi: 10.1093/jnci/djr319.
- ⁴² Sankaranarayanan R, Prabhu PR, Pawlita M, Gheit T, Bhatla N, Muwonge R, et al. Indian HPV Vaccine Study Group. Immunogenicity and HPV infection after one, two, and three doses of quadrivalent HPV vaccine in girls in India: a multicentre prospective cohort study. *Lancet Oncology*. 2016; 17:67-77. doi: 10.1016/S1470-2045(15)00414-3.
- ⁴³ Romanowski B, Schwarz TF, Ferguson L, Peters K, Dionne M, Behre Ue, et al. Sustained immunogenicity of the HPV-16/18 AS04-adjuvanted vaccine administered as a two-dose schedule in adolescent girls: five-year clinical data and modeling predictions from a randomized study. *Human Vaccines & Immunotherapeutics*. 2016; 12:20-9. doi: 10.1080/21645515.2015.1065363.
- ⁴⁴ Dobson SR, McNeil S, Dionne M, Dawar M, Ogilvie G, Krajden M, et al. Immunogenicity of 2 doses of HPV vaccine in younger adolescents vs 3 doses in young women: a randomized clinical trial. *Journal of the American Medical Association*. 2013; 309(17):1793-1802. doi: 10.1001/jama.2013.1625.
- ⁴⁵ Multiple vaccines and immune system. Centers for Disease Control and Prevention Website. <http://www.cdc.gov/vaccinesafety/concerns/multiple-vaccines-immunity.html>. Updated October 27, 2015. Accessed October 24, 2016.
- ⁴⁶ Vaccine ingredients- Aluminum. The Children's Hospital of Philadelphia Website. <http://www.chop.edu/centers-programs/vaccine-education-center/vaccine-ingredients/aluminum#.VseQx0bN4Yk>. Published November 04, 2014. Accessed December 29, 2016.
- ⁴⁷ Study reports Aluminum in vaccines poses extremely low risk to infants. U.S. Food and Drug Administration Website.

<http://www.fda.gov/BiologicsBloodVaccines/ScienceResearch/ucm284520.htm>. Updated February 6, 2015. Accessed July 21, 2016.

⁴⁸ Common ingredients in U.S. licensed vaccines U.S. Food and Drug Administration Website. <http://www.fda.gov/BiologicsBloodVaccines/SafetyAvailability/VaccineSafety/ucm187810.htm>. Published May 1, 2014. Updated December 31, 2014. Accessed February 17, 2016.

⁴⁹ Bruni L, Diaz M, Barrionuevo-Rosas L, et al. Global estimates of human papillomavirus vaccination coverage by region and income level: a pooled analysis. *Lancet Global Health*. 2016; 4(7):e453-63.

⁵⁰ Frequently Asked Questions about HPV Vaccine Safety. Centers for Disease Control and Prevention Website. http://www.cdc.gov/vaccinesafety/Vaccines/HPV/hpv_fags.html. Published July 23, 2014. Updated September 12, 2016. Accessed October 7, 2016.

⁵¹ Increase the vaccination coverage level of 3 doses of human papillomavirus (HPV) vaccine for females by age 13 to 15 years. Healthy People 2020 Website. https://www.healthypeople.gov/node/4657/data_details#revision_history_header. Updated February 09, 2016. Accessed December 29, 2016.

⁵² Reagan-Steiner S, Yankey D, Jeyarajah J, et al. National, regional, state, and selected local area vaccination coverage among adolescents aged 13–17 Years — United States, 2015. *Morbidity and Mortality Weekly Report*. 2016; 65:850–858. doi: 10.15585/mmwr.mm6533a4.

⁵³ Wong K, Do Y. Are there socioeconomic disparities in women having discussions on human papillomavirus vaccine with health care providers? *BioMed Central Women’s Health*. 2012; 12(33):1-7. doi:10.1186/1472-6874-12-33.

⁵⁴ Ge S, Gong B, Cai X, Yang X, Gan X, Tong X, et al. Prevent cervical cancer by screening with reliable human papillomavirus detection and genotyping. *Cancer Medicine*. 2012;1(1):59-67. doi: 10.1002/cam4.9.

⁵⁵ Stewart A. Childhood vaccine and school entry laws: the case of HPV vaccine. *Public Health Reports*. 2008; 123:801-803.

⁵⁶ Ryser M, McGoff K, Herzog D, Sivakoff D, Myer E. Impact of coverage dependent marginal costs on optimal HPV vaccination strategies. *Epidemics*. 2015; 11:32-47.

⁵⁷ Juedin P, Liveright E, Carmen M, Perkins R. Race, ethnicity and income as factors for HPV vaccine acceptance and use. *Human Vaccines & Immunotherapeutics*. 2013; 9(7):1413-1420.

⁵⁸ Young J, Bernheim R, Korte J, et al. Human papillomavirus vaccination recommendation may be linked to reimbursement: a survey of Virginia family practitioners and gynecologists. *Journal of Pediatric & Adolescent Gynecology*. 2011; 24:380–5.

-
- ⁵⁹ Hendry M, Lewis R, Clements A, Damery S, Wilkinson C. HPV? Never heard of it!: a systematic review of girls' and parents' information, views and preferences about human papillomavirus vaccination. *Vaccine*. 2013; 31(45):5152-5167.
- ⁶⁰ Trim K, Nagji N, Elit L, Roy K. Parental knowledge, attitudes, and behaviors toward human papillomaviruses vaccination for their children: a systematic review from 2001 to 2011. *Obstetrics and Gynecology International*. 2012; 2012:1-12. doi:10.1155/2012/921236.
- ⁶¹ Polonijo A, Carpiano R. Social inequalities in adolescent human papillomavirus vaccination: a test of fundamental cause theory. *Social Science and Medicine*. 2013; 82:115-125. doi: 10.1016/j.socscimed.2012.12.020.
- ⁶² Rosenthal S, Weiss T, Zimet G, Ma L, Good M, Vichnin M. Predictors of HPV vaccine uptake among women aged 19–26: importance of a physician's recommendation. *Vaccine*. 2011; 29:890–895.
- ⁶³ Vadaparampil ST, Murphy D, Rodriguez M, Malo TL, Quinn GP. Qualitative response to a national physician survey on HPV vaccination. *Vaccine*. 2013;31(18):2267-2272. doi: 10.1016/j.vaccine.2013.02.063.
- ⁶⁴ Vadaparampil ST, Kahn JA, Salmon D, Lee JH, Quinn GP, Roetzheim R, et al. Physicians' human papillomavirus vaccine recommendations, 2009 and 2011. *American Journal of Preventive Medicine*. 2014; 46(1):90-84. doi: 10.1016/j.amepre.2013.07.009.
- ⁶⁵ Vadaparampil ST, Kahn JA, Salmon D, Lee JH, Quinn GP, Roetzheim R, et al. Missed clinical opportunities: provider recommendations for HPV vaccination for 11-12 year old girls are limited. *Vaccine*. 2011; 29(47):8634-8641. doi: 10.1016/j.vaccine.2011.09.006.
- ⁶⁶ Addressing parents' top questions about HPV Vaccine. Centers for Disease Control and Prevention Website. <http://www.cdc.gov/vaccines/who/teens/for-hcp-tipsheet-hpv.html>. Published August 26, 2013. Updated August 26, 2013. Accessed December 29, 2016.
- ⁶⁷ Bocchini, J. Five key steps to improve vaccination rates in your practice [webinar]. Council of State and Territorial Epidemiologist/National Foundation for Infectious Diseases Webinar Series. December 9, 2014. http://c.ymcdn.com/sites/www.cste.org/resource/resmgr/Webinars/Five_Key_Steps_to_Improve_HP.pdf. Accessed December 29, 2016.
- ⁶⁸ Gilkey MB, Malo TL, Shah PD, Hall ME, Brewer NT. Quality of physician communication about human papillomavirus vaccine: findings from a national survey. *Cancer Epidemiology, Biomarkers and Prevention*. 2015; 24(11):1-8. doi: 10.1158/1055-9965.Epi-15-0326.
- ⁶⁹ Gerend M, Shepherd M, Lustria M, et al. Predictors of provider recommendations for HPV vaccine among young adult men and women: findings from a cross-sectional survey. *Sexually Transmitted Infections*. 2016; 92(2):104-107

-
- ⁷⁰ Goff S, Mazor K, Gagne S, Corey K, Blake D. Vaccine counseling: a content analysis of patient-physician discussions regarding human papillomavirus vaccine. *Vaccine*. 2011; 29(43):7343-7349. doi: 10.1016/j.vaccine.2011.07.082.
- ⁷¹ Hoffstetter A, Rosenthal S. Factors impacting HPV vaccination: lessons for health care professionals. *Vaccines*. 2014; 13(8):1013-1026
- ⁷² Daley M, Crane L, Markowitz L, et al. Human papillomavirus vaccination practices: a survey of US physicians 18 months after licensure. *Pediatrics*. 2010; 128(3):425-433
- ⁷³ Noronha A, Markowitz L, Dunne E. Systematic review of human papillomavirus vaccine coadministration. *Vaccine*. 2014; 32(23):2670-2674. doi: 10.10/j.vaccine.2013.12.037.
- ⁷⁴ Wheeler C, Harvey B, Pichichero M, et al. Immunogenicity and safety of human papillomavirus- 16/18 AS04-adjuvanted vaccine coadministered with tetanus toxoid, reduced diphtheria toxoid, and acellular pertussis vaccine and/or meningococcal conjugate vaccine to healthy girls 11 to 18 years of age: results from a randomized open trial. *The Pediatric Infectious Disease Journal*. 2011; 30(12):e225-e234. doi: 10.1097/INF.0b013e31822d28df.
- ⁷⁵ Wong C, Taylor J, Wright J, Opel D, Katzenellenbogen R. Missed opportunities for adolescent vaccination, 2006-2011. *Journal Adolescent Health*. 2013;53(4):492-7.
- ⁷⁶ Gilkey MB, Moss JL, Coyne-Beasley T, Hall ME, Shah PD, Brewer NT. Physician communication about adolescent vaccination: how is human Papillomavirus vaccine different? *Preventive Medicine*. 2015; 77:181-185. doi: 10.1016/j.ypmed.2015.05.024.
- ⁷⁷ Dunne EF, Stokley S, Chen W, Zhou F. Human Papillomavirus vaccination of females in a large claims database in the United States, 2006-2012. *The Journal of Adolescent Health*. 2015; 56:408-413.
- ⁷⁸ Think About the Link education awareness campaign: Survey Research Executive Summary. Prevent Cancer Foundation Website. <http://preventcancer.org/wp-content/uploads/2016/01/TATL-Campaign-Research-Executive-Summary.pdf>. Published January 2016. Accessed December 29, 2016.
- ⁷⁹ Bynum SA, Staras SA, Malo TL, Giuliano AR, Shenkman E, Vadaparampil ST. Factors associated with Medicaid providers' recommendation of the HPV vaccine to low-income adolescent girls. *Journal of Adolescent Health*. 2014; 54(2):190-196. doi: 10.1016/j.jadohealth.2013.08.006.
- ⁸⁰ Perkins RB, Clark JA, Apte G, Vercruyse JL, Sumner JJ, Wall-Haas CL. Missed opportunities for HPV vaccination in adolescent girls: a qualitative study. *Pediatrics*. 2014; 134:666-674. doi: 10.1542/peds.2014-0442.
- ⁸¹ Rambout L, Tashkandi M, Hopkins L, Tricco A. Self-reported barriers and facilitators to preventive human papillomavirus vaccination among adolescent girls and young women: a systematic review. *Preventive Medicine*. 2014; 58:22-32. doi: 10.1016/j.ypmed.2013.10.009.

-
- ⁸² Small S, Sampsel C, Martyn K, Dempsey A. Modifiable influences on female HPV vaccine uptake at the clinic encounter level: a literature review. *Journal of American Association of Nurse Practitioners*. 2014; 26(9):519-525. doi: 10.1002/2327-6924.12057.
- ⁸³ Price list: affordable health in your neighborhood. CVS Pharmacy Website. <http://www.cvs.com/minuteclinic/services/price-lists#vaccination>. Updated May 1, 2015. Accessed September 21, 2016.
- ⁸⁴ Pourat N, Jones J. Role of insurance, income and affordability in human papillomavirus Vaccination. *American Journal of Managed Care*. 2012; 18(6):320-330.
- ⁸⁵ Malo TL, Hassani D, Staras SA, Vadaparampil S. Do Florida Medicaid providers' barriers to HPV vaccination vary based on VFC Program participation? *Maternal and Child Health Journal*. 2013;17(4):609-615. doi: 10.1007/s10995-012-1036-5.
- ⁸⁶ Keating KM¹, Brewer NT, Gottlieb SL, Liddon N, Ludema C, Smith JS. Potential barriers to HPV vaccine provision among medical practices in an area with high rates of cervical cancer. *Journal of Adolescent Health*. 2008; 43(4):S61-S67. doi: 10.1016/j.jadohealth.2008.06.015.
- ⁸⁷ Gerend M, Shepherd M, Liza M, Lustria L. Increasing human papillomavirus vaccine acceptability by tailoring messages to young adult women's perceived barriers. *Sexually Transmitted Diseases*. 2013; 40(5):401-405. doi: 10.1097/OLQ.0b013e318283c8a8.
- ⁸⁸ Zimet G, Rosberger Z, Fisher W, Perez S, Stupiansky N. Beliefs, behaviors and HPV vaccine: correcting the myths and the misinformation. *Preventive Medicine*. 2013; 57(5):414-418. doi: 10.1016/j.ypmed.2013.05.013.
- ⁸⁹ Tan T, Bhattacharaya L, Gerbie M. Awareness, perceptions and knowledge of recommended adult vaccines among a nationwide sample of adult primary care providers. *Journal of Reproductive Medicine*. 2011; 56(7):301-307
- ⁹⁰ Brownson RC, Seiler R, Eyer A. Measuring the impact of public health policy. *Preventing Chronic Disease*. 2010; 7(4):A77-84.
- ⁹¹ Meyerson B, Lawrence C, Smith J. Attend to the "Small p" stuff: state policy issues affecting cervical cancer efforts. *Open Journal of Obstetrics and Gynecology*. 2014; 4:455-461.
- ⁹² Affordable Care Act implementation FAQs – Set 12. Centers for Medicare and Medicaid Services Website. http://www.cms.gov/CCIIO/Resources/Fact-Sheets-and-FAQs/aca_implementation_faqs12.html. Accessed December 29, 2016.
- ⁹³ Dillard, C. Achieving universal vaccination against cervical cancer in the United States: the need and the means. *Guttmacher Policy Review*. 2006; 9(4):12-16.

-
- ⁹⁴ License for use of current procedural terminology, Fourth Edition (“CPT”). Centers for Medicare and Medicaid Services Website. <https://www.cms.gov/apps/physician-fee-schedule/search/search-results.aspx?Y=0&T=0&HT=0&CT=3&H1=90473&M=5>. Accessed December 29, 2016.
- ⁹⁵ Lipton B, Decker S. ACA provisions associated with increase in percentage of young adult women initiating and completing the HPV vaccine. *Health Affairs*. 2015; 34(5):757-764.
- ⁹⁶ Vaccines for Children Program (VFC). Centers for Disease Control and Prevention Website. <http://www.cdc.gov/vaccines/programs/vfc/about/index.html>. Published August 31, 2012. Updated February 14, 2014. Accessed December 29, 2016.
- ⁹⁷ Human papillomavirus (HPV) vaccines. National Cancer Institute Website. <http://www.cancer.gov/cancertopics/factsheet/prevention/HPV-vaccine>. Published December 29, 2011. Accessed December 29, 2016.
- ⁹⁸ State coverage of preventive services for women under Medicaid: findings from a state-level survey. Kaiser Family Foundation Website. <http://kaiserfamilyfoundation.files.wordpress.com/2013/01/8330.pdf>. Published November 2012. Accessed December 28, 2016.
- ⁹⁹ Questions answered on vaccines purchased with 317 funds. Centers for Disease Control and Prevention Website. <http://www.cdc.gov/vaccines/imz-managers/guides-pubs/qa-317-funds.html>. Published October 26, 2012. Updated July 19, 2013. Accessed December 29, 2016.
- ¹⁰⁰ Merck Vaccine Patient Assistance Program. Merck Help Website. <http://www.merckhelps.com/Programs.aspx>. Accessed December 29, 2016.
- ¹⁰¹ State mandates on immunization and vaccine-preventable diseases. Immunization Action Coalition Website. <http://www.immunize.org/laws/>. Accessed December 29, 2016.
- ¹⁰² Giffin R, Stratton K, and Chalk R. Childhood vaccine finance and safety issues. *Health Affairs*. 2004; 23(5):98-111. doi: 10.1377/hlthaff.23.5.98.
- ¹⁰³ Stewart A, Cox M. HPV vaccine school entry requirements: confronting the myths, misperceptions and misgivings. *Journal of Health and Biomedical Law*. 2008; 4:311-332.
- ¹⁰⁴ Policies and Regulations. Virginia Beach City Public Schools Website. http://www.vbschools.com/policies/5-10_1r.asp. Published July 16, 1993. Updated July 7, 2014. Accessed December 29, 2016.
- ¹⁰⁵ Human papillomavirus (HPV) vaccination opt-out certificate. Government of the District of Columbia Department of Health Website. <http://doh.dc.gov/sites/default/files/dc/sites/doh/HPV%20Opt-Out%202015-2016%20FINAL.pdf>. Updated January, 2015. Accessed December 29, 2016.

-
- ¹⁰⁶ Borg, L. Rhode Island to mandate HPV vaccine for all 7th graders. Providence Journal. July 28, 2015. <http://www.providencejournal.com/article/20150728/NEWS/150729287>. Accessed September 30, 2016.
- ¹⁰⁷ Calo WA, Gilkey MB, Shah PD, Moss JL, Brewer NT. Parents' support for school-entry requirements for human papillomavirus vaccination: a national study. *Cancer Epidemiology, Biomarkers & Prevention*. 2016; 25(9):1317-25. doi: 10.1158/1055-9965.EPI-15-1159
- ¹⁰⁸ Tompa R. HPV vaccines work, so why do so few states require them? Fred Hutch Cancer Research Center. July 17, 2015. <https://www.fredhutch.org/en/news/center-news/2015/07/why-few-states-require-HPV-vaccines.html>. Accessed October 10, 2016.
- ¹⁰⁹ 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. *Human Vaccines & Immunotherapeutics*. 2016; 12(6):1615-1622. doi: 10.1080/21645515.2016.1150394.
- ¹¹⁰ Cuff RD, Buchanan T, Pelkofski E, Korte J, Modesitt SP, Pierce JY. Rates of human papillomavirus vaccine uptake amongst girls five years after introduction of statewide mandate in Virginia. *American Journal of Obstetrics and Gynecology*. 2016; 214(6):752.e1-752.e6. doi: 10.1016/j.ajog.2016.03.022.
- ¹¹¹ Pierre-Victor D, Page TF, Trepka MJ, Stephens DP, Li T, Madhivanan P. Impact of Virginia's school-entry vaccine mandate on human papillomavirus vaccination among 13-17-year-old females. *Journal of Women's Health*. October 2016, ahead of print. 2016; 214(6),752.e1-752.e6. doi: 10.1089/jwh.2016.5869.
- ¹¹² The HPV vaccine: access and use in the U.S. Keiser Family Foundation Website. <http://kff.org/womens-health-policy/fact-sheet/the-hpv-vaccine-access-and-use-in/>. Published September 3, 2015. Accessed July 21, 2016.
- ¹¹³ Society for Adolescent Health and Medicine, English A, Ford CA, Kahn JA, Kharbanda EO, Middleman AB. Adolescent consent for vaccination: a position paper of the Society for Adolescent Health and Medicine. *Journal of Adolescent Health*. 2013; 53(2013): 550-553. doi: 10.1016/j.jadohealth.2013.07.039.
- ¹¹⁴ Stewart, A., Cox, M., Rosenbaum, S. The epidemiology of U.S. immunization law. Translating CDC immunization guidelines into practice: state laws related to the use of standing orders covering immunization practice. http://hsrc.himmelfarb.gwu.edu/sphhs_policy_facpubs/289/. Published November 2005. Accessed December 29, 2016.
- ¹¹⁵ Pharmacist administered vaccines [presentation]. American Pharmacists Association. January 31, 2015. http://www.pharmacist.com/sites/default/files/files/Pharmacist_IZ_Authority_1_31_15.pdf. Accessed December 29, 2016.

-
- ¹¹⁶ Rothholz, Mitchel, Litjen L J Tan. Promoting the immunization neighborhood: benefits and challenges of pharmacies as additional locations for HPV vaccination. *Human Vaccines & Immunotherapeutics*. 2016; 12(6):1646-1648.
- ¹¹⁷ Dunne EF, Markowitz LE, Saraiya M, Stokley S, Middleman A, Unger ER, et al. CDC Grand Rounds: reducing the burden of HPV- Associated Cancer and Disease. *Morbidity and Mortality Weekly Report*. 2014; 63(04):69-72
- ¹¹⁸ Smulian EA, Mitchell KR, Stokley S. Interventions to increase HPV vaccination coverage: A systematic review. *Human Vaccines & Immunotherapeutics*, 2016; 12(6):1566-88. doi: 10.1080/21645515.2015.1125055.
- ¹¹⁹ Szilagyi PG, Albertin C, Humiston SG, Rand CM, Schaffer S, Brill H, et al. A randomized trial of the effects of centralized reminder/recall on immunizations and preventive care visits for adolescents. *Academic Pediatrics*. 2013; 13(3):204-213.
- ¹²⁰ Chao C, Preciado M, Slezak J, Lanfang X. A randomized intervention of reminder for human papillomavirus vaccine series completion. *Journal of Adolescent Health*. 2014; 56(2015):85-90.
- ¹²¹ Social Ecological Model: a framework for prevention. Centers for Disease Control and Prevention Website. <http://www.cdc.gov/violenceprevention/overview/social-ecologicalmodel.html>. Published December 27, 2013. Updated March 25, 2015. Accessed December 29, 2016.
- ¹²² Wolfe R, Sharp L. Anti-vaccinationists past and present. *British Medical Journal*. 2002; 325:430-432.
- ¹²³ Dube E, Vivion M, MacDonald N. Vaccine hesitancy, vaccine refusal and the anti-vaccine movement: influence, impact and implications. *Expert Reviews*. 2015; 14(1):99-17. doi:10.1586/14760584.2015.964212.
- ¹²⁴ Wolfe R, Sharp L, Martin L. Content and design attributes of antivaccination websites. *The Journal of the American Medical Association*. 2002; 287(24):3245-3248. doi: 10.1001/jama.287.24.3245.
- ¹²⁵ Winnike A. History of compulsory immunization laws and the development of the anti-vaccine movement [webinar]. University of Houston Law Center. November 20, 2014. https://www.networkforphl.org/_asset/8gb0c9/Immunization-Laws-Webinar-11-4-14.pdf. Accessed December 29, 2016.