

WHY IT IS IMPORTANT TO INCREASE HPV VACCINATION UPTAKE AMONG
US ADOLESCENTS AGES 11-14 FOR THE PREVENTION OF HPV-ASSOCIATED
CANCERS

By

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DEDICATION

This work is dedicated to all who have suffered, are suffering or are at risk for Human Papillomavirus associated cancers. The goal is to bring awareness to the importance of protecting our youth ages 11-14 years old against HPV through full vaccination to prevent HPV associated cancers. There are many barriers to HPV vaccination that exist, but with the proper public health implementations they can be overcome.

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ABSTRACT

This research analysis provides an overview of why it is important to increase Human papillomavirus (HPV) vaccination uptake among adolescents ages 11-14 for the prevention of HPV-associated cancers within the United States. HPV is a sexually transmitted infection that affects a high proportion of adolescents shortly after becoming sexually active. HPV is known to cause various types of cancers over time. Unfortunately, only cervical cancer can be detected early through a screening test. The other cancers caused by HPV can go undetected until they become more serious. The best preventive measure against HPV is the HPV vaccine starting early at ages 11-14 years. However, while HPV vaccine coverage among US adolescents ages 11-14 has increased recently, it still remains low in comparison to other vaccines.

METHODS

MEDLINE/PubMed, The Journal of Infectious Diseases, JAMA Network Open, National Cancer Institute, and the International Journal of Environmental Research and Public Health database searches were conducted for US-based original research articles and studies to examine the ins and outs of HPV vaccination among adolescents within the United States. In addition, I reviewed information from The Center for Disease Control and Prevention. The search focused on identifying why it is important to increase HPV vaccination uptake among adolescents 11-14 years old for the prevention of HPV- associated cancers. Overall, 15 of the most relevant research articles and studies were included in this analysis, providing evidence-based research on what future efforts could prevent HPV-associated cancers in the United States.

INTRODUCTION

Human papillomavirus (HPV) is the most common sexually transmitted infection within the United States. There is no known cure for HPV infection, only treatment to control the related health effects from it. HPV is easy to contract through skin-to-skin contact. This includes vaginal, anal, and oral sex. Almost all HPV infections are transmitted sexually.

There are 6 million new HPV infections each year in the United States, but most people never know they are infected, making this public health concern an endemic.¹ That means nearly every American may be infected with HPV at some point in their life. The best preventive measure against HPV is vaccination of our youth because HPV vaccine works best when received before someone has the chance to becoming exposed to the virus. Yet only a little over half of adolescents ages 11-14 are up to date on HPV vaccination in the United States.¹

HPV infection often clears within 1 to 2 years on its own, but persistent HPV infections can lead to both precancers and cancers. There are more than 100 varieties of HPV that fall into two categories, low risk and high risk.¹ Certain types of low-risk HPV strains cause warts, while high-risk HPV strains can cause various HPV-associated cancers. Out of 14 types of high-risk HPV strains, HPV 16, and HPV 18 lead to majority of HPV-associated cancers.¹ Cancers of the cervix, vulva, vagina, penis, anus, and oropharynx all can develop due to HPV infection. Cervical cancer used to be the leading cause of cancer death for women in the United States.¹ Over the years, the number of cases of cervical cancer and the number of deaths from it in women has decreased but it remains a public health concern. Some high-risk HPV types cause a greater percentage of cervical cancer than others (See Table 1). HPV accounts for roughly 36,000 cases of cancer each year in the United States.¹ This is why it is crucial to bring

awareness to the importance of increasing HPV vaccination uptake among adolescents ages 11-14 years old, to reduce the number of HPV-associated cancers in the United States.

TABLE 1. High-risk HPV types and the percent of cervical cancer they cause

High-risk HPV Types	% of Cervical Cancer Caused
16,18	70%
31,33,35,45,52,58	20%
39,51,56,59,66,68	10%

Source: (<https://www.cdc.gov/cancer/cervical/statistics/>)

(This table represents high-risk HPV types combined and the percent of cervical cancer they cause together, not individually)

HISTORY OF THE VACCINE RECOMMENDATIONS

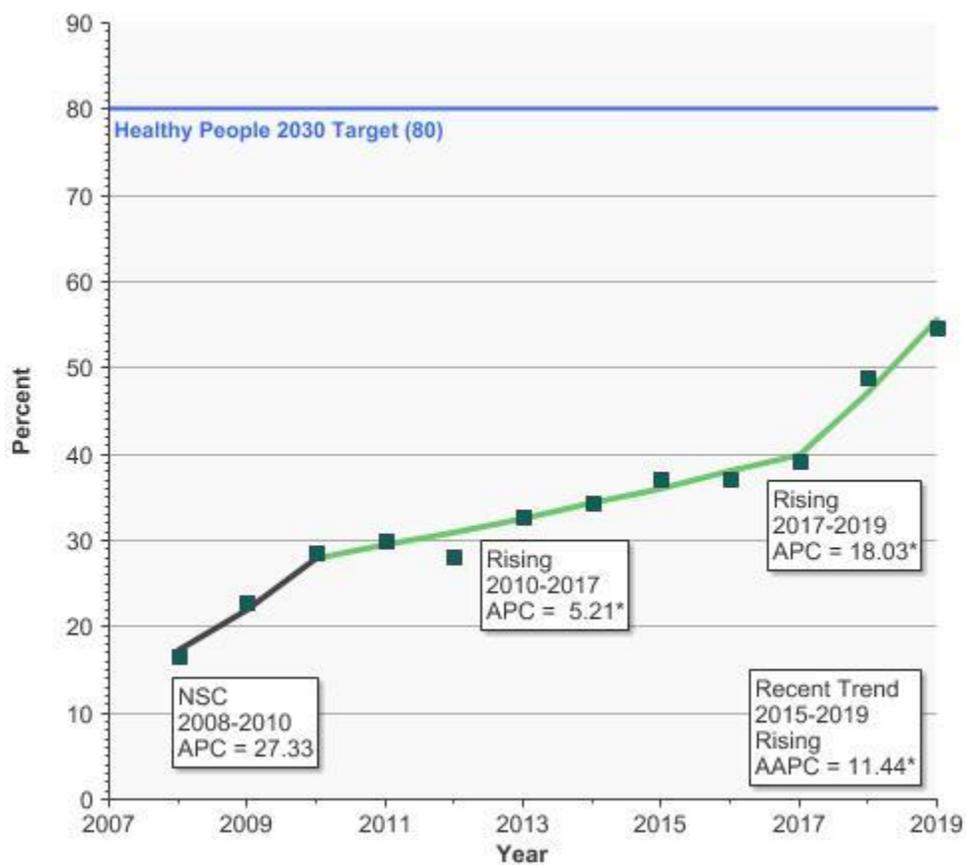
Many organizations develop vaccine recommendations. The Center for Disease Control and Prevention's (CDC) Advisory Committee on Immunization Practices (ACIP) is the most authoritative for developing all vaccination recommendations in the United States, including the use of HPV vaccines. When the HPV vaccine HPV4 (Gardasil) was first introduced to the United States in 2006, it was recommended for routine vaccination for females ages 11 to 12 years old by the ACIP as a form of cervical cancer prevention.² In 2009 the ACIP extended their recommendations to include males ages 11 to 12 years old.² However, the HPV vaccine may be given as early as age 9. In 2011, the ACIP extended their recommendations again for females aged 13 to 26 years old, and males aged 13 through 21 years old who have not been previously vaccinated.² Depending on the opinion of one's primary health provider individuals aged 27-45 years old may still be able to get the HPV vaccine although by that age most people will not

benefit from it.² (See Table 2 for the full history of HPV recommendations made by the ACIP over the years.)

The standard dose schedule for HPV4 and HPV9 vaccines require a 3-dose series of shots.² It can be reduced to 2 doses of the HPV4 and HPV9 if taken before the age of 15 years old in the span of 6 to 12 months apart.² Any adolescent who does not receive the HPV vaccine until after 15 years old is recommended three doses by the ACIP.³ The second dose is recommended to be given 1-2 months after receiving the first dose, and the third dose is recommended to be given 6 months after the first dose.² The U.S. Food and Drug Administration (FDA) approved a total of three HPV vaccines over the past several years. HPV4 was approved by the FDA in 2006, HPV2 (Cervarix) was the second HPV vaccine approved by the FDA in 2009, and HPV9 (Gardasil-9) was the final HPV vaccine approved by the FDA in 2014.² All three vaccines target high risk HPV 16 and 18.² HPV9 targeted additional low and high-risk HPV types and has replaced HPV4. HPV2 never provided protection for the prevention of any low-risk HPV types, so the manufacturers of HPV2 withdrew their vaccine due to the financial concerns from steep competition.²

As of 2016, HPV9 is the only vaccine distributed within the United States. It protects against HPV types 6, 11 that cause genital warts as well as additional high risk HPV types 31, 33, 45, 53, and 58 for the prevention of HPV associated cancers.³ The ACIP has changed their recommendations in the United States since introducing the HPV vaccine to cover 90% of HPV-associated cancers within the United States.³ Despite, the ACIP routine recommendations made to encourage full vaccination against HPV in adolescents, the HPV vaccination uptake is just beginning to gradually improve (See Figure 1).

FIGURE 1. Percent of adolescents aged 13-15 years who had received 2 or 3 doses of the HPV vaccine as recommended at time of immunization, 2008-2019



Source: (https://progressreport.cancer.gov/prevention/hpv_immunization)

Abbreviation: ACCP = Average Annual Percent Change, APC = Annual Percent Change

TABLE 2. ACIP recommendations for HPV vaccination, 2006-2019

ACIP recommendations 2006	Females: Routine vaccination series of three doses recommended at age 11 to 12 years old and up until 26 years old, if the individual has not been vaccinated before.
ACIP recommendations 2009	Males: Routine vaccination series of three doses recommended at age 11 to 12 years old, and up until 21 years old.
ACIP recommendations 2011	<p>Females: Routine vaccination series of three doses recommended at age 11 to 12 years old.</p> <p>Males: Routine vaccination series if three doses recommended at age 11 to 12 years old and up until 21 years old, if not vaccinated before. Vaccination is also recommended for men who are sexually active with men and for men who are immunocompromised (including those infected by HIV) up until 26 years old.</p>

ACIP recommendations 2016	The ACIP reduced the recommended doses from three to two for females and males under 15 years old.
ACIP recommendations 2019	Females and Males: Recommended three series doses catch up HPV vaccination for all individuals up until 26 years old. ACIP also recommended clinical decision making regarding catch up vaccination for adults 27 through 45 years old.

Source: (<https://www.cdc.gov/vaccines/hcp/acip-recs/vacc-specific/hpv.html>)

Abbreviation: ACIP = Advisory Committee on Immunization Practices

EFFECTIVENESS AND SAFETY OF THE VACCINE

Over 15 years of monitoring and research has gone into ensuring that the HPV vaccination is safe, effective and provides long lasting protection from cancers caused by HPV. In the United States there are three different systems the safety of all vaccinations goes through. The first one is the Vaccine Adverse Events Reporting System (VAERS) that allows anyone to submit a report about any adverse events they are experiencing from the vaccine.⁴ Adverse events are defined as any health problems that occurs after a vaccine and requires immediate medical attention.⁴ Next, Vaccine Safety Datalink (VSD) is a project between the CDC and other healthcare organizations responsible for monitoring the safety of vaccines and conducts extensive vaccine safety assessments.⁴ Finally, Clinical Immunization Safety Assessment Project (CISA) is responsible for conducting clinical research and evaluates adverse events after vaccination.⁴ HPV4, HPV9, and HPV2 were each studied thoroughly in clinical trials for

effectiveness and safety. HPV4 was studied in a clinical trial with over 29,000 females and males, HPV9 was studied in a clinical trial with over 15,000 females and males, and HPV2 was studied in a clinical trial with over 30,000 females.⁴ All three vaccines were deemed safe and effective. In fact, findings from more than 160 studies revealed that each one of the HPV vaccines consisted of an excellent safety profile with little to no adverse events occurring after vaccination.⁴ Besides being safe, the HPV vaccines work very well against preventing HPV-associated cancers. Since the HPV vaccine was introduced in 2006 it reduced HPV-associated cancers by 88% and genital warts among females decreased by 61%.⁴ Efficacy of each HPV vaccine has been determined to be close to 100% in preventing HPV infections leading to precancers, cancers and genital warts.⁴ On top of that, HPV vaccination delivers long-lasting protection. People who get vaccinated against HPV remain protected for more than ten years, with no record of the protection from the vaccine declining over time.⁴ Without doubt HPV vaccines are safe and effective. Research has concluded the HPV vaccine does not work against any HPV type in one who is already infected with it. Therefore, the sooner it is received among adolescents ages 11- 14 the better for reaching herd immunity, limiting the further spread of the infection in the United States.

STATISTICS ON THE UNDERUSE OF THE VACCINE

Although there is evidence displaying the safety and effective of the vaccine, HPV vaccination remains underutilized for adolescents 11-14 years old. A 2019 study involving a total of 20,475 adolescents revealed that only 16% of adolescents in the United States completed HPV vaccination before turning 13 years old.⁵ The study also revealed only 35% of adolescents completed HPV vaccination before the age of 15 years old.⁵ 44% of males and 35% of females never initiated HPV vaccination before the ages 13-15 years old.⁵ This is a concern considering

the National Survey of Family Growth estimates that 11% of males and 16% of females are sexually active by the time they turn 15 years old.⁵

For both age points in this study, female adolescents had a higher rate of completed HPV vaccination than males. In one study, 20.1% of females completed HPV vaccination before 13 years of age compared to 11.6% of male adolescents.⁵ Before 15 years of age 41.6% female adolescents completed HPV vaccination, compared to 28.3% of males (See Table 3).⁵ Statistics on completed HPV vaccination for adolescents 11-14 years old varies based on sex, race, and income. Hispanics had the highest rate of completed HPV vaccination before the ages of 13 and 15 years old compared to other ethnicities. 18.9% of Hispanic adolescents were fully vaccinated against HPV before turning age 13 compared to 14.1% of Caucasians, 16.6% of African Americans, and 16.1% of other ethnicities.⁵ Hispanic adolescents continued to take the lead for full vaccination against HPV before turning age 15 at 41.3% versus 31.1% of Caucasians, 36.9% of African Americans and 36.2% of other ethnicities adolescents.⁵ Moreover, adolescents living below the poverty level had a higher level of completed HPV vaccination than adolescents living at/above the poverty level prior to becoming 13 and 15 years of age (See Table 3).⁵

TABLE 3. 2016 HPV status among US adolescents before ages 13 and 15

Characteristics	Percentage UTD on HPV vaccination prior to age 13	Percentage that never initiated HPV vaccination prior to age 13
Below poverty level	19.6	29.8
At/above poverty level	14.7	42.7
Male	11.6	44.0
Female	20.1	35.0
Characteristics	Percentage UTD on HPV vaccination prior to age 15	Percentage that never initiated HPV vaccination prior to age 15
Below poverty level	42.1	29.8
At/above poverty level	32.8	42.7
Male	28.3	44.0
Female	41.6	35.0

Abbreviation: UTD = Up To Date

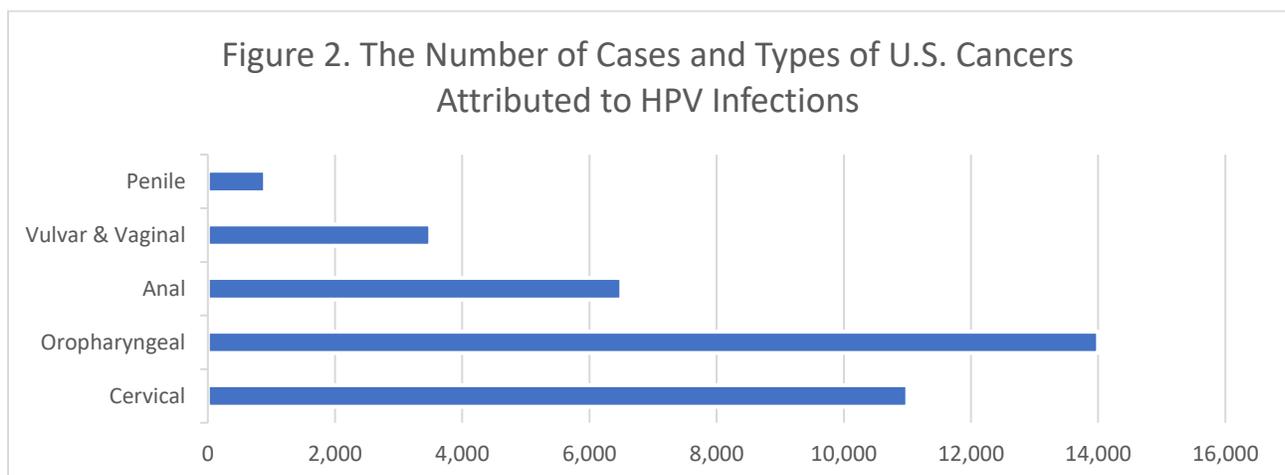
Source: (Bednarczyk et al., 2019)

THE AMOUNT OF HPV- ASSOICATED CANCERS THE VACCINE COULD PREVENT

HPV vaccination could prevent more than 90% of cancers caused by HPV, which causes an estimated 36,000 cases of cancer in the United States per year.⁶ Cervical cancer is the only cancer caused by HPV that can be detected early through a screening test, a pap smear. A pap

smear tests for abnormal cells in the cervix caused by HPV infection that have the possibility of turning into cervical cancer and is recommended for women starting at age 21. Cancers of the vulva, vagina, penis, anus, and oropharynx are all caused by HPV infections, and cannot be detected early in females or males. As a result, those cancers usually remain hidden until they have developed into a more serious stage that is harder to treat.

The number of HPV-associated cancers is steadily on the rise. Cervical cancer once was the most common cancer linked to HPV, but as of today oropharyngeal cancer cases have surpassed cervical cancer cases. Recent data determined 14,000 cases of oropharyngeal cancer and 11,000 cases of cervical cancers are linked to HPV.⁷ HPV infections cause an estimated 70% of oropharyngeal cancers, 70% of cervical cancers, over 90% of anal cancers, over 60% of penile cancers, 75% of vaginal cancers and 70% vulvar cancers (See Figure 2).⁷ The World Health Organization (WHO) has a goal of achieving 80% HPV vaccination coverage among girls aged 9-14 years old to reduce the risk of HPV infection by 2030.⁸ Widespread use of the HPV vaccine is going to be key in reducing both the incidence and prevalence rate of HPV-associated cancer cases each year in the United States.



Source: (Acampora et al., 2020)

WHY THE VACCINE IS UNDERUSED

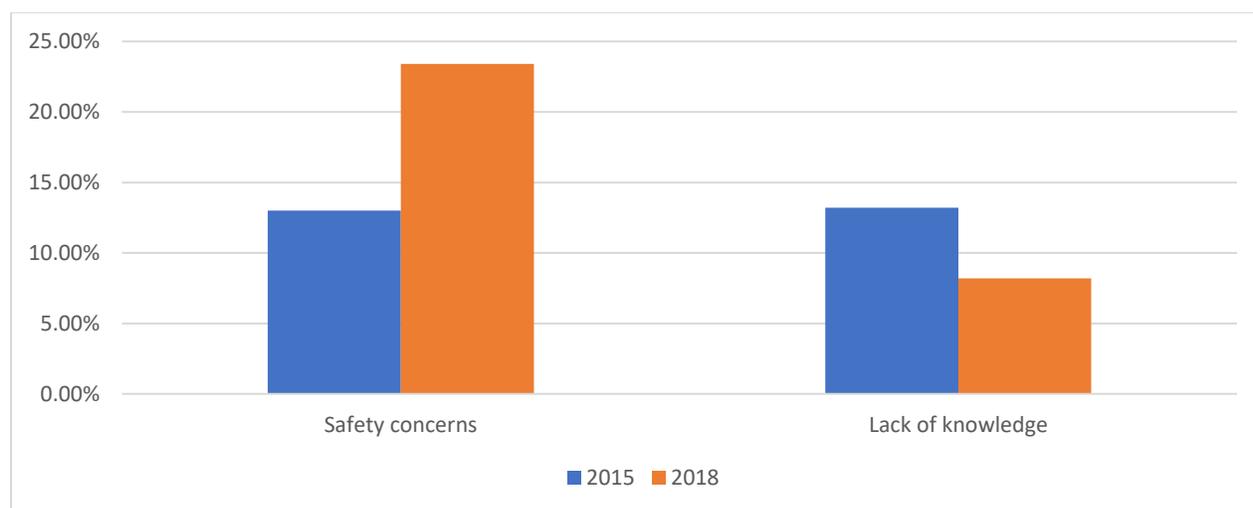
Regardless of the reliable evidence supporting the effectiveness and safety of HPV vaccines, parents are still declining HPV vaccination for their children due to safety concerns and the lack of knowledge on the HPV vaccine itself. Data from the 2015 to 2018 National Immunization Survey-Teen (NIS) indicated that almost all parents had doubts about the safety of HPV vaccines.⁹ In the United States the NIS-Teen is a randomized telephone survey collecting the immunization status of adolescents aged 13 to 17 years old reported by parents. The NIS-Teen was completed by the parents of 39,364 unvaccinated adolescents with a mean age of 15 years old.⁹ The survey was used to identify the main reasons behind low HPV vaccination rates. Parents of unvaccinated adolescents were asked if they planned to vaccinate their child in the next 12 months. Any parent who responded with “No”, “Not too likely”, and “Don’t know/not sure” was asked a sequence of additional questions to distinguish the primary reasons for HPV vaccine hesitancy.⁹ Responses of those parents were recoded and categorized into 28 categories.⁹ Safety concerns and lack of knowledge were the top two reasons that made up almost 60% of HPV vaccine hesitancy by parents.⁹ The proportion of adolescents whose parents’ main uncertainty was because of “Safety concerns” increased from 13.0% to 23.4% from 2015 to 2018.⁹ Parents of adolescents who cited “Lack of knowledge” reasons for HPV vaccine uncertainty decreased between 2015 to 2018. “Lack of knowledge” decreased from 13.2% to 8.2% (See Figure 3).⁹

The rise in safety concerns may have resulted from several different factors, especially misinformation from social media. In a 2017 study, parents who had seen or heard negative things about the HPV vaccine via social media were over 50% more likely to refuse the HPV vaccine for their child than parents who had not.¹⁰ Unfortunately, false reports of adverse

reactions to the HPV vaccine have been circulating on social media for years that may have led parents to believe the vaccine is unsafe. In reality, reports of health issues following HPV vaccination were extremely rare from 2015 to 2018, yet it still affected parents perception of the HPV vaccine.¹¹

The slight decrease between “Lack of knowledge” reported by HPV in hesitant parents is correlated with public health efforts to educate and inform people about the benefits of vaccines. Education is a major key to improving HPV vaccination uptake among adolescents, by giving comfort to parents.¹¹ Nonetheless, these findings highlight the importance and challenges of improving vaccine confidence to increase HPV vaccination among adolescents 11-14 years old.

FIGURE 3. Change in top 2 reasons for HPV vaccine hesitancy from parents 2015 to 2018



Source: (Sonawane et al., 2020)

HPV VACCINE POLICY PROPOSALS

HPV vaccination requirement for school entry has been a controversial topic in the United States, because it touches on teenage sexuality. The public's negative perception about HPV being a sexually transmitted infection makes it difficult to make HPV vaccine mandatory for school admission. People who oppose HPV vaccine being mandated for school entry feel that it limits a parent's right to discuss sexuality with their children on their own terms.¹² Others are also concerned that mandatory HPV vaccination will encourage teenage sexual activities, although the evidence available disproves this claim.¹² Vaccine requirements for school entry has been proven to be a great method for increasing youth immunization rates and decreasing the incidence of preventable diseases.¹² In the past 10 years, 42 states in America have seen legislation proposed on HPV vaccination requirements for school entry, but most were unsuccessful.¹² Texas was the first state to require HPV vaccination in 2007.¹² That was until legislature overrode the decision the following year due to extreme outrage.¹² Now, a minimum of three jurisdictions require adolescents to obtain the HPV vaccine for school entry like Virginia, Rhode Island, and District of Columbia.¹² All three jurisdictions have broad exemptions to the HPV vaccination requirement, making it more practical when issues arise that prevent vaccination. In Rhode Island, students can be made exempt from the vaccine if a medical professional approves, or a parent insists that it conflicts with their religious beliefs.¹² Having exemptions to school vaccine requirements is necessary for the comfort of parents.

WHY HPV VACCINE POLICY CHANGE IS NEEDED

School vaccine requirements increase the percent of children vaccinated and decrease the incidence of vaccine preventable disease.¹³ Of the three U.S. jurisdictions that passed HPV vaccine mandates, Rhode Island has the highest HPV vaccination rates for both male and female

adolescents resulting from their school requirement on August 1, 2015.¹⁴ In Rhode Island, 91% of adolescents reported being up to date with HPV vaccination before age 13.¹⁵ Overall, the states with policies requiring HPV vaccine as a school requirement had considerably higher HPV vaccination completion rates for adolescents before the age of 13 than the nearby states that do not have an HPV vaccine school requirement policy in place.¹⁵ Policy changes can make a huge difference in the health of all by reducing the risk of up to 90% of cancers attributed to HPV.¹⁵ This shows that mandatory HPV vaccination for school entry is a step in the right direction that will improve the health of the public by protecting adolescents ages 11-14 years old against HPV-related cancers in the United States.

PUBLIC HEALTH PRACTICE RECOMMENDATIONS

HPV vaccination uptake among adolescents ages 11-14 years old is highly important for the prevention of HPV-associated cancers. However, the HPV vaccination uptake has continuously been low in the United States due to safety concerns despite evidence proving HPV vaccination safety and effectiveness to be excellent. In addition, lack of knowledge also contributes to low HPV vaccine coverage. Vaccines are a key public health tool for addressing infectious diseases such as HPV. That is why policy change in the United States is essential to improving HPV vaccination uptake. Mandating HPV vaccination as a school requirement for all states would provide protection against HPV-associated cancers. Education and awareness regarding the HPV vaccine also plays a major role in increasing HPV vaccination uptake among adolescents ages 11-14 years. Lastly, having free webinars and workshops to educate adolescents and parents on the importance of HPV vaccination would be greatly beneficial for reducing the amount of HPV-associated cancer cases in the United States.

LIMITATIONS

There was only one limitation encountered. That was a lack of statistical data and studies specifically on adolescents aged 11-14 years old for HPV vaccination in the United States.

However, all the data used was still relevant and credible.

CONCLUSION

Although the ACIP recommends the HPV vaccination for ages 11-12, HPV vaccination uptake remains extremely low in the United States. This is a major public health issue considering the impact of HPV-associated cancers. Most HPV infections are not detected until they have progressed to more serious health conditions. That is why HPV vaccination among adolescents ages 11-14 years old is important to reduce the burden of HPV-associated cancers.

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