Human papillomavirus (HPV) vaccine: Updated recommendations and strategies to improve immunization rates

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Abstract

HPV infection is the most common sexually transmitted disease. Persistent HPV infection is associated with many epithelial cell cancers, with cervical cancer being the most common. Vaccination with nonavalent HPV vaccine (9vHPV) covers about 90% of HPV-associated cancers. Traditional dosing for HPV vaccines has been a 3-dose series at 0, 1–2, and 6 months. Recently, a 2-dose series for 9vHPV has been approved and recommended for patients aged 9 through 14 years at 0 and 6–12 months. Common barriers to HPV vaccination completion include inappropriate education, cost, and forgetfulness about subsequent doses, and lack of interaction with healthcare providers. Pharmacists can use their role in the community to promote and educate patients on the need for HPV vaccination. Additionally, pharmacists can use technology to reach out to patients to educate them and remind them to complete the vaccination series.
Introduction
HPV infection is considered to be the most common sexually transmitted disease in the United States.1-3 There are about 41 million people between the ages of 10 and 19 years currently living in the US, and more than half of the sexually transmitted diseases occur in these patients.3 Therefore, this is a large population that can be targeted to try and reduce human papillomavirus (HPV) infection.

Although HPV is considered a single type of infection, there are more than 150 different strains of HPV.4 Each HPV strain is numbered based on the order it has been discovered and classified based on its oncogenic potential.1,5,6 HPV strains that have higher likelihood of being oncogenic are HPV 16, 18, 31, 33, 45, 52, and 58, whereas HPV strains 6 and 11 are associated with most cases of genital or respiratory warts.6 Patient factors that increase the risk of HPV persistence and development of HPV-associated cancers are: immunosuppression, cigarette smoking, oral contraceptive use, and having had multiple children.5,6

Luckily, although HPV infection is extremely common, including among the high-risk strains, 90% of patients who acquire HPV will clear it within 12 to 18 months without consequence.7 Even if the body does clear the infection, however, the individual would have immunity to that strain only, making the patient susceptible to the many other strains of HPV and, as such, a vaccine candidate.5

It is those who do not clear the HPV virus and instead have it persist for years who are at risk for HPV-associated cancers. Further, HPV can also cause genital warts and recurrent respiratory papillomatosis (warts of the upper airway).4,6 Specifically, HPV has been associated with epithelial mucosal cervical, vulvar, vaginal, anogenital, and oropharyngeal cancers.4,5 For cervical cancer, cancer precursors of cervical intraepithelial neoplasia (CIN) can be identified and monitored. CIN ranges from 1 to 3, with 3 being the most severe. HPV 16 and 18 are most commonly associated with high-level CIN and cervical cancer. Because of the association of high-risk HPV strains and cervical cancer, the FDA has approved molecular testing to be done with Papanicolaou tests as routine screening to help identify patients who are at increased risk for HPV-associated cervical cancer.6

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Humans papillomavirus epidemiology
Rates of HPV-associated cancers continued to climb in the years 2008 to 2012 as compared to the years 2004 to 2008, with cervical cancer remaining the most common.2 It is believed that this increase is likely because HPV causes cancer years after infection and these patients likely did not receive HPV vaccination.2 More than 30,000 patients are diagnosed with HPV-associated cancers each year in the US, with 93% caused by strains covered by the 9-valent HPV vaccine (9vHPV).2 Therefore, with more than 90% of the strains associated with HPV-related cancer being included in the 9vHPV, it has the potential to drastically reduce the incidence of these cancers with significant vaccine uptake.

Over the past few years, rates of HPV vaccination in adolescents and young adults have slowly begun to increase. Highest rates occur in girls between the ages of 13 and 17 years.8 Specifically, single doses of HPV vaccination in adolescent females increased from 16% (Mississippi) to 55% (Rhode Island) in 2008, to 48% (Wyoming) to 89% (Rhode Island) in 2015.9 Rhode Island is the only state reporting a vaccination rate of over 80%, while 11 other states had HPV vaccination rates between 70% and 80%.

Even with increasing rates of initial HPV dose uptake, most patients have not completed their HPV vaccination series. Among current adolescents, only 40% of female and 22% of male adolescents have completed the HPV vaccine.10 Young adult patients, age 19 to 26 years, are estimated to have extremely low rates of HPV vaccine completion, at 5.9% for males and 37% for females.4 Therefore, many patients are still under-vaccinated (having not completed the full series of vaccination) or unvaccinated (having not received any of the vaccination series), showing an opportunity for pharmacist vaccination.

Although the vaccination rates have not been as robust as one would want, HPV vaccination has resulted in a positive impact on HPV infection in adolescent females from age 14 to 24 years. The prevalence of HPV decreased in teenagers and young adults from 11.5% and 18.5% in the years before the first HPV vaccine was approved, to 4.3% and 12.1% in 2009 and 2012, respectively.11 The prevalence, however, did not change at all in women age 25 to 34 years.11 Thus, there will likely be a resultant reduction in cancers in these populations as they approach the age when cancers would occur and as vaccination rates increase, further reductions can be expected.

Human papillomavirus vaccine
Over the years, 3 vaccines have received approval from the FDA for the
Vaccine recommendations

The HPV vaccine is routinely recommended to be administered to patients of both genders, beginning at age 11 or 12 years. There are multiple reasons for providing the vaccination at such a young age. First, the vaccine is effective at preventing infection, not at treating infection. As such, it should be given before patients are exposed to the virus. Because 50% of adolescents are reported to be sexually active in high school, patients should receive the vaccine prior to starting high school. Second, patients vaccinated before their 15th birthday have stronger immune responses to the vaccine. Therefore, if patients are vaccinated at age 11 or 12, the 7th grade visit, the goal is to provide protection prior to being exposed to the virus. Vaccination continues to be recommended for females and high-risk males (men who have sex with men or men who are immunocompromised) through age 26 years and males without risk factors through age 21 years. Although the vaccine is not recommended to be started after the age of 26 years, the Advisory Committee on Immunization Practices (ACIP) has clarified that it can be finished after that age. Additionally, ACIP still allows for the vaccine to be given in patients as young as age 9 years, especially if the patient has specific risk factors for HPV infection. If patients initiated the vaccination with the 2vHPV or 4vHPV, they can continue their series with 9vHPV.

Dosing schedule. Two dosing schedules are currently FDA approved for 9vHPV (Table 1). The first is a 3-dose series that is administered at 0, 1 to 2 months, and at 6 months. This schedule is approved for patients age 9 through 26 years. FDA approved and ACIP recently voted (October 2016 meeting) to reduce the number of doses needed for patients age 9 through 14 years.

The HPV vaccine is routinely recommended to be administered to patients of both genders, beginning at age 11 or 12 years.
cine. Vaccine responses for all 3 vaccines were noninferior to the vaccines independently. This is important, as these vaccines are recommended to be administered during adolescence and caught up through early adulthood.

**Administration.** The HPV vaccine is a white cloudy suspension and must be agitated prior to administration. It is recommended to be administered as a 0.5-mL dose intramuscularly. It should not be counted if given anywhere except in the deltoid or by any route other than intramuscularly. If it is inadvertently given subcutaneously by mistake, the Centers for Disease Control and Prevention (CDC) recommends revaccination. The HPV vaccine is associated with more pain than other vaccines. When multiple vaccines are being given, the HPV vaccine should be given last. Patients need to be observed for 15 minutes after vaccine administration.

Cases of syncope, sometimes with seizure-like activity, have occurred following administration of the HPV vaccine. These seizure-like movements are usually temporary and often improve if patients are placed in a supine or Trendelenburg position to restore blood flow to the brain.

The HPV vaccine comes as a single-dose vial or prefilled syringes. The prefilled syringes come with a 22-gauge needle that will need to be attached before administration. If the vial is being used, the pharmacist should inject the vaccine using a 22–25 gauge needle. In addition to the needle gauge, the length of the needle is important. The length of the needle should be chosen based on the patient’s weight (Table 2). A 1” needle is appropriate for most patients, including those up to 200 pounds for a female or 260 pounds for a male. Alternatively, a 5/8” needle can be used on patients who weigh less than 130 pounds if the skin is not bunched and it is administered in the deltoid muscle. A 1 1/2” needle is needed for females weighing more than 200 pounds and males weighing more than 260 pounds. A 1 or 1 1/2” needle can be used for patients between 152 and 200/260 pounds weight. When administering vaccines into the deltoid, such as the HPV vaccine, it should be injected into the lower half of the deltoid muscle at a 90° angle. If a vaccine is administered too high in the deltoid, it has the potential to inject into bursa space, acromion, or synovial space instead of the muscle. Additionally, 4vHPV is not recommended during pregnancy. If patients are inadvertently vaccinated during pregnancy, they should be enrolled in the pregnancy registry for 9vHPV by calling 1-800-986-8999 or faxing 215-933-1220 and future doses held until after delivery.

**Adverse effects/contraindications.** Patients who received the 9vHPV vaccine were more likely than those who received the 4vHPV to experience injection site reactions. Both swelling (40% females, 27% males) and erythema (34% females, 25% males) were more common in those who received the 9vHPV. Importantly, the incidence of these reactions increased with subsequent doses. The 9vHPV is contraindicated in patients with a history of allergic reaction to a prior dose or any component of the vaccine, including yeasts. Additionally, 4vHPV is not recommended during pregnancy. If patients are inadvertently vaccinated during pregnancy, they should be enrolled in the pregnancy registry for 9vHPV by calling 1-800-986-8999 or faxing 215-933-1220 and future doses held until after delivery.

**Barriers to human papillomavirus vaccination**

There are multiple barriers to receiving and completing HPV vaccination. A systematic review of the literature from 2009 to 2014 summarized 55 studies.

Parental barriers included lack of education about the vaccine and recommended age, not receiving a provider recommendation, and concerns about adverse effect, cost, and availability of the vaccine. Barriers to completion of the vaccine series included misunderstanding or forgetting additional doses were needed, insufficient insurance coverage.

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**Which population will you target to improve HPV vaccination rates?**

"Pharmacists are in an optimal position to target the barriers associated with HPV vaccination and improve on HPV immunization rates."
rates of adolescents and young adults are often poor for multidose vaccinations.21 These studies have either demonstrated or alluded to the issue that the lack of contact of adolescents and young adults with the healthcare system is a significant barrier for obtaining and completing a vaccination series.19–21

A recent meta-analysis has evaluated the impact of the role of pharmacists on vaccination rates.22 It reviewed 22 studies in which pharmacists were facilitators or educators and 14 studies in which pharmacists were administering vaccines.22 In these studies, the pharmacist’s roles included one-on-one education, mailings, phone calls, and advertisements. Importantly, all of the studies demonstrated some level of increase in vaccinations, with an overall risk ratio of 2.74 (confidence interval, 1.58–4.74).22 The meta-analysis attributed the improvements to multiple factors, including first, that patients have come to trust the pharmacist, and second, that the pharmacy provides a convenient location with hours of operation beyond the typical Monday through Friday workday of physicians’ offices and allows the patient to just walk in for care.22

When reviewing the literature regarding pharmacists’ impact on improving vaccination as well as the issues with multidose vaccines, a few trends appear. The most important of these is that pharmacists are in an optimal position to target the barriers associated with HPV vaccination and improve on HPV immunization rates. Pharmacists are trusted healthcare providers who are accessible in the community. Pharmacists may interact with adolescent and young adult patients more frequently than other healthcare providers, such as when these young patients pick up prescriptions (eg, oral contraceptives) or ask questions about over-the-counter products for minor conditions. During these interactions, pharmacists have the opportunity to educate patients about HPV infection, promote HPV vaccination, and provide (if allowed by state law) the HPV vaccine. Many patients do not like getting vaccines, but if they and/or their parents understand that the vaccine will help them, promotion of the 2-dose series for those younger than age 15 years may increase the willingness to receive the vaccine on time. Additionally, to help improve patient and parent knowledge about the vaccine, the CDC provides great promotional flyers and educational materials that focus on HPV infection, associated cancers, and HPV vaccination. These materials can be easily downloaded, printed, and promoted in the community pharmacy (see http://www.cdc.gov/vaccines/who/teens/products/print-materials.html). Another way that pharmacists can provide education about the HPV vaccination and the need to receive 2 to 3 doses is to reach out to patients through the use of technology. More than 90% of adolescents and young adults are online at least daily, 81% have a social media account, and adolescents are the highest users of text messages.3 Examples of such outreach include providing HPV education to the adolescent and young adult patients through the pharmacy’s website or social media account and the use of text-message reminder systems.

Pharmacy technicians can also help the pharmacist improve HPV vaccination rates. The technician can assist in identifying those patients who may be indicated to receive the HPV vaccine. Such patients can be identified based on their age when prescription medications are being filled or refilled, with paper notices stapled to the outside of their prescription that will prompt the technician to have the patient speak with the pharmacist if the patient has not yet received the vaccine. Additionally, the pharmacy technician can also post educational information from the CDC on the pharmacy’s website or social media and post the CDC educational flyers around the pharmacy.

Pharmacist-administered vaccination for HPV

Different states have varying laws regarding pharmacist immunization (see https://www.pharmacist.com/pharmacist-administered-immunizations-what-does-your-state-allow). Some states allow pharmacists to provide all vaccines to all patients, while others restrict which vaccines or which age patients can be given vaccinations. It is important as highlighted previously that pharmacists have been successful at improving vaccination rates for HPV in both the role of facilitator and administrator. Pharmacists can provide education via their pharmacist–patient relationship with the adolescent/youth patient as well as the parent of the adolescent. Therefore, even if pharmacists are unable to provide the vaccination in their state they can still make an impact.

How technicians can help identify patients in need of HPV vaccination

The HPV vaccine as discussed here is routinely recommended to be administered to patients beginning at age 11 and
continuing through age 21 to age 26, depending on the gender and risk factors of the patient. The technician can also assist the pharmacist by identifying patients who are picking up prescriptions, asking questions, or purchasing OTC agents. The Immunization Action Coalition provides screening questions that can be used (see http://www.immunize.org/catg.d/p4036.pdf). Similarly, technicians can help to promote vaccination by providing educational flyers and by use of social media and other technologies. Once patients are identified, they should be referred to the pharmacist to answer questions and provide vaccinations.

**TEST QUESTIONS**

**FOR PHARMACISTS**

1. Tim is a 17-year-old youth (280 lbs) who is picking up an antibiotic at your pharmacy. Your technician inquires what vaccines he has received, and has identified that he may not have received the HPV vaccine. Which of the following is your recommendation for Tim?
   a. He does not need the HPV vaccine.
   b. He should get the HPV vaccine at 0 and 6 months.
   c. He should get the HPV vaccine at 0, 1-2, and 6 months.
   d. He should get the HPV vaccine at 0, 6, and 12 months.

2. Tim is a 17-year-old youth (280 lbs) who has decided to get the HPV vaccine, based on your recommendation. Which of the following is recommended needle size to administer the vaccine in Tim?
   a. 5/8”
   b. 1”
   c. 1.5”
   d. Whatever size comes with the syringe

3. Sally is a healthy 12-year-old girl. Her mother asks you if she should get the HPV vaccine now or wait until she is older. Which of the following is correct regarding vaccine administration in Sally at her current age?
   a. She should get the HPV vaccine at 0 and 6 months.
   b. She should get the HPV vaccine at 0, 1-2, and 6 months.
   c. She should get the HPV vaccine at 0, 6, and 12 months.
   d. She should get the HPV vaccine at 0, 6, 12, and 24 months.

4. What is the outcome of most patients who acquire HPV infection?
   a. Most patients have persistent infection without consequence.
   b. Most patients have persistent infection that goes on to cause cancer.
   c. Most patients clear the infection within a few years.
   d. There is no association between HPV infection and cancer.

5. Which of the following strains of HPV is the most likely to be associated with cervical cancer?
   a. 10
   b. 16
   c. 35
   d. 59

6. Betsy is a 20-year-old patient who is known to be infected with a strain of HPV. Which of the following is recommended for Betsy?
   a. She should be assessed for HPV vaccination, just like any other patient.
   b. She should find out if the type of HPV she is infected with is oncogenic. She only should get the vaccine if it is oncogenic.
   c. She should find out if the type of HPV she is infected with is oncogenic. She only should get the vaccine if it is oncogenic.
   d. She is not indicated to get the vaccine because she is positive for a strain of the HPV.

7. Paris is a 23-year-old woman who has agreed to be vaccinated for HPV. How should the vaccine be administered?
   a. IM in the gluteus
   b. IM in the deltoid
   c. SQ in the belly
   d. SQ in the back of the arm

8. Based on the literature, which of the following are barriers to multidose vaccinations, including HPV vaccination?
   a. Lack of education
   b. Cost
   c. Lack of access to providers
   d. All of the above

9. If you wanted to improve your patient’s knowledge of HPV disease, where could you obtain educational posters?
   a. CDC
   b. MMWR
   c. IDSA
   d. SIDP

10. Which of the following is a way that the pharmacist is likely to be most successful reaching out to younger patients to provide information about HPV vaccination?
    a. Phone calls
    b. Educational messages on social media
    c. Notices on their chronic medications
    d. Advertisement in the newspaper

11. Which of the following is most likely to be a good method for reminding adolescents and young adults, based on their common practices, to come back to complete their vaccination series?
    a. Phone calls
    b. Text messages
    c. Notices in their chronic medication refills
    d. Providing the information at the time when they get their first dose

12. What is the likely manner that the majority of patients acquire HPV infection?

**Conclusion**

Rates of HPV vaccination have been slowly increasing. HPV vaccination with the 9vHPV can lead to decreased rates of HPV-associated cancers and warts. Patients from age 9 through 14 years can be vaccinated with a 2-dose series, while older patients require 3 doses. The pharmacist can help to increase the vaccination rates for HPV by providing educational materials, recommending the vaccine, and providing the vaccine to patients who may not otherwise interact with a healthcare provider. Some easy ways to promote the vaccine include flyers from the CDC, reminder tags on prescriptions, talking with the patient, using technology and social media to promote the vaccine, and providing reminders for second and, when indicated, third doses of the HPV vaccine.

**References are available online at www.drugtopics.com/cpe.**
TEST QUESTIONS

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13. What makes it difficult for patients to be protected from HPV by the vaccine?
   a. It is a live attenuated vaccine that many patients cannot receive.
   b. It is a multidose vaccine that patients may forget to complete.
   c. It is a subcutaneous vaccine that patients do not like in regard to how it is administered.
   d. It is a vaccine that needs to be restarted if it is not completed within a year, which makes it difficult in regard to compliance.

14. In addition to being a trusted reference, another reason that pharmacists have a potential role in increasing vaccination efforts is:
   a. It costs less to get vaccinated in a pharmacy.
   b. Hours are more convenient in a pharmacy than provider’s office.
   c. Communication skills are stronger than other professions.
   d. It is the only place that carries any vaccines.

15. Patricia is a 23-year-old healthy patient who comes in to receive her second dose of the HPV vaccine. You have her complete an intake form prior to vaccination. You review the form and notice she indicates that she is pregnant. Which of the following is recommended for Patricia?
   a. Provide her the vaccine today
   b. Have her check with her doctor and vaccinate her as long as he/she says it is okay
   c. Defer vaccination until after the baby is delivered
   d. Tell her she does not need the HPV vaccine.

16. If Patricia tells you that she was pregnant during her first dose of the HPV vaccine, which of the following is recommended?
   a. Nothing needs to be done
   b. She should be enrolled in the pregnancy registry for 9vHPV.
   c. She should be told that many adverse effects have been seen with other HPV vaccines given during pregnancy.
   d. You should report the administration to VAERS (vaccine adverse events reporting system).

17. What is the recommended dose of HPV vaccine?
   a. 0.5 mL  b. 0.65 mL  c. 1 mL  d. 1.5 mL

18. Where in the deltoid should the HPV vaccine be administered?
   a. Anywhere in the deltoid
   b. Top 2/3 of the deltoid
   c. Bottom 2/3 of the deltoid
   d. It should not be administered in the deltoid.

19. The 9vHPV vaccine is estimated to cover approximately what percentage of HPV-associated cancers.
   a. 15%  b. 45%  c. 60%  d. 90%

20. HPV infection has been associated with:
   a. Cancers  b. Genital warts  c. Recurrent respiratory papillomatosis  d. All of the above

FOR PHARMACY TECHNICIANS

1. Why are patients recommended to receive HPV vaccination at such a young age?
   a. To prevent the virus from being able to cause infection
   b. To treat the virus after it causes infection
   c. To treat persistence of the virus
   d. To treat the virus to make it not able to cause cancer

2. What is the HPV vaccine indicated to prevent?
   a. HPV-associated acne
   b. HPV-associated cancers
   c. HPV-associated seizures
   d. HPV-associated pneumonia

3. In addition to its primary disease prevention what other conditions does the vaccine prevent?
   a. HPV-associated genital warts
   b. HPV-associated respiratory warts
   c. HPV foot warts
   d. A & B

4. Where should the HPV vaccine be stored?
   a. At room temperature
   b. In a refrigerator
   c. In a freezer
   d. Any of the above are reasonable locations for HPV vaccine storage.

5. Why should the vaccine not be stored in a dorm-type refrigerator?
   a. Too small size
   b. Does not reach freezing temperatures
   c. Inconsistent temperature
   d. None of the above

6. If the vaccine is inadvertently left out of refrigeration at 68°F overnight, which of the following should be done?
   a. Throw out the vaccine
   b. Use the vaccine that day
   c. Call the CDC
   d. Put it in the freezer

7. You identify an 18 year old who is underimmunized for HPV. They have some clinical questions about the vaccine. Which of the following is the best recommended action?
   a. Provide them a handout on HPV disease
   b. Recommend they go to their physician
   c. Refer them to talk with the pharmacist
   d. Refer them to the pregnancy registry for 9vHPV

8. Which patient should be screened to determine if they are in need of HPV vaccination?
   a. 7 year old picking up an antibiotic
   b. 16 year old picking up an oral contraceptive
   c. 30 year old picking up a cardiac medication
   d. All of the above

9. The 9vHPV is expected to have a larger impact on HPV-associated cancers than 4vHPV or 2vHPV because:
   a. It covers more oncogenic strains of HPV
   b. It has a longer protection against HPV
   c. It requires more doses of HPV vaccination (4 doses versus 3 doses)
   d. There is no difference in protection against HPV with the different vaccines

10. At which age is HPV vaccine routinely recommended to begin being given?
    a. 11 or 12 years  b. 16 or 18 years  c. 20 or 21 years  d. 26 or 27 years

HUMAN PAPILLOMAVIRUS (HPV) VACCINE
REFERENCES


