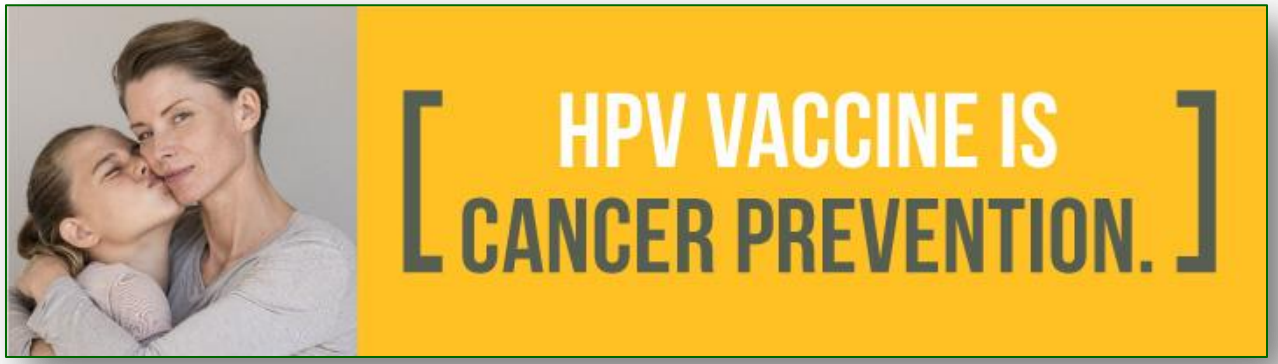

2017 HPV Vaccine Update

HPV 2-Dose Schedule Recs

Adult Coalition Meeting
January 11, 2017

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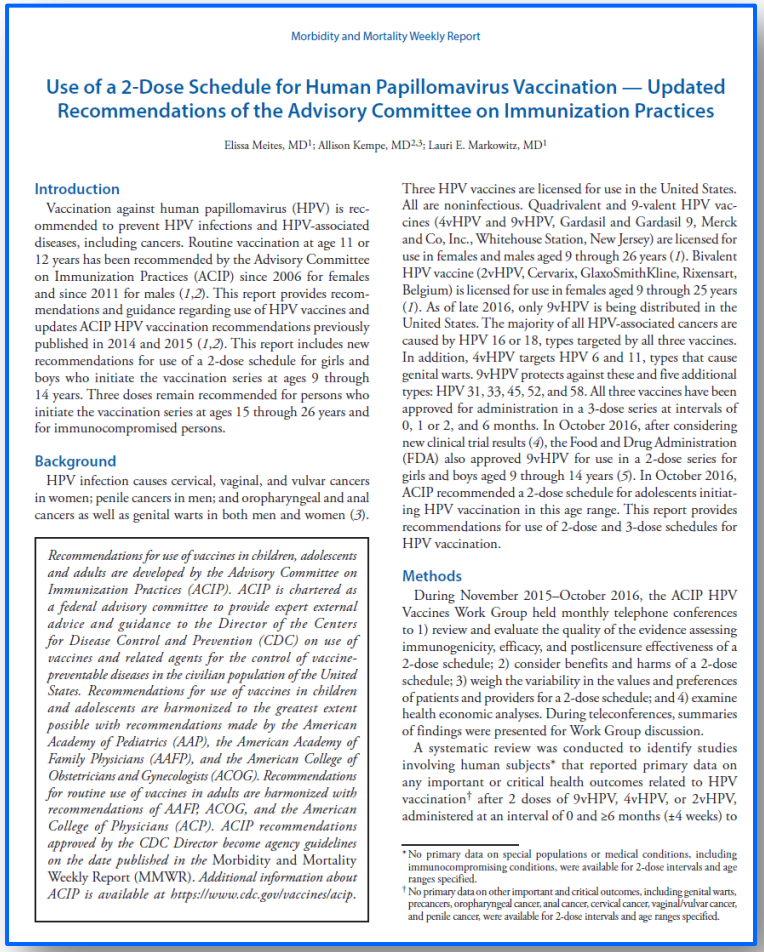
Susan M. Lett Disclosure

- I, Susan Lett, have been asked to disclose any significant relationships with commercial entities that are either providing financial support for this program or whose products or services are mentioned during my presentations.
  - I have no relationships to disclose.
- I may discuss the use of vaccines in a manner not approved by the U.S. Food and Drug Administration.
  - But in accordance with ACIP recommendations.

Outline

- HPV Vaccine Coverage
- HPV 2-dose schedule
  - Background
  - Summary of evidence reviewed on 2-dose schedules
  - Updated HPV vaccination recommendations
  - Case examples
  - Resources
- Evidence Based Strategies to Implement the New Recommendations and Improve HPV Rates

Updated ACIP Recommendations for a 2-Dose HPV Vaccine Schedule



Morbidity and Mortality Weekly Report

Use of a 2-Dose Schedule for Human Papillomavirus Vaccination — Updated Recommendations of the Advisory Committee on Immunization Practices

Elissa Meites, MD[1]; Allison Kempe, MD[2,3]; Lauri E. Markowitz, MD[1]

Introduction

Vaccination against human papillomavirus (HPV) is recommended to prevent HPV infections and HPV-associated diseases, including cancers. Routine vaccination at age 11 or 12 years has been recommended by the Advisory Committee on Immunization Practices (ACIP) since 2006 for females and since 2011 for males (*1*,*2*). This report provides recommendations and guidance regarding use of HPV vaccines and updates ACIP HPV vaccination recommendations previously published in 2014 and 2015 (*1*,*2*). This report includes new recommendations for use of a 2-dose schedule for girls and boys who initiate the vaccination series at ages 9 through 14 years. Three doses remain recommended for persons who initiate the vaccination series at ages 15 through 26 years and for immunocompromised persons.

Background

HPV infection causes cervical, vaginal, and vulvar cancers in women; penile cancers in men; and oropharyngeal and anal cancers as well as genital warts in both men and women (*3*).

Recommendations for use of vaccines in children, adolescents and adults are developed by the Advisory Committee on Immunization Practices (ACIP). ACIP is chartered as a federal advisory committee to provide expert external advice and guidance to the Director of the Centers for Disease Control and Prevention (CDC) on use of vaccines and related agents for the control of vaccine-preventable diseases in the civilian population of the United States. Recommendations for use of vaccines in children and adolescents are harmonized to the greatest extent possible with recommendations made by the American Academy of Pediatrics (AAP), the American Academy of Family Physicians (AAFP), and the American College of Obstetricians and Gynecologists (ACOG). Recommendations for routine use of vaccines in adults are harmonized with recommendations of AAFP, ACOG, and the American College of Physicians (ACP). ACIP recommendations approved by the CDC Director become agency guidelines on the date published in the Morbidity and Mortality Weekly Report (MMWR). *Additional information about ACIP is available at https://www.cdc.gov/vaccines/acip.*

Three HPV vaccines are licensed for use in the United States. All are noninfectious. Quadrivalent and 9-valent HPV vaccines (4vHPV and 9vHPV, Gardasil and Gardasil 9, Merck and Co, Inc., Whitehouse Station, New Jersey) are licensed for use in females and males aged 9 through 26 years (*1*). Bivalent HPV vaccine (2vHPV, Cervarix, GlaxoSmithKline, Rixensart, Belgium) is licensed for use in females aged 9 through 25 years (*1*). As of late 2016, only 9vHPV is being distributed in the United States. The majority of all HPV-associated cancers are caused by HPV 16 or 18, types targeted by all three vaccines. In addition, 4vHPV targets HPV 6 and 11, types that cause genital warts. 9vHPV protects against these and five additional types: HPV 31, 33, 45, 52, and 58. All three vaccines have been approved for administration in a 3-dose series at intervals of 0, 1 or 2, and 6 months. In October 2016, after considering new clinical trial results (*4*), the Food and Drug Administration (FDA) also approved 9vHPV for use in a 2-dose series for girls and boys aged 9 through 14 years (*5*). In October 2016, ACIP recommended a 2-dose schedule for adolescents initiating HPV vaccination in this age range. This report provides recommendations for use of 2-dose and 3-dose schedules for HPV vaccination.

Methods

During November 2015–October 2016, the ACIP HPV Vaccines Work Group held monthly telephone conferences to 1) review and evaluate the quality of the evidence assessing immunogenicity, efficacy, and postlicensure effectiveness of a 2-dose schedule; 2) consider benefits and harms of a 2-dose schedule; 3) weigh the variability in the values and preferences of patients and providers for a 2-dose schedule; and 4) examine health economic analyses. During teleconferences, summaries of findings were presented for Work Group discussion.

A systematic review was conducted to identify studies involving human subjects* that reported primary data on any important or critical health outcomes related to HPV vaccination† after 2 doses of 9vHPV, 4vHPV, or 2vHPV, administered at an interval of 0 and ≥6 months (±4 weeks) to

* No primary data on special populations or medical conditions, including immunocompromising conditions, were available for 2-dose intervals and age ranges specified.

† No primary data on other important and critical outcomes, including genital warts, precancers, oropharyngeal cancer, anal cancer, cervical cancer, vaginal/vulvar cancer, and penile cancer, were available for 2-dose intervals and age ranges specified.

Published in the MMWR on December 16, 2016

https://www.cdc.gov/mmwr/volumes/65/wr/pdfs/mm6549a5.pdf

CDC. MMWR 2016;65:1405-1408.

HPV Vaccine Background

HPV vaccine use

- Through 2014, almost all HPV vaccine used was 4vHPV
- In 2016, almost all HPV vaccine used is 9vHPV

HPV vaccine availability

- After the end of October 2016, only 9vHPV will be distributed in U.S.
- 2vHPV and 4vHPV will continue to be available outside U.S.

HPV 2-dose Recommendations

- In October 2016, the FDA approved a 2 dose schedule of 9vHPV in teens initiating the series before their 15th birthday
- In October 2016, the ACIP revised their recommendations for HPV vaccine after a thorough review of available studies over several meetings.

HPV 2-dose Schedule Summary of Evidence

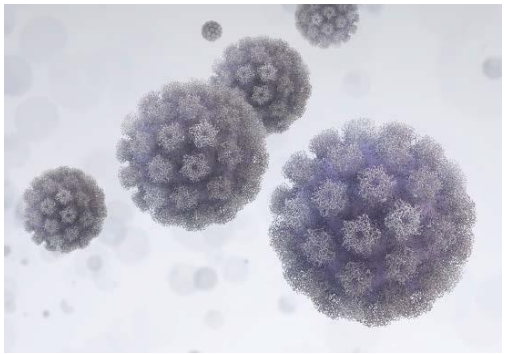
- Immunogenicity trials including all HPV formulations found antibody response after 2 doses (0,6 months or 0,12 months) in ~ 9–14 year olds were **significantly higher** for all 9v HPV types compared to the response after 3 doses in the age ~16–26 years of age
- Data from 10 years of follow-up of 3-dose vaccine trials show that duration of protection after HPV vaccination is long lasting
  - No evidence waning immunity
- Modelling data suggest **duration of protection will be the same** after 2-dose and 3-dose schedules
- Experts project the 2-dose schedule will improve HPV coverage

Implementation of the new 2-dose schedule provides the opportunity to achieve protection against vaccine preventable HPV cancers with just 2 office visits!

CDC. MMWR 2016;65:1405-1408.

Updated Recommendations for HPV Vaccination

- Routine and catch-up age groups (no changes)
- Dosing schedules
- Medical conditions
- Special populations (no changes)



CDC. MMWR 2016;65:1405-1408.

Routine and Catch-up Age Groups (no changes)

- ACIP recommends routine HPV vaccination at age 11 or 12 years. Vaccination can be given starting at age 9 years.
- ACIP also recommends vaccination for females through age 26 years and for males through age 21 years who were not previously adequately vaccinated. Males aged 22 through 26 years may be vaccinated.
- (See also: Special populations, Medical conditions)

CDC. MMWR 2016;65:1405-1408.

Schedule Basics

- Number of recommended doses is now based on **age at administration of the first dose.**
- Persons initiating the series **before** the 15th birthday will only need 2 doses
- Persons starting the series on or after the 15th birthday; and those with certain immunocompromsing conditions, regardless of age will need 3 doses
- Persons who began their HPV series with 2vHPV or 4vHPV vaccines can complete with 9vHPV, using either a 2-dose or a 3-dose schedule
- If the vaccination schedule is interrupted, the vaccination series does not need to be restarted.

CDC. MMWR 2016;65:1405-1408.

Dosing Schedules

- **For persons initiating vaccination before the 15th birthday**
  - The recommended immunization schedule is 2 doses of HPV vaccine. The second dose should be administered 6–12 months after the first dose (0, 6–12 month schedule).
    - The minimum interval between the 1st and 2nd doses in a 2-dose schedule is 5 months.
    - If at least 1 valid dose is given before the 15th birthday, only 2 doses will be needed, **even if they are now ≥15 years**

- **For persons initiating vaccination on or after the 15th birthday**
  - The recommended immunization schedule is 3 doses of HPV vaccine.
    - The second dose should be administered 1–2 months after the first dose, and the third dose should be administered 6 months after the first dose (0, 1–2, 6 month schedule).

CDC. MMWR 2016;65:1405-1408.

Recommended Number of Doses and Dosing Schedule for HPV Vaccine

Age/Immunocompromising Conditions	Recommended Number of Doses	Recommended Dosing Schedule
Persons initiating vaccination at ages 9 through 14 years; **except** persons with certain immunocompromising conditions (see later slide for details)	2	0, 6–12 months[1]
Persons initiating vaccination at ages 15 through 26 years	3	0, 1–2, 6 months[2]
Persons with certain immunocompromising conditions that might reduce cell mediated or humoral immunity initiating the vaccine series at **9 through 26 years**	3	0, 1–2, 6 months[2]

[1] In a 2-dose schedule of HPV vaccine, the minimum between the 1st and 2nd dose is 5 calendar months. If the 2nd dose is administered at a shorter interval, a 3rd dose should be administered a minimum of 12 weeks after the 2nd dose and a minimum of 5 months after the 1st dose.

[2] In a 3-dose schedule of HPV vaccine, the minimum intervals are: 4 weeks between the 1st and 2nd dose, 12 weeks between the 2nd and 3rd dose, and 5 months between the 1st and 3rd doses. If a vaccine dose is administered after a shorter interval, it should be re-administered after another minimum interval has elapsed after the most recent dose.

CDC. MMWR 2016;65:1405-1408.

Medical Conditions

- ACIP recommends HPV vaccination for certain immunocompromised persons aged 9 through 26 years with 3 doses (0, 1–2, 6 months).
- Persons who should receive **3 doses** are those with **certain** primary or secondary immunocompromising conditions that might reduce cell-mediated or humoral immunity:
  - B lymphocyte antibody deficiencies, T lymphocyte complete or partial defects, HIV infection, malignant neoplasm, transplantation, autoimmune disease, or immunosuppressive therapy
    - Because their immune response to vaccination may be attenuated

Only 2 Doses Are Needed for Immunocompromised Persons <15 years with:
Asplenia; sickle cell disease; asthma; chronic granulomatous disease; chronic liver disease; chronic lung disease; chronic renal disease; CNS anatomic barrier defects (e.g., cochlear implant); persistent complement component deficiencies; diabetes and heart disease.

CDC. MMWR 2016;65:1405-1408.

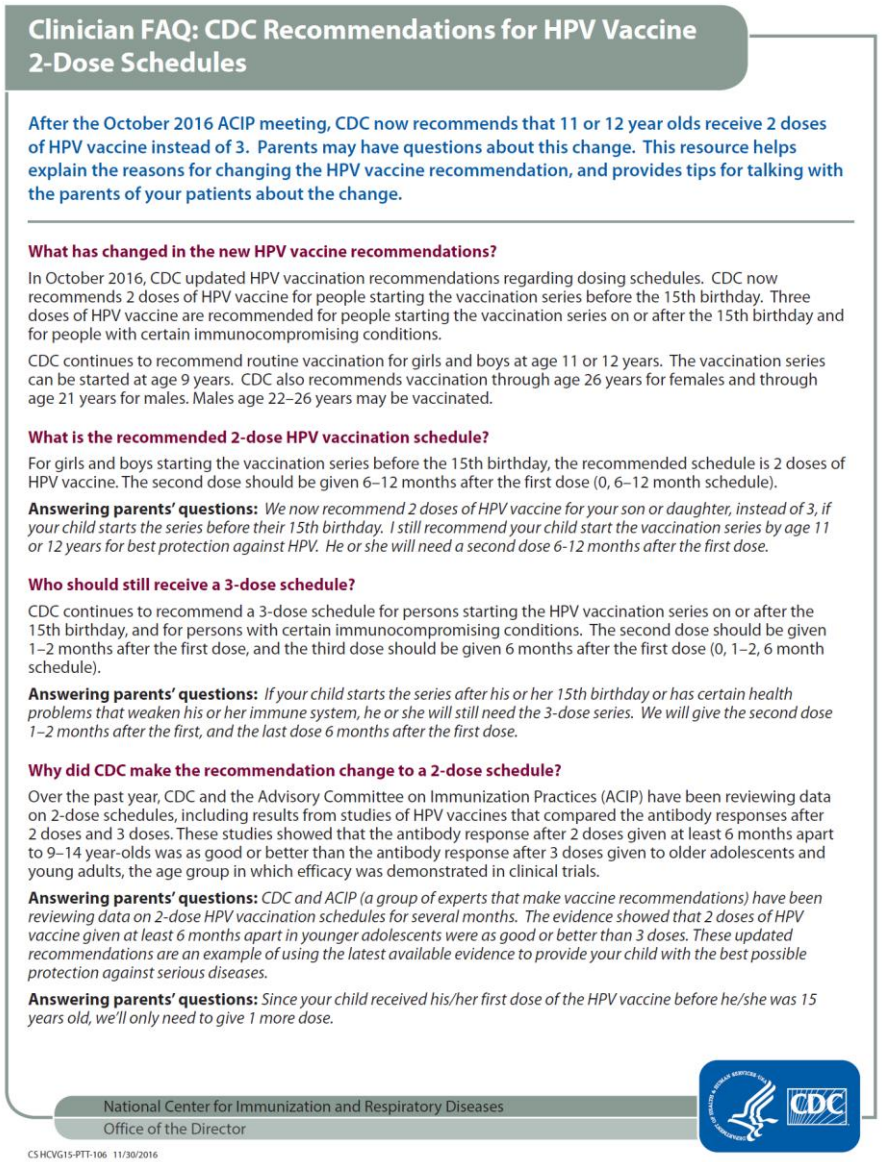
Special Populations (no change)

- For men who have sex with men (MSM)*, ACIP recommends routine HPV vaccination as for all males, and initiation of vaccination through age 26 years for those who were not adequately vaccinated previously.

- For transgender persons, ACIP recommends routine HPV vaccination as for all adolescents, and initiation of vaccination through age 26 years for those who were not adequately vaccinated previously.

*Including those who identify as gay or bisexual, or who intend to have sex with men

CDC. MMWR 2016;65:1405-1408.



Clinician FAQ: CDC Recommendations for HPV Vaccine 2-Dose Schedules

After the October 2016 ACIP meeting, CDC now recommends that 11 or 12 year olds receive 2 doses of HPV vaccine instead of 3. Parents may have questions about this change. This resource helps explain the reasons for changing the HPV vaccine recommendation, and provides tips for talking with the parents of your patients about the change.

What has changed in the new HPV vaccine recommendations?

In October 2016, CDC updated HPV vaccination recommendations regarding dosing schedules. CDC now recommends 2 doses of HPV vaccine for people starting the vaccination series before the 15th birthday. Three doses of HPV vaccine are recommended for people starting the vaccination series on or after the 15th birthday and for people with certain immunocompromising conditions.

CDC continues to recommend routine vaccination for girls and boys at age 11 or 12 years. The vaccination series can be started at age 9 years. CDC also recommends vaccination through age 26 years for females and through age 21 years for males. Males age 22–26 years may be vaccinated.

What is the recommended 2-dose HPV vaccination schedule?

For girls and boys starting the vaccination series before the 15th birthday, the recommended schedule is 2 doses of HPV vaccine. The second dose should be given 6–12 months after the first dose (0, 6–12 month schedule).

Answering parents' questions: *We now recommend 2 doses of HPV vaccine for your son or daughter, instead of 3, if your child starts the series before their 15th birthday. I still recommend your child start the vaccination series by age 11 or 12 years for best protection against HPV. He or she will need a second dose 6-12 months after the first dose.*

Who should still receive a 3-dose schedule?

CDC continues to recommend a 3-dose schedule for persons starting the HPV vaccination series on or after the 15th birthday, and for persons with certain immunocompromising conditions. The second dose should be given 1–2 months after the first dose, and the third dose should be given 6 months after the first dose (0, 1–2, 6 month schedule).

Answering parents' questions: *If your child starts the series after his or her 15th birthday or has certain health problems that weaken his or her immune system, he or she will still need the 3-dose series. We will give the second dose 1–2 months after the first, and the last dose 6 months after the first dose.*

Why did CDC make the recommendation change to a 2-dose schedule?

Over the past year, CDC and the Advisory Committee on Immunization Practices (ACIP) have been reviewing data on 2-dose schedules, including results from studies of HPV vaccines that compared the antibody responses after 2 doses and 3 doses. These studies showed that the antibody response after 2 doses given at least 6 months apart to 9–14 year-olds was as good or better than the antibody response after 3 doses given to older adolescents and young adults, the age group in which efficacy was demonstrated in clinical trials.

Answering parents' questions: *CDC and ACIP (a group of experts that make vaccine recommendations) have been reviewing data on 2-dose HPV vaccination schedules for several months. The evidence showed that 2 doses of HPV vaccine given at least 6 months apart in younger adolescents were as good or better than 3 doses. These updated recommendations are an example of using the latest available evidence to provide your child with the best possible protection against serious diseases.*

Answering parents' questions: *Since your child received his/her first dose of the HPV vaccine before he/she was 15 years old, we'll only need to give 1 more dose.*

National Center for Immunization and Respiratory Diseases
Office of the Director

CS HCVG15-PTT-106 11/30/2016

https://www.cdc.gov/hpv/downloads/hcvg15-ptt-hpv-2dose.pdf

HPV Case Examples

HPV Case Example

- **A 13 year old received of 1 dose of 4vHPV at age 10 years. Does he need 1 or 2 more HPV vaccine doses to complete the series?**

HPV Case Example

- **A 13 year old received of 1 dose of 4vHPV at age 10 years. Does he need 1 or 2 more HPV vaccine doses to complete the series?**

This adolescent needs 1 more dose to complete the series, because he initiated vaccination before the 15th birthday.

He received the first dose more than a year ago; the second dose can be given as soon as possible.

Note: This child began the series with 4vHPV and can complete it with 9vHPV.

HPV Case Example

- **A 14 year old has a history of 2 doses of HPV vaccine: 4vHPV given at age 11 years and 9vHPV given 2 months later. Are any more HPV vaccine doses needed to complete the vaccination series?**

HPV Case Example

- **A 14 year old has a history of 2 doses of HPV vaccine: 4vHPV given at age 11 years and 9vHPV given 2 months later. Are any more HPV vaccine doses needed to complete the vaccination series**?

Yes, although he initiated the vaccination series before his 15th birthday, he needs a third dose because the 2 HPV vaccine doses were administered less than 5 months apart.

Note: This child has received 2 different HPV vaccine formulations and can complete the series with 9vHPV vaccine.

HPV Case Example

- **A 19 year old received 1 dose of 4vHPV at age 14 years. Does she need 1 or 2 more HPV vaccine doses to complete the series?**

HPV Case Example

- **A 19 year old received 1 dose of 4vHPV at age 14 years. Does she need 1 or 2 more HPV vaccine doses to complete the series?**

This person needs 1 more dose to complete the series, because she initiated vaccination before the 15th birthday (even though she is now beyond her 15th birthday)

She received the first dose several years ago; the second dose can be given as soon as possible.

Note: This person began the series with 4vHPV and can complete it with 9vHPV.

HPV Case Example

- **A 12 year old with a history of autoimmune disease on immunosuppressive therapy is starting the HPV vaccine series. How many doses does she need?**

HPV Case Example

- **A 12 year old with a history of autoimmune disease on immunosuppressive therapy is starting the HPV vaccine series. How many doses does she need?**

Even though this adolescent is initiating the vaccine series before her 15th birthday, she will needs **3 doses** (0, 1-2, 6 months) to complete the series, because she has an immunocompromising condition that might reduce cell-mediated or humoral immunity:

- B lymphocyte antibody deficiencies; T lymphocyte complete or partial defects; HIV infection; malignant neoplasm; transplantation; autoimmune disease; or immunosuppressive therapy
  - Because their immune response to vaccination may be attenuated

Updated HPV Vaccine Recommendations: Implementation Issues

Evidence-Based Strategies to Improve HPV Vaccine Coverage

- Make an effective recommendation for HPV vaccination as cancer prevention for every 11- or 12-year-old patient
- Assess HPV vaccine coverage for each provider in your practice and develop an office-wide strategy to improve it
- Engage the entire practice – not just healthcare providers – in committing to improve HPV vaccine coverage
- Implement systems strategies to improve HPV vaccine coverage

Evidence-Based Systems Strategies to Improve HPV Vaccine Coverage

- Establish standing orders for HPV vaccination beginning at age 11-12 years in your practice
- Conduct reminder/recall beginning at 11-12 years of age
- Assess HPV vaccine coverage at every visit and prompt clinical staff to give HPV vaccine at that visit
- Schedule return visit for next dose before the patient leaves the office
- Document each dose in the child's medical record and the state's immunization information system

New Recommendations To-Do List

- Make sure everyone involved in immunization delivery in the clinic understands the new recommendation
- Update standing orders to reflect the new recommendation
- Update reminder/recall protocols
- Update clinical decision support/forecasting functions for assessment of needed immunizations in electronic health records and immunization information systems
- Update systems for scheduling return visits for next dose

Resources for 2-Dose HPV Vaccine Implementation

- CDC's **Main HPV website**: www.cdc.gov/hpv
- CDC's ***MMWR* policy note** contains more information on the recent ACIP recommendations: https://www.cdc.gov/mmwr/volumes/65/wr/mm6549a5.htm?s_cid=mm6549a5_e
- CDC's **Clinician FAQ: CDC Recommendations for HPV Vaccine 2-Dose Schedules explains the reasons for changing the HPV vaccine recommendation and provides tips for talking with parents about the change:** https://www.cdc.gov/hpv/downloads/hcvg15-ptt-hpv-2dose.pdf
- **HPV Vaccine Information Statement (VIS)** has been updated**:**: https://www.cdc.gov/vaccines/hcp/vis/vis-statements/hpv.pdf
- **CDC's "tip sheet"** for guidance on answering questions parents may have about the HPV vaccine: https://www.cdc.gov/vaccines/who/teens/for-hcp-tipsheet-hpv.pdf
- **Package insert for 9-valent HPV vaccine,** updated after FDA approval for use in a 2-dose series for adolescents aged 9 through 14 years: http://www.fda.gov/BiologicsBloodVaccines/Vaccines/ApprovedProducts/ucm426445.htm
- **Current Issues in Immunization NetConference**. Lauri E Markowitz, MD - CDC's Associate Director of Science for HPV, reviews the updated HPV vaccination recommendations: http://www.cdc.gov/vaccines/ed/ciinc/2016-10-26.html
- **CDC's HPV Toolkit** is designed to help partners and programs increase HPV vaccination rates: https://www.cdc.gov/hpv/partners/index.html