



Human Papillomavirus (HPV) Vaccination Recommendations

Lloyd Fisher, MD, FAAP

Assistant Professor of Pediatrics, UMass Chan Medical School;

Chief Medical Informatics Officer, Reliant Medical Group;

Medical Director, MCAAP Immunization Initiative



Disclosure

I, Lloyd Fisher, have been asked to disclose any relevant financial relationships with ACCME-defined commercial entities that are either providing financial support for this program or whose products or services are mentioned during this presentation.

I have no relevant financial relationships to disclose.



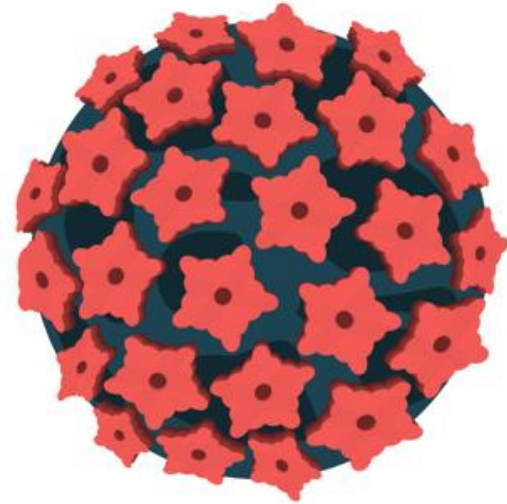
Agenda

1. HPV epidemiology and pathophysiology
2. Timeline of approvals from FDA and ACIP
3. Current vaccine recommendations, schedule, and contraindications
4. Differences between ACIP and AAP recommendations (initiation at age 9)
5. Understanding the recommendation for persons 27-45
6. Strategies for improving rates in your practice



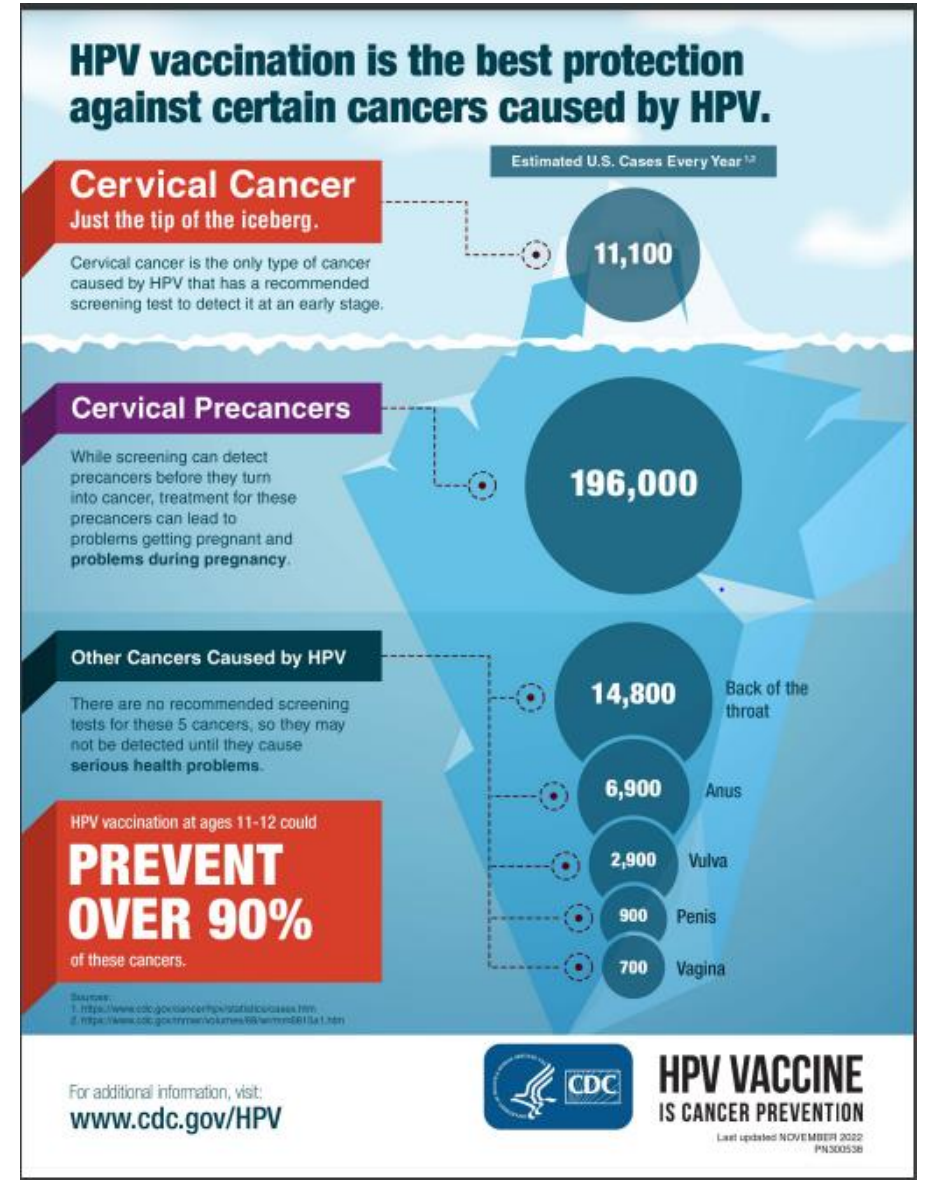
- Human papillomavirus (HPV) is a common virus spread through intimate skin-to-skin contact.
- Nearly everyone will get HPV at some point in their lives.
- More than 42 million Americans are infected with types of HPV that cause disease.
- About 13 million Americans, including teens, become infected each year.
- 9 out of 10 HPV infections clear within two years. However, some HPV infections will last longer and can cause cancer. Among those who do not clear their infections, chronic infection can lead to pre-malignant and malignant lesions in numerous anatomic sites.

HUMAN PAPILOMAVIRUS
HPV



HPV-Associated Cancers

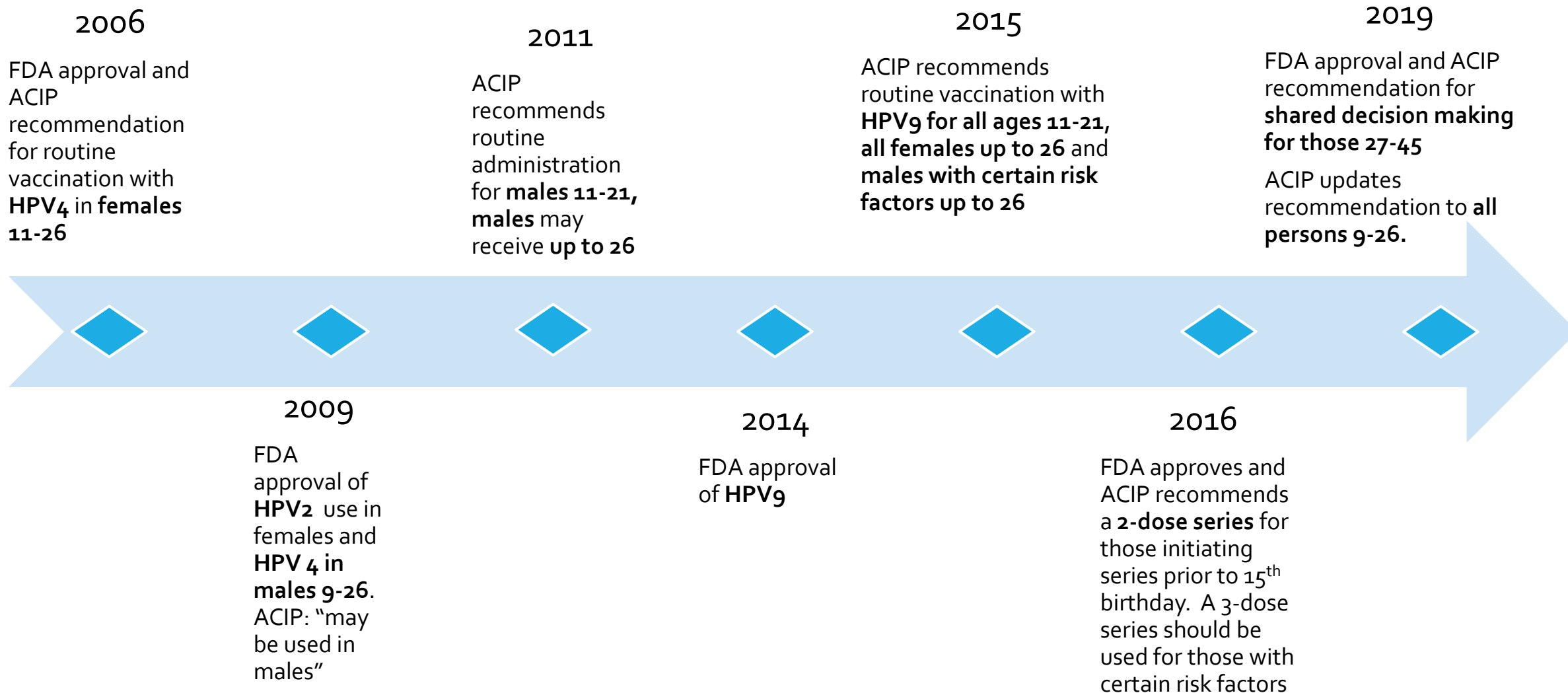
- Every year in the United States, HPV causes about **37,000** cases of cancer in both men and women.
- HPV is associated with cervical, vulvar, and vaginal cancer in females, penile cancer in males, and anal cancer and oropharyngeal cancer in both females and males.
- The burden of HPV infection also includes cervical precancers, including cervical intraepithelial neoplasia grade 2 or 3 and adenocarcinoma in situ (\geq CIN2).
- Most HPV-associated cancers are caused by **HPV 16** or **HPV 18**.
- HPV-associated cancers can also be caused by **HPV 6** and **HPV 11**, which can cause anogenital warts, and five additional high-risk types: **HPV 31, 33, 45, 52, and 58**.





Highlights of FDA Approval and ACIP Recommendation Timeline

See Appendix for full details





Current ACIP-Recommended HPV Vaccination Schedule

Routine vaccination	Age 11–12 years; can be started at age 9 years
Catch-up Vaccination*	Age 13–26 years, if not adequately vaccinated
Shared clinical decision-making*	Some adults age 27–45 years, if not adequately vaccinated

*MMWR. 2019;68(32);698-702



Currently Available (US) HPV Vaccine

- Human Papillomavirus 9-valent Vaccine, Recombinant (Gardasil 9) – contains HPV types 6, 11, 16, 18, 31, 33, 45, 52, and 58
- 9vHPV vaccine can be administered as recommended to all persons 9 through 45 years of age.
- 9vHPV vaccine is state-supplied for persons 9 through 18 years of age.
- HPV vaccine is not required for school entry in Massachusetts.



ACIP-Recommended HPV Vaccination Dosage and Schedule

- A **2-dose schedule** is recommended for **people who get the first dose before their 15th birthday**.
 - In a 2-dose series, the second dose should be given 6–12 months after the first dose (0, 6–12-month schedule).
 - The minimum interval is 5 months between the first and second dose. If the second dose is administered after a shorter interval, a third dose should be administered a minimum of 5 months after the first dose and a minimum of 12 weeks after the second dose.
 - If the vaccination schedule is interrupted, vaccine doses do not need to be repeated (no maximum interval).
- A **3-dose schedule** is recommended for **people who get the first dose on or after their 15th birthday**, and for people with certain immunocompromising conditions.
 - In a 3-dose series, 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).
 - The minimum intervals are 4 weeks between the first and second dose, 12 weeks between the second and third doses, and 5 months between the first and third doses. If a vaccine dose is administered after a shorter interval, it should be re-administered after another minimum interval has elapsed since the most recent dose.
 - If the vaccination schedule is interrupted, vaccine doses do not need to be repeated (no maximum interval).



Contraindications to HPV Vaccination

- HPV vaccines are contraindicated for persons with a history of allergic reaction to the vaccine or to any of its components.
- HPV vaccines are contraindicated in persons who are pregnant.



FAQ: Why are the ACIP and AAP recommendations for initiation of HPV vaccination at age 9 different?

- For almost every childhood and adolescent vaccine, American Academy of Pediatrics (AAP) policy reflects ACIP recommendations. AAP has worked with ACIP for decades to harmonize recommendations to prevent confusion among providers. In rare cases, however, recommendations may differ. One example is the subtle difference in the wording of the AAP and ACIP recommendations regarding HPV vaccination.
 - ACIP's recommendation: "ACIP recommends that routine HPV vaccination be initiated at age **11 or 12 years**. The vaccination series can be started beginning at age 9 years."
 - AAP's recommendation, introduced in its 2018-2021 *Red Book* series: "The American Academy of Pediatrics and the Advisory Committee on Immunization Practices (ACIP) of the Centers for Disease Control and Prevention recommend routine HPV vaccination for females and males. The AAP recommends starting the series between 9 and 12 years, at an age that the provider deems optimal for acceptance and completion of the vaccination series."

FAQ: AAP reasoning for initiation of HPV vaccination at age 9

- The AAP recommendations are designed to promote immunization when the vaccine is most effective - before the initiation of sexual activity and exposure to HPV and at a younger age when the immune response is most robust.
- The vaccine is safe and effective, but uptake continues to lag behind other adolescent vaccines.
- There is no evidence of significant waning protection after antibody levels plateau approximately 18 to 24 months after series completion.
- Offering the vaccine earlier provides the opportunity to complete the series before the 11-12-year vaccines (MenACWY, Tdap).
- Initiating the vaccine at age 9 or 10 also may be preferable for parents or adolescents who do not want to receive three or four concomitant vaccines at age 11 or 12. If a vaccine is delayed at the 11- or 12-year visit, it almost always is the HPV vaccine.
- Offering the vaccine earlier reduces parents considering it a “sex vaccine”



FAQ: Understanding ACIP recommendations for use of HPV vaccine in people aged 27 through 45 years

- In 2019, after reviewing new evidence, ACIP updated its HPV vaccination recommendations for U.S. adults as follows:
 - Catch-up HPV vaccination is now recommended for **all** persons through age 26 years.
 - For adults aged 27 through 45 years, public health benefit of HPV vaccination in this age range is minimal; **shared clinical decision-making** (discussion between the provider and the patient) is recommended because some persons who are not adequately vaccinated might benefit.
- HPV vaccine works to prevent infection among persons **who have not been exposed to vaccine-type HPV before vaccination**. While new HPV infections are most commonly acquired in adolescence and young adulthood, at any age, **having a new sex partner is a risk factor for acquiring a new HPV infection**. In addition, **some persons have specific behavioral or medical risk factors for HPV infection** or disease, including men who have sex with men, transgender persons and persons with immunocompromising conditions.
- While most health insurance plans cover the cost of the HPV vaccine for adults aged 27 and older, coverage should be confirmed.



Research has shown that a strong recommendation from a healthcare provider is the main reason that parents and patients decide to get vaccinated.

- The COVID-19 pandemic disrupted routine healthcare delivery, causing declines in recommended vaccination rates throughout the lifespan.
- Strategies for improving HPV vaccination update in your practice:
 - Ensure a consistent, practice-wide message about the importance of HPV vaccination
 - Take time to answer patient/parent questions
 - Share personal stories as relevant
 - Utilize alerts in EHRs
 - Use every opportunity to vaccinate
 - Use Reminder/Recall strategies to reach out to patients who are behind on their vaccines

Massachusetts Chapter

INCORPORATED IN MASSACHUSETTS

American Academy of Pediatrics 
DEDICATED TO THE HEALTH OF ALL CHILDREN®

Thank you!

Massachusetts Chapter

INCORPORATED IN MASSACHUSETTS

American Academy of Pediatrics 
DEDICATED TO THE HEALTH OF ALL CHILDREN®

Appendix!



Timeline of US HPV Vaccine Approval and Recommendations

YEAR	FDA	ACIP
2006	FDA licensure of HPV ₄ vaccine (Gardasil®) for use in females to prevent infection of four strains of HPV (6, 11, 16, and 18).	ACIP <u>recommendation</u> for routine vaccination of females aged 11 or 12 years with three doses of HPV ₄ vaccine. Catch-up vaccination is recommended for females aged 13 through 26 years. Can be started at age 9.
2009	<p>FDA licensure of bivalent HPV₂ vaccine (Cervarix) for use in females aged 10 through 25 years.</p> <p>FDA licensure of HPV₄ vaccine (Gardasil®) for use in males aged 9 through 26 years for prevention of genital warts caused by human papillomavirus (HPV) types 6 and 11.</p>	<p>ACIP <u>recommendation</u> for routine vaccination of females aged 11 or 12 years with three doses of either HPV₂ or HPV₄ vaccine. Catch-up vaccination is recommended for females aged 13 through 26 years. Can be started at age 9.</p> <p>ACIP guidance that the 3-dose series of HPV₄ may be given to males aged 9 through 26 years to reduce their likelihood of acquiring genital warts. ACIP does not recommend HPV₄ for routine use among males.</p>
2010	FDA adds prevention of anal cancer in males and females as an indication for use of HPV ₄ .	
2011		ACIP <u>recommendation</u> for routine use of HPV ₄ in males aged 11 or 12 years. Recommendation for HPV vaccination for males aged 13 through 21 years who have not been vaccinated previously or who have not completed the 3-dose series; males aged 22 through 26 years may be vaccinated.



Timeline of US HPV Vaccine Approval and Recommendations

YEAR	FDA	ACIP
2014	FDA licensure of Gardasil 9 (9vHPV) for protection against HPV types 6/11/16/18/31/33/45/52/58.	ACIP <u>recommendation</u> for routine use of HPV ₄ or HPV ₂ for females aged 11 or 12 years and with HPV ₄ for males aged 11 or 12 years. Vaccination also recommended for females aged 13 through 26 years and for males aged 13 through 21 years who were not vaccinated previously. Males aged 22 through 26 years may be vaccinated. ACIP recommends vaccination of men who have sex with men and immunocompromised persons (including those with HIV infection) through age 26 years if not previously vaccinated.
2015		ACIP <u>recommendation</u> of 9-valent human papillomavirus (HPV) vaccine (9vHPV) (Gardasil 9) as one of three HPV vaccines that can be used for routine vaccination. HPV vaccine is recommended for routine vaccination at age 11 or 12 years. ACIP also recommends vaccination for females aged 13 through 26 years and males aged 13 through 21 years not vaccinated previously. Vaccination is also recommended through age 26 years for men who have sex with men and for immunocompromised persons (including those with HIV infection) if not vaccinated previously.

Timeline of US HPV Vaccine Approval and Recommendations

YEAR	FDA	ACIP
2016	FDA approved 9vHPV for use in a 2-dose series for girls and boys aged 9 through 14 years.	<p>ACIP <u>recommended</u> 2 doses of HPV vaccine for persons initiating vaccination before their 15th birthday. The second dose should be administered 6–12 months after the first dose (0, 6–12-month schedule). For persons initiating vaccination on or after their 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).</p> <p>ACIP recommended vaccination with 3 doses of HPV vaccine (0, 1–2, 6 months) for females and males aged 9 through 26 years with primary or secondary immunocompromising conditions that might reduce cell-mediated or humoral immunity.</p>
2019	FDA approves Gardasil 9 to include individuals 27 through 45 years old.	<p>ACIP <u>recommendation</u> for children and adults aged 9 through 26 years: HPV vaccination is routinely recommended at age 11 or 12 years; vaccination can be given starting at age 9 years. Catch-up HPV vaccination is recommended for all persons through age 26 years who are not adequately vaccinated.</p> <p>For adults aged >26 years: catch-up HPV vaccination is not recommended for all adults aged >26 years. Instead, shared clinical decision-making regarding HPV vaccination is recommended for some adults aged 27 through 45 years who are not adequately vaccinated. (Box). HPV vaccines are not licensed for use in adults aged >45 years.</p>
2020	FDA adds oropharyngeal and other head and neck cancers to the list of indications for the Gardasil 9 HPV vaccine based on effectiveness in preventing HPV-related anogenital disease.	