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Human Papillomavirus (HPV), Burden of Disease, and Vaccination Uptake

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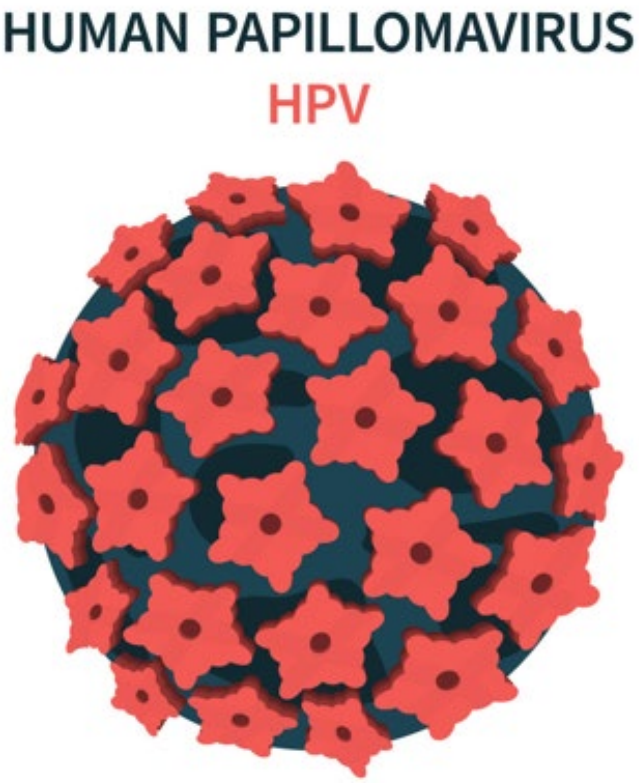
Agenda

1. HPV epidemiology and pathophysiology
2. Timeline of approvals from FDA and ACIP
3. Current vaccine recommendations, schedule, and contraindications
4. Understanding the recommendation for persons 27-45
5. State of HPV vaccination in Massachusetts
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.

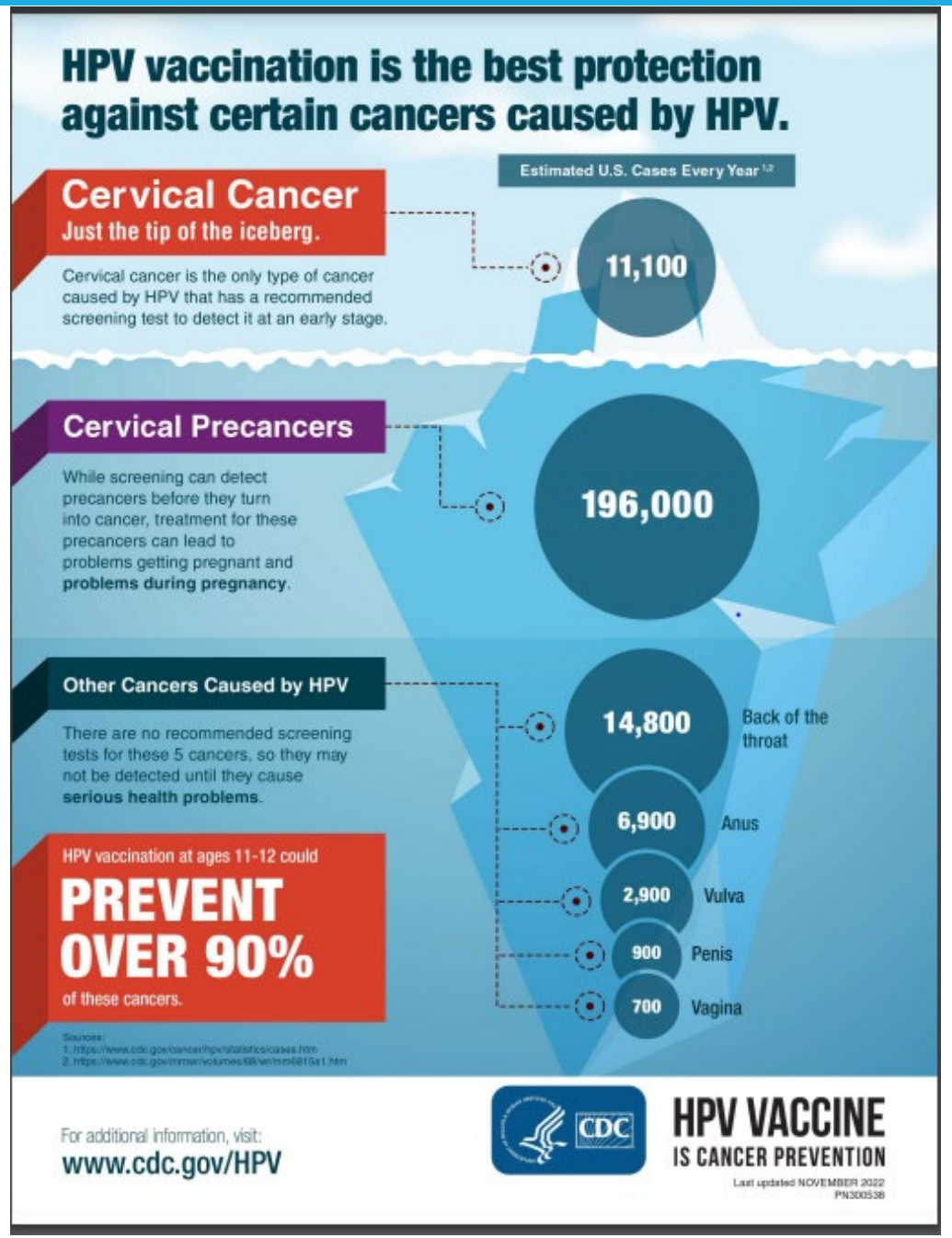


https://www.cdc.gov/hpv/parents/about-hpv.html

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 (≥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**.

https://www.cdc.gov/mmwr/pdf/wk/mm6411.pdf#page=12



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Highlights of FDA Approval and ACIP Recommendation Timeline

See Appendix for full details

2006

FDA approval and ACIP recommendation for routine vaccination with **HPV4** in **females 11-26, *with an option to start as early as age 9***

2009

FDA approval of **HPV2** use in females and **HPV 4 in males 9-26**. ACIP: "may be used in males"

2011

ACIP recommends routine administration for **males 11-21, males** may receive **up to 26**

2014

FDA approval of **HPV9**

2015

ACIP recommends routine vaccination with **HPV9 for all ages 11-21, all females up to 26** and **males with certain risk factors up to 26**

2016

FDA approves and ACIP recommends a **2-dose series** for those initiating series prior to 15th birthday. A 3-dose series should be used for those with certain risk factors

2019

FDA approval and ACIP recommendation for **shared decision making for those 27-45**

ACIP updates recommendation to **all persons 9-26 SHOULD receive.**

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

https://www.cdc.gov/hpv/hcp/schedules-recommendations.html

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).

https://www.cdc.gov/hpv/hcp/schedules-recommendations.html

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.

VERY FEW CONTRAINDICATIONS. THE VACCINE IS SAFE WITH ADVERSE EFFECTS SIMILAR TO OTHER IMMUNIZATIONS

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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.

https://www.cdc.gov/mmwr/volumes/68/wr/mm6832a3.htm

Adolescent (13-17 Years of Age) HPV Vaccination Coverage – NIS, 2022

	1+ Dose		UTD*	
	MA	US	MA	US
Male	85%	74%	78%	61%
Female	87%	78%	76%	65%
Overall	86%	76%	77%	67%

MA rates higher than US rates

Male and female rates are similar

*HPV-UTD – 2 doses if the first dose was given before the 15th birthday and doses were separated by five months; otherwise, 3 doses

MA Adolescent (13-17 Years of Age) HPV Vaccination Coverage – MIIS, 2022

	1+ Dose	UTD
	MA	MA
Male	87%	71%
Female	87%	72%
Overall	87%	71%

Overall, MIIS rates similar to NIS rates

Male and female rates are also similar

Denominator Source: UMass Donahue Institute 2020 Population Estimates

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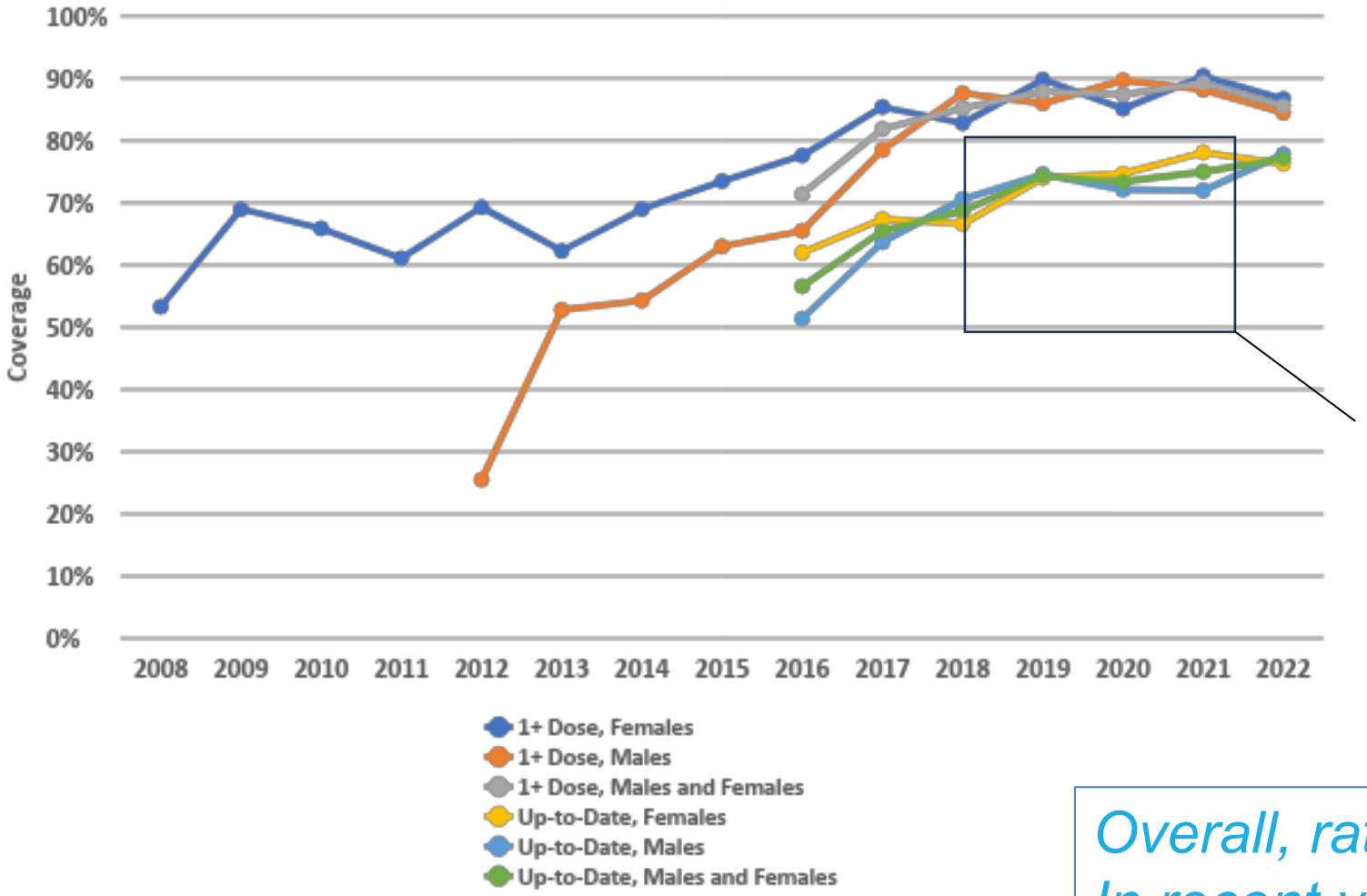
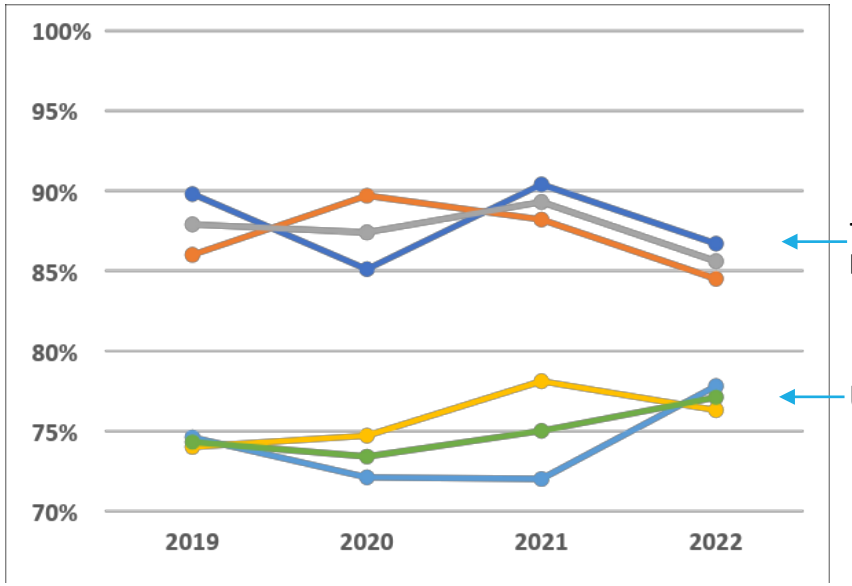
Trends in MA Adolescent (13-17 Years of Age) HPV Vaccination Coverage over Time – NIS, 2008-22





Overall, rates have increased over time
In recent years, these gains have plateaued

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Age of Initial HPV Vaccination over Time – MIIS, 2016-23

	2016	2017	2018	2019	2020	2021	2022	2023
9 Years	2%	2%	3%	4%	5%	8%	10%	12%
10 Years	2%	3%	4%	6%	7%	10%	10%	12%
11 Years	18%	21%	27%	32%	37%	36%	36%	35%
12 Years	19%	20%	22%	22%	22%	19%	19%	18%
13 Years	16%	16%	15%	13%	11%	10%	10%	8%
14 Years	13%	13%	11%	9%	7%	6%	6%	5%
15 Years	10%	8%	6%	4%	3%	3%	3%	3%
16 Years	8%	6%	5%	4%	3%	3%	2%	2%
17 Years	6%	5%	4%	4%	2%	2%	2%	2%
18 Years	5%	4%	3%	3%	2%	2%	2%	2%

HPV initiation shifting to younger ages over time

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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

Thank you!

Appendix

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Timeline of US HPV Vaccine Approval and Recommendations

YEAR	FDA	ACIP
2006	FDA licensure of HPV4 vaccine (Gardasil®) for use in females to prevent infection of four strains of HPV (6, 11, 16, and 18).	ACIP recommendation for routine vaccination of females aged 11 or 12 years with three doses of HPV4 vaccine. Catch-up vaccination is recommended for females aged 13 through 26 years. Can be started at age 9.
2009	FDA licensure of bivalent HPV2 vaccine (Cervarix) for use in females aged 10 through 25 years. 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.	ACIP recommendation 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. 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.
2010	FDA adds prevention of anal cancer in males and females as an indication for use of HPV4.	
2011		ACIP recommendation for routine use of HPV4 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.

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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 recommendation for routine use of HPV4 or HPV2 for females aged 11 or 12 years and with HPV4 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 recommendation 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.

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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.	ACIP recommended 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). 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.
2019	FDA approves Gardasil 9 to include individuals 27 through 45 years old.	ACIP recommendation 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. 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.
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.	