Human Papillomavirus Vaccine

Pink Book Web-on-Demand Series
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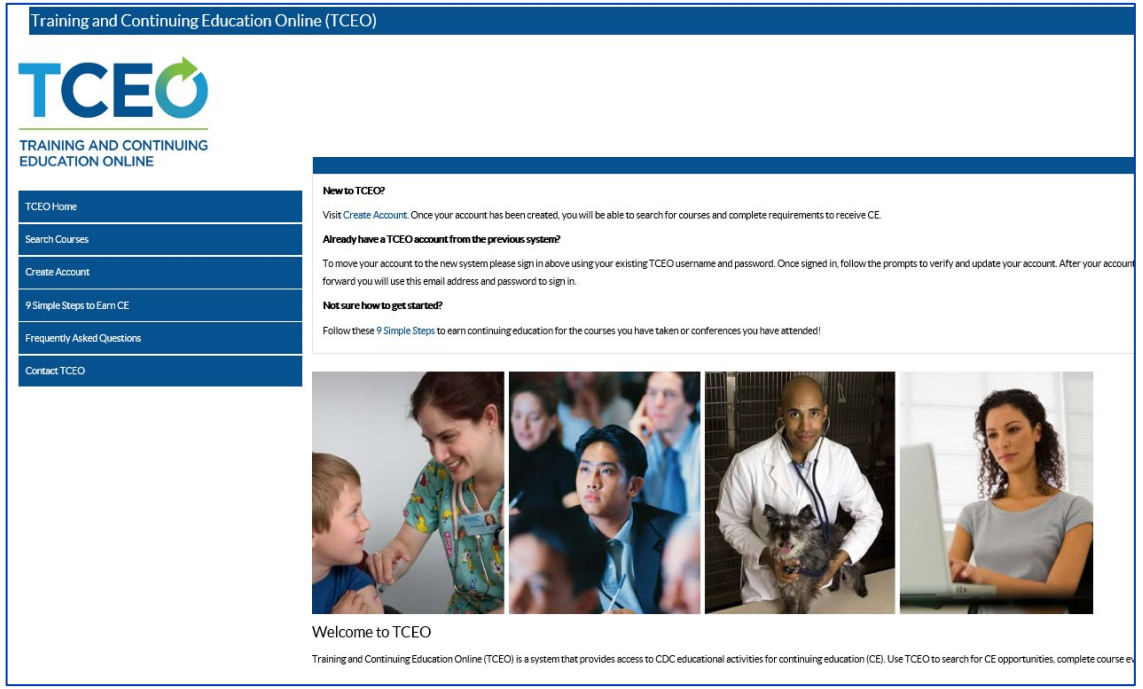
Learning Objectives

- Describe the Advisory Committee on Immunization Practices General Best Practice Guidelines on Immunization.
- Describe an emerging immunization issue.
- For each vaccine-preventable disease, identify those for whom routine immunization is recommended.
- For each vaccine-preventable disease, describe characteristics of the vaccine used to prevent the disease.
- Locate current immunization resources to increase knowledge of team's role in program implementation for improved team performance.
- Implement disease detection and prevention health care services (e.g., smoking cessation, weight reduction, diabetes screening, blood pressure screening, immunization services) to prevent health problems and maintain health.

Continuing Education Information

- **CE credit, go to**: https://tceols.cdc.gov/
- **Search course number: WD4564-100422**
- **CE credit expires: July 1, 2024**
- **CE instructions are available on the Pink Book Web-on-Demand Series web page**
- **Questions and additional help with the online CE system, e-mail** CE@cdc.gov



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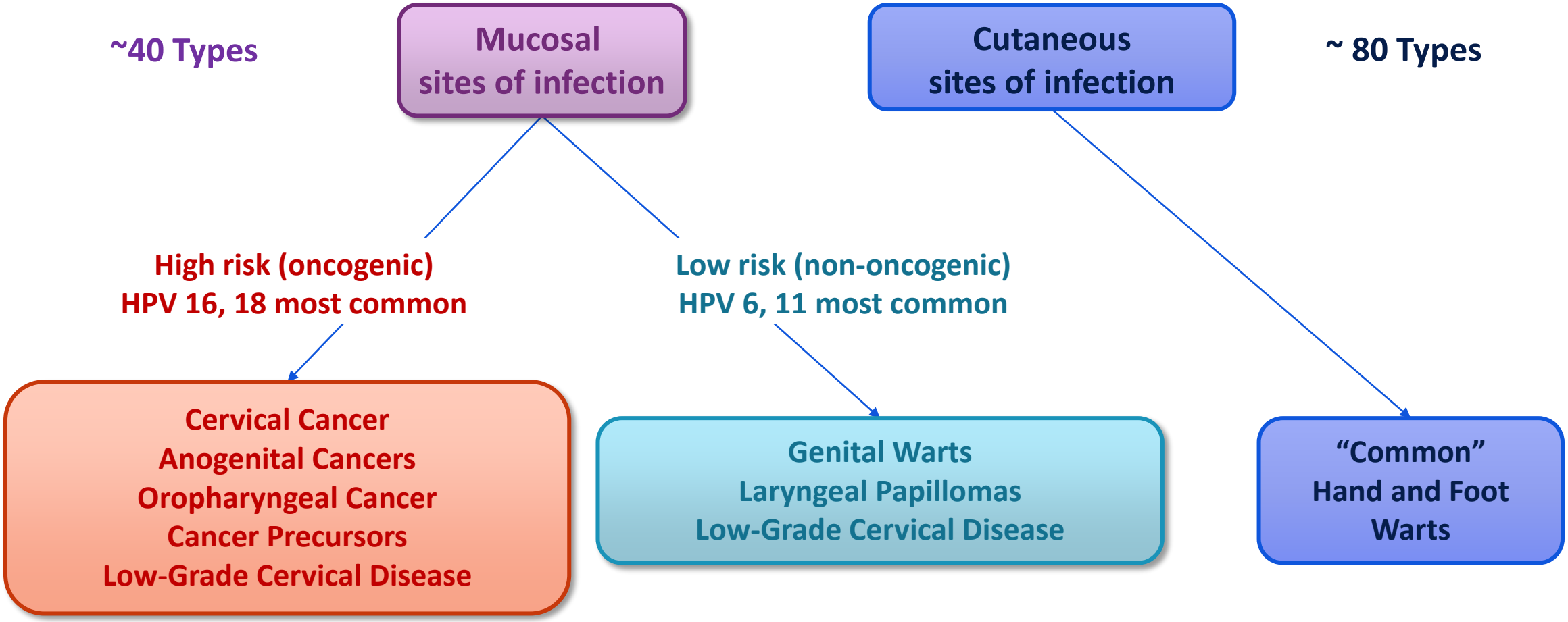
Human Papillomavirus

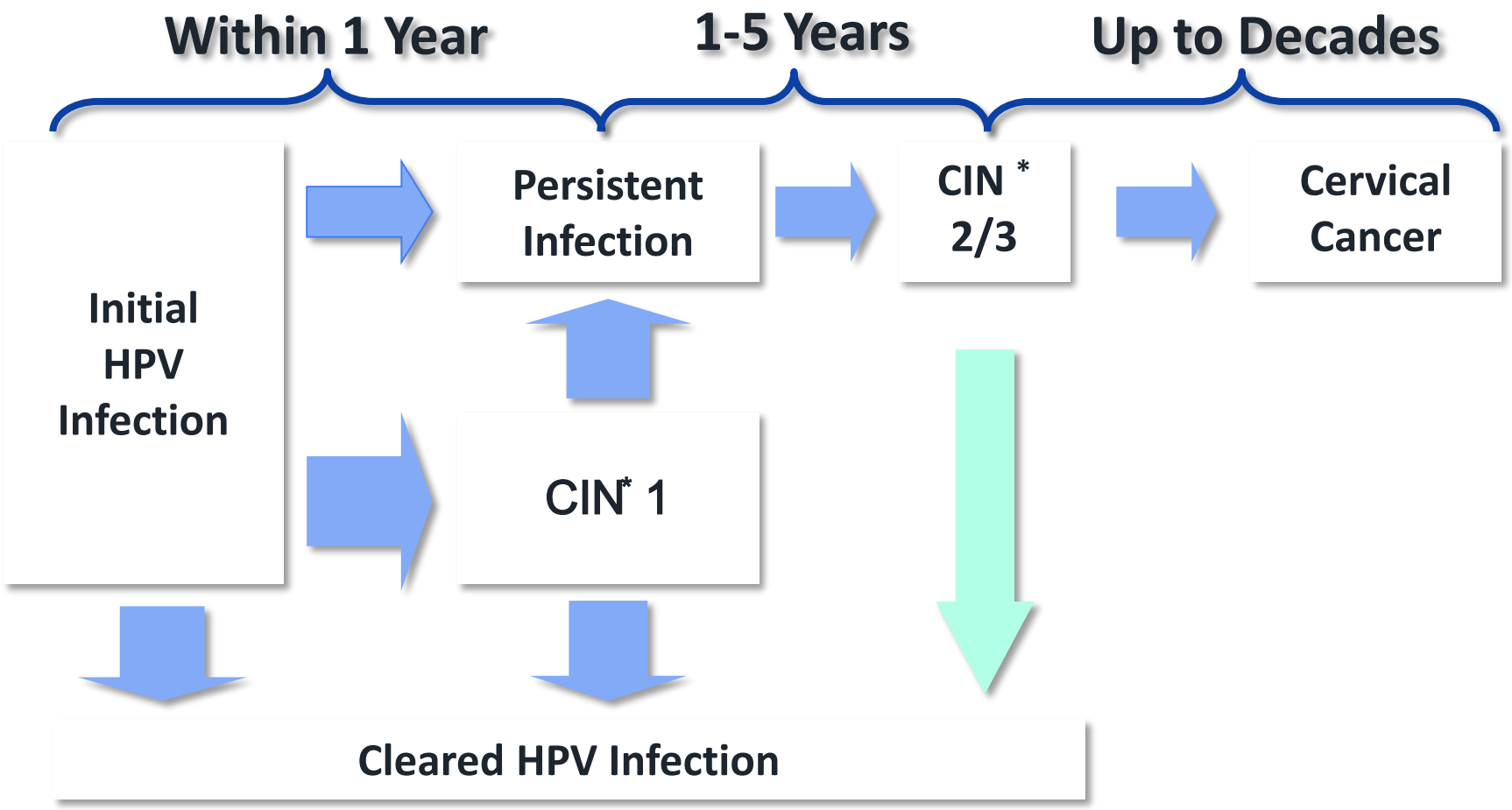
Human Papillomavirus (HPV)

- Most common sexually transmitted infection in the U.S.
- Small DNA virus
- More than 200 types
- First vaccine was licensed in 2006

HPV Types Differ in Their Disease Associations



Natural History of HPV Infection



*CIN = cervical intraepithelial neoplasia

HPV Clinical Features

- **Most HPV infections are asymptomatic and result in no clinical manifestations**

- **Clinical manifestations of HPV infection include:**
  - Anogenital warts
  - Recurrent respiratory papillomatosis
  - Cervical cancer precursors (cervical intraepithelial neoplasia)
  - Cancer (cervical, anal, vaginal, vulvar, penile, and some oropharyngeal cancers)

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

Number of HPV-Associated and HPV-Attributable Cancer Cases Per Year, U.S., 2014–2018

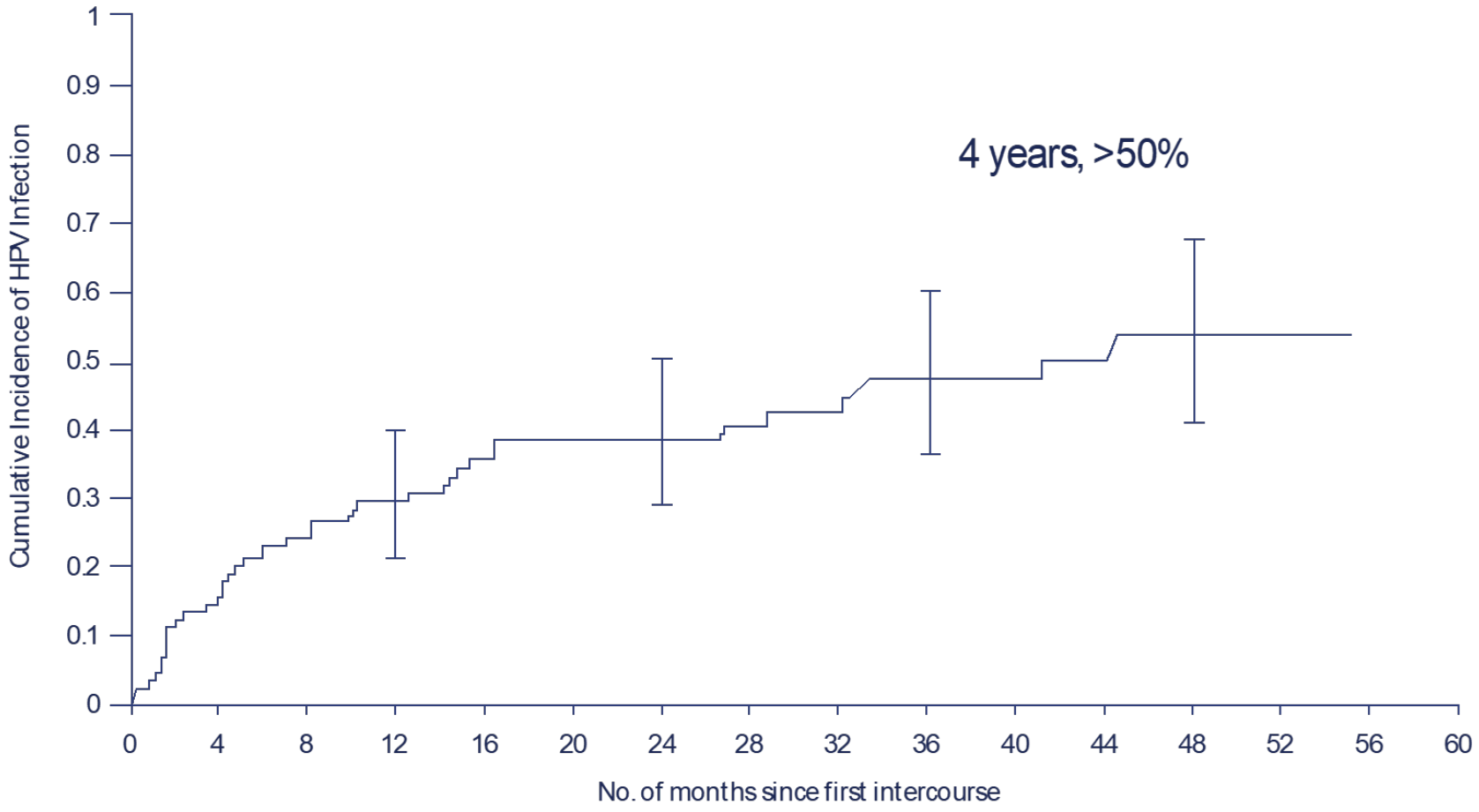
Cancer site	Number of HPV-associated cancers	Percentage probably caused by any HPV type	Estimated number probably caused by any HPV type*		
			Female	Male	Both sexes
Cervix	12,200	91%	11,100	0	11,100
Vagina	863	75%	600	0	600
Vulva	4,191	69%	2,900	0	2,900
Penis	1,365	63%	0	900	900
Anus**	7,288	91%	4,500	2,100	6,600
Oropharynx	20,236	70%	2,300	12,100	14,400
TOTAL	**46,143**	**79%**	**21,400**	**15,100**	**36,500**

*Estimates were rounded to the nearest 100. Estimated counts might not sum to total because of rounding.
**Includes anal and rectal squamous cell carcinomas
Sources: https://www.cdc.gov/cancer/hpv/statistics and http://www.cdc.gov/cancer/dataviz

HPV Epidemiology

Reservoir	Human
Transmission	Direct contact (skin to skin)
Temporal pattern	None
Communicability	Presumed to be high

Cumulative Incidence of any HPV Infection Months after Sexual Initiation



Am J Epidemiol 2003;157(3):218–26

HPV Disease Burden in the U.S.

- **Estimated 42 million persons are infected**
  - ~13 million persons with a new infection annually
- **Common among adolescents and young adults**
  - 50% of new infections occur in persons 15–24 years of age
- **Approximately $10.8 billion spent annually on management of sequelae of HPV infections**
- **Most people will never know that they have been infected**

Chesson HW et al., Vaccine 2012; 30: 6016–19. Updated to 2021 US dollars using the "medical care" component of the consumer price index (https://www.bls.gov/cpi/)
Lewis R et al. STD 2021; 48: 273-77

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Human Papillomavirus Vaccine

HPV Vaccine

- **HPV vaccine (9vHPV, Gardasil 9) is currently licensed for use in the United States**
  - Only HPV vaccine currently available in the United States
- **Two other HPV vaccines, quadrivalent HPV vaccine (4vHPV, Gardasil 4) and a bivalent HPV vaccine (2vHPV, Cervarix) are licensed in the United States, but are no longer available in this country**

HPV Children and Adult Vaccination Schedule

Vaccine	Birth	1 mo	2 mos	4 mos	6 mos	9 mos	12 mos	15 mos	18 mos	19–23 mos	2–3 yrs	4–6 yrs	7–10 yrs	11–12 yrs	13–15 yrs	16 yrs	17–18 yrs
Human papillomavirus (HPV)														See Notes			

Vaccine	19–26 years	27–49 years	50–64 years	≥65 years
Human papillomavirus (HPV)	2 or 3 doses depending on age at initial vaccination or condition	27 through 45 years		

- Non-live vaccine
- Administered by intramuscular (IM) injection

HPV Vaccine

HPV Vaccines	9-valent 9vHPV (Gardasil 9)
L1 VLP types	6, 11, 16, 18, 31, 33, 45, 52, 58
Manufacturer	Merck
Contraindications	Hypersensitivity to yeast
FDA indications	Females (9–45 yrs): Anal, cervical, vaginal, vulvar, oropharyngeal and other head and neck cancers, genital wars; precancerous or dysplastic lesions
	Males (9–45 yrs): Anal, oropharyngeal and other head and neck cancers, genital warts, and precancerous or dysplastic lesions

- **Only 9vHPV vaccine is available in the U.S.**

https://www.fda.gov/vaccines-blood-biologics/vaccines/Gardasil-9

HPV Vaccine Efficacy

- High efficacy among females without evidence of infection with vaccine HPV types (more than 95%)

- No evidence of efficacy against disease caused by vaccine types participants were infected with at the time of vaccination

- Prior infection with one HPV type did not diminish the efficacy of the vaccine against other vaccine HPV types

Expanded age indication for 9-valent HPV vaccine

- Manufacturer filed an application with FDA in April 2018 to expand age indication through 45 years
- FDA approved October 2018
- Evidence based on bridging data from a study of the quadrivalent HPV vaccine in this age group
- ACIP made a recommendation for shared clinical decision-making in this age group in 2019.

9vHPV (Gardasil 9) Efficacy and Safety

- Efficacy
- Noninferior immunogenicity to 4vHPV
- 5 additional types account for 11% of invasive cancers
- Safety profile similar to 4vHPV across age, gender, race, ethnic groups

HPV Vaccine Duration of Protection

- **Studies suggest that vaccine protection is long-lasting**
- **No evidence of waning protection**
  - Available evidence indicates protection for *at least* 12 years
  - Multiple studies are in progress to monitor

Knowledge Check

- **A provider is evaluating a 52-year-old woman with a history of multiple sex partners and genital warts. She has not previously received any HPV vaccine. Is HPV vaccine recommended for her?**
  - A. Yes
  - B. No

Answer

- A provider is evaluating a 52-year-old woman with a history of multiple sex partners and genital warts. She has not previously received any HPV vaccine. Is HPV vaccine recommended for her?

  - B. No

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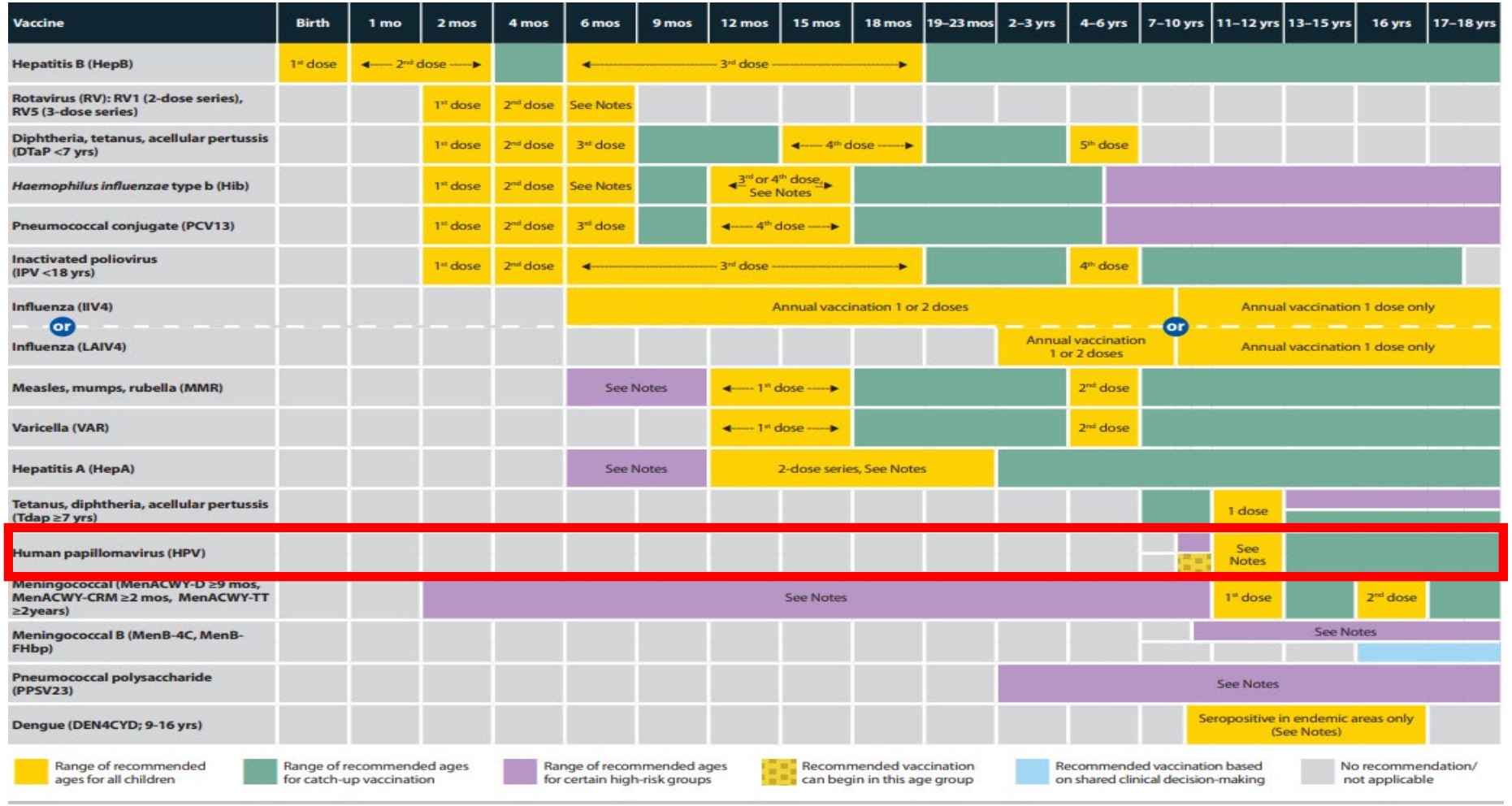
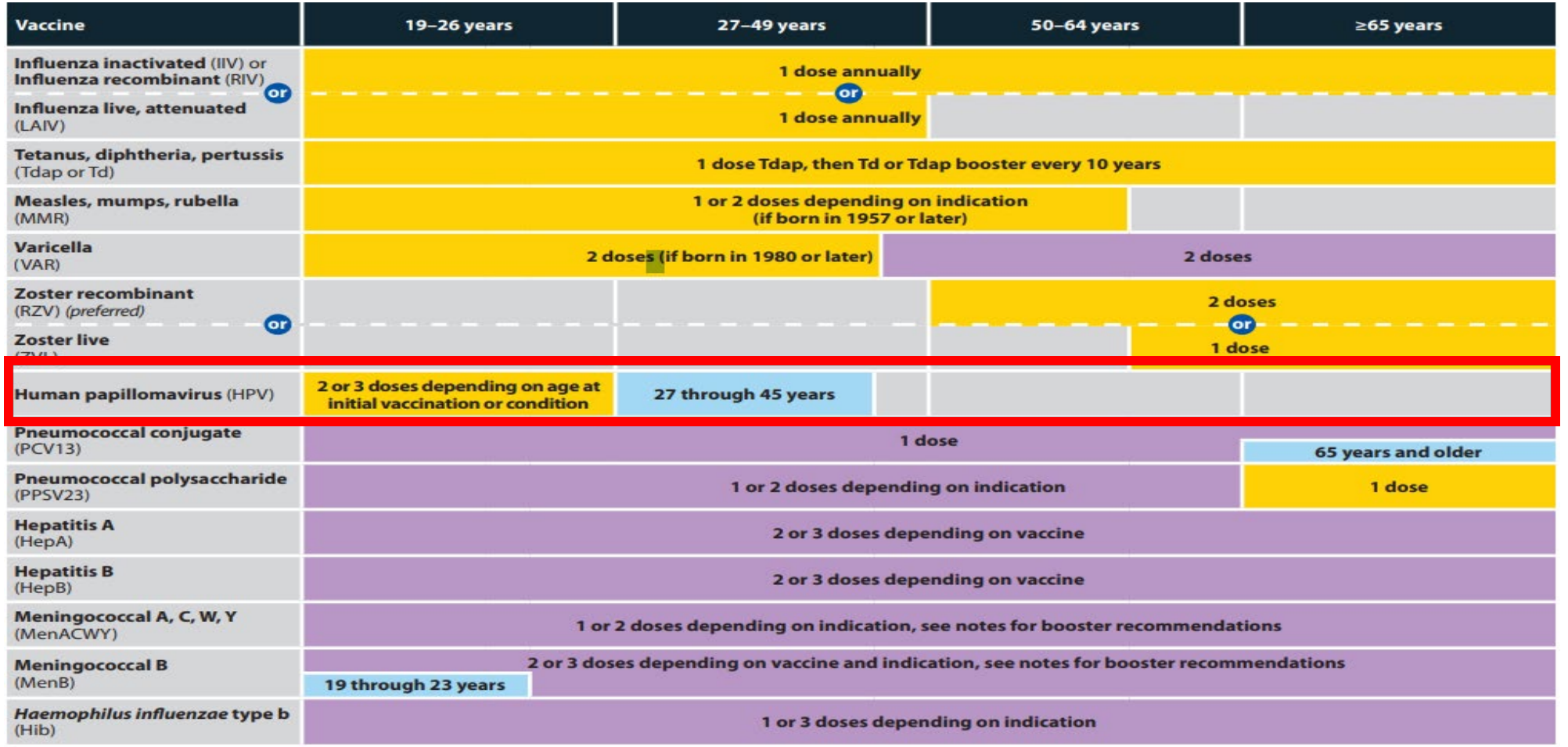
Clinical Considerations

Recommended Child and Adolescent Immunization Schedule for ages 18 years and younger, 2022



https://www.cdc.gov/vaccines/schedules/downloads/child/0-18yrs-child-combined-schedule.pdf

Recommended Adult Immunization Schedule for ages 19 years or older, 2022



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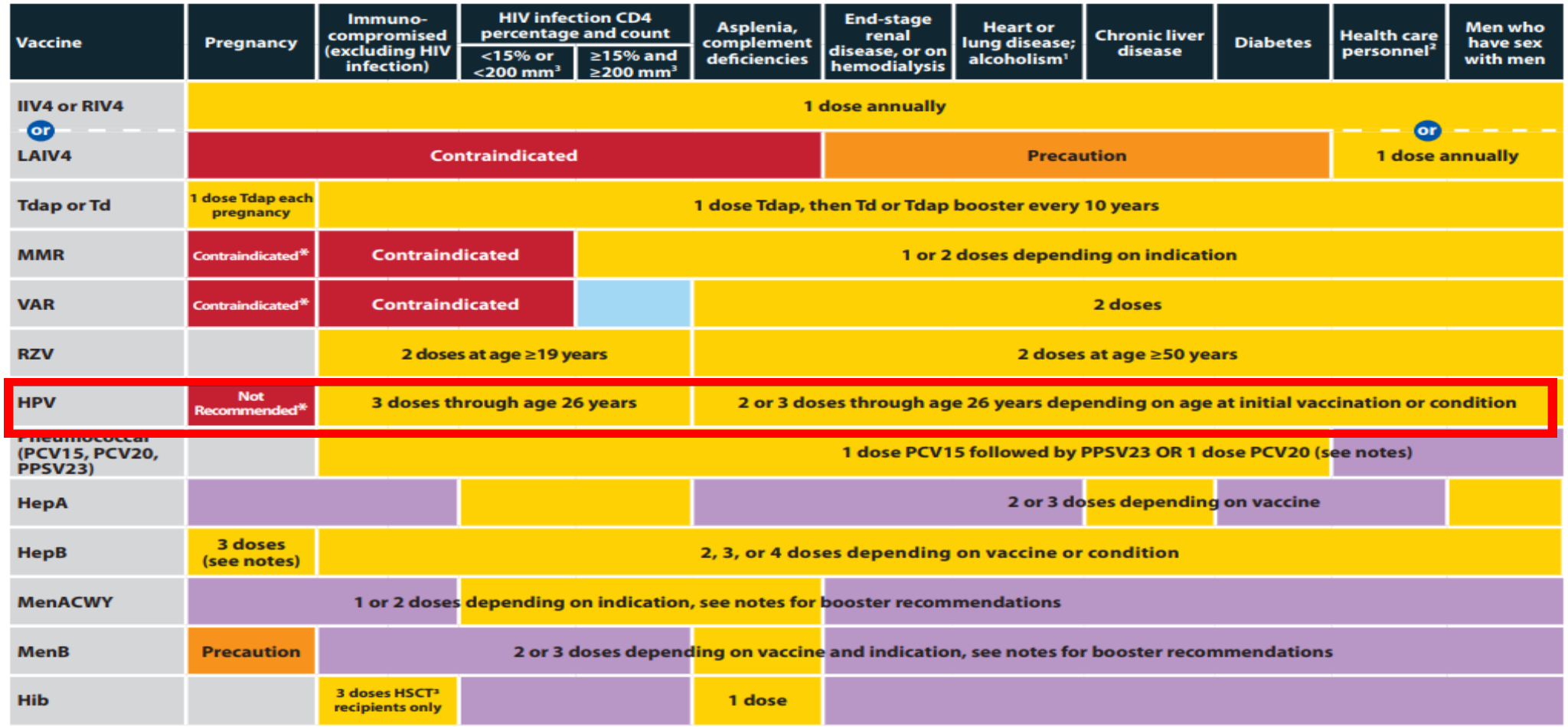

1. Precaution for LAIV4 does not apply to alcoholism. **2.** See notes for influenza; hepatitis B; measles, mumps, and rubella; and varicella vaccinations. **3.** Hematopoietic stem cell transplant.

Human Papillomavirus Vaccine Routine Recommendations

- **Routinely vaccinate boys and girls at 11–12**
  - Vaccination series can be started at 9 years of age
    - HPV vaccination recommended for all males and females aged 13 through age 26 years: if not adequately vaccinated

MMWR 2015;64:300–4

HPV Vaccine Dosing Schedule, United States

Population	Number of vaccine doses	Interval between doses
Persons initiating vaccination at **9 through 14** years, except persons with immunocompromising conditions	2	0, 6–12 months*
Persons initiating vaccination at **15 through 26** years and persons with immunocompromising conditions initiating vaccination at 9 through 26 years	3	0, 1–2, 6 months[+]

* In a 2-dose schedule of HPV vaccine, the minimum interval between first and second doses is 5 months.

[+] In a 3-dose schedule of HPV vaccine, the minimum intervals are 4 weeks between the first and second doses, 12 weeks between the second and third doses, and 5 months between the first and third doses

- **Persons are considered adequately vaccinated if they completed a recommended schedule with 9vHPV, 4vHPV, or 2vHPV vaccine.**

Meites, et al *MMWR Morb Mortal Wkly Rep* 2016

HPV Vaccination Schedules

- Data from clinical trials showed 2 doses of HPV vaccine given in younger adolescents (9–14 years) produced an immune response similar to or higher than the response in young adults (16–26 years) who received 3 doses

- Data available to date show that a 3-dose schedule in older adolescents and young adults provides long-lasting protection

- Data suggest that a 2-dose schedule given to younger adolescents will also provide long-lasting protection

ACIP HPV Immunization Recommendations
Previously Unvaccinated Adolescents: Age 9–14 years

- **Administer 2 doses of HPV vaccine to adolescents starting the series at 9–14 years of age.**
- **Follow the routine 2-dose schedule:**
  - Administer the second dose 6-12 months after the first dose.
- **If a second dose is inadvertently administered prior to 5 months, default to a 3-dose series.**

https://www.cdc.gov/vaccines/pubs/pinkbook/supplement.html

ACIP HPV Immunization Recommendations
Previously Unvaccinated Adolescents: Age 15 years or older

- **Administer 3 doses to adolescents starting the series on or after the 15th birthday**
  - Even those who initiate vaccination at age
- **Routine 3-dose schedule: 0, 1–2, 6 months**
  - Dose #2 should be administered at least 1 month after dose 1
  - Dose #3: Administer at least:
    - 12 weeks after dose 2 AND
    - 5 months after dose 1
- **An accelerated schedule using minimum intervals is not recommended**

MMWR 2016;65(49):1405–08

ACIP HPV Immunization Recommendations
Previously Unvaccinated Adolescents: Immunocompromised

- **Administer 3 doses for persons who have immunocompromising conditions**
  - Even for those who initiated vaccination at age 9–14 years
- **Routine 3-dose schedule: 0, 1–2, 6 months**

MMWR 2016;65(49):1405–08

ACIP HPV Immunization Recommendations for Persons with an Incomplete Series or Who Previously Received 4vHPV or 2vHPV

- **Adolescents who initiated vaccination with 9vHPV, 4vHPV, or 2vHPV**
  - Before their 15th birthday, are fully vaccinated if they received:
    - 2 doses at the recommended dosing schedule (0, 6–12 months) OR
    - 3 doses at the recommended dosing schedule (0, 1–2, 6 months)
  - On or after the 15th birthday are fully vaccinated if they received:
    - 3 doses at the recommended dosing schedule (0, 1–2, 6 months)
- **All of the doses do not have to be 9vHPV**

MMWR 2016;65(49):1405–08

HPV Vaccination of Adults 27–45 Years of Age

- **Shared clinical decision-making is recommended for adults 27–45 years of age**

- **Shared clinical decision-making includes adults who may have received doses prior to the 27th birthday**

https://www.cdc.gov/mmwr/volumes/68/wr/pdfs/mm6832a3-H.pdf

Considerations for Shared Clinical Decision-Making Regarding HPV Vaccination of Adults Aged 27–45 Years

- **HPV is a very common sexually transmitted infection. Most HPV infections are transient and asymptomatic and cause no clinical problems.**

- **Although new HPV infections are most commonly acquired in adolescence and young adulthood, some adults are at risk for acquiring new HPV infections. At any age, having a new sex partner is a risk factor for acquiring a new HPV infection.**

- **Persons who are in a long-term, mutually monogamous sexual partnership are not likely to acquire a new HPV infection.**

- **Most sexually active adults have been exposed to some HPV types, although not necessarily all of the HPV types targeted by vaccination.**

https://www.cdc.gov/mmwr/volumes/68/wr/pdfs/mm6832a3-H.pdf

Considerations for Shared Clinical Decision-Making Regarding Human Papillomavirus (HPV) Vaccination of Adults Aged 27 through 45

- **No clinical antibody test can determine whether a person is already immune or still susceptible to any given HPV type.**

- **HPV vaccine efficacy is high among persons who have not been exposed to vaccine-type HPV before vaccination.**

- **Vaccine effectiveness might be low among persons with risk factors for HPV infection or disease (e.g., adults with multiple lifetime sex partners and likely previous infection with vaccine-type HPV), as well as among persons with certain immunocompromising conditions.**

- **HPV vaccines are prophylactic (i.e., they prevent new HPV infections). They do not prevent progression of HPV infection to disease, decrease time to clearance of HPV infection, or treat HPV-related disease.**

https://www.cdc.gov/mmwr/volumes/68/wr/pdfs/mm6832a3-H.pdf

Knowledge Check

- **A 30-year-old woman received a first dose of HPV vaccine at 25 years of age. Is shared clinical decision-making recommended to continue the series?**

  - A. Yes
  - B. No

Answer

- A 30-year-old woman received a first dose of HPV vaccine at 25 years of age. Is shared clinical decision-making recommended to continue the series?
  - A. Yes

ACIP HPV Immunization Recommendations: Additional Considerations

- **No therapeutic effect on HPV infection, genital warts, cervical lesions**

- **Prevaccination assessments not recommended**
  - HPV
  - Pregnancy

Human Papillomavirus Vaccine and Pregnancy

- HPV vaccination should be delayed until after pregnancy.
- If a person is found to be pregnant after starting the HPV vaccine series, second and/or third doses should be delayed until they are no longer pregnant.
- If a person receives HPV vaccine and later learns that they are pregnant, there is no reason to be alarmed.
- Anyone who learns they are pregnant when they received an HPV vaccine can contact the manufacturer at 1-877-888-4231
- Any suspected adverse events following HPV vaccination during pregnancy should be reported to VAERS.

https://www.cdc.gov/vaccines/vpd/hpv/hcp/recommendations.html

Knowledge Check

- **A woman becomes pregnant while receiving HPV vaccine. Do you continue with the series?**

  - A. Yes
  - B. No

Answer

- A woman becomes pregnant while receiving HPV vaccine. Do you continue with the series?
  - B. No

HPV Vaccine Administration

- **Administer HPV vaccine via IM injection:**
  - Needle size: 1- through 1½-inch, 22- to 25-gauge
  - Site: Deltoid muscle in the upper arm

- **Follow proper injection practices:**
  - Use aseptic technique
  - Use a new needle and syringe for each injection

- **Administer HPV vaccine at the same medical visit as other vaccines.**

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Safety

Contraindications

HPV
Severe allergic reaction (e.g., anaphylaxis) after a previous dose or to a vaccine component, including yeast

Precautions

HPV
Moderate or severe acute illness with or without fever

HPV Vaccine Safety Summary: Selected Sources of data and Key Findings

- **Over 135 million doses distributed in the United States through 2020**
  - More than 14 years of monitoring
- **Vaccine Adverse Event Reporting System (VAERS)**
  - No unusual outcomes identified; syncope are one of the common reports
  - 4vHPV, 2vHPV and 9vHPV
- **Vaccine Safety Data Link (VDS)***
  - Other studies to investigate associations**
  - No safety concerns for pre-specified autoimmune, neurologic or other diseases
- **World Health Organization Global Advisory Committee on Vaccine Safety**
  - Multiple reviews – most recently 2020[+]

*Gee et al. Vaccine 2011; Gee et al. Vaccine 2017; Donahue et al. Pediatrics 2019; **Chao et al. J Intern Med 2012; Arnheim-Dahlstrom et al. BMJ 2013. Grimaldi-Bensouda et al. J Intern Med 2013; Scheller et al. JAMA 2015; Gee et al. Hum Vaccin Immunother. 2016; [+] WHO WER. July 2017 and https://www.who.int/publications/m/item/WER-2020-95-28-(full-issue) http://www.who.int/vaccine_safety/committee/topics/hpv/June_2017/en/
https://www.cdc.gov/vaccinesafety/vaccines/hpv/hpv-safety-faqs.html#A10

HPV Vaccine Adverse Reactions

- Reactions after vaccination can include:
  - Injection site reactions: pain, redness, and/or swelling in the arm where the shot was given
  - Systemic: fever, headaches, nausea, muscle or joint pain
- Life threatening allergic reaction can occur after any vaccine, including HPV vaccines
- Brief fainting spells (syncope) and related symptoms (such as jerking movements) can happen soon after any injection, including HPV vaccine
  - Patients should be seated (or lying down) during vaccination and remain in that position for 15 minutes

HPV Vaccine Safety and Effectiveness Data | CDC

https://www.cdc.gov/vaccinesafety/vaccines/hpv/hpv-safety-faqs.html

Gee, et al. *Hum Vaccine Immunother.* 2016

Knowledge Check

- **All of the following strategies can be used to help to prevent syncope when vaccinating adolescents EXCEPT?**
  - a. vaccinating while in a sitting position?
  - b. vaccinating while in a standing position?
  - c. vaccinating while in a lying down position?
  - d. observing patients for 15 minutes following vaccination?

Answer

- **All of the following strategies can be used to help to prevent syncope when vaccinating adolescents EXCEPT?**
  - A. vaccinating while in a sitting position?
  - B. vaccinating while in a standing position?
  - C. vaccinating while in a lying down position?
  - D. observing patients for 15 minutes following vaccination?

B. vaccinating while in a standing position

HPV Vaccination Coverage Adolescents 13 through 17 Years of Age, 2021

HPV Vaccine	U.S.	
	Females	Males
1 or more doses*	78.5%	75.4%
HPV UTD**	61.7%	56.0%

For HPV percentage of ≥1 dose measure and HPV UTD measure and included 9vHPV, 4vHPV or 2vHPV vaccines used.

**HPV UTD includes those with ≥3 doses and with 2 doses when the first HPV vaccine dose was initiated before age 15 years and there was at least 5 months minus 4 days between the first and second dose.

https://www.cdc.gov/mmwr/volumes/71/wr/mm7135a1.htm#F1_down

HPV Vaccine Communications during the Health Care Encounter

- **HPV vaccine is often presented as optional, whereas other adolescent vaccines are recommended.**
- **Some providers expressed mixed or negative opinions about relatively new vaccines and concerns over safety and efficacy.**
- **When parents' express reluctance, providers are hesitant to engage in discussion.**
- **Some providers share parents' views that a teen is not at risk for HPV and vaccination can be delayed until the teen is older.**

Goff S, et al. *Vaccine* 2011;10:7343–9
Hughes C, et al. *BMC Pediatrics* 2011;11:74

Strategies for Increasing HPV Vaccination Coverage in Clinical Practices

- **Recommend HPV vaccine**
  - Include HPV vaccine when discussing other recommended vaccines.
- **Integrate standard procedures supporting vaccination:**
  - Assess for needed vaccines at every clinical encounter
  - Vaccinate at every opportunity
  - Use standing orders
- **Reminder and recall**
- **Tools for improving uptake of HPV vaccine at www.cdc.gov/vaccines/teens**

5

Storage & Handling

Vaccine Storage and Handling

- **Store HPV vaccine in a refrigerator between 2°C and 8°C (36°F and 46°F)**
- **Store HPV vaccines:**
  - In the original packaging with the lids closed
  - In a clearly labeled bin of the storage unit
- **Do not freeze the vaccine**
- **Protect the vaccine from light**

Vaccine storage label example is available at: https://www.cdc.gov/vaccines/hcp/admin/storage/guide/vaccine-storage-labels.pdf

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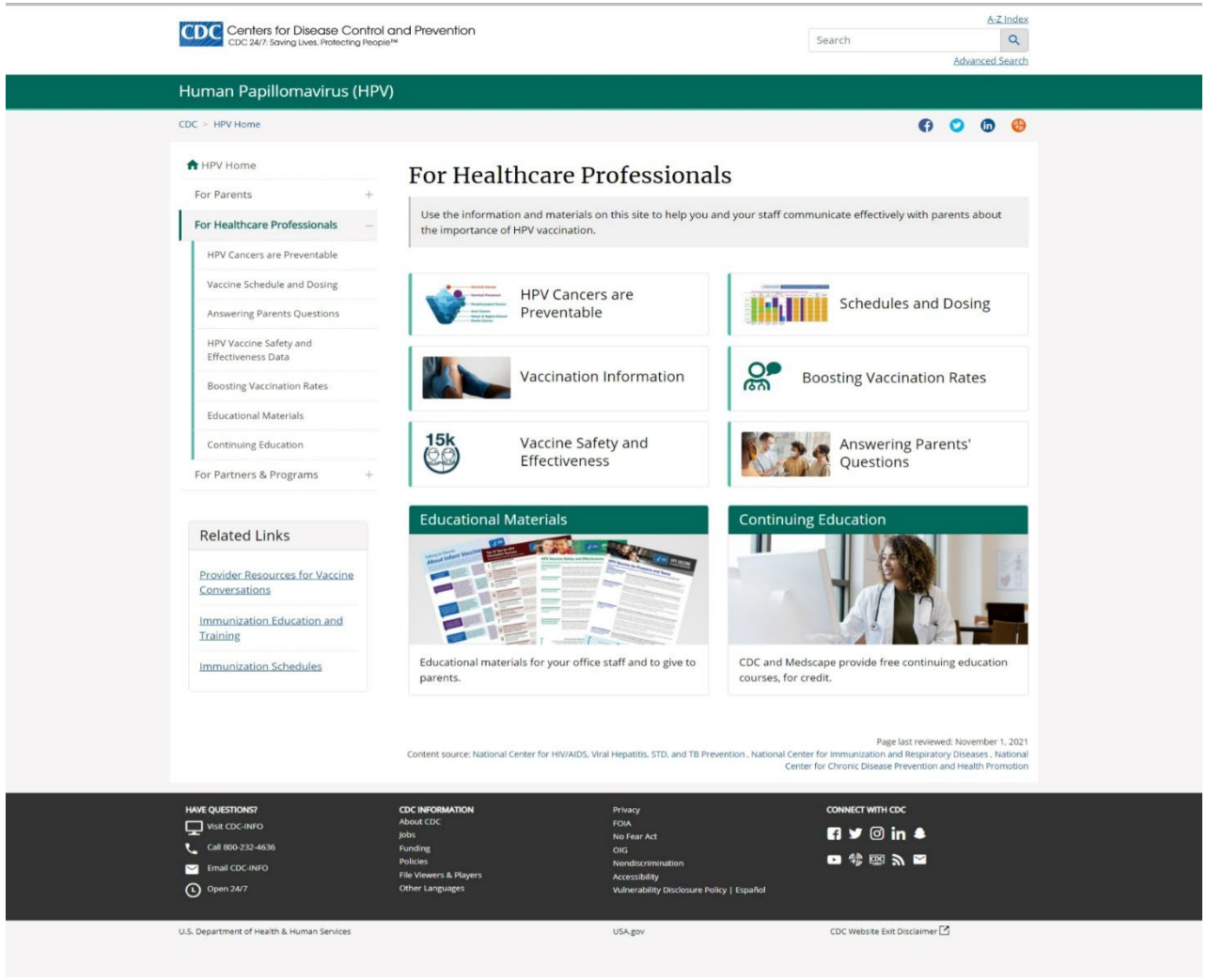
Resources

HPV Vaccination Resources for HCP



https://www.cdc.gov/hpv/hcp/index.html?CDC_AA_refVal=https%3A%2F%2Fwww.cdc.gov%2Fvaccines%2Fyouarethekey%2Findex.html

HPV Vaccine Resources

- **Human papillomavirus resource pages at**
  - https://www.cdc.gov/vaccines/ed/webinar-epv/
- **Includes information for:**
  - Health care providers on:
    - Disease and treatment
    - Vaccine administration, storage, and handling
  - Parents and patients on:
    - Disease
    - Vaccine safety
  - Partners and programs
    - Print materials, articles, online, video and audio resources

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- **Questions and additional help with the online CE system, e-mail** CE@cdc.gov

E-mail Your Immunization Questions to Us

- NIPINFO@cdc.gov

Thank You From Atlanta!