**Centers for Disease Control and Prevention** National Center for Immunization and Respiratory Diseases



# Human Papillomavirus – 2019

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# Human Papillomavirus (HPV) Disease

Most common sexually transmitted infection in the U.S.

Small DNA virus

More than 150 types

First vaccine was licensed in 2006

# Human Papillomavirus Type and Disease Association

Mucosal (~40 types) Cutaneous (other types) "Common" Warts (hands/feet) "Low-risk" "High-risk" Types **Types** (16,18, others) (6, 11, others) Low-grade cervical Low-grade cervical abnormalities abnormalities **Genital warts** 

- High grade abnormalities/
- Cancer precursors

Anogenital cancers

Respiratory papillomas

https://www.cdc.gov/vaccines/acip/meetings/downloads/slides-2019-06/HPV-4-Chesson-508.pdf

# **Natural History of HPV Infection**



### **HPV Clinical Features**

### Most HPV infections are asymptomatic and result in no clinical disease

#### 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)

TABLE 1. Average annual number and rate of human papillomavirus (HPV)–associated cancers and estimated percentage and annual number of cancers attributable to HPV, by HPV type, cancer type, and sex — United States,\* 2012–2016

	Reported HPV-associa	ated cancers⁺	ancers <sup>+</sup> Estimated no. <sup>s</sup> (%) of cancers attributable to HPV types <sup>1</sup>			
Cancer type	Total no.**	Rate*	9vHPV-targeted	Other HPV	HPV-negative	
Cervix	12,015	7.2	9,700 (81)	1,200 (10)	1,100 (9)	
Vagina	862	0.4	600 (73)	0 (2)	300 (25)	
Vulva	4,009	2.1	2,500 (63)	300 (6)	1,200 (31)	
Penis	1,303	0.8	700 (57)	100 (6)	500 (37)	
Anus	6,810	1.8	6,000 (88)	200 (3)	600 (9)	
Female	4,539	2.3	4,100 (90)	100 (2)	300 (8)	
Male	2,270	1.3	1,900 (83)	100 (6)	300 (11)	
Oropharynx	19,000	4.9	12,600 (66)	900 (5)	5,500 (29)	
Female	3,460	1.7	2,100 (60)	100 (3)	1,300 (37)	
Male	15,540	8.5	10,500 (68)	800 (5)	4,200 (28)	
Total	43,999	12.2	32,100 (73)	2,700 (6)	9,200 (21)	
Female	24,886	13.7	19,000 (76)	1,700 (7)	4,200 (17)	
Male	19,113	10.6	13,100 (69)	1,000 (5)	5,000 (26)	

Abbreviations: 9vHPV = 9-valent HPV vaccine; ICD-O-3 = International Classification of Diseases for Oncology, Third Edition.

\* Compiled from population-based cancer registries that participate in the CDC National Program of Cancer Registries, and/or the National Cancer Institute's Surveillance, Epidemiology, and End Results Program and meet the criteria for high data quality for all years during 2012–2016, covering 100% of the U.S. population. <sup>+</sup> HPV-associated cancers were defined as invasive cancers at anatomic sites with cell types in which HPV DNA frequently is found. All cancers were histologically confirmed. Cervical cancers (ICD-O-3 site codes C53.0–C53.9) are limited to carcinomas (ICD-O-3 histology codes 8010–8671, 8940–8941). Vaginal (ICD-O-3 site code C52.9), vulvar (ICD-O-3 site codes C51.0–C51.9), penile (ICD-O-3 site codes C60.0–60.9), anal (ICD-O-3 site codes C20.9, C21.0–C21.9) and oropharyngeal (ICD-O-3 site codes C01.9, C02.4, C02.8, C05.1, C05.2, C09.0, C09.1, C09.8, C09.9, C10.0, C10.1, C10.2, C10.3, C10.4, C10.8, C10.9, C14.0, C14.2, and C14.8) cancer sites are limited to squamous cell carcinomas (ICD-O-3 histology codes 8050–8084, 8120–8131).

<sup>5</sup> HPV-attributable cancers are cancers that are probably caused by HPV (<u>https://academic.oup.com/jnci/article/107/6/djv086/872092</u> ]). Estimates for attributable fraction were based on studies that used population-based data from cancer tissue studies to estimate the percentage of those cancers probably caused by HPV. The

### **HPV Epidemiology**

Reservoir

Human

Transmission

Direct contact (usually sexual)

Temporal pattern

None

• **Communicability** Presumed to be high

# **Cumulative Incidence of any HPV Infection Months after Sexual Initiation**



### **HPV Disease Burden in the U.S.**

### Estimated 79 million persons are infected

• ~ 14 million new infections annually

#### Common among adolescents and young adults

• 50% of new infections occur in persons 15–24 years of age

# About \$8 billion spent annually on management of sequelae of HPV infections

**Cervical Cancer Screening** 

- Revised in 2018
- Screening should begin at age 21 years
- Screen women 21 to 29 years of age with Pap test every 3 years
- Screen women 30 to 65 years of age with Pap test every 3 years; HPV test every 5 years; or Co-testing (Pap and HPV testing) every 5 years

Human Papillomavirus Vaccine

• HPV L1 major capsid protein of the virus is antigen used for immunization

L1 protein produced using recombinant DNA technology

L1 proteins self-assemble into virus-like particles (VLP)

VLPs are noninfectious and nononcogenic

# Human Papillomavirus Vaccine

HPV Vaccines	9-valent 9vHPV (Gardasil9)
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, and vulvar precancer and cancer; genital warts
	Males (9—45 yrs): Anal precancer and cancer; genital warts

# Only 9vHPV vaccine is available in the US

# Human Papillomavirus Vaccine Efficacy

High efficacy among females without evidence of infection with vaccine HPV types (>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 efficacy of the vaccine against other vaccine HPV types

### 9vHPV (Gardasil9)

Licensed by the FDA for males and females 9 through 45 years of age

- Trials conducted with 3-dose schedule
- Targets 5 additional high-risk types:
  - 6, 11, 16, 18, **31, 33, 45, 52, 58**

# **9vHPV (Gardasil9) Efficacy and Safety**

## Efficacy

- ~97% protection against 31-,33-,45-,52-,58-related outcomes
- Similar protection against 6-,11-,16-,18-related disease
- Noninferior immunogenicity to 4vHPV
- 5 additional types account for 11% of invasive cancers
  - Differences by gender: 14% for females; 4% for males
- 9vHPV can be administered at the same medical visit with MenACWY and Tdap
- Safety profile similar to 4vHPV across age, gender, race, ethnicity groups

# 9vHPV (Gardasil9) Efficacy and Safety – 27 through 45 years

Immunogenicity – 94-100%

# Safety – few serious adverse events and no vaccine related deaths

# Human Papillomavirus Vaccine Duration of Immunity

- The duration of immunity after a complete 3-dose schedule is not known
  - Available evidence indicates protection for at least 8 years for 4vHPV and at least 9 years for 2vHPV
  - Multiple cohort studies are in progress to monitor the duration of immunity

# **Recommended Schedule for Children and Adolescents Aged 18 Years and Younger 2019**

#### Table 1 Recommended Child and Adolescent Immunization Schedule for ages 18 years or younger United States, 2019

These recommendations must be read with the Notes that follow. For those who fall behind or start late, provide catch-up vaccination at the earliest opportunity as indicated by the green bars in Table 1. To determine minimum intervals between doses, see the catch-up schedule (Table 2). School entry and adolescent vaccine age groups are shaded in gray.



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

# **Recommended Schedule for Children and Adolescents Aged 18 Years and Younger 2019**

#### Catch-up immunization schedule for persons aged 4 months—18 years who start late or who are more than 1 month behind, United States, 2019

The figure below provides catch-up schedules and minimum intervals between doses for children whose vaccinations have been delayed. A vaccine series does not need to be restarted, regardless of the time that has elapsed between doses. Use the section appropriate for the child's age. Always use this table in conjunction with Table 1 and the notes that follow.

Vaccine	Minimum Age for		Minimum Interval Between Doses		
	Dose 1	Dose 1 to Dose 2	Dose 2 to Dose 3	Dose 3 to Dose 4	Dose 4 to Dose 5
Hepatitis B	Birth	4 weeks	8 weeks and at least 16 weeks after first dose. Minimum age for the final dose is 24 weeks.		
Rotavirus	6 weeks Maximum age for first dose is 14 weeks, 6 days	4 weeks	<b>4 weeks</b> Maximum age for final dose is 8 months, 0 days.		
Diphtheria, tetanus, and acellular pertussis	6 weeks	4 weeks	4 weeks	6 months	6 months
Haemophilus influenzae type b	6 weeks	No further doses needed if first dose was administered at age 15 months or older. 4 weeks If first dose was administered before the 1 <sup>d</sup> birthday. 8 weeks (as final dose) If first dose was administered at age 12 through 14 months.	No further doses needed if previous dose was administered at age 15 months or older. 4 weeks If current age is younger than 12 months and first dose was administered at younger than age 7 months, and at least 1 previous dose was PRP-T (ActHib, Pentacel, Hiberix) or unknown. 8 weeks and age 12 through 59 months (as final dose) If current age is younger than 12 months and first dose was administered at age 7 through 11 months; OR If current age is 12 through 59 months and first dose was administered before the 1 <sup>st</sup> birthday, and second dose administered at younger than 15 months; OR If both doses were PRP-OMP (PedvaxHiB; Comvax) and were administered before the 1 <sup>st</sup> birthday.	8 weeks (as final dose) This dose only necessary for children age 12 through 59 months who received 3 doses before the 1 <sup>st</sup> birthday.	
Pneumococcal conjugate	6 weeks	No further doses needed for healthy children if first dose was administered at age 24 months or older. 4 weeks If first dose administered before the 1* birthday. 8 weeks (as final dose for healthy children) If first dose was administered at the 1* birthday or after.	No further doses needed for healthy children if previous dose administered at age 24 months or older. 4 weeks if current age is younger than 12 months and previous dose given at <7 months old. 8 weeks (as final dose for healthy children) if previous dose given between 7-11 months (wait until at least 12 months old): OR if current age is 12 months or older and at least 1 dose was given before age 12 months.	8 weeks (as final dose) This dose only necessary for children age 12 through 59 months who received 3 doses before age 12 months or for children at high risk who received 3 doses at any age.	
Inactivated poliovirus	6 weeks	4 weeks	4 weeks if current age is < 4 years. 6 months (as final dose) if current age is 4 years or older.	6 months (minimum age 4 years for final dose).	
Measles, mumps, rubella	12 months	4 weeks		A Designed and the second s	
Varicella	12 months	3 months			
Honatitic A	12 months	6 months			
Hepatus A	Tz monuis	6 months			
Meningococcal	2 months MenACWY- CRM 9 months MenACWY-D	8 weeks	See Notes	See Notes	
			Children and adolescents age 7 through 18 years		
Meningococcal	Not Applicable (N/A)	8 weeks			
Tetanus, diphtheria; tetanus, diphtheria, and acellular pertussis	7 years	4 weeks	4 weeks If first dose of DTaP/DT was administered before the 1* birthday. 6 months (as final dose)	6 months if first dose of DTaP/ DT was administered before the 1ª birthday.	
			in hist dose of Drap/Dr or Tdap/Td was administered at or after the T* Dirtiday.		
Human papillomavirus	9 years	Routine dosing intervals are recomme	nded.		
Hepatitis A	N/A	6 months			
Hepatitis B	N/A	4 weeks	8 weeks and at least 16 weeks after first dose.		
Inactivated poliovirus	N/A	4 weeks	6 months A fourth dose is not necessary if the third dose was administered at age 4 years or older and at least 6 months after the previous dose.	A fourth dose of IPV is indicated if all previous doses were administered at <4 years or if the third dose was administered <6 months after the second dose.	
Measles, mumps, rubella	N/A	4 weeks			
Varicella	N/A	3 months if younger than age 13 years. 4 weeks if age 13 years or older.			

# **Recommended Schedule for Children and Adolescents Aged 18 Years and Younger 2019**

 Table 3
 Recommended Child and Adolescent Immunization Schedule by Medical Indication

 United States, 2019
 Value States

INDICATION									
VACCINE	Pregnancy	Immunocom- promised status (excluding HIV infection)	HIV infection CD4+ count <sup>1</sup> <15% and ≥15% and total CD4 total CD4 cell count of <200/mm3 ≥200/mm3	Kidney failure, end-stage renal disease, on hemodialysis	Heart disease, chronic lung disease	CSF leaks/ cochlear implants	Asplenia and persistent complement component deficiencies	Chronic liver disease	Diabetes
Hepatitis B								J	
Rotavirus		SCID <sup>2</sup>							
Diphtheria, tetanus, & acellular pertussis (DTaP)									
Haemophilus influenzae type b									
Pneumococcal conjugate									
Inactivated poliovirus									
Influenza (IIV)									
Influenza (LAIV)					Asthma, wheezing: 2-4yrs <sup>3</sup>				
Measles, mumps, rubella									
Varicella									
Hepatitis A									
Meningococcal ACWY									
Tetanus, diphtheria, &	1818285858								
Human papillomavirus									
Meningococcal B									
Pneumococcal polysaccharide		856555555555				E SESSEE		2202020	1999999
Vaccination according to the routine schedule recommended	Recommen persons with additional I for which th would be in	nded for th an risk factor he vaccine ndicated	Vaccination is recommended, and additional doses may be necessary based on medical condition. See Notes.	Contraindicated recommended- should not be ac because of risk f adverse reaction	or use not -vaccine dministered or serious adverse i adverse i	on—vaccine indicated if f protection hs risk of reaction	Delay vaccination until after pregnancy if vaccine indicated	No rec	ommendation

1 For additional information regarding HIV laboratory parameters and use of live vaccines, see the General Best Practice Guidelines for Immunization "Altered Immunocompetence" at www.cdc.gov/vaccines/hcp/acip-recs/general-recs/immunocompetence.html, and Table 4-1 (footnote D) at: www.cdc.gov/vaccines/hcp/acip-recs/general-recs/contraindications.html, 2 Severe Combined Immunodeficiency

3 LAIV contraindicated for children 2-4 years of age with asthma or wheezing during the preceding 12 months.

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# **Recommended Immunization Schedule for Adults Aged 19 Years or Older 2019**

accine	19–21 years	22–26 years	27–49 years	50–64 years	≥65 years
nfluenza inactivated (IIV) or			1 dose annually		
nfluenza live attenuated LAIV)			1 dose annually		
<b>etanus, diphtheria, pertussis</b> Tdap or Td)		1 dose Td	ap, then Td booster ev	ery 10 yrs	
<b>feasles, mumps, rubella</b> MMR)		1 or 2 doses dependin	g on Indication (if bor	n in 1957 or later)	
<b>/aricella</b> VAR)	2 doses (If bo	rn in 1980 or later)			
RZV) (preferred)					2 doses
Oster live					1 dage
luman papillomavirus (HPV) emale	2 or 3 doses depending on ag	e at initial vaccination			
luman papillomavirus (HPV) Nale	2 or 3 doses depending on age	e at initial vaccination			
PCV13)					1 d <mark>ose</mark>
neumococcal polysaccharide PPSV23)		1 or 2 c	doses depending on in	dication	1 dose
<b>lepatitis A</b> HepA)		2 or 3	doses depending on v	accine	
<b>lepatitis B</b> HepB)		2 or 3	doses depending on v	accine	
<b>Neningococcal A, C, W, Y</b> MenACWY)	1	or 2 doses depending on	Indication, then boost	er every 5 yrs if risk remai	ns
<b>feningococcal B</b> MenB)		2 or 3 doses d	lepending on vaccine a	ind Indication	
lasses and the state of the second second being the					

# **Recommended Immunization Schedule for Adults Aged 19 Years or Older 2019**

Table 2	Recommended Adult Immunization Schedule by Medical Condition and Other Indications United States, 2019							
Vaccine	Pregnancy	Immuno- compromised (excluding HIV Infection)	fection count Asplenia, complement deficiencies	End-stage renal la disease, on hemodialysis	Heart or ing disease, sicoholism	Diabetes	Health care personnel <sup>3</sup>	Mon who have sex with mon
IIV or RIV	1 dose annually							_
LAIV		CONTRAINDICATED PRECAUTION 1 dose annually						annually
Tdap or Td	1 dose Tdap each pregnancy		1 do	se Tdap, then Td boo	oster every 10 yrs			
MMR	CONT	RAINDICATED		1	or 2 doses depending on in-	lication		
VAR	CONT	CONTRAINDICATED 2 doses						
RZV (preferred)	DELAY	ELAY 2 doses at age 250 yrs						
714	CONT							
HPV Female	DELAY	3 doses through age	age 26 yrs 2 or 3 doses through age 26 yrs					
LIDV Mala		3 doses through age	gh age 26 yrs 2 or 3 doses through age 21 yrs 2 or 3 through				2 or 3 doses through pos 26 yrs	
THE R PRODUCT								
PCV13				1 dos	•			
PCV13 PPSV23				1 dos	a 1, 2, or 3 doses dependin	g on age and Indi	cation	
PCV13 PPSV23 HepA				1 des	e 1, 2, or 3 doses dependin 2 o <mark>r</mark> 3 doses depen	g on age and Indi Iding on vaccine	cation	
PCV13 PPSV23 HepA HepB				1 dos	e 1, 2, or 3 doses dependin 2 or 3 doses depen 2 o <mark>r</mark> 3 doses depen	g on age and ind nding on vaccine nding on vaccine	ication	
PCV13 PPSV23 HepA HepB MenACWY		1 or 2 doses de	pending on indication	1 dos , then booster every	e 1, 2, or 3 doses dependin 2 o <mark>r 3 doses depen</mark> 2 o <mark>r 3 doses depen</mark> 5 yrs if risk remains	g on age and Ind ding on vaccine iding on vaccine	cation	
PCV13 PPSV23 HepA HepB MenACWY MenB	PRECAUTION	1 or 2 doses de	pending on indication	then booster every on vaccine and India	e 1, 2, or 3 doses dependin 2 or 3 doses depen 2 or 3 doses depen 5 yrs if risk remains cation	g on age and indi iding on vaccine iding on vaccine	kation	
PCV13 PPSV23 HepA HepB MenACWY MenB Hib	PRECAUTION	1 or 2 doses de 2 3 doses HSCT) recipiente cely	pending on indication t or 3 doses depending	then booster every on vaccine and indi	e 1, 2, or 3 doses dependin 2 or 3 doses depen 2 or 3 doses depen 5 yrs if risk remains cation	g on age and ind nding on vaccine nding on vaccine	ication	
PCV13 PPSV23 HepA HepB MenACWY MenB Hib Recommentation	PRECAUTION Red vaccination for a ge requirement, lack ion of vaccination, o past infection	1 or 2 doses de 2 3 doses HSCT <sup>2</sup> notpients only duits Recommended for adults with r lack risk factor or ar indication	pending on indication t or 3 doses depending fvaccination an additional sother	then booster every on vaccine and indi- dose fion—vaccine might cated if benefit of ion outweight mik of a reaction	e 1, 2, or 3 doses dependin 2 or 3 doses depen 2 or 3 doses depen 5 yrs if risk remains cation Delay vaccination until after programs y if vaccine is indicated	g on age and indi ding on vaccine ading on vaccine contraindicated—w should not be admis because of risk for w adverse reaction	ection section nistered effour	o recommendation

# Human Papillomavirus Vaccine Routine Recommendations

- Routinely vaccinate boys and girls at 11–12 years of age\*
- Catch-up those previously unvaccinated or are missing doses including:
  - Females and males age 13 through 26 years

# **HPV Vaccination Schedules**

- FDA has approved a 2-dose schedule for 9vHPV (Gardasil9)
- ACIP reviewed data on 2-dose schedules including studies of immune response, vaccine effectiveness, and duration of protection. Specifically:
  - Data from clinical trials showed two doses of HPV vaccine given in younger adolescents (aged 9-14 years) produced an immune response that that was similar or higher than the response in young adults (aged 16-26 years) who received three doses
  - Data available to date show that a 3-dose schedule in older adolescents and young adults provides long-lasting protection.
  - Study data suggest that a 2-dose schedule given to younger adolescents will also provide long-lasting protection

# ACIP HPV Immunization Recommendations Previously Unvaccinated Adolescents

Administer 2 doses of HPV vaccine to adolescents starting the series at 9 through 14 years of age

Follow the routine 2-dose schedule
 Administer dose 2 6-12 months after the 1<sup>st</sup> dose

If a 2<sup>nd</sup> dose is inadvertently administered prior to 5 months default to a 3-dose series

# ACIP Immunization Recommendations Previously Unvaccinated Adolescents

- Administer 3 doses of HPV vaccine to adolescents starting the series on or after the 15th birthday
- Routine 3-dose schedule\*: 0, 1-2, 6 months
  - Dose #2: Administer at least 1 to 2 months after dose 1
  - Dose #3: Administer at least:
    - o 12 weeks after dose 2 AND
    - o 6 months (24 weeks) after dose 1

# An accelerated schedule using minimum intervals is not recommended

MMWR 2016;65(49):1405-08

# ACIP Immunization Recommendations Persons with an Incomplete Series

- 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 month), OR
     3 doses at the recommended dosing schedule (0, 1-2, 6 month)
  - On or after the 15th birthday are fully vaccinated if they received,
     3 doses at the recommended dosing schedule (0, 1-2, 6 month)
- All doses do not have to 9vHPV
- No additional doses are recommended, regardless of their current age

# ACIP HPV Immunization Recommendations Medical Condition Considerations

- ACIP recommends HPV vaccination for immunocompromised females and males aged 9 through 26 years with 3 doses of HPV vaccine (0, 1-2, 6 months)
- Administer a 3-dose series to immunocompromised persons including those with:
  - Primary or secondary immunocompromising conditions that might reduce cell-mediated or humoral immunity, such as B lymphocyte antibody deficiencies, T lymphocyte complete or partial defects, HIV infection, malignant neoplasm, transplantation, autoimmune disease or immunosuppressive therapy

# HPV Vaccination of Adults 27 Through 45 Years of Age

- Catch up HPV vaccination is not recommended for all adults who would initiate vaccination after the 27<sup>th</sup> birthday
- Shared clinical decision-making regarding HPV vaccination is recommended for some unvaccinated adults age 27 through 45 years of age
- Criteria for making the shared clinical decision-making available at "Box" at
  - https://www.cdc.gov/mmwr/volumes/68/wr/pdfs/mm6832a 3-H.pdf

### **Box:**

# https://www.cdc.gov/mmwr/volumes/68/wr/pdfs/mm 6832a3-H.pdf

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.

### Box : <u>https://www.cdc.gov/mmwr/volumes/68/wr/pdfs/mm6832a3-</u> <u>H.pdf</u>

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.

### Human Papillomavirus Vaccine Administration

#### Administer HPV vaccines via intramuscular (IM) injection

- Needle size: 1- to 1½- inch, 22- to 25-gauge
- Site: Deltoid muscle in the upper arm

#### **Goldow proper injection practices**

- Use aseptic technique
- Use a new needle and syringe for each injection

#### Administer at the same medical visit as other vaccines

# ACIP HPV Immunization Recommendations Schedule Considerations

- Number of recommended doses is based on:
  - Age at administration of the first dose OR
  - Health status immunosuppression
- Series does not need to be restarted if interrupted
  - There is NO maximum interval between HPV vaccine doses
- HPV vaccine can be administered during the same clinical visit other vaccines
- 9vHPV may be used to continue or complete a series started with 4vHPV or 2vHPV regardless of the dosing schedule

# **2-Dose Clinical FAQs**

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 vacche instead of 3. Parents may have questions about this change. This resource helps explain the reasons for changing the HPV vacche recommendation, and provides tipe 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, recommends 2 doses of HPV vaccine for people starting the vaccination series before the 15th b doses of HPV vaccine are recommended for people starting the vaccination series on or after the for people with certain immunocompromising conditions.

CDC continues to recommend routine vaccination for girls and boys at age 11 or 12 years. The vi can be started at age 9 years. CDC also recommends vaccination through age 26 years for femal 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 sch HPV vaccine. The second dose should be given 6–12 months after the first dose (0, 6–12 month s

Answering parents' questions: We now recommend 2 doses of HPV vaccine for your son or daugh your child starts the series before their 15th birthday. 1still recommend your child start the vaccinatic or 12 years for best protection against HPV. He or she will need a second dose 6-12 months after the f

#### Who should still receive a 3-dose schedule?

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

Answering parents' questions: If your child starts the series after his or her 15th birthday or has ce problems that weaken his or her immune system, he or she will still need the 3-dose series. We will giv 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 bee on 2-dose schedules, including results from studies of HPV vaccines that compared the antibody 2 doses and 3 doses. These studies showed that the antibody response after 2 doses given at leas to 9-14 year-olds was as good or better than the antibody response after 3 doses given to loder 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 recommenda reviewing data on 2-dose HPV vaccination schedules for several months. The evidence showed that 1 vaccine given at least 6 months apart in younger adolescents were as good or better than 3 doses. Th recommendations are an example of using the latest available evidence to provide your child with th protection against serious diseases.

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

National Center for Immunization and Respiratory Dis

#### Office of the Director

CS HCVG15-PTT-106 11/30/2016

#### Why is the 2-dose schedule change recommended only for girls and boys age 9–14 years?

ACIP makes recommendations based on the best available scientific evidence. Immunogenicity studies have shown that 2 doses of HPV vaccine given to 9–14 year-olds at least 6 months apart were as good, or better, than 3 doses given to older adolescents and young adults. Studies have not been done to show this in adolescents age 15 years or older.

Answering parents' questions: The data we currently have from scientific studies (clinical trials) showed that 2 doses of HPV vaccine given at least 6 months apart were as good or better than 3 doses in children 9–14 years of age. Older adolescents haven't been studied in the same way, so we don't have information available for that age group. For that reason, the recommendation for number of doses has not been changed for older adolescents.

#### What is the recommendation for persons with immunocompromising conditions?

CDC recommends 3 doses of HPV vaccine (0, 1–2, 6 months) for immunocompromised people age 9 through 26 years. People whose Immune responses might be lower, for example due to HIV infection, cancer, autoimmune disease, or taking Immunosuppressant medications, should receive 3 doses to make sure they get the most benefit. However, children with asthma, diabetes, and other conditions that would not suppress Immune response to HPV vaccination can receive a 2-dose schedule.

Answering parents' questions: Even though CDC has recommended just 2 doses of HPV for kids under 15 years, we'll need to give your child 3 doses because he/she has a health problem that weakens his or her immune system.

#### If a HPV vaccine series was started with quadrivalent HPV vaccine or bivalent HPV vaccine and will be completed with 9-valent HPV vaccine, what are the intervals for the remaining doses in a 3-dose or 2-dose series?

If the first dose of any vaccine was given before the 15th birthday, vaccination should be completed according to a 2-dose schedule. In a 2-dose series, the second dose is recommended 6–12 months after the first dose (0, 6–12 month schedule).

If the first dose of any vaccine was given on or after the 15th birthday, vaccination should be completed according to a 3-dose schedule. In a 3-dose series, the second dose is recommended 1–2 months after the first dose, and the third dose is recommended 6 months after the first dose (0, 1–2, 6 month schedule

If a vaccination schedule is interrupted, vaccine doses do not need to be repeated.

#### If a girl or boy received 2 doses of HPV vaccine less than 5 months apart, do they need a third HPV vaccine dose?

Yes. In a 2-dose schedule of HPV vaccine, the recommended interval is 6–12 months, and the minimum interval is 5 months between the first and second dose. If the second dose is given earlier than 5 months, a third dose should be administered.

Answering parents' questions: The recommended schedule is 2 doses given 6 to 12 months apart. The minimum amount of time between those doses is 5 months. Because your child received 2 doses less than 5 months apart, we'll need to give your child a third dose.

#### If someone is age 15 years or older and started the vaccination series at age 11 but only received 1 dose, how many more doses do they need?

This person needs 1 more dose to complete a 2-dose series, which is recommended because the vaccination was started before turning 15 years old. In a 2-dose series, the second dose is recommended 6-12 months after the first dose. In this case, the first dose was given several years ago, so the second dose can be given right away.

#### Is the 9-valent HPV vaccine approved by FDA for use as a 2-dose schedule?

Yes, in October 2016, FDA approved a 2-dose schedule (0, 6–12 months) of 9-valent HPV vaccine for use in girls and boys age 9–14 years in the United States.

#### What HPV vaccines are currently available in the United States?

Three HPV vaccines are licensed for use in the United States: 9-valent HPV vaccine, quadrivalent HPV vaccine, and bivalent HPV vaccine. However, after the end of 2016, only 9-valent HPV vaccine will be sold in the United States.

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

# ACIP HPV Immunization Recommendations Additional Considerations

- For persons who have completed a series of 4vHPV or 2vHPV, there is no ACIP recommendation for additional vaccination with 9vHPV
- No therapeutic effect on HPV infection, genital warts, cervical lesions
- Prevaccination assessments not recommended
  - HPV
  - Pregnancy

# Human Papillomavirus Vaccine Special Situations

# Administer vaccine to:

- Females who:
  - Have equivocal or abnormal Pap test
  - Have positive HPV DNA test
  - o Are breast-feeding
- Males and females who:
  - o Have genital warts
  - o Are immunosuppressed

# **Human Papillomavirus Vaccine and Pregnancy**

- Initiation of the vaccine series should be delayed until after completion of pregnancy
- If a woman is found to be pregnant after initiating the vaccination series, remaining doses should be delayed until after the pregnancy
- If a vaccine dose has been administered during pregnancy, there is no indication for intervention
- Women vaccinated during pregnancy should be reported to the respective manufacturer
  - Active pregnancy registry for 9vHPV established; others are closed
  - Contact information is in the package insert

## Human Papillomavirus Vaccine Contraindications and Precautions

### Contraindication

• Severe allergic reaction to a vaccine component or following a prior dose

### Precaution

• Moderate or severe acute illnesses (defer until symptoms improve)

# Adverse Events Following Any Dose of HPV Vaccine Among Females<sup>\*</sup>

Adverse Event	2vHPV	4vHPV	9vHPV
Pain	92%	84%	89%
Swelling	44%	29%	40%
Erythema	48%	25%	34%
Fever	13%	13%	5%
Nausea	7%	GI 28% <sup>**</sup>	4%
Headache	12%	55%	11%

\*FDA product approval data

\*\*GI = Gastrointestinal symptoms, including nausea, vomiting, diarrhea, and/or abdominal pain

# Adverse Events Following Any Dose of HPV Vaccine Among Females<sup>\*</sup>

- Postural Orthostatic Tachycardia Syndrome (POTS)
- Guillain-Barré syndrome (GBS)
- Complex Regional Pain Syndrome (CRPS)

# **Syncope Following Vaccination**

 An increase in the number of reports of syncope has been detected by the Vaccine Adverse Event Reporting System (VAERS)

• Most of the increase among females 11-18 years

Serious injuries have resulted

ACIP recommends providers strongly consider observing patients for 15 minutes after they are vaccinated

# **Vaccine Storage and Handling**

Store HPV vaccine in a refrigerator between 2°C - 8°C (36°F - 46°F)

### Store HPV vaccines:

- In the original packaging with the lids closed
- In a clearly labeled bin and/or area of the storage unit

# Do not freeze the vaccineProtect the vaccine from light

Available at www.cdc.gov/vaccines/hcp/admin/storage/guide/vaccine-storage-labels.pdf



Administer to females and males

Use for: 9 years through 26 years Recommended ages: 11 years or 12 years Catch-up ages: 13 years through 26 years Route: Intramuscular (IM) injection

# HPV Immunization Rates Females 13-17 Years of Age, 2018

	U.S.			
<b>HPV Vaccine</b>	Females	Males		
1 or more doses*	69.9%	66.3%		
HPV UTD**	53.7%	48.7%		

Percentages ≥1 human papillomavirus vaccine, either 4vHPV, or 2vHPV

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

https://www.cdc.gov/vaccines/imz-managers/coverage/teenvaxview/data-reports/hpv/dashboard/2018.html

### **HPV Vaccine Communications during the Health Care Encounter**

- HPV vaccine is often presented as optional, whereas other adolescent vaccines are recommended
- Some 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 teen is not at risk for HPV and vaccination can be delayed until older

# **Strategies for Increasing HPV Vaccination Rates 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.
  - Immunize at every opportunity
  - Use standing orders
- Reminder and recall
- Tools for improving uptake of HPV at <u>www.cdc.gov/vaccines/teens</u>

### **HPV Vaccination Resources for HCP**





# Human Papillomavirus Vaccine Resources

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