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Human Papillomavirus (HPV): Current Status & Controversies

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Current Status & Controversies

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Objectives

- **1.** Discuss the epidemiology of HPV infections in the United States.
- **2.** Describe the pathophysiology, risk factors, signs and symptoms, and modes of HPV transmission.
- **3.** Identify the negative health consequences associated with HPV.

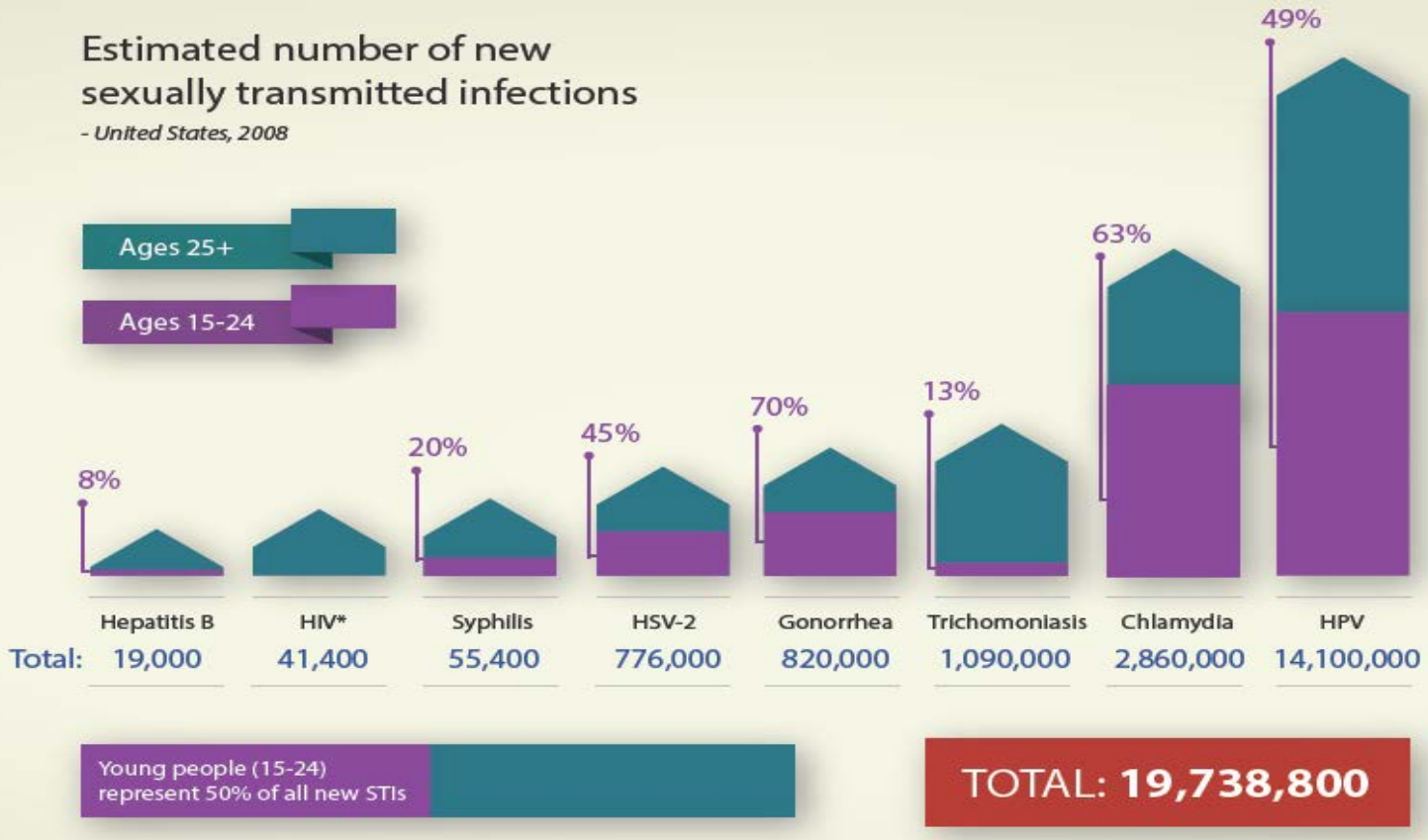
Objectives

- **4.** Summarize the current recommendations for preventing HPV infections.
- **5.** Identify the different HPV vaccinations available and describe the latest recommendations for their use.
- **6.** Discuss controversies related to HPV infections and vaccinations.

Pre-Test

- **Question 1:** The most common sexually transmitted infections in the United States are HPV infections.
- **Question 2:** An individual can become infected with only one strain of HPV at a time.
- **Question 3:** The only type of cancer linked to HPV is cervical cancer.

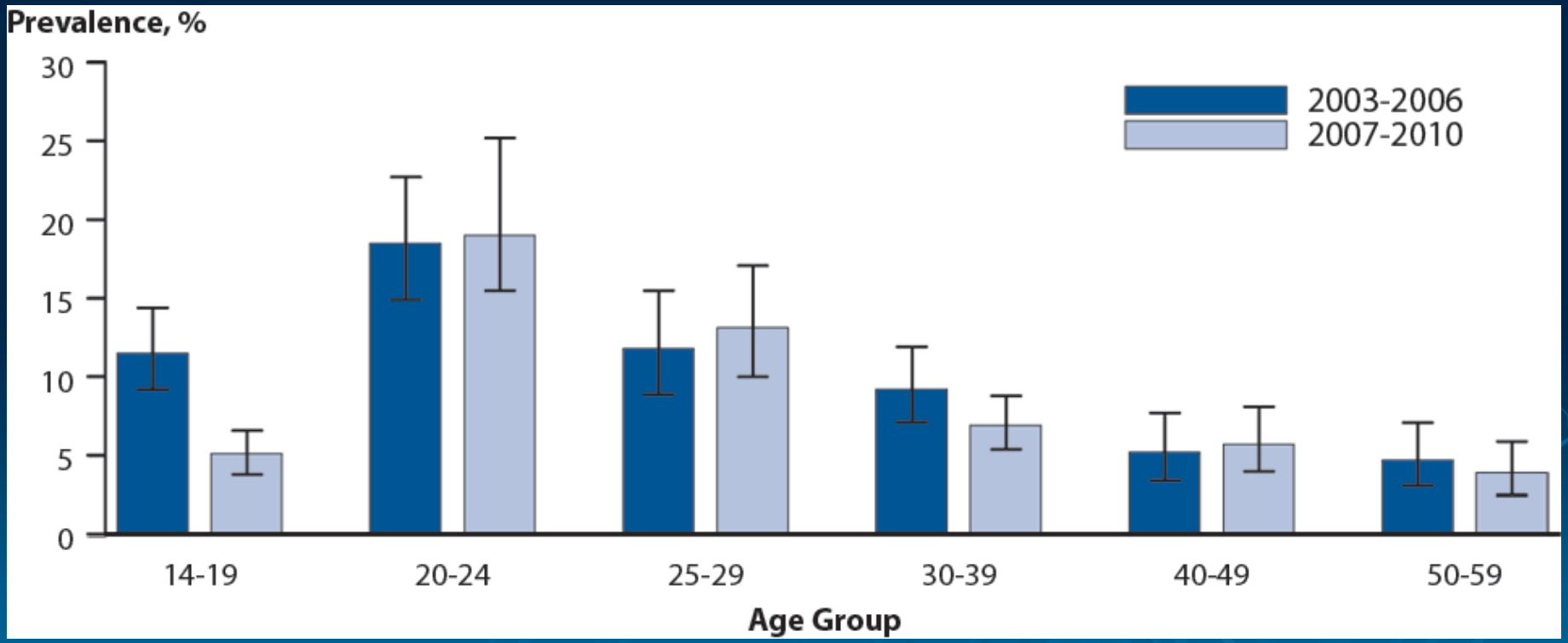
Epidemiology



Epidemiology

Epidemiology

- Cervicovaginal Prevalence of Types 6, 11, 16 and 18 Among Women Aged 14–59 Years by Age Group and Time Period



HPV

- Family of >200 non-enveloped, double-stranded DNA viruses that target human epithelial cells
  - >40 types are sexually transmitted
  - >13 types may cause cancer
- Numbered in order of discovery
- Classified into groups based on anatomic areas they affect

HPV

- Individuals may be infected with more than one type at a time
- The most common viral infection of the reproductive tract
- The most common sexually transmitted infection (STI) in the United States

Risk Factors

- Early first sexual intercourse
- Multiple sexual partners
- Tobacco use
- Immunosuppression

Signs and Symptoms

- Most HPV infections are asymptomatic and resolve spontaneously
- Persistent, untreated high risk infections may result in precancerous lesions

Modes of Transmission

- Spreads from one person to another by skin-to-skin contact
  - Sexual intercourse
  - Intimate, non-penetrative encounters

Sexually Transmitted HPV

- Two categories:

  1. Low risk: Cause skin warts around the mouth, throat, genitals/anus as well as respiratory papillomatosis
    - HPV 6, 11

  2. High risk: Cause cancer
    - HPV 16, 18

Sexually Transmitted HPV

- Affects 6.2 million 14-44 year olds every year
  - 74% between the ages of 15 and 24

- Up to 70% of young women will be infected with at least 1 type of HPV within the first 5 years of starting sexual activity

Complications

- Precancerous lesions may progress to different types of cancer
  - Cervical
  - Anal
  - Oropharyngeal
  - Vaginal
  - Vulvar
  - Penile

Complications: HPV-Associated Cancers

- Based on data from 2008-2012, 38,793 HPV-associated cancers occur in the U.S. each year
  - ~23,000 among women
  - ~16,000 in men
- Cervical cancer is the most common among women
- Oropharyngeal cancers are the most common among men

Complications: HPV-Associated Cancers

Number of HPV-Associated and HPV-Attributable Cancer Cases per Year							
Cancer site	Average number of cancers per year in sites where HPV is often found (HPV-associated cancers)	Percentage probably caused by any HPV type[a]	Number probably caused by any HPV type[a]	Percentage probably caused by HPV types 16/18[b]	Number probably caused by HPV types 16/18[b]	Percentage probably caused by HPV types 31/33/45/52/58[c]	Number probably caused by HPV types 31/33/45/52/58[c]
Cervix	11,771	91%	10,700	66%	7,800	15%	1,700
Vagina	802	75%	600	55%	400	18%	100
Vulva	3,554	69%	2,400	49%	1,700	14%	500
Penis	1,168	63%	700	48%	600	9%	100
Anus	5,010	91%	4,600	79%	4,000	8%	400
Female	3,260	93%	3,000	80%	2,600	11%	400
Male	1,750	89%	1,600	79%	1,400	4%	100
Rectum	750	91%	700	79%	600	8%	100
Female	513	93%	500	80%	400	11%	100
Male	237	89%	200	79%	200	4%	<100
Oropharynx	15,738	70%	11,000	60%	9,500	6%	900
Female	3,100	63%	2,000	51%	1,600	10%	300
Male	12,638	72%	9,100	63%	8,000	4%	600
TOTAL	**38,793**		**30,700**		**24,600**		**3,800**

Complications: Cervical Cancer

- HPV 16 & 18 cause 70% of all cases

- Symptoms
  - Fatigue
  - Weight loss, loss of appetite
  - Back, leg, or pelvic pain
  - Single swollen leg
  - Vaginal discomfort or odorous discharge
  - Irregular, intermenstrual, or abnormal vaginal bleeding after sexual intercourse

Treatment

- Aimed at genital warts and precancerous lesions
  - Cryotherapy
  - Electrocautery
  - Surgical excision
  - Topical therapies

Prevention

- Abstinence
- Safe sex practices
- Cervical cancer screening
- HPV testing for oncogenic types
- Immunizations

Prevention: Cervical Cancer Screening

- Females 21-65 years old
  - Conventional or liquid-based cytologic testing (Papanicolaou test) every 3 years

- Females 30-65 years old
  - Co-testing with oncogenic HPV tests every 5 years

American Cancer Society Guidelines for the Early Detection of Cervical Cancer

Ages 21 to 29 years
Get a Pap test every 3 years.

Ages 30 to 65 years
Get a Pap test and an HPV test every 5 years (this is best) or get just a Pap test every 3 years.

If you are at high risk for cervical cancer, talk with your doctor or nurse to make a testing plan that's right for you.

Women over 65 years
Stop testing if you've had regular testing for the past 10 years and have not had any bad pre-cancers in the past 20 years.

Women who have had cervical pre-cancer
Get tested for at least 20 years after the cell changes were found and treated.

Women who had a hysterectomy and their cervix was removed
Stop testing unless the surgery was done to treat cervical cancer or pre-cancer.

Women who got the HPV vaccine
Follow the same screening plan as above.

These guidelines are not for women who have cervical cancer.

Prevention: Cervical Cancer Screening

- Positive HPV test
  - Second HPV test in 1 year and/or
  - Test to identify HPV type

Prevention:
HPV Testing for Oncogenic Types

- Detect viral DNA or messenger RNA (mRNA)
- Indications
  - In conjunction with conventional cervical screening in females 30-65 years old
  - To triage abnormal results of conventional cervical screening
  - As follow-up after treatment of cervical precancers

Prevention: Screening in Men

- No Food and Drug Administration (FDA)-approved tests to detect HPV in men
- No recommended screening methods to detect HPV-related cell changes in men

Prevention: Immunizations

- Healthy People 2020
  - *Goal:* Increase immunization rates and reduce preventable infectious diseases
  - *Objectives:*

IID-11	Increase routine vaccination coverage levels for adolescents		
IID-11.1	Increase the vaccination coverage level of 1 dose of tetanus-diphtheria-acellular pertussis (Tdap) booster vaccine for adolescents by age 13 to 15 years	Revised	⊕
IID-11.2	Increase the vaccination coverage level of 2 doses of varicella vaccine for adolescents by age 13 to 15 years (excluding children who have had varicella)	Revised	⊕
IID-11.3	Increase the vaccination coverage level of 1 dose meningococcal conjugate vaccine for adolescents by age 13 to 15 years	Revised	⊕
IID-11.4	Increase the vaccination coverage level of 3 doses of human papillomavirus (HPV) vaccine for females by age 13 to 15 years	Revised	⊕
IID-11.5	Increase the vaccination coverage level of 3 doses of human papillomavirus (HPV) vaccine for males by age 13 to 15 years		⊕

Prevention: Immunizations

Estimated Vaccination Coverage[*,†] With Vaccines Included in Healthy People 2020 Immunization Objectives, Among Adolescents Aged 13-15 Years[§], by State and Selected Area -- National Immunization Survey-Teen, United States, 2014

			Females	Males	
	≥ 1 Tdap[¶]	≥ 1 MenACWY[**]	≥ 3 HPV[††]	≥ 3 HPV[††]	≥ 2 doses varicella vaccine if had no history of disease[§§]
	% (95% CI)	% (95% CI)	% (95% CI)	% (95% CI)	% (95% CI)
Healthy People 2020 Target	80%	80%	80%	80%	90%
US National	**88.3(±1.1)**	**79.4(±1.4)**	**34.4(±2.3)**	**20.6(±2.1)**	**82.1(±1.4)**
Alabama	87.0(±5.8)	69.8(±7.8)	36.8(±12.1)	NA	82.7(±6.7)
Alaska	71.9(±6.8)	56.8(±7.9)	22.8(±8.3)	NA	81.0(±7.0)
Arizona	84.1(±6.1)	86.3(±5.9)	24.3(±9.6)	16.8(±7.3)	73.9(±7.9)
Arkansas	87.9(±5.8)	65.4(±7.9)	23.7(±10.6)	12.4(±7.1)	71.2(±8.7)
California	88.1(±5.6)	78.1(±7.5)	43.2(±13.0)	29.5(±11.1)	82.1(±6.9)
Colorado	89.3(±4.6)	76.7(±6.4)	41.1(±11.0)	23.7(±9.6)	86.2(±6.0)
Connecticut	96.2(±3.1)	97.3(±2.1)	36.9(±11.4)	19.9(±8.4)	97.1(±2.3)
Delaware	91.4(±4.8)	86.5(±6.2)	40.3(±12.5)	26.3(±11.9)	91.7(±5.1)
Dist. of Columbia	80.9(±7.7)	92.3(±4.2)	55.9(±13.8)	37.6(±15.3)	92.1(±5.2)
Florida	89.4(±6.0)	72.9(±8.2)	21.4(±10.7)	21.5(±12.0)	79.3(±8.2)
Georgia	89.4(±5.2)	80.4(±7.0)	43.9(±12.4)	18.1(±8.3)	95.6(±3.1)
Hawaii	82.1(±5.9)	77.3(±6.5)	32.0(±10.1)	28.4(±10.3)	78.1(±7.0)
Idaho	75.7(±7.4)	82.8(±6.8)	39.4(±11.7)	20.1(±9.3)	69.6(±9.3)

Prevention: Immunizations

Table 67. Vaccination coverage for selected diseases among adolescents aged 13–17, by selected characteristics: United States, 2008–2014

Updated data when available, Excel, and PDF: http://www.cdc.gov/nchs/hus/contents2015.htm#067.

[Data are based on telephone interviews of a sample of the civilian noninstitutionalized population, supplemented by a survey of interview participants' immunization providers]

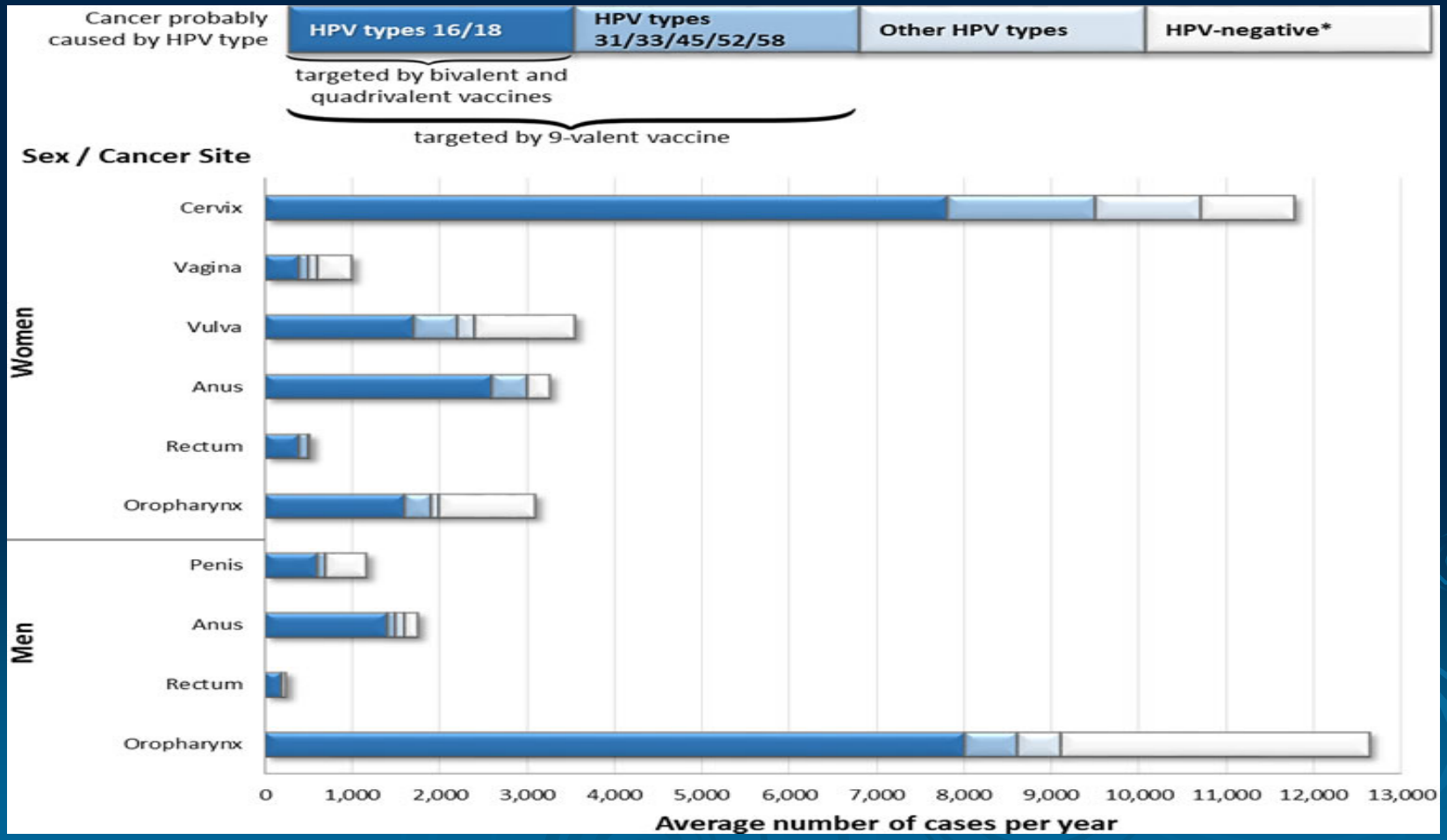
Vaccination coverage	*2008*	*2009*	*2010*	*2011*	*2012*	*2013*[1]	*2014*[1]
				Percent of adolescents aged 13–17			
Measles, mumps, rubella (2 doses or more)	89.3	89.1	90.5	91.1	91.4	89.6	90.7
Hepatitis B (3 doses or more)	87.9	89.9	91.6	92.3	92.8	91.3	91.4
History of varicella or received varicella vaccine (2 doses or more)[2]	73.5	75.7	76.8	79.9	82.6	82.7	85.0
Tdap (1 dose or more)[3]	40.8	55.6	68.7	78.2	84.6	84.7	87.6
Meningococcal conjugate vaccine (MenACWY) (1 dose or more)[4]	41.8	53.6	62.7	70.5	74.0	76.6	79.3
Human papillomavirus (HPV) (3 doses or more among females)[5]	17.9	26.7	32.0	34.8	33.4	36.8	39.7
Human papillomavirus (HPV) (3 doses or more among males)[5]	...	...	...	1.3	6.8	13.4	21.6

Prevention: Immunizations

Vaccine type	Brand name	HPV types covered
Bivalent (2vHPV)	Cervarix®	16, 18
Quadrivalent (4vHPV)	Gardasil®	6, 11 16, 18
9-valent (9vHPV)	Gardasil®9	6, 11 16, 18 31, 33, 45, 52, 58

- Gardasil®9 replaced the bivalent and quadrivalent HPV vaccines by the end of 2016

Prevention: Immunizations



Cervarix®

- **Initial U.S. approval:** 2009
- **Manufacturer:** GlaxoSmithKline
- **FDA indication:** Females 9-25 years old
- **Dosage & administration:**
  - Three 0.5 mL intramuscular (IM) injections at 0, 1, and 6 months

Gardasil®

- **Initial U.S. approval:** 2006
- **Manufacturer:** Merck Sharp & Dohme Corp.
- **FDA indications:**
  - Females 9-26 years old
  - Males 9-26 years old
- **Dosage & administration:**
  - Three 0.5 mL IM injections at 0, 2, and 6 months

Gardasil®9

- **Initial U.S. approval:** 2014
- **Manufacturer:** Merck Sharp & Dohme Corp.
- **FDA indications:**
  - Females 9-26 years old
  - Males 9-26 years old
- **Dosage & administration:**
  - Three 0.5 mL IM injections at 0, 2, and 6 months

Gardasil®9

- If the 3-dose HPV vaccination series is initiated with the bivalent or quadrivalent vaccines, it may be continued or completed with Gardasil®9

- If the 3-dose HPV vaccination series has been completed with the bivalent or quadrivalent vaccines, Gardasil®9 is not recommended

Gardasil®9

- Safety assessed across 7 Phase III trials involving >15,000 patients aged 9-26 years

- Common side effects
  - Injection site reactions [pain, swelling, erythema] (84.8%)
  - Headache (13.2%)
  - Fever (6.1%)

Prevention: Immunizations

Characteristic	Bivalent (2vHPV)*	Quadrivalent (4vHPV)†	9-valent (9vHPV)§
Brand name	Cervarix	Gardasil	Gardasil 9
VLPs	16, 18	6, 11, 16, 18	6, 11, 16, 18, 31, 33, 45, 52, 58
Manufacturer	GlaxoSmithKline	Merck and Co., Inc.	Merck and Co., Inc.
Manufacturing	*Trichoplusia ni* insect cell line infected with L1 encoding recombinant baculovirus	*Saccharomyces cerevisiae* (Baker's yeast), expressing L1	*Saccharomyces cerevisiae* (Baker's yeast), expressing L1
Adjuvant	500 μg aluminum hydroxide, 50 μg 3-O-desacyl-4' monophosphoryl lipid A	225 μg amorphous aluminum hydroxyphosphate sulfate	500 μg amorphous aluminum hydroxyphosphate sulfate
Volume per dose	0.5 ml	0.5 ml	0.5 ml
Administration	Intramuscular	Intramuscular	Intramuscular

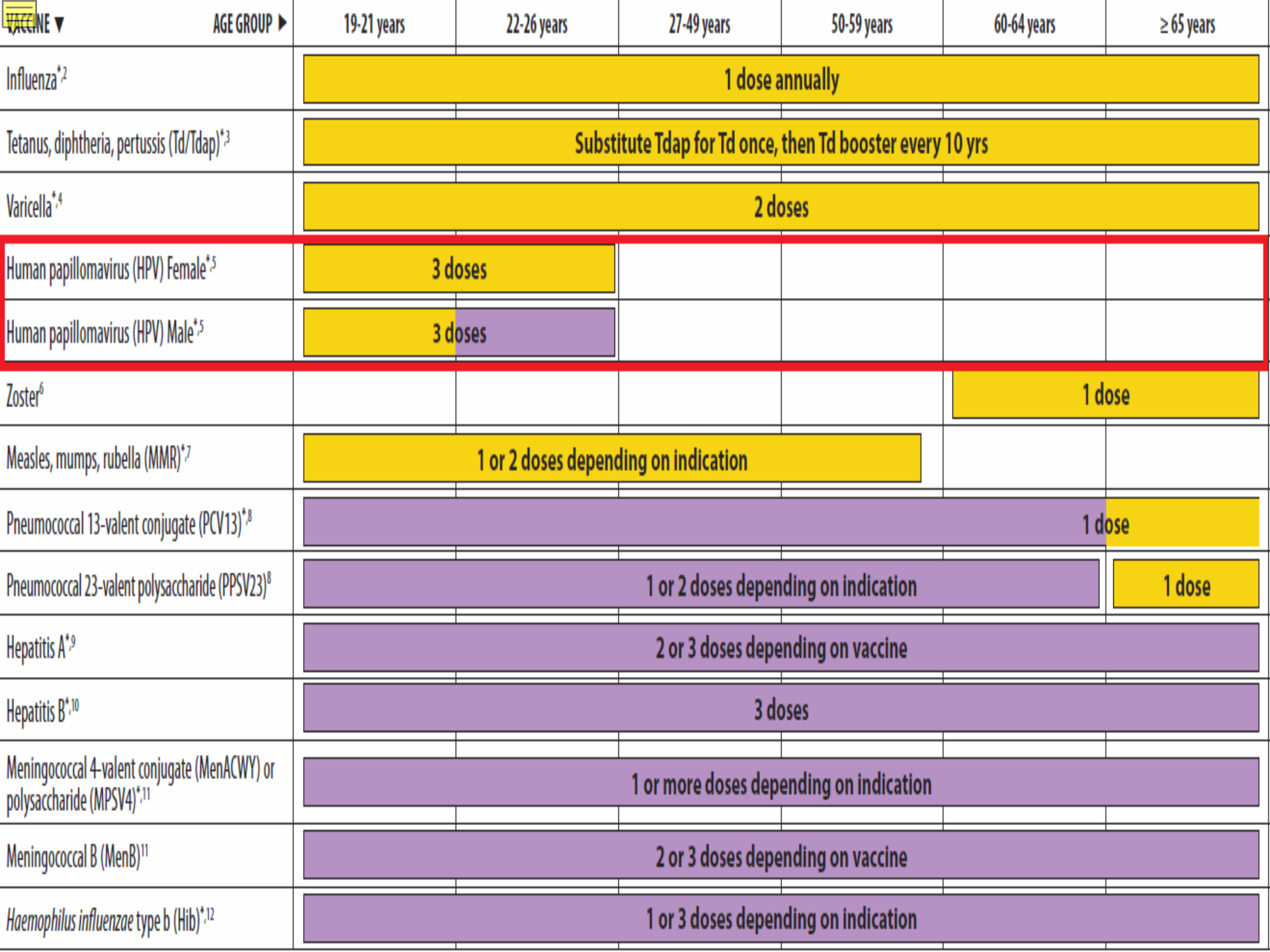
Abbreviation: L1 = the HPV major capsid protein; VLPs = virus-like particles.

* Only licensed for use in females in the United States. Package insert available at http://www.fda.gov/downloads/BiologicsBloodVaccines/Vaccines/ApprovedProducts/UCM186981.pdf.

† Package insert available at http://www.fda.gov/downloads/BiologicsBloodVaccines/Vaccines/ApprovedProducts/UCM111263.pdf.

§ Package insert available at http://www.fda.gov/downloads/BiologicsBloodVaccines/Vaccines/ApprovedProducts/UCM426457.pdf.

Vaccines	18 mos	19-23 mos	2-3 yrs	4-6 yrs	7-10 yrs	11-12 yrs	13-15 yrs	16-18 yrs
Hepatitis B[1] (HepB)	←3rd dose→							
Rotavirus[2] (RV) RV1 (2-dose series); RV5 (3-dose series)								
Diphtheria, tetanus, & acellular pertussis[3] (DTaP: <7 yrs)	←4th dose→			5th dose				
Haemophilus influenzae type b[4] (Hib)								
Pneumococcal conjugate[5] (PCV13)								
Inactivated poliovirus[6] (IPV)(<18 yrs)	←3rd dose→			4th dose				
Influenza[7] (IIV; LAIV)	Annual vaccination (IIV only) 1 or 2 doses		Annual vaccination (LAIV or IIV) 1 or 2 doses		Annual vaccination (LAIV or IIV) 1 dose only			
Measles, mumps, rubella[8] (MMR)				2nd dose				
Varicella[9] (VAR)				2nd dose				
Hepatitis A[10] (HepA)	←2 dose series, See footnote 10→							
Meningococcal[11] (Hib-MenCY ≥ 6 weeks; MenACWY-D ≥9 mos; MenACWY-CRM ≥ 2 mos)	See footnote 11					1st dose		Booster
Tetanus, diphtheria, & acellular pertussis[12] (Tdap: ≥7 yrs)						(Tdap)		
Human papillomavirus[13] (2vHPV:females only; 4vHPV, 9vHPV:males and females)						(3 dose series)		


VACCINE ▼
AGE GROUP ▶
19-21 years
22-26 years
27-49 years
50-59 years
60-64 years
≥ 65 years
Influenza*,2
1 dose annually
Tetanus, diphtheria, pertussis (Td/Tdap)*,3
Substitute Tdap for Td once, then Td booster every 10 yrs
Varicella*,4
2 doses
Human papillomavirus (HPV) Female*,5
3 doses
Human papillomavirus (HPV) Male*,5
3 doses
Zoster6
1 dose
Measles, mumps, rubella (MMR)*,7
1 or 2 doses depending on indication
Pneumococcal 13-valent conjugate (PCV13)*,8
1 dose
Pneumococcal 23-valent polysaccharide (PPSV23)8
1 or 2 doses depending on indication
1 dose
Hepatitis A*,9
2 or 3 doses depending on vaccine
Hepatitis B*,10
3 doses
Meningococcal 4-valent conjugate (MenACWY) or polysaccharide (MPSV4)*,11
1 or more doses depending on indication
Meningococcal B (MenB)11
2 or 3 doses depending on vaccine
Haemophilus influenzae type b (Hib)*,12
1 or 3 doses depending on indication

Prevention: Immunizations

- Routine vaccination:
  - Administer a 3-dose series of HPV vaccine on a schedule of 0, 1-2, and 6 months to all adolescents aged 11-12 years.
  - Administer the second dose 1-2 months after the first dose (minimum interval of 4 weeks), administer the third dose 16 weeks after the second dose (minimum interval of 12 weeks) and 24 weeks after the first dose.
  - Administer HPV vaccine beginning at age 9 years to children and youth with any history of sexual abuse or assault who have not initiated or completed the 3-dose series.

Prevention: Immunizations

- Catch-up vaccination:
  - Administer the vaccine series to females (2vHPV, 4vHPV, or 9vHPV) and males (4vHPV or 9vHPV) at age 13-18 years if not previously vaccinated.
  - Use recommended routine dosing intervals (see previous slide) for vaccine series catch-up.

Prevention: Immunizations

- For men who have sex with men and immunocompromised individuals, use:
  - Gardasil®, or
  - Gardasil®9

Prevention: Immunizations

- Not recommended during pregnancy
- Pregnancy testing is not needed before vaccination
- If a woman is found to be pregnant after initiating the vaccination series, no intervention is needed
  - The remainder of the 3-dose series should be delayed until completion or termination of pregnancy
- Ongoing pregnancy registry

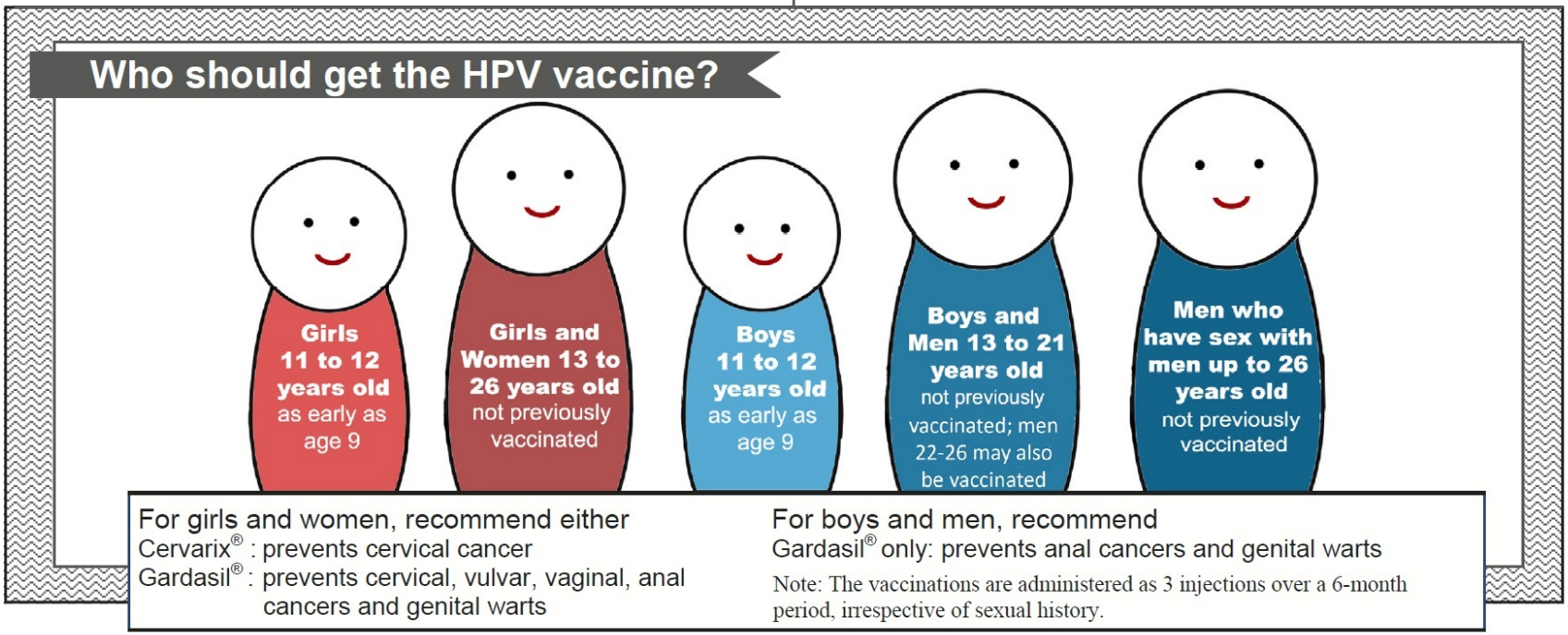
Prevention: Immunizations Update

- October 20th, 2016:
  - CDC and ACIP state that children 9-14 years old may receive just 2 doses of the vaccine, 6 months apart.
- The first HPV vaccine dose is routinely recommended at 11-12 years old. The second dose of the vaccine should be given 6-12 months after the first dose.
- Teens and young adults who start getting the vaccination at ages 15-26 years will continue to need 3 doses.
- Children and teens ages 9-14 who already received 2 doses of the HPV vaccine less than 6 months apart will require a third dose.
- Three doses are recommended for people with weakened immune systems aged 9-26 years.

Prevention: Immunizations

ACIP *recommendations*

The Advisory Committee on Immunization Practices: Human Papillomavirus Vaccine



Immunizations & Controversies

- For optimal effectiveness, HPV vaccines should be administered prior to engaging in sexual activity

Controversies: Age-related Concerns

- Parents, pro-abstinence activists, and social conservatives have expressed concern about the recommended age for vaccination

- They argue that it should be up to the parents to decide when their child gets vaccinated and when to discuss the topic of sex

Controversies: Age-related Concerns

- Many believe that the added protection from the vaccine will prompt adolescents to start engaging in sexual activity

- Others maintain that it will increase the rate of teenage promiscuity

Controversies: Misconceptions About HPV

- Surveys of parents have found several misconceptions that hinder vaccine acceptability:
  - Failure to recognize HPV as an STI
  - Low concern about child's risk of acquiring HPV
  - Lack of knowledge about disease features and sequelae

Controversies: Cost of Vaccination

- Each dose of the HPV vaccine costs approximately $120-$200
- The total cost for the 3-dose series ranges from ~$360-$600
- Administration fees may apply

Controversies: Cost of Vaccination

- Many insurance plans cover the cost for all 3 doses
- Vaccines for Children (VFC) Program covers HPV vaccination
  - Males and females up to 18 years old

Controversies:
Side Effects vs. Adverse Events

- *Side effects*: Health problems that have been shown to be linked to a vaccine by scientific studies

- *Adverse events*: Health problems that occur after vaccination that may or may not be caused by a vaccine

Controversies: Serious Adverse Events

- An adverse event is <u>defined by law</u> as serious if it is:
  - Life threatening, or
  - Results in death, a persistent or significant disability or incapacity, congenital anomaly or birth defect, hospitalization, or prolongation of existing hospitalization

Controversies: Serious Adverse Events

- ~90 million doses of HPV vaccines have been distributed in the U.S. from June 2006-March 2016

HPV vaccine	Number of doses distributed
Cervarix®	720,000
Gardasil®	79 million
Gardasil®9	10 million

Controversies: Serious Adverse Events

- In this same time period, the most commonly reported symptoms to the Vaccine Adverse Event Reporting System (VAERS) database were non-serious:
  - Fainting
  - Dizziness
  - Headache
  - Nausea
  - Fever
  - Pain, redness, swelling in the arm where the vaccine was given

Controversies: Serious Adverse Events

- 2011: Safety assessment of Gardasil® in 9-26 year old female vaccine recipients between August 2006-October 2009
  - 600,558 doses analyzed
  - No statistically significant increased risk for Guillain-Barré syndrome, stroke, venous thromboembolism, appendicitis, seizures, syncope, allergic reactions, or anaphylaxis

Controversies: Damage to Ovaries

- After over a decade of experience, neither the CDC nor the FDA have noted patterns between HPV vaccination and reproductive problems, including
  - Premature ovarian failure
  - Premature menopause
  - Amenorrhea

Controversies: Vaccine Safety in Pregnancy

- 2015: Analysis of VAERS data for pregnant women who received Gardasil® from June 2006-December 2013
  - No unexpected patterns in maternal or fetal outcomes
  - No safety concerns for pregnant women or their babies
- Gardasil® Pregnancy Registry
  - No evidence that the vaccine affects fertility, pregnancy, or the baby's health

Controversies:
Venous Thromboembolism (VTE)

- 2014: Analysis of Denmark data from October 2006-July 2013
  - 1,613,798 females aged 10-44 years
  - Found no association between Gardasil® and VTE during 42 days following vaccination
  - Subgroup analyses by age, anticoagulant treatment, and oral contraceptive use also found no association

Controversies:
Complex Regional Pain Syndrome (CRPS)

- A chronic, painful condition that typically affects a single limb following an episode of trauma or immobilization

- Occurs in the general population, including adolescents

Controversies:

Postural Orthostatic Tachycardia Syndrome (POTS)

- An abnormally large and sustained increase in heart rate when changing from a lying down to an upright position
- Relatively common in young adolescents
- Difficult to distinguish from normal physiologic responses in this age group

Controversies:
CRPS & POTS

- Review of >80 million females who received the vaccine worldwide
- Rates of syndromes in vaccinated females were no different from expected rates in their age groups
- Review of data provides no evidence of association with HPV vaccination
- No evidence justifies leaving individuals vulnerable to HPV-related cancers

Controversies:
Guillain-Barré Syndrome (GBS)

- A rare disorder in which a person's own immune system damages nerve cells, causing muscle weakness and sometimes paralysis
- Most individuals fully recover
- CDC's Vaccine Safety Datalink was monitored for GBS following administration of >1.4 million doses of Gardasil® from August 2006-February 2012
  - No cases of GBS were identified

Controversies: Autoimmune Diseases

- 2012: Kaiser Permanente Vaccine Study Center
- 2013: Department of Medical Epidemiology and Biostatistics at the Karolinska Institute in Sweden and the Statens Serum Institute in Denmark
- 2014: Institute Pasteur and 113 medical centers in Europe
- 2015: HPV vaccine safety data from the United States and Europe
- 2015: Cohort study from 2006-2013 in Denmark and Sweden
  - No statistically significant differences in the incidence of immune thrombocytopenia, autoimmune hemolytic anemia, systemic lupus erythematosus, rheumatoid arthritis, juvenile rheumatoid arthritis, type 1 diabetes, Hashimoto's disease, Graves' disease, multiple sclerosis, acute disseminated encephalomyelitis, GBS, neuromyelitis optica, optic neuritis, or uveitis

Controversies: Deaths

- CDC reviews all available information on reports of death following vaccines

- It has concluded that there is no evidence suggesting that HPV vaccination has resulted in death
  - There is no pattern of death occurring with respect to time after vaccination
  - There is no consistent vaccine dose number or combination of vaccines given among the reports

Post-Test

- **Question 1:** The most common sexually transmitted infections in the United States are HPV infections.

  Answer: True
- **Question 2:** An individual can become infected with only one strain of HPV at a time.

  Answer: False
- **Question 3:** The only type of cancer linked to HPV is cervical cancer.

  Answer: False

Thank you.

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