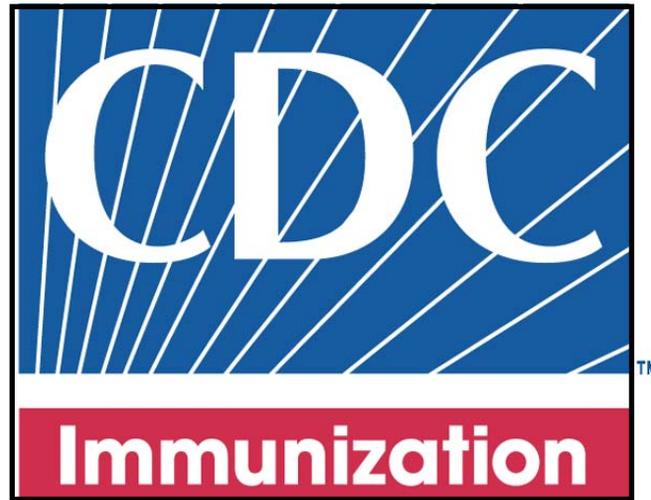


HPV: A New Era in the Prevention of Cervical Cancer

**William L. Atkinson, MD, MPH
National Center for Immunization and
Respiratory Diseases**

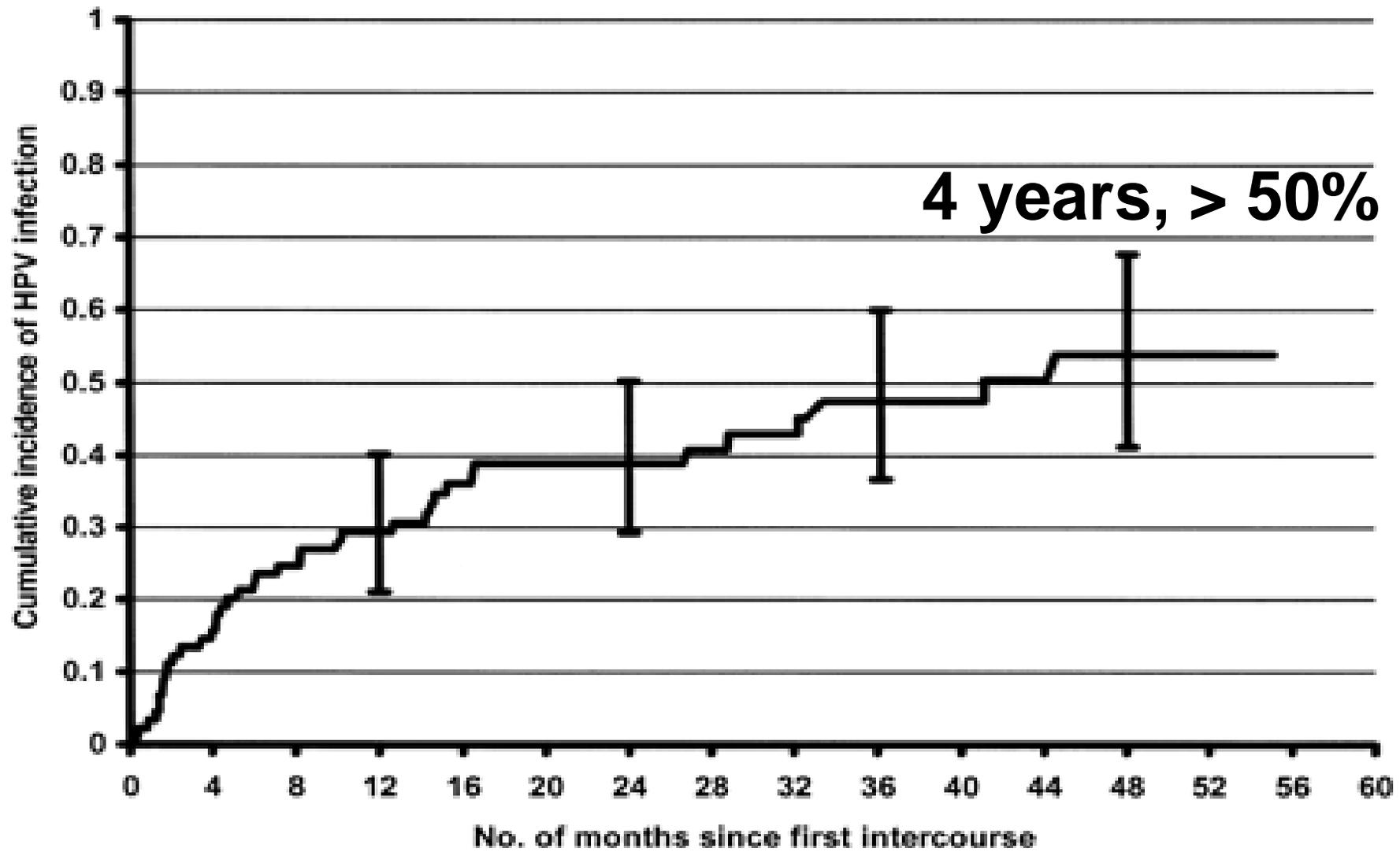


May 2007

Human Papillomavirus (HPV)

- **Genital HPV is the most prevalent sexually transmitted infection in the US**
 - **~20 million currently infected**
 - **6 million new infections/year**
 - **Estimated 80% of sexually active persons will have been infected by age 50**
- **Vast majority of infections are transient and asymptomatic**
- **Persistent infection may lead to anogenital cancer decades after initial infection**

Cumulative Incidence of Any HPV Infection Months after sexual initiation

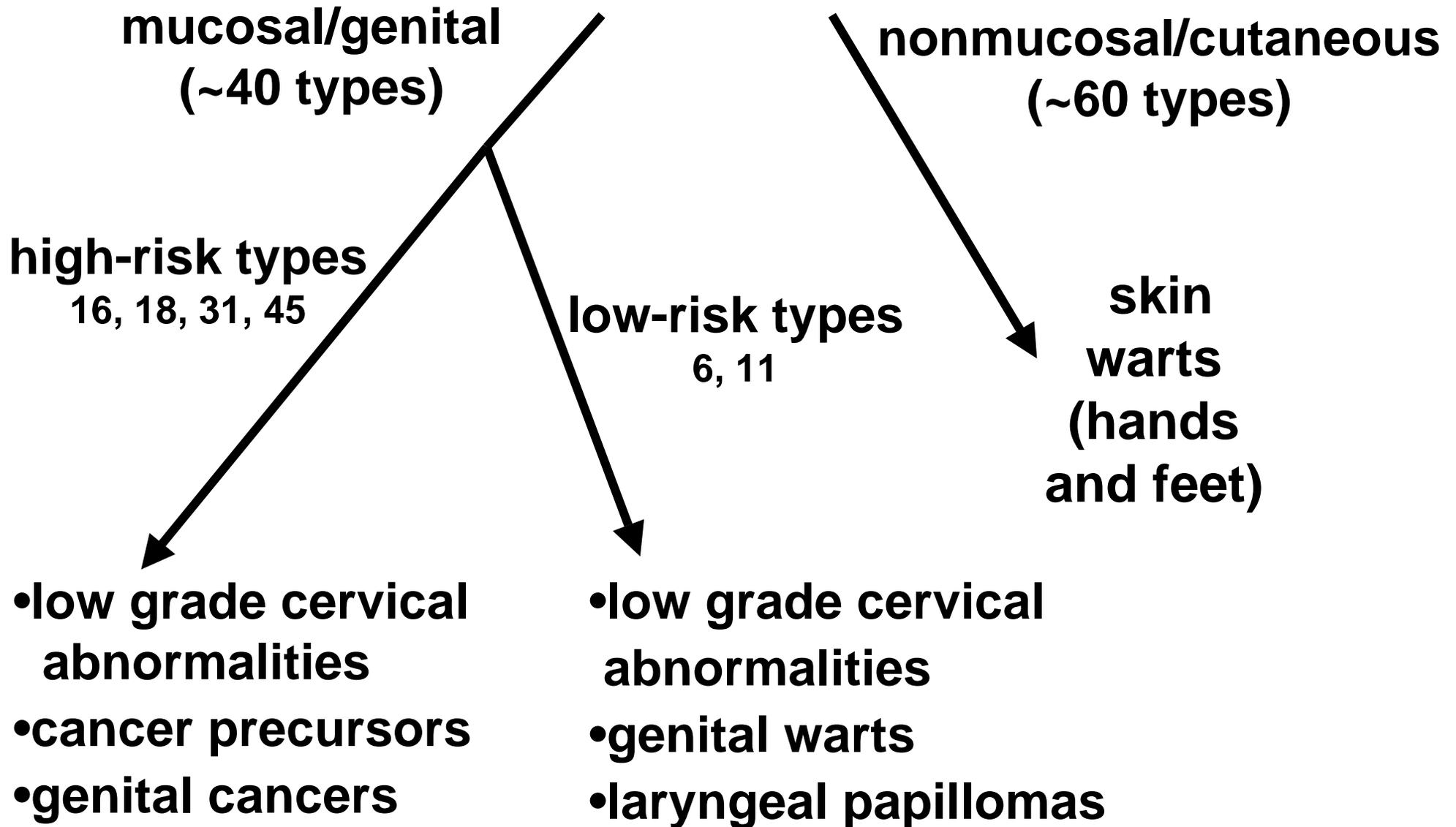


Winer: Am J Epidemiol, 2003;157

Cervical Cancer Disease Burden in the United States

- **The National Cancer Institute estimates that in 2007**
 - **11,150 new cervical cancer cases**
 - **3,670 cervical cancer deaths**
- **Almost 100% of these cervical cancer cases will be caused by one of the 40 HPV types that infect the mucosa**

Human Papillomavirus Types and Disease Association



HPV-Associated Disease

Type	Women	Men
16/18	70% of Cervical Cancer 70% of Anal/genital Cancer	70% of Anal Cancer Transmission to women
6/11	90% of Genital Warts 90% of RRP lesions	90% of Genital Warts 90% of RRP lesions Transmission to women

Correct and consistent condom use may have a protective effect on HPV acquisition, reduce the risk for HPV-associated diseases, and mitigate the adverse consequences of infection with HPV.

This statement is required by section 317 of the Public Health Service Act, 42 U.S.C., 243

Human Papillomavirus Vaccine

- **HPV L1 major capsid protein of the virus is antigen used for immunization**
- **Expression of L1 protein uses recombinant technology similar to that used to produce hepatitis B vaccine**
- **L1 proteins self-assemble into virus-like particles (VLP)**
- **Noninfectious, nononcogenic, and very effective**

Efficacy for Prevention of Clinical HPV Disease Due to HPV 6/11/16/18 Among 16-26 year-old Females*

<u>Endpoint</u>	<u>Vaccine</u>		<u>Placebo</u>		<u>Efficacy</u>	<u>(95% CI)</u>
	<u>N</u>	<u>Cases</u>	<u>N</u>	<u>Cases</u>		
HPV 16/18-related CIN2/3 or AIS	8487	0	8460	53	100	(93,100)
HPV 6/11/16/18 related CIN	7858	4	7861	83	95	(87, 99)
HPV 6/11/16/18 related genital warts	7897	1	7899	91	99	(94,100)

*Package insert: Gardasil®. Integrated dataset; results in the per-protocol populations
 CIN – cervical intraepithelial neoplasia; AIS – adenocarcinoma *in situ*

Serologic “Bridging” Studies of HPV Vaccine

- **Clinical trials among women 16-26 years defined serologic response and clinical efficacy against CIN and AIS**
- **Girls 9-15 years were evaluated with serologic testing only**
 - **Younger girls developed higher level of antibodies than older girls and women**
 - **Clinical efficacy assumed based on serology studies of older females**

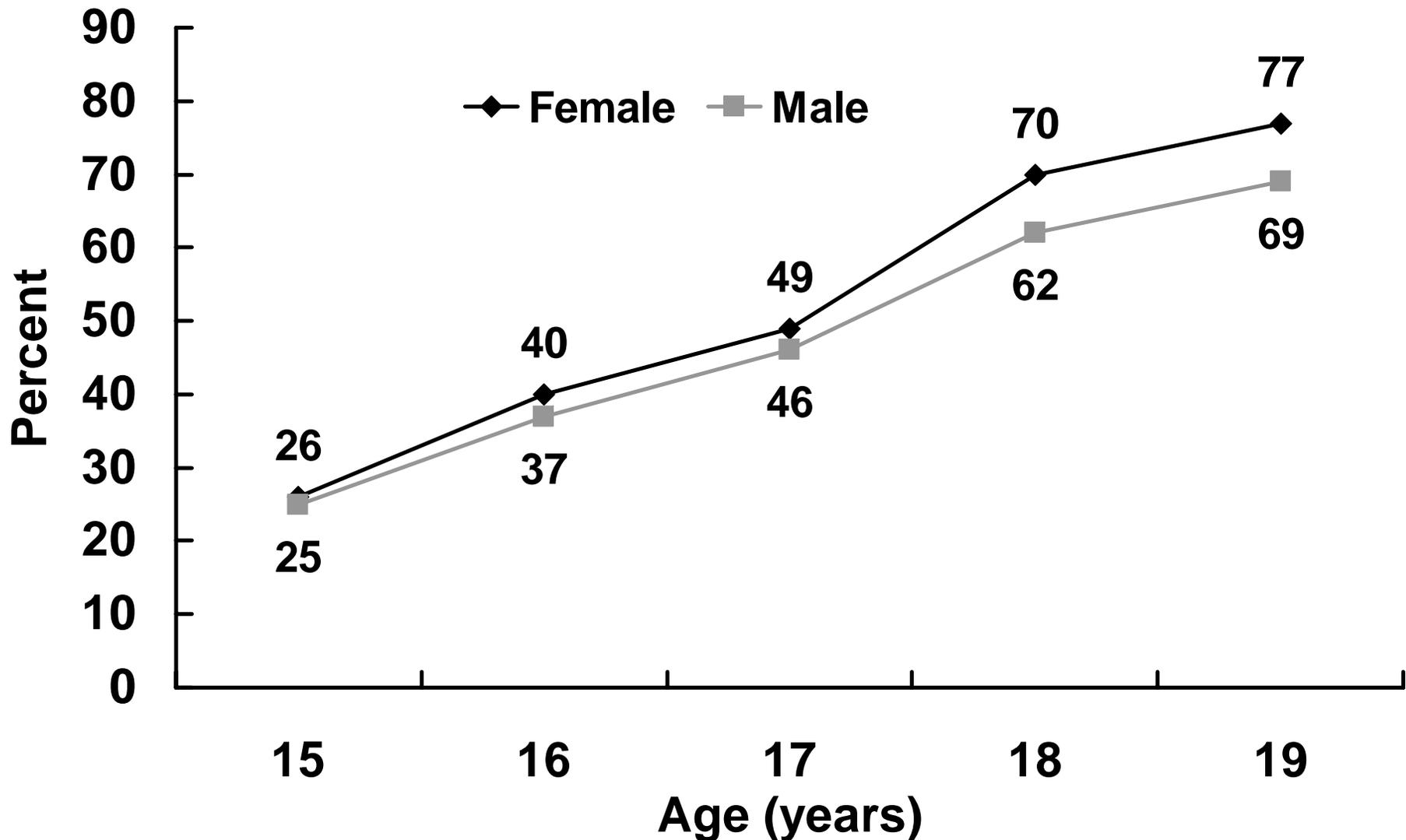
Quadrivalent HPV Vaccine

- **High efficacy among females without evidence of infection with vaccine HPV types**
- **No evidence that the vaccine had efficacy against existing disease or infection (i.e., the vaccine is not therapeutic)**
- **Prior infection with one HPV type did not diminish efficacy of the vaccine against other vaccine HPV types**

Routine HPV Vaccination Recommendations

- **ACIP recommends routine vaccination of females 11-12 years of age with three doses of quadrivalent HPV vaccine**
- **The vaccination series can be started as young as 9 years of age at the clinician's discretion**
- **“Catch-up” vaccination through age 26 years**

Percentage of Adolescents Who Have Had Vaginal Sex, By Gender and Age



National Survey of Family Growth, 2002. Mosher et al., 2005; Vital and Health Statistics: No. 362

HPV Vaccination Schedule

- **Routine schedule is 0, 2, 6 months**
- **Intramuscular injection in the deltoid**
- **Minimum intervals**
 - **4 weeks between doses 1 and 2**
 - **12 weeks between doses 2 and 3**
- **Minimum age is 9 years**
- **Maximum age is 26 years**

Incomplete Schedules and Duration of Immunity

- **The efficacy of less than three doses of HPV vaccine is not known**
- **The duration of immunity after a complete 3-dose schedule is not known**
 - **Available evidence indicates protection for at least 5 years**
 - **Multiple studies are in progress to monitor the duration of immunity**

Quadrivalent HPV Vaccine

- **HPV vaccine should not be administered to males and women older than 26 years**
 - **Limited safety and immunogenicity data available**
 - **No clinical efficacy data**
 - **Off-label use not recommended**
- **Studies of clinical efficacy in progress now**

Special Situations - HPV Vaccine May Be Administered

- **Equivocal or abnormal Pap test**
- **Positive HPV test**
- **Genital warts**
- **Immunosuppression**
- **Lactating women**

HPV 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)**

HPV Vaccination During 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**
- **Woman vaccinated during pregnancy should be reported to Merck registry (800.986.8999)**

MMWR 2006;56(No. RR-2):1-23. March 23, 2007

Cervical Cancer Screening

- **Cervical cancer screening – no change**
 - **30% of cervical cancers caused by HPV types not prevented by the quadrivalent HPV vaccine**
 - **Vaccinated females could subsequently be infected with non-vaccine HPV types**
 - **Sexually active females could have been infected prior to vaccination**
- **Providers should educate women about the importance of cervical cancer screening**

National Immunization Program Contact Information

- **Telephone** **800.CDC.INFO**
- **Email** **nipinfo@cdc.gov**
- **Website** **www.cdc.gov/nip**
- **Vaccine Safety**
<http://www.cdc.gov/od/science/iso/>