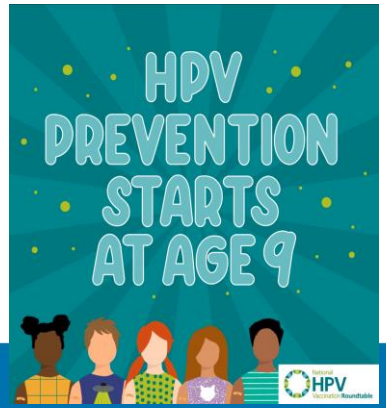
HPV Vaccination: an update



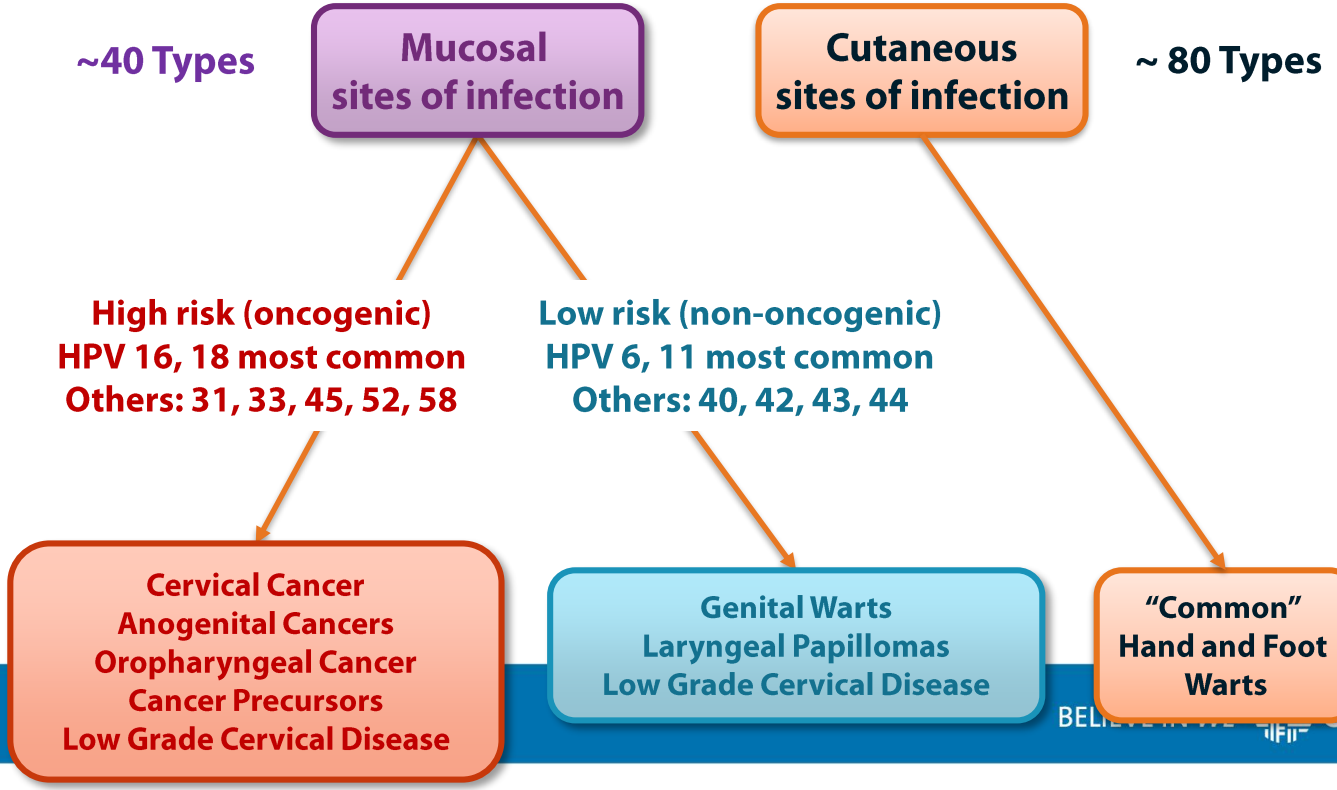
Kellie Rath, MD

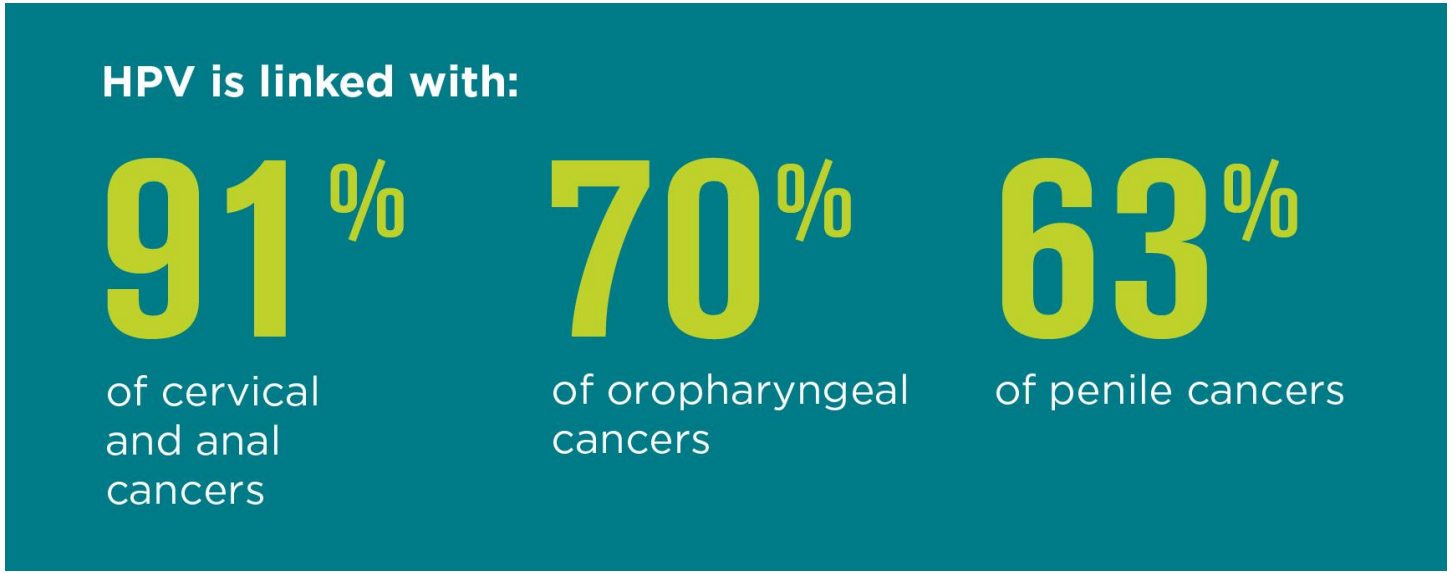
Ohio Health Gynecologic Oncology

HPV -- Human papillomavirus

Nonenveloped
double-stranded
DNA virus

HPV Types Differ in their Disease Associations

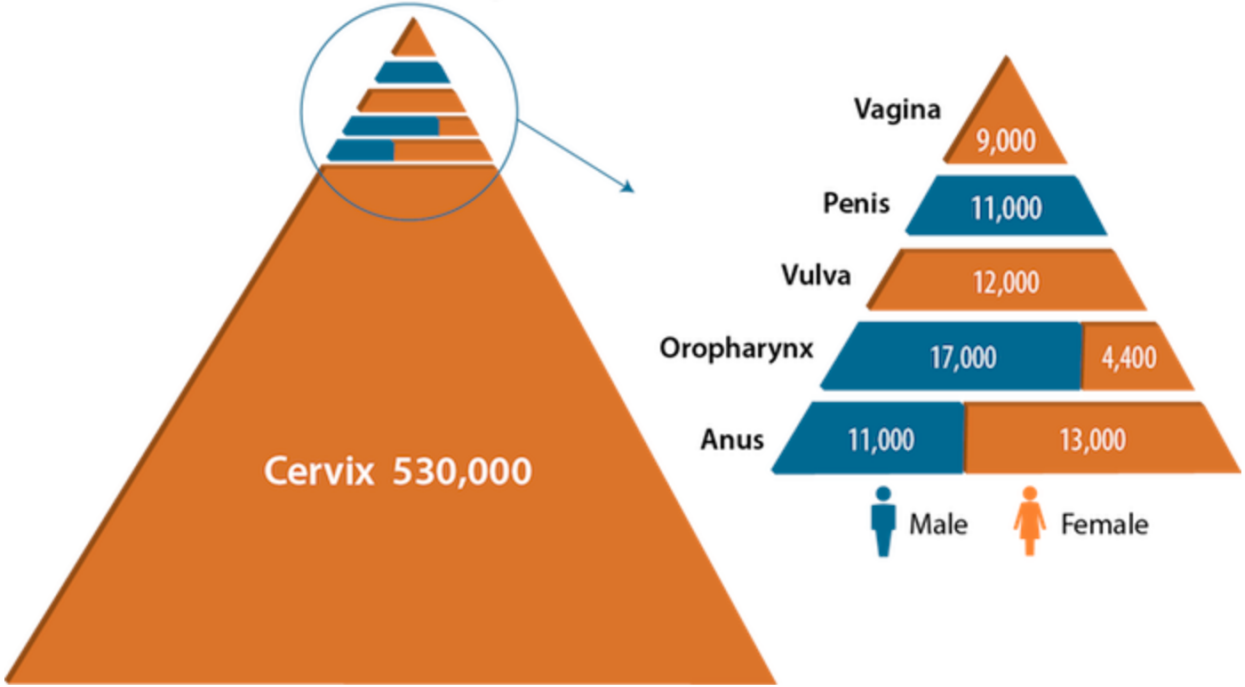




https://www.cdc.gov/cancer/hpv/statistics/

Figure 1

Numbers of Cancers Caused by HPV Worldwide Each Year



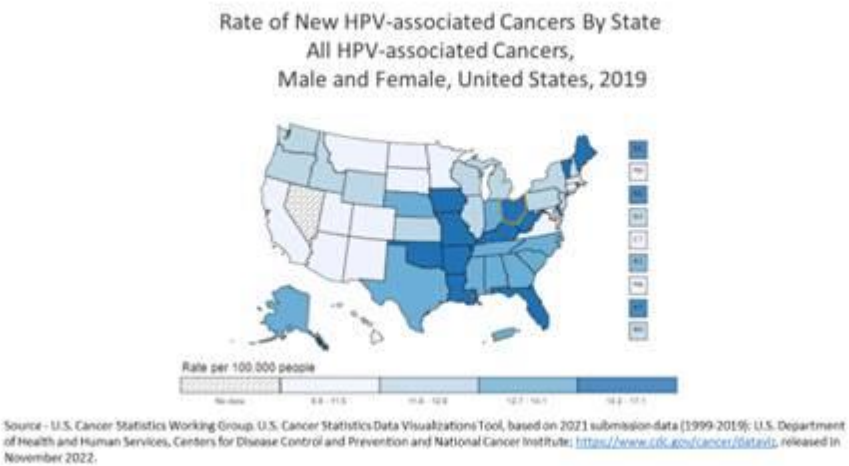
Note: Global estimates of genital warts and recurrent respiratory papillomatosis incidence are not available.

Source: de Martel C, Ferlay J, Franceschi S, Vignat J, Bray F, Forman D, et al. Global burden of cancers attributable to infections in 2008: a review and synthetic analysis. Lancet Oncol. 2012;13(6):607-15. Available from: http://www.ncbi.nlm.nih.gov/pubmed/22575588

Number of HPV-Attributable Cancer Cases per Year

Cancer site	Average number of cancers per year	Percentage probably caused by any HPV type	Estimated number probably caused by any HPV type
Cervix	12,293	91%	11,100
Vagina	879	75%	700
Vulva	4,282	69%	2,900
Penis	1,375	63%	900
Anus	7,531	91%	6,900
Female	5,106	93%	4,700
Male	2,425	89%	2,200
Oropharynx	20,839	70%	14,800
Female	3,617	63%	2,300
Male	17,222	72%	12,500
TOTAL	**47,199**	**79%**	**37,300**
Female	**26,177**	**83%**	**21,700**
Male	**21,022**	**74%**	**15,600**

Data source: National Program of Cancer Registries SEER*Stat Database: U.S. Cancer Statistics Incidence Analytic file 1998–2018. United States Department of Health and Human Services, Centers for Disease Control and Prevention. Released June 2021, based on the 2020 submission. From: https://www.cdc.gov/cancer/hpv/statistics/cases.htm. accessed 12/3/22.



Source - U.S. Cancer Statistics Working Group. U.S. Cancer Statistics Data Visualizations Tool, based on 2021 submission data (1999-2019): U.S. Department of Health and Human Services, Centers for Disease Control and Prevention and National Cancer Institute; https://www.cdc.gov/cancer/dataviz, released in November 2022.

HPV-associated Cancers Ohio 2019

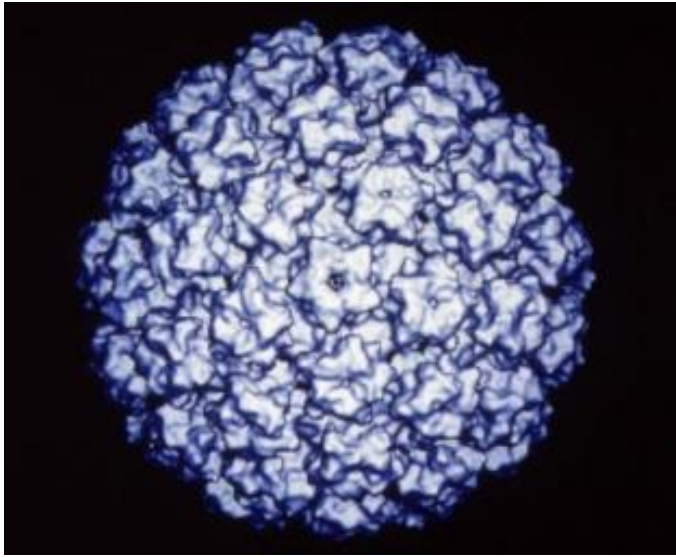
	% attributed to HPV	Ohio Cases	Ohio Cases Attributed to HPV
Cervix	90%	481	433
Vagina	75%	47	35
Vulva	70%	221	155
Penis	60%	65	39
Anus and Rectum	90%	303	273
Oropharynx	70%	923	646
Total		**2,040**	**1581**

Definitions of Risk Factor-Associated Cancers, https://www.cdc.gov/cancer/uscs/public-use/predefined-seer-stat-variables.htm

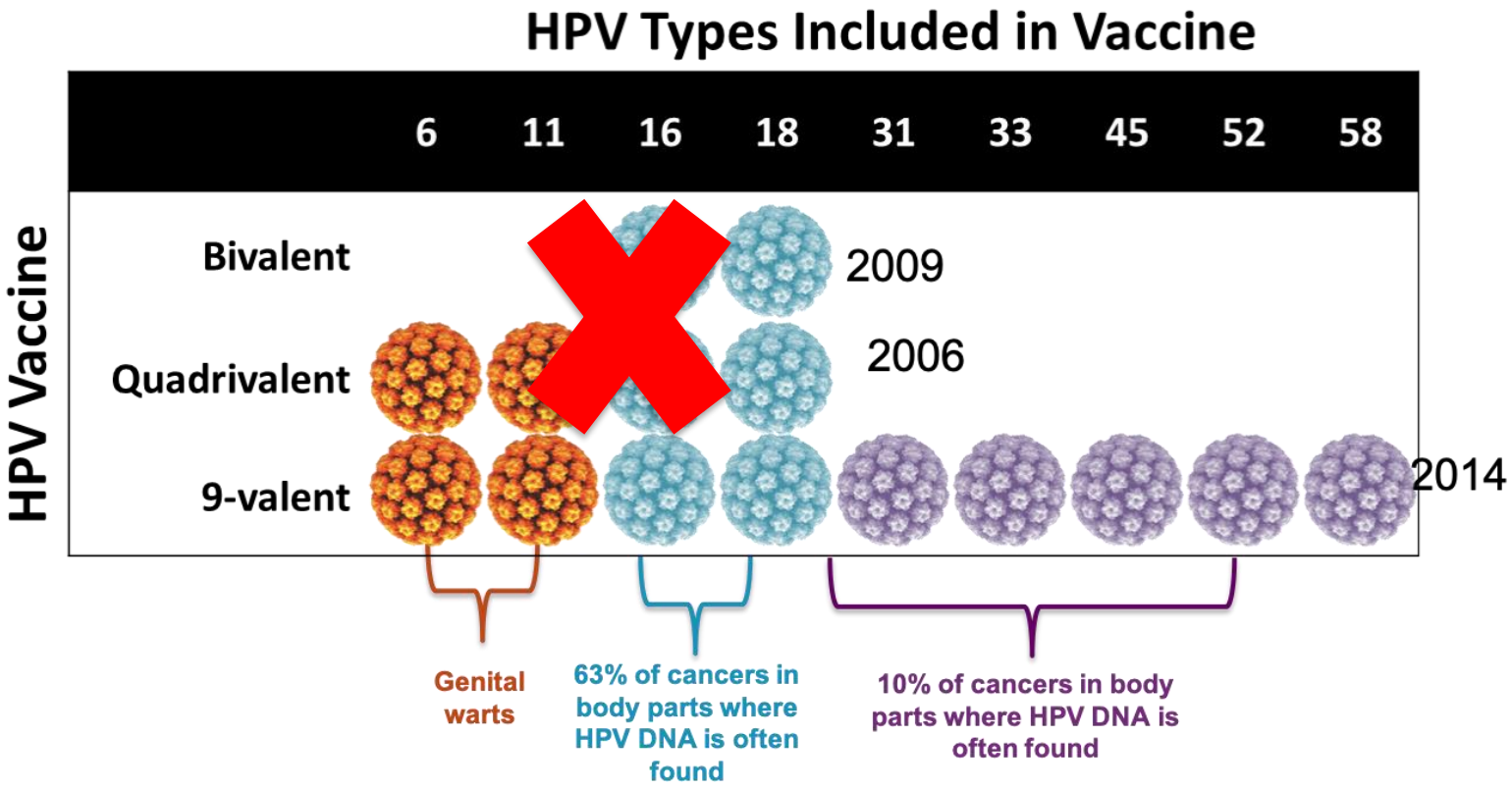
HPV Vaccines and vaccine recommendations

HPV Vaccines

- Recombinant L1 capsid proteins that form “virus-like” particles (VLP)
- Non-infectious and non-oncogenic
- Produce higher levels of neutralizing antibody than natural infection



HPV Virus-Like Particle

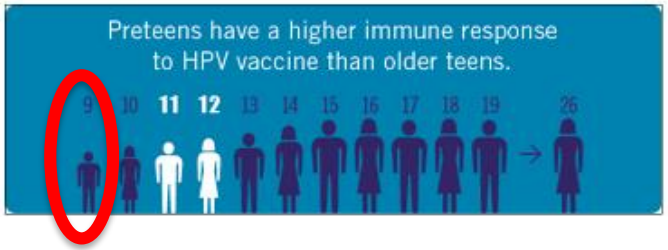


Adapted from Petrosky et al. *MMWR*. 2015.

TABLE. 2019 HPV VACCINATION RECOMMENDATIONS FROM ACIP[13]

Age	Gender	Regimen	Schedule
Initial Vaccination			
9-14 years	Females and males	2 doses	0, 6 to 12 months
Catch-up Vaccination			
15-26 years	Females and males	3 doses	0, 2, 6 months
27-45 years[a]	Females and males	3 doses	0, 2, 6 months

ACIP indicates Advisory Committee on Immunization Practices; HPV, human papillomavirus.
[a]Based on shared clinical decision making between patient and practitioner.



Immunocompromised all ages
– HIV infection, cancer, autoimmune disease.

Why Age 9?

- Offers more time for completion of the series by the age of 13
- Results in a strong immune response to the HPV vaccine
- Increases the likelihood of vaccinating prior to first HPV exposure
- Decreases questions about sexual activity by parents and guardians
- Decreases requests for only vaccines that are "required" for school
- Decreases the number of administered shots per visit
- Increases vaccinations and therefore the number of cancers prevented
- Has been shown by several systems to increase vaccination rates
- Has been shown to be highly acceptable to systems, providers, and parents

HPV Vaccine Recommendations: Catch-Up/Late

- Vaccination for everyone through age 26 years if not previously adequately vaccinated.
- Vaccination is not recommended for everyone older than 26 years.
  - However, some adults ages 27 through 45 years may decide to get the HPV vaccine based on discussion with their clinician, if they were not adequately vaccinated when they were younger.
  - HPV vaccination of people in this age range provides less benefit, as more have already been exposed to HPV.

Meites, et al. *MMWR Morb Mortal Wkly Rep*. 2019

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 vaccines should *not* be given to:

Patients with an allergic reaction to:

- A previous dose of Gardasil; yeast

Moderate or severe acute illnesses

- Wait until illness improves before vaccinating.

Pregnant women

- Delay initiation and completion until after delivery.
- HOWEVER →Vaccine not linked to adverse pregnancy outcomes or possible side effects to developing fetus.

HPV Vaccine Safety

CDC Vaccine Safety Monitoring Systems

System	Collaborators	Description
Vaccine Adverse Event Reporting System (VAERS)	CDC and FDA	Frontline, spontaneous reporting system to detect potential vaccine safety issues
Vaccine Safety Datalink (VSD)	CDC and 9 integrated health care systems	Large, linked database system used for active surveillance and research ~13 million members (~4% of US pop)
Clinical Immunization Safety Assessment (CISA) Project	CDC and 7 academic centers	Expert collaboration that conducts individual clinical vaccine safety assessments and clinical research

HPV Vaccine Safety in the United States

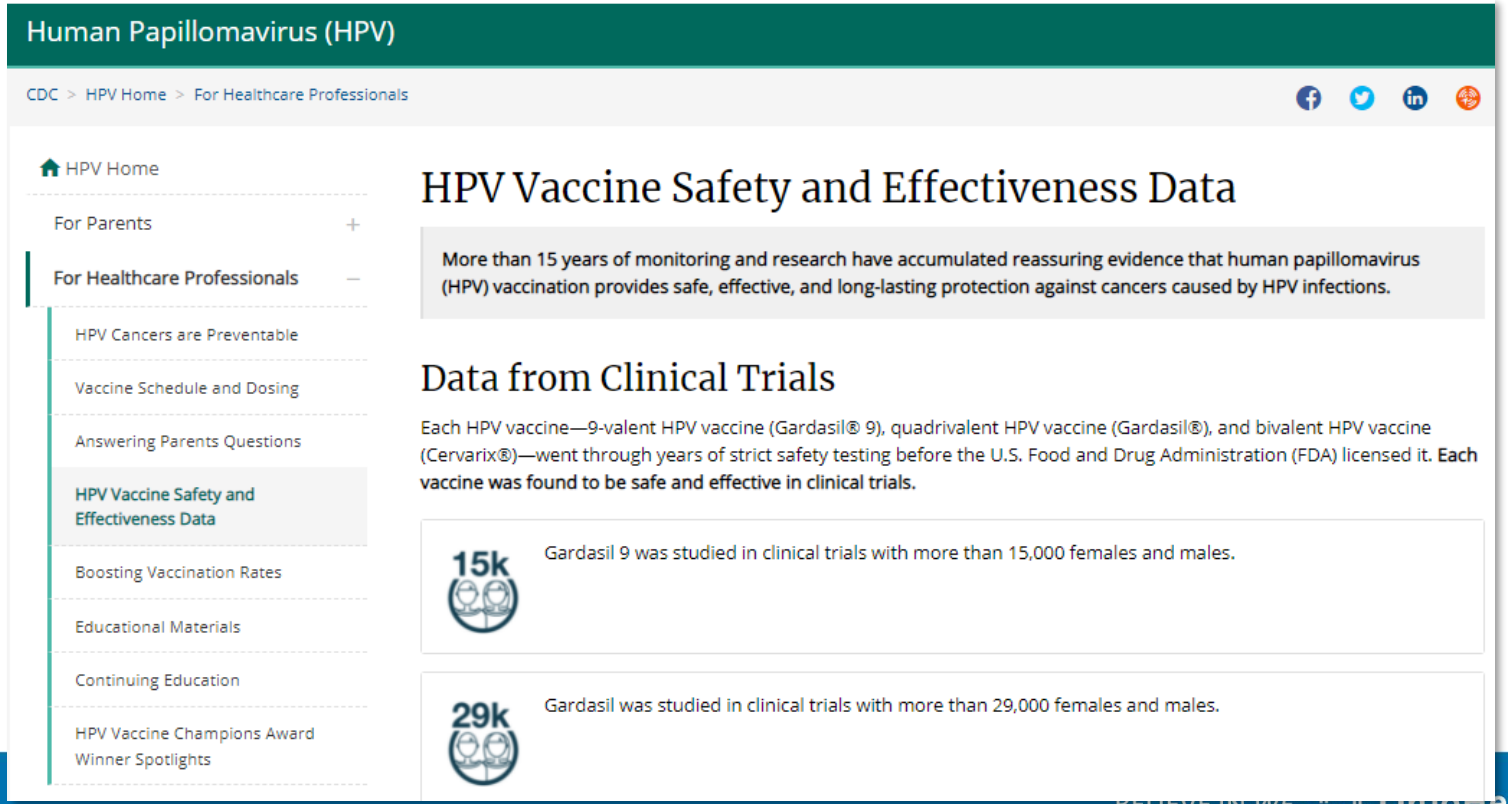
- We have more than **15 years** of HPV vaccine safety data.
- With more than **135 million doses** of HPV vaccines distributed in the United States, there are robust data showing that HPV vaccines are safe.
- As with all vaccines, CDC and FDA continue to monitor and evaluate the safety of HPV vaccines.
- **Clinicians can reassure parents who may have concerns about HPV vaccination.**

https://www.cdc.gov/hpv/hcp/vaccine-safety-data.html

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



https://www.cdc.gov/hpv/hcp/vaccine-safety-data.html

Impact of HPV Vaccination Program

Does this vaccine work ?????

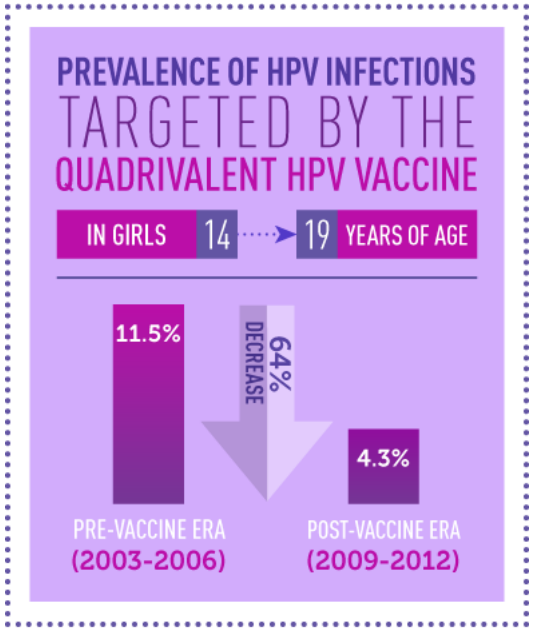
- Post-licensure evaluations are important to assess real-world effectiveness of vaccines
- Population impact against early and mid outcomes has been reported in many countries

CIN; cervical intraepithelial neoplasia

HPV Vaccine Impact in the United States

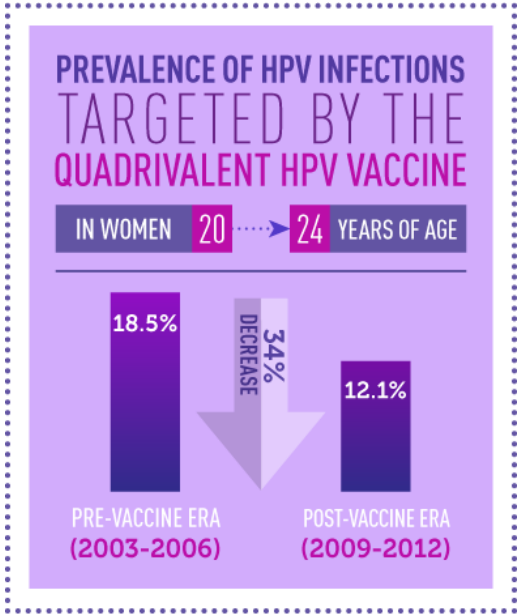
- Declines observed in:
  - Vaccine-type infections
  - Genital warts
  - Cervical precancers
  - Juvenile-onset recurrent respiratory papillomatosis

It works! HPV Prevalence Rates



www.cancer.gov

Source: Markowitz LE, Liu G, Hariri S, et al. Pediatrics. 2016 Mar;137(3):1-9

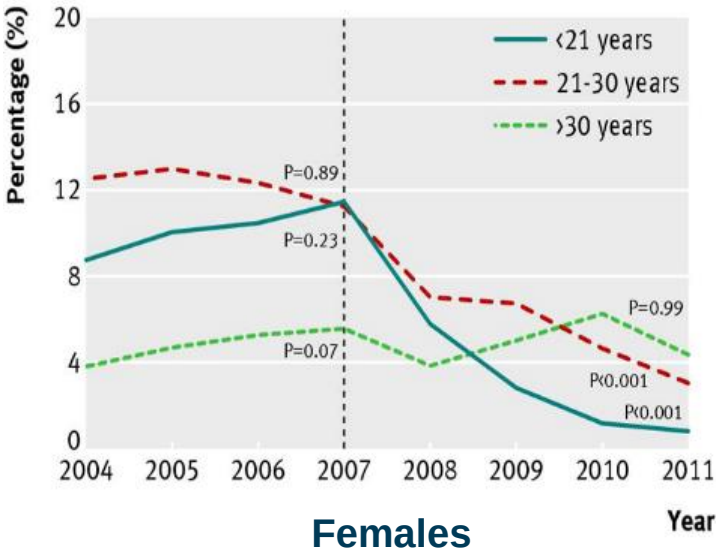


www.cancer.gov

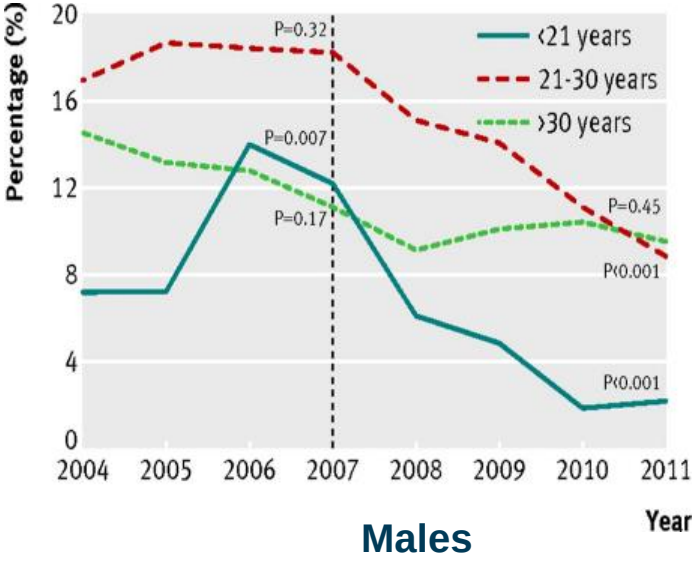
Source: Markowitz LE, Liu G, Hariri S, et al. Pediatrics. 2016 Mar;137(3):1-9

Impact of HPV Vaccination in Australia

Proportion of Australian-born females and males diagnosed as having genital warts at first visit, by age group, 2004-11



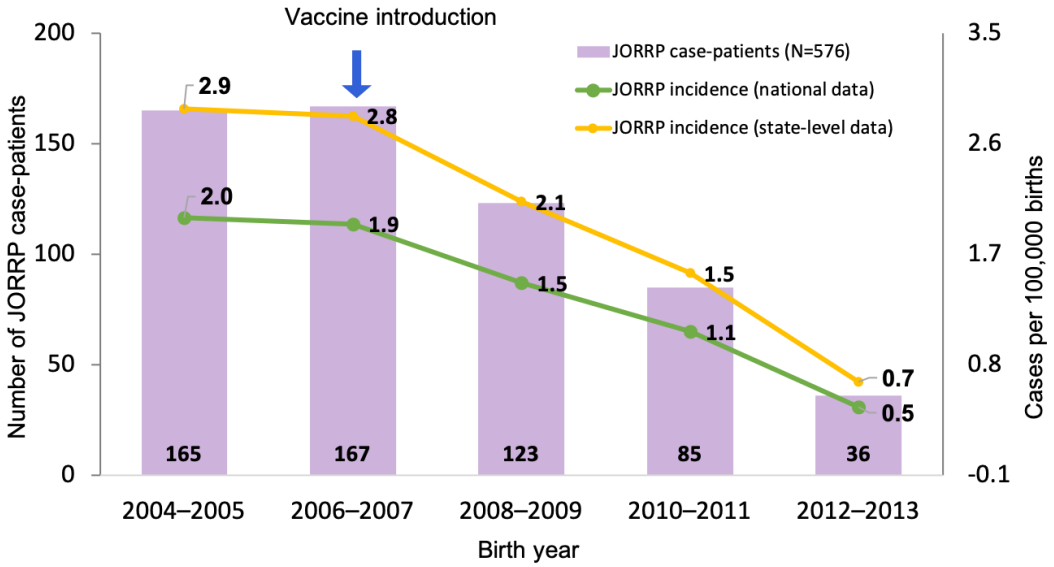
Females



Males

Ali, et al., Genital warts in young Australians five years into national human papillomavirus vaccination programme: national surveillance data. British Med J 2013;346:f2032

JORRP by Birth Year and Incidence Based on National or State-Level Denominator Data



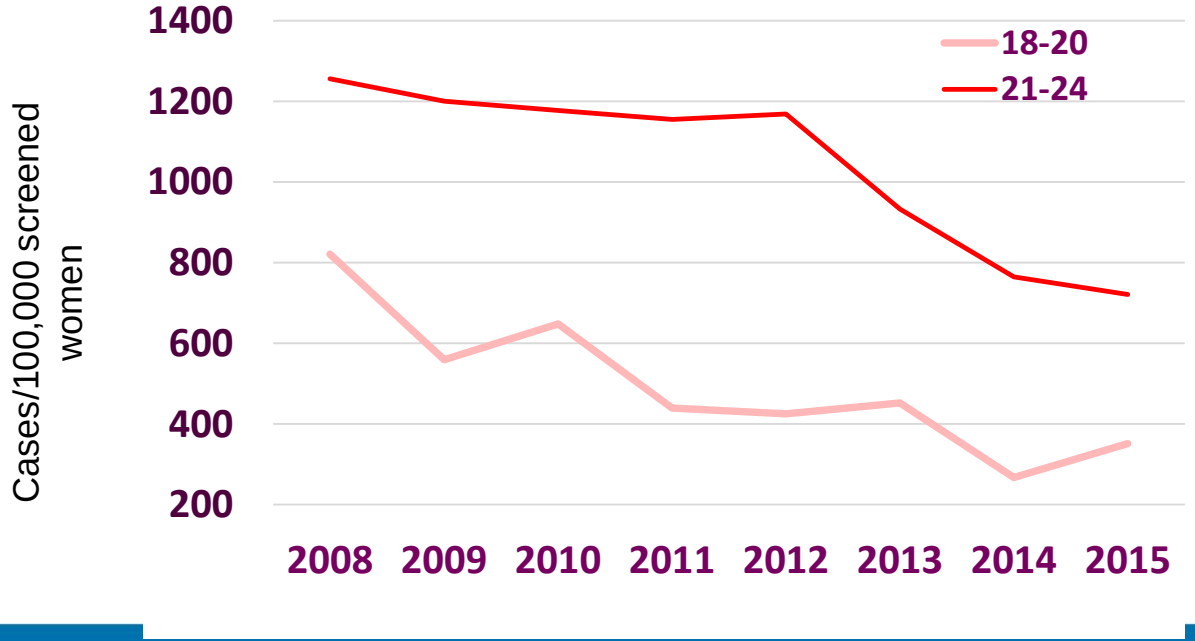
JORRP, juvenile-onset recurrent respiratory papillomatosis; Meites, et al. *Clin Infect Dis.* 2021

Effective at preventing cervical, vaginal, vulvar pre cancer

- Preventing CIN 2+
  - Not exposed: 97-100% effective
  - overall population: 44% effective
- Preventing VIN 2-3
  - Never exposed: 100% effective
  - Overall population: 66%

N Engl J Med. 2007;356(19):1928, N Engl J Med. 2007;356(19):1915, N Engl J Med. 2015;372(8):711., Lancet. 2014 Dec 20;384(9961):2213-27

Cervical Precancer Incidence Rates among Screened Women, HPV IMPACT Project, 2008-2015



Cervical precancer rates decreased significantly in screened women aged 18–20 and 21–24 years

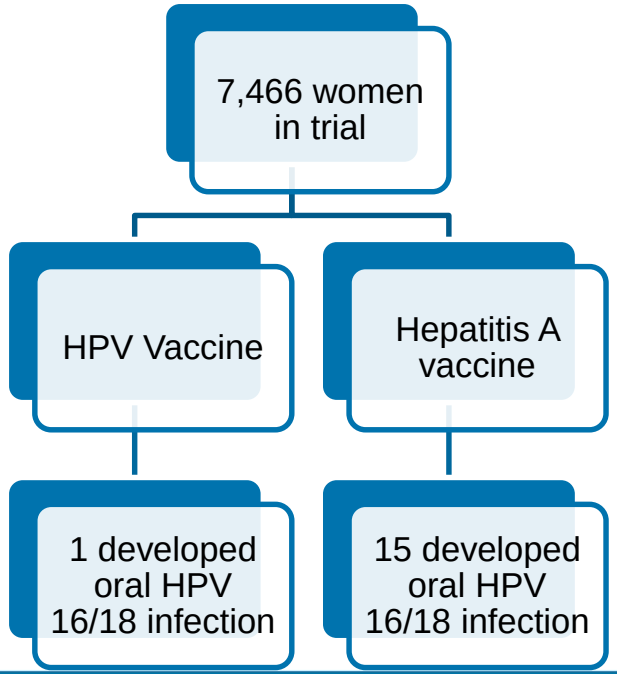
Gargano, et al. *Clin Infect Dis.* 2019

Systematic Review and Meta-Analysis: Population-Level Impact of HPV Vaccination

- Review of 65 studies in 14 high-income countries
- Evidence of herd effects
  - Anogenital warts decreased among men – in countries where men were not vaccinated
- After ~5-8 years of vaccination
  - Among 13- to 19-year-old girls
    - HPV 16/18 prevalence decreased by 83%
    - Anogenital warts decreased by 67%
  - Among 20- to 24-year-old women
    - HPV 16/18 prevalence decreased by 66%
    - Anogenital warts decreased by 54%
  - Among 20- to 24-year-old women screened for cervical cancer
    - Cervical precancers decreased by 31%

Drolet, et al. *Lancet Infect Dis*. 2019

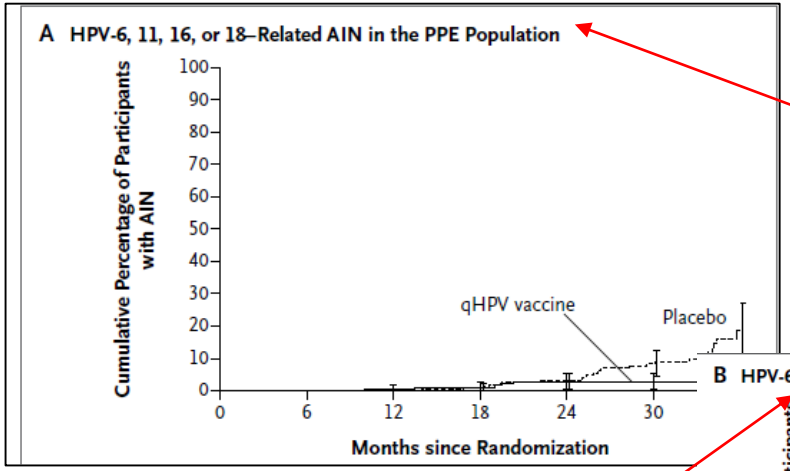
Impact of HPV 16/18 Vaccine on Oral HPV Infection



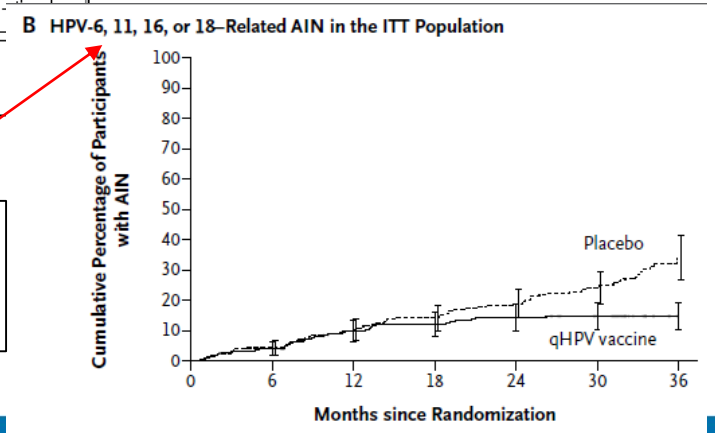
- Vaccine 93.3% effective in preventing oral HPV infection

Herrero R, et al. Reduced prevalence of oral human papillomavirus (HPV) 4 years after bivalent HPV vaccination in a randomized clinical trial in Costa Rica. PLOS ONE 2013;8:e68329

HPV vaccination (6,11,16,18) prevents anal dysplasia: MSM age 16-26



Men without HPV infection at Time of vaccination
-- 77.5% effective



All men included in the study
50.3% effective

Palefsky J, et al. HPV vaccine against anal HPV infection and anal intraepithelial neoplasia. N Engl J Med. 2011 Oct 27;365(17):1576-85

So what's the data behind vaccine approval to age 45????

- N=3819 women 24-45yo (international)
- Exclusion: pregnancy, hysterectomy, h/o genital warts, cervical dysplasia, cervical cancer, cervical biopsy in last 5 years, HIV, other immunocompromised state
- Outcomes: persistent infection at 6m, external genital HPV disease, cervical HPV disease

- Efficacy against PI/CIN/EGL:
  - 88.7% in per protocol population
  - 66.9% if sero+ but DNA negative for HPV type at time of enrollment
  - 47.2% in intention to treat population
- Follow up: median 4 years
- Safety: no concerns

End-of-study safety, immunogenicity, and efficacy of quadrivalent HPV (types 6, 11, 16, 18) recombinant vaccine in adult women 24-45 years of age. Br J Cancer. 2011 Jun 28;105(1):28-37.

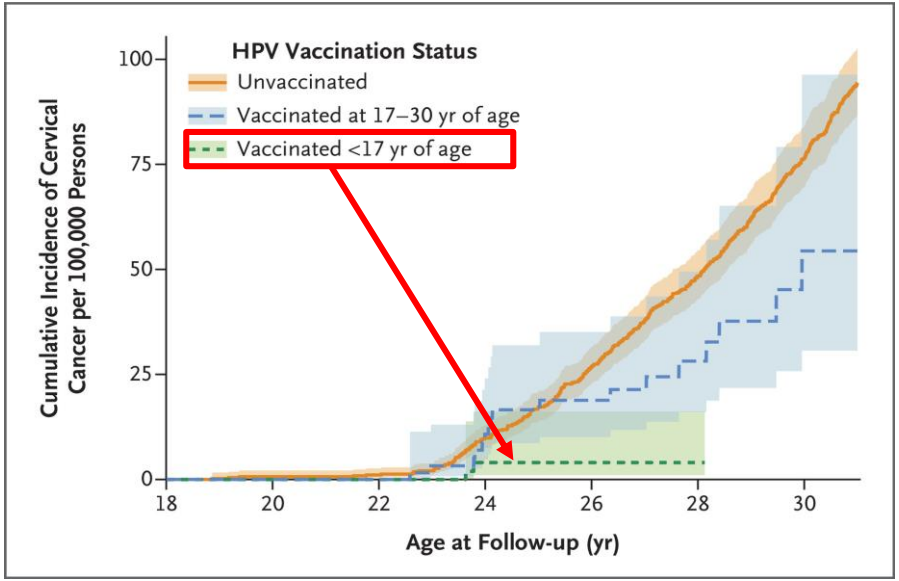
The NEW ENGLAND JOURNAL of MEDICINE

ORIGINAL ARTICLE

HPV Vaccination and the Risk of Invasive Cervical Cancer

Jiayao Lei, Ph.D., Alexander Ploner, Ph.D., K. Miriam Elfström, Ph.D., Jiangrong Wang, Ph.D., Adam Roth, M.D., Ph.D., Fang Fang, M.D., Ph.D., Karin Sundström, M.D., Ph.D., Joakim Dillner, M.D., Ph.D., and Pär Sparén, Ph.D.

N ENGL J MED 383;14 NEJM.ORG OCTOBER 1, 2020



- Swedish registry of 1,672,983 females age 10-30 years from 2006-2017.
- assessed the association between HPV vaccination and the risk of invasive cervical cancer
- controlling for age at follow-up, calendar year, county of residence, and parental characteristics, including education, household income, mother's country of birth, and maternal disease history

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

ACIP. Summary Report. June 22-23, 2016; Ferris, et al. *Pediatrics.* 2017; Goldstone, et al. *Lancet.* 2021; Kjaer, et al. EClinicalMedicine. 2020

HPV Vaccine Is SAFE

- Benefits far outweigh any potential risks
- Safety studies findings for HPV vaccination are reassuring and similar to MenACWY and Tdap vaccine safety reviews

HPV Vaccine WORKS

- Population impact against early and mid outcomes has been reported in multiple countries

HPV Vaccine Protection LASTS

- Studies suggest that vaccine protection is long-lasting
- No evidence of waning protection

How many cancers might we prevent?

Number of HPV-Attributable Cancer Cases per Year

Cancer site	Average number of cancers per year	Percentage probably caused by any HPV type	Estimated number probably caused by any HPV type
Cervix	12,293	91%	11,100
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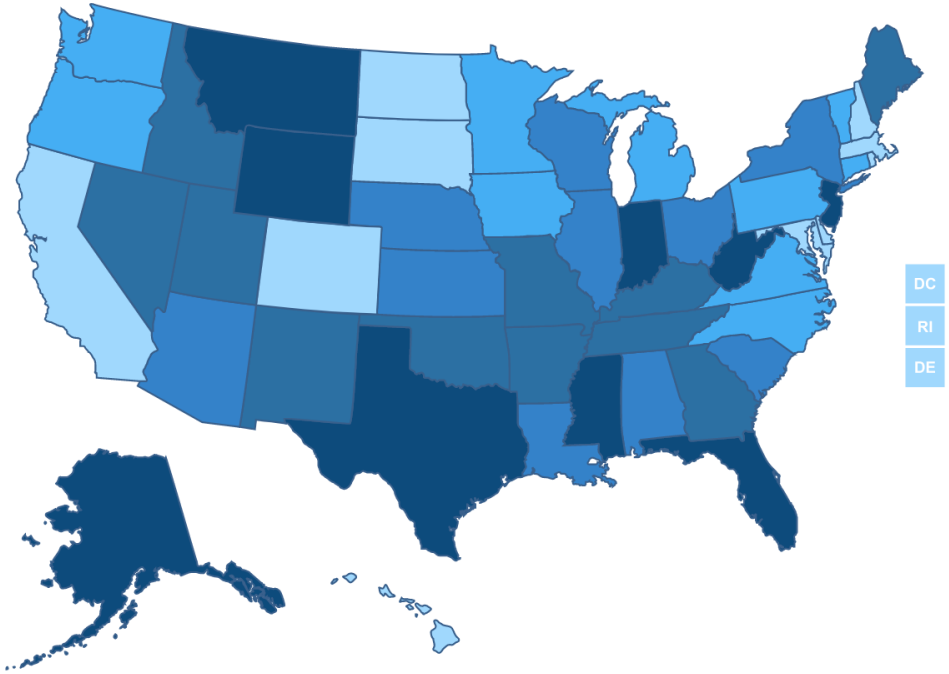
So how are we doing???

Percentage of adolescents ages 13-17 who received all recommended doses of the human papillomavirus (HPV) vaccine

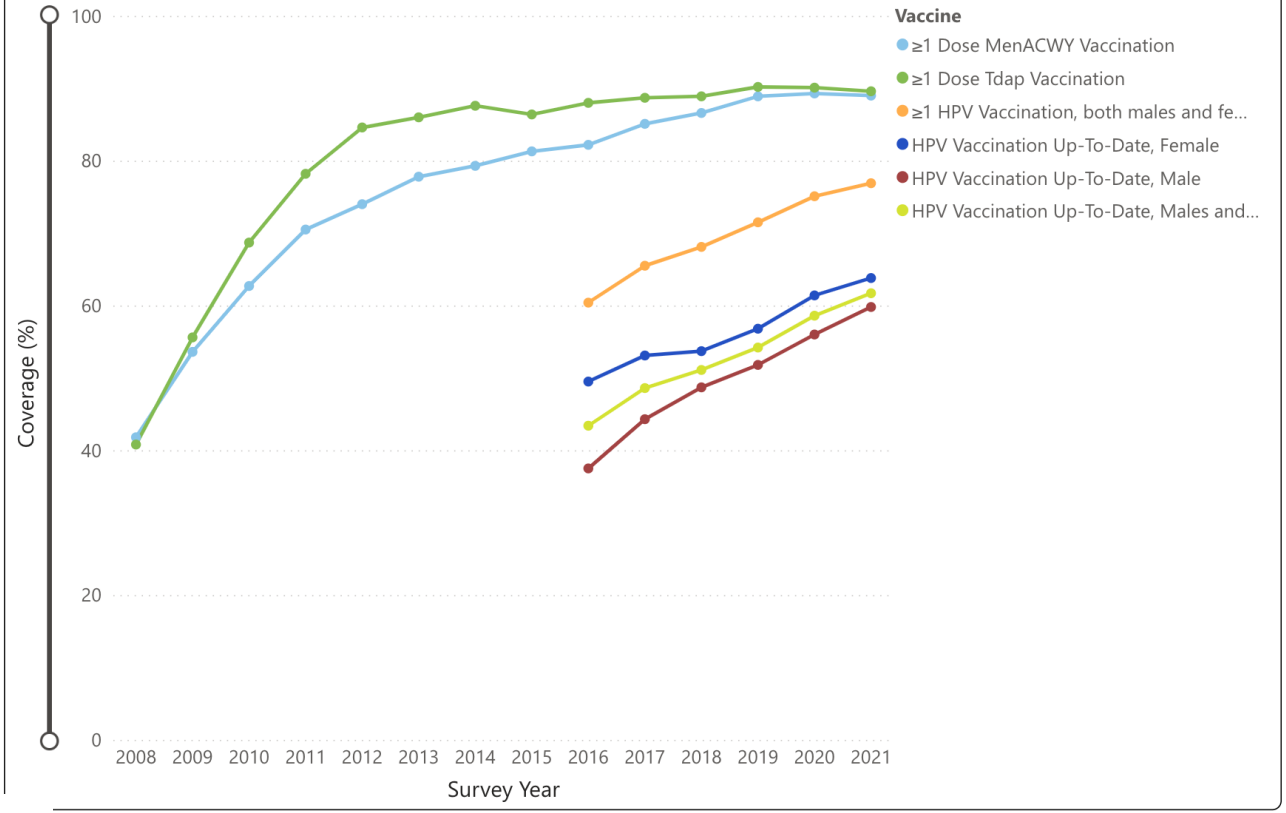


>= 68.9%	64.7% - 68.8%	61.7% - 64.6%	56.5% - 61.6%	<= 56.4%

Source:

- CDC, National Immunization Survey-Teen

Vaccination Coverage by Year among Adolescents Age 13-17 Years, United States, National Immunization Survey-Teen



Source:

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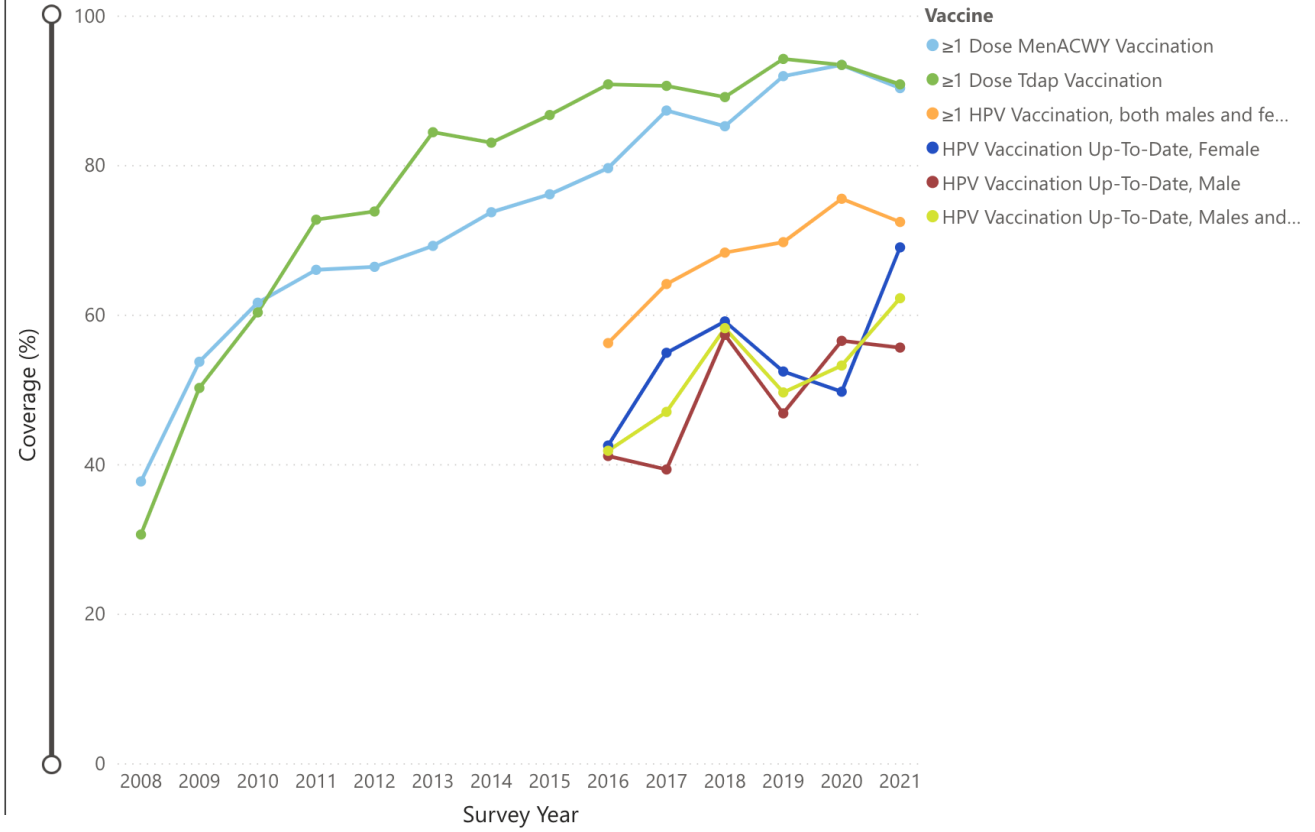
Vaccination Coverage by Year among Adolescents Age 13-17 Years, Ohio, National Immunization Survey-Teen



Source:

- CDC, National Immunization Survey-Teen

Talking about the HPV Vaccine

BELIEVE IN *WE*™ OhioHealth

A **clear** and **concise** **recommendation**

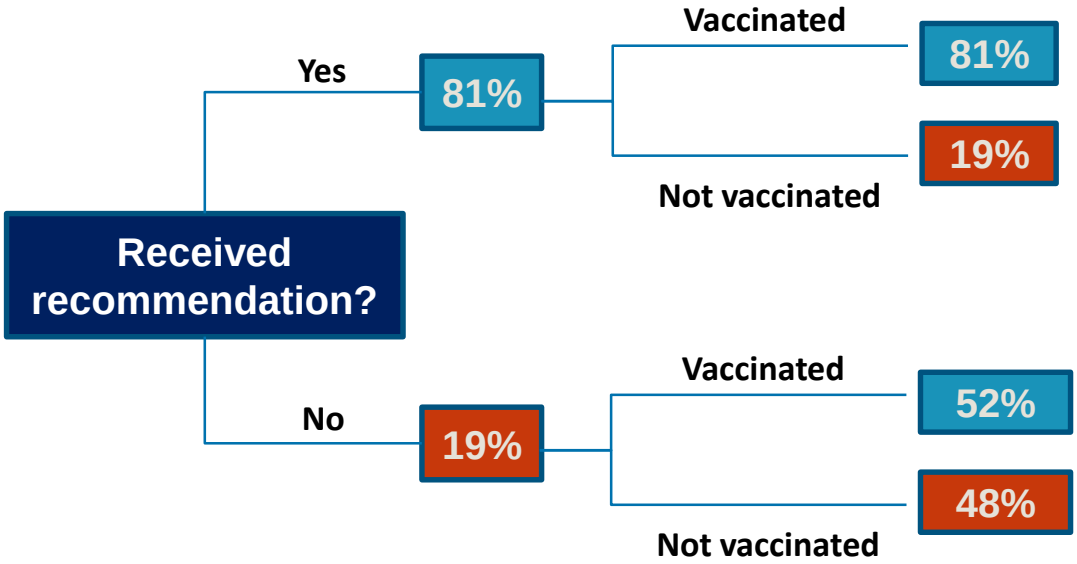
from a healthcare provider

INCREASES **vaccination rates**

among children and adults.

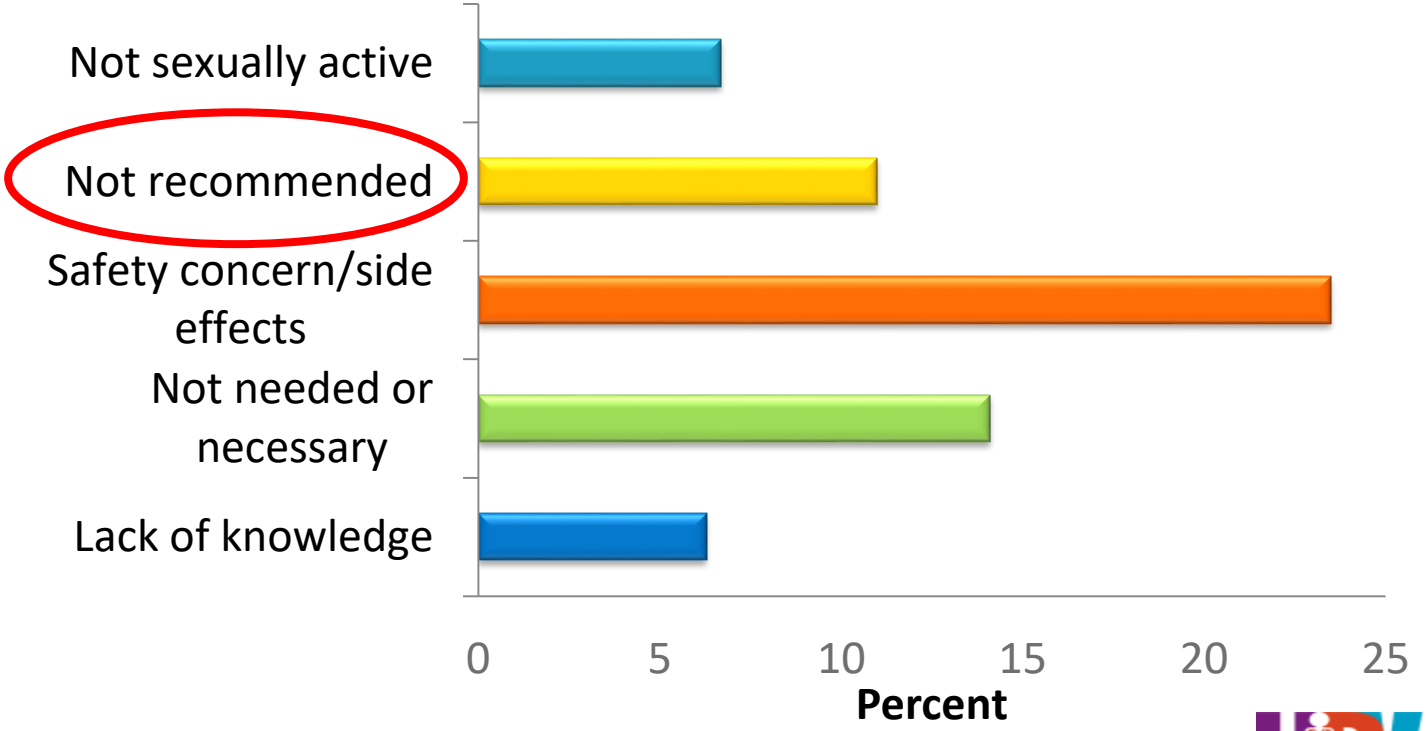
AND Is the main reason parents decide to vaccinate

Vaccination Coverage Higher among Those Reporting a Recommendation

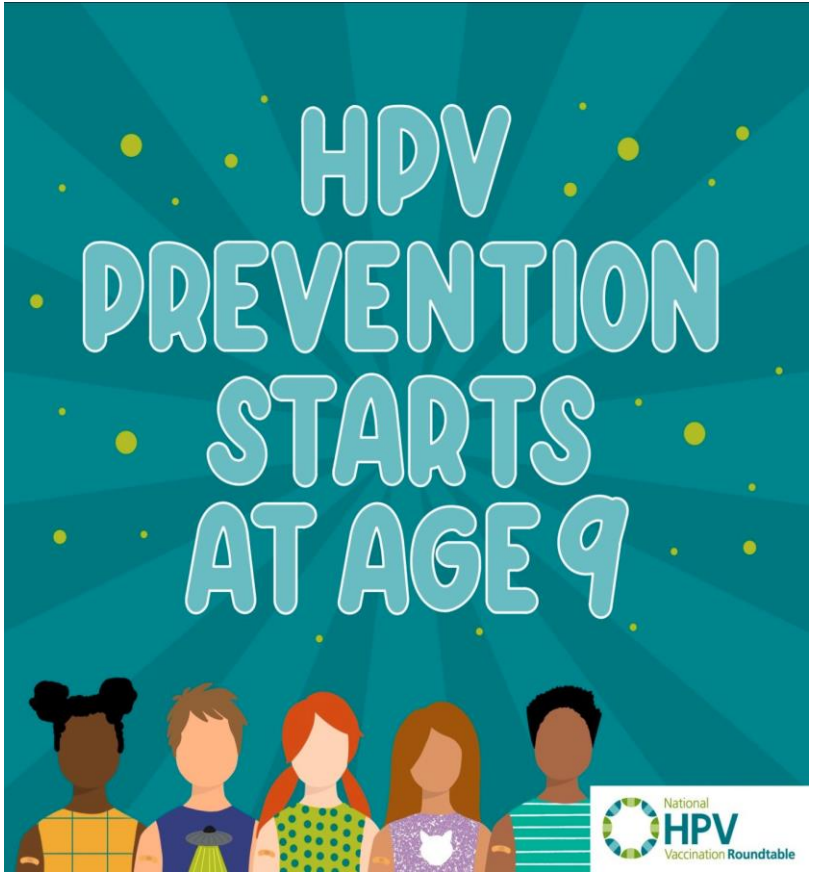


Source: CDC unpublished, NIS-Teen 2020

Top Reasons for Not Vaccinating against HPV



Source: CDC unpublished, NIS-Teen 2020


HPV
PREVENTION
STARTS
AT AGE 9
National
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Vaccination Roundtable


PREVENT
SIX CANCERS
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- Decreases the number of administered shots per visit
- Increases vaccinations and therefore the number of cancers prevented
- Has been shown by several systems to increase vaccination rates
- Has been shown to be highly acceptable to systems, providers, and parents

Protect Your Preteen/Teen with Vaccines

Protect them from serious diseases including HPV cancers, meningitis, tetanus, whooping cough, flu, and COVID-19.

AGES 9 - 10

- HPV dose 1 (human papillomavirus)
- HPV dose 2 (6 - 12 months after dose 1)

AGES 11 - 12

- Meningitis dose 1 (MenACWY)
- Tdap (tetanus, diphtheria, pertussis)
- HPV (if 2 doses haven't been given)

AGE 16

- Meningitis dose 2 (MenACWY)
- Meningitis B series (MenB)

YEARLY

- Flu (seasonal influenza)

Preteens and teens should stay up-to-date with COVID-19 vaccine to help protect them from COVID-19.

National HPV Vaccination Roundtable

This publication was supported in part by funding from the Centers for Disease Control and Prevention through Cooperative Agreement grant number 6 NU66IP000682. The content of this publication does not necessarily represent the official views of, nor an endorsement by, the CDC/HHS or the U.S. Government.

Recommended Vaccination Schedule Guideline

On Time
AGE 9-12
2 Doses
6-12 months apart

Late
AGES 13-14
2 Doses
6-12 months apart

Critical
AGES 15-26
3 Doses
1st dose at visit one
2nd dose 1-2 months later
3rd dose 6 months after 2nd

If not started prior to age 11 and visit for other preteen vaccines….
SAME WAY, SAME DAY

Group all the adolescent vaccines

- Recommend HPV vaccination the same way you recommend Tdap and meningococcal vaccines

Recommend HPV vaccine *TODAY*

- Recommend HPV vaccination the same day you recommend Tdap and meningococcal vaccines

Brewer, et al. *Pediatrics*. 2017

“Would you give it to your child?”

As soon as my children are old enough they will get the vaccine (only 1.5 years away)!

I also recommend it to all my patients, friends, and family members!

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