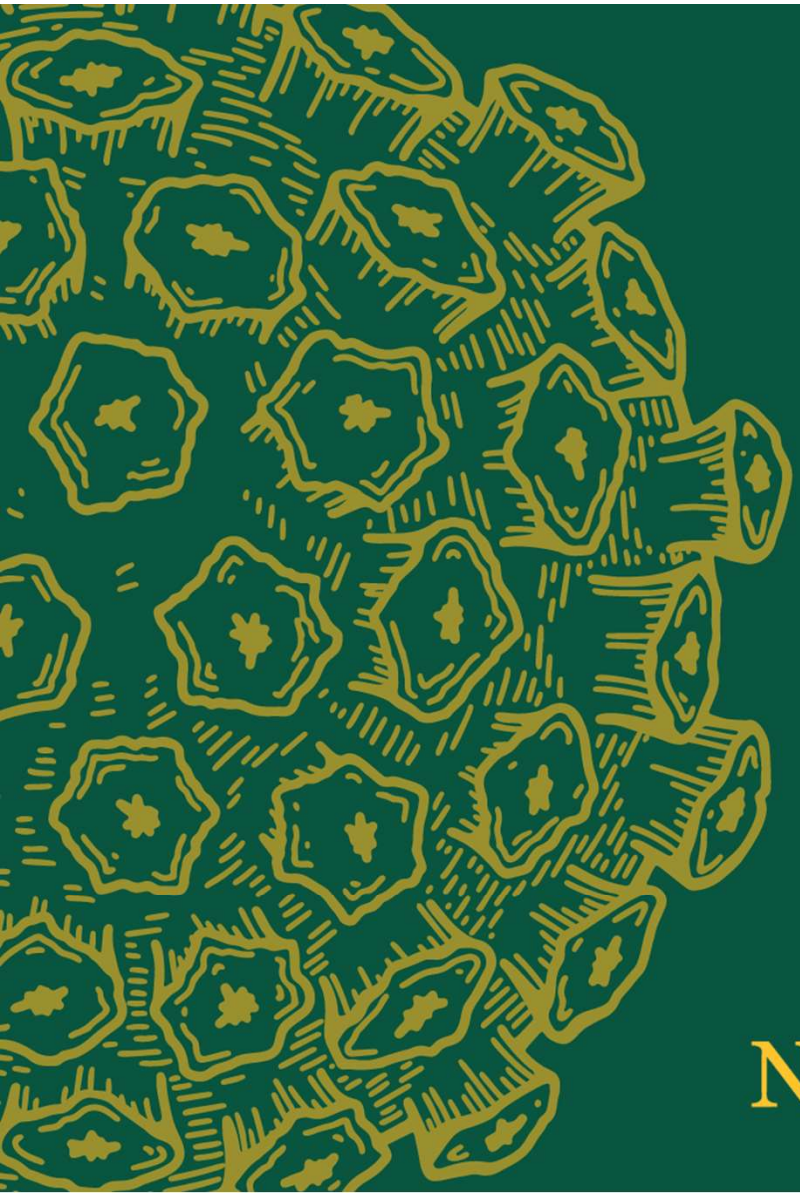

HPV Infection

Immunizing for Cancer Prevention

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Associate Professor of Practice &
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NDSU | CENTER FOR IMMUNIZATION RESEARCH AND EDUCATION

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MINNESOTA MEDICAL ASSOCIATION

Disclosure:

It is the policy of the Minnesota Medical Association (MMA) to ensure balance, independence, objectivity, and scientific rigor in its CME activities. To comply with the Standards for Integrity and Independence of the Accreditation Council for Continuing Medical Education (ACCME), the MMA requires planning committee members and faculty to disclose all financial relationship they have with an ineligible company. The members of the faculty and planning committee for this conference have indicated that they have no financial relationships to disclose related to the content of the CME activity. Faculty members have declared that they will uphold the MMA's standards regarding CME activities and that any clinical recommendations are based on the best available evidence or are consistent with generally accepted medical practice. Please indicate in the comments section of the evaluation form whether you detect any instances of bias toward products manufactured by an ineligible company.

CME & MOC Statements:

This activity has been planned and implemented in accordance with the accreditation requirements and polices of the Accreditation Council for Continuing Medical Education through the Minnesota Medical Association and NDSU. The Minnesota Medical Association (MMA) is accredited by the Accreditation Council for Continuing Medical Education to provide continuing medical education for physicians.

The Minnesota Medical Association designates this live activity for a maximum of 1 *AMA PRA Category 1 Credit(s)™*. Physicians should claim only the credit commensurate with the extent of their participation in the activity.

Successful completion of this CME activity, which includes participation in the evaluation component, enables the learner to earn up to 1 MOC point in the American Board of Pediatrics' (ABP) Maintenance of Certification (MOC) program. It is the CME activity provider's responsibility to submit learner completion information to ACCME for the purpose of granting ABP MOC credit.

Financial Support:

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Disclosure

Dr. Tracie Newman has no relevant financial relationships with ineligible companies to disclose.

Provider recommendation is strongly correlated with vaccination:

initiation, completion, and follow-through

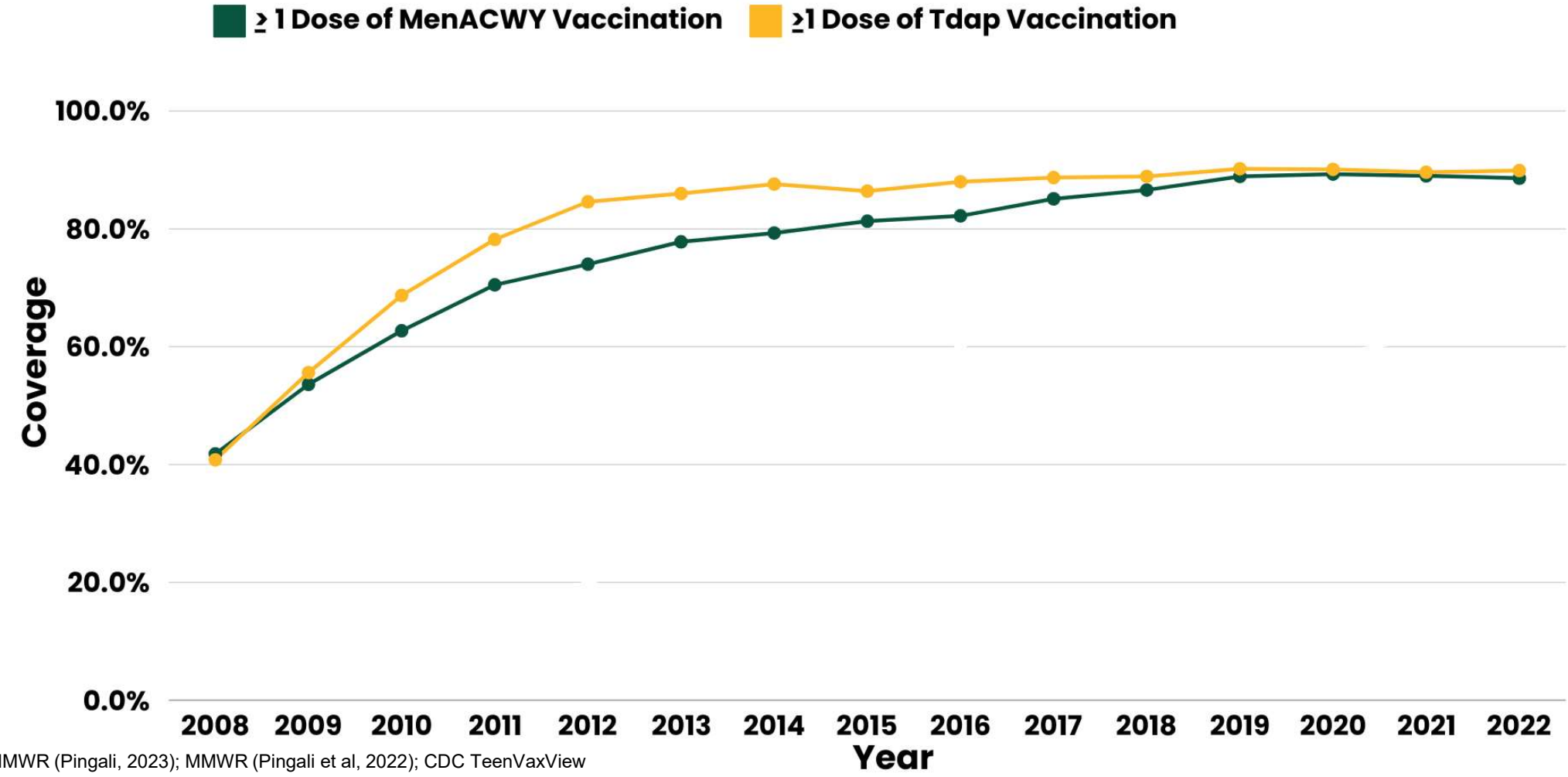
Prev Med (Oh et al, 2021)

- **Lack of general HPV and vaccine knowledge**
- **Low self-confidence in counselling and addressing parental concerns**
- **Discomfort in discussing sexual issues related to vaccination**

Vaccine (Shuk et al, 2019)

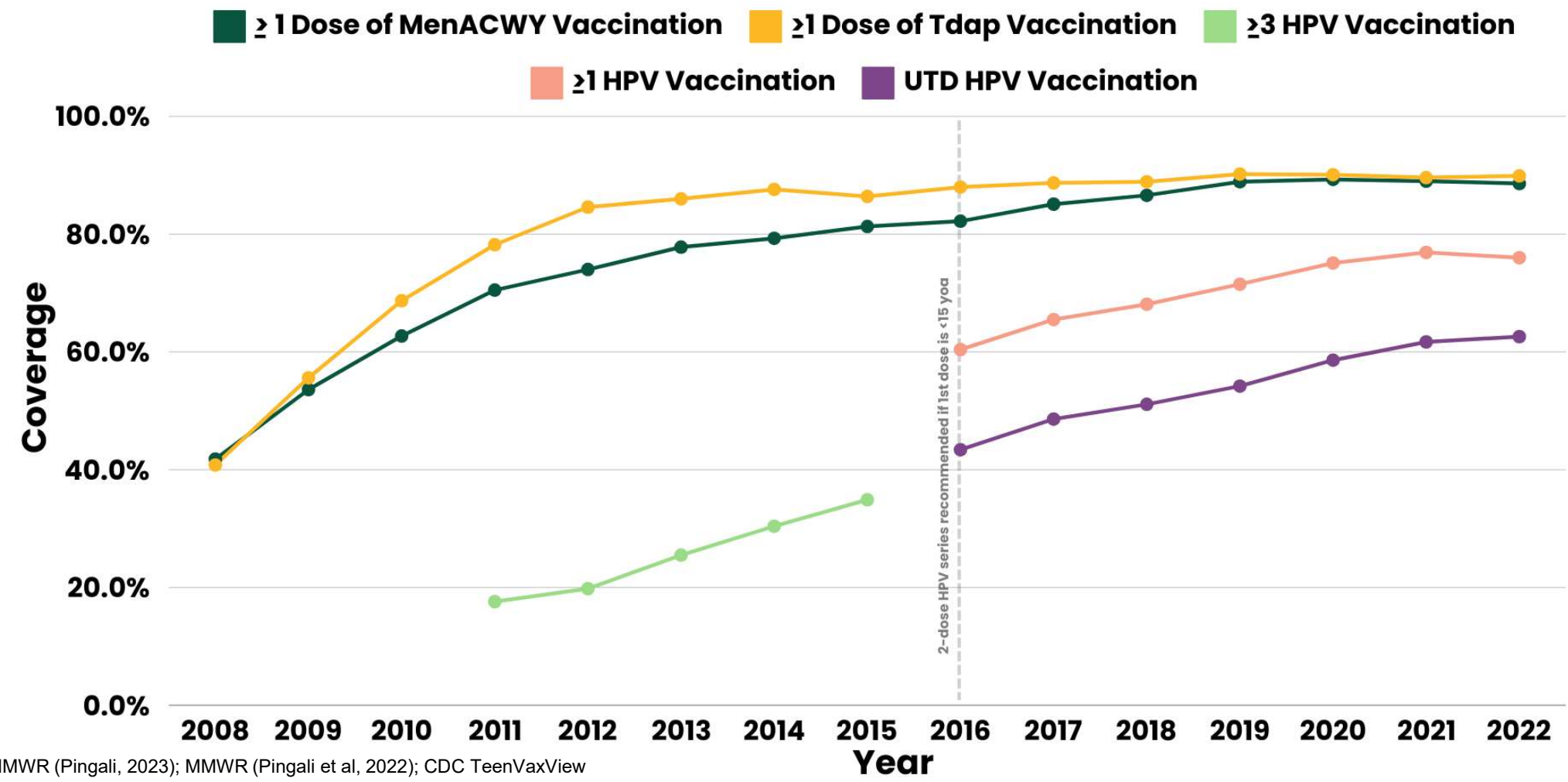
BUT, are providers equipped to address the HPV-related conversation with patients?

Vaccination Coverage by Year among Adolescents 13-17 Years Old, U.S. NIS-Teen

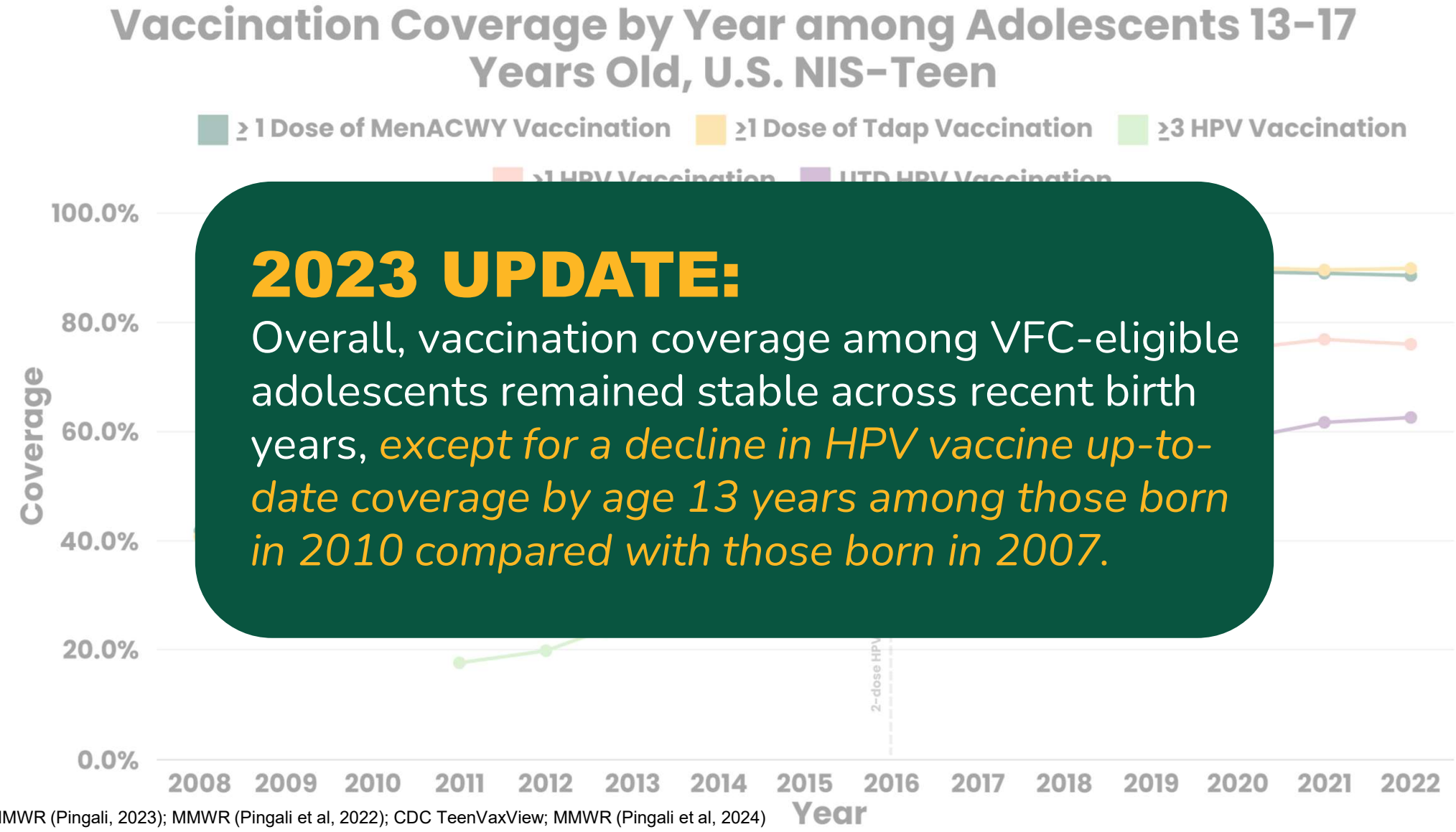


MMWR (Pingali, 2023); MMWR (Pingali et al, 2022); CDC TeenVaxView

Vaccination Coverage by Year among Adolescents 13-17 Years Old, U.S. NIS-Teen

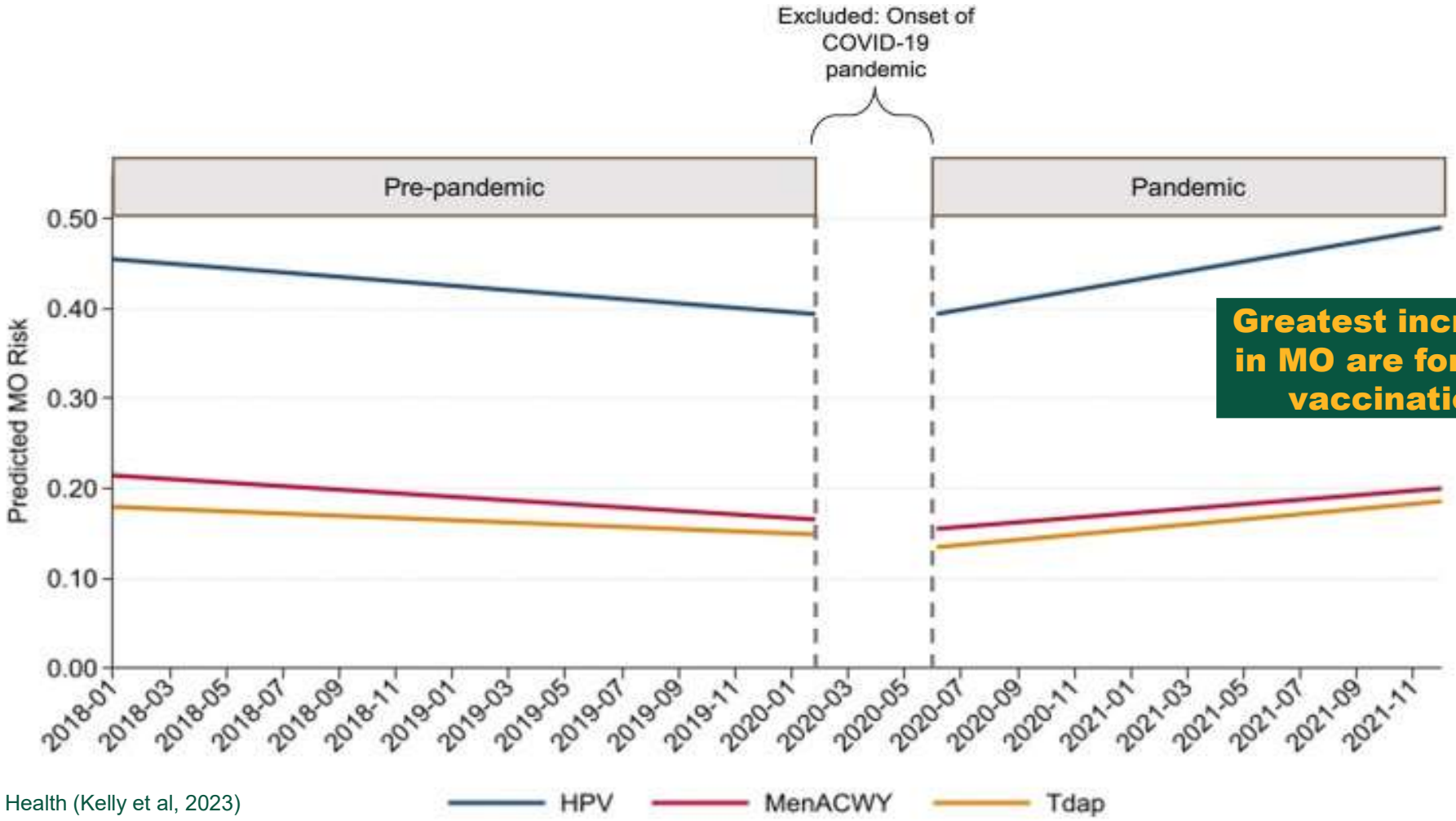


MMWR (Pingali, 2023); MMWR (Pingali et al, 2022); CDC TeenVaxView



MMWR (Pingali, 2023); MMWR (Pingali et al, 2022); CDC TeenVaxView; MMWR (Pingali et al, 2024)

Proportion of adolescent vaccine missed opportunities (MO) at well child visits



Greatest increase in MO are for HPV vaccination

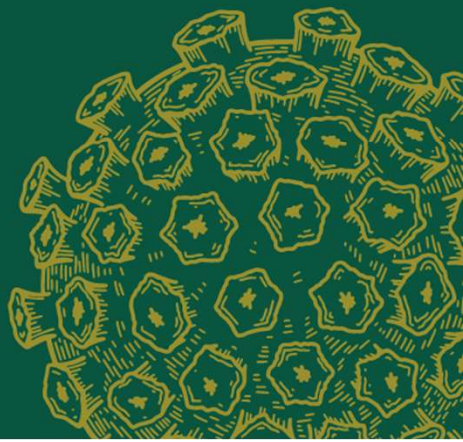
J Adolesc Health (Kelly et al, 2023)

By the end of today we hope you feel more confident in addressing HPV vaccination with patients and have fewer missed opportunities!

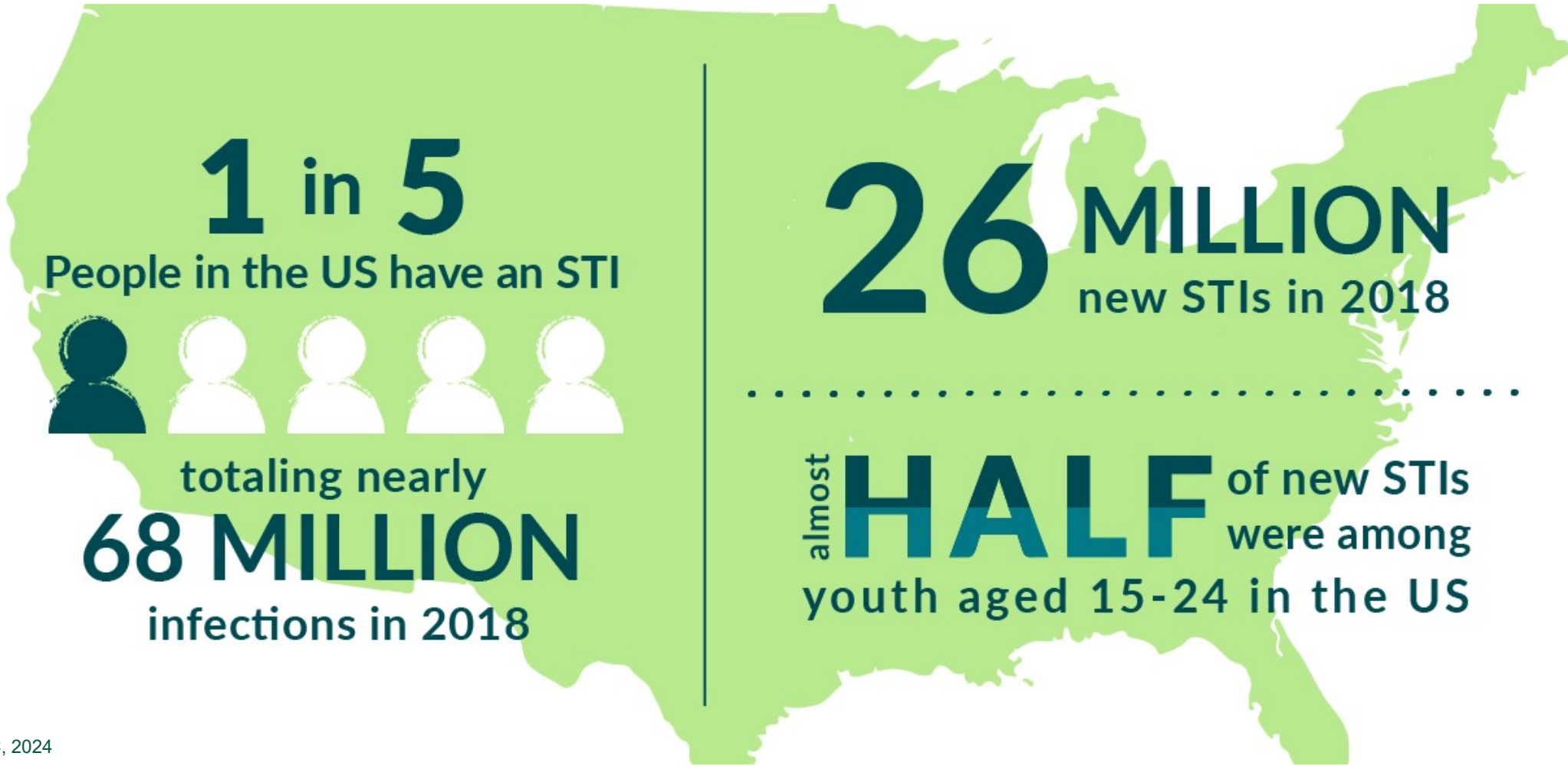
Outline:

- HPV epidemiology and pathology
- HPV Vaccination
  - Efficacy
  - Real world data
  - Coverage
- Communicating about HPV Vaccination

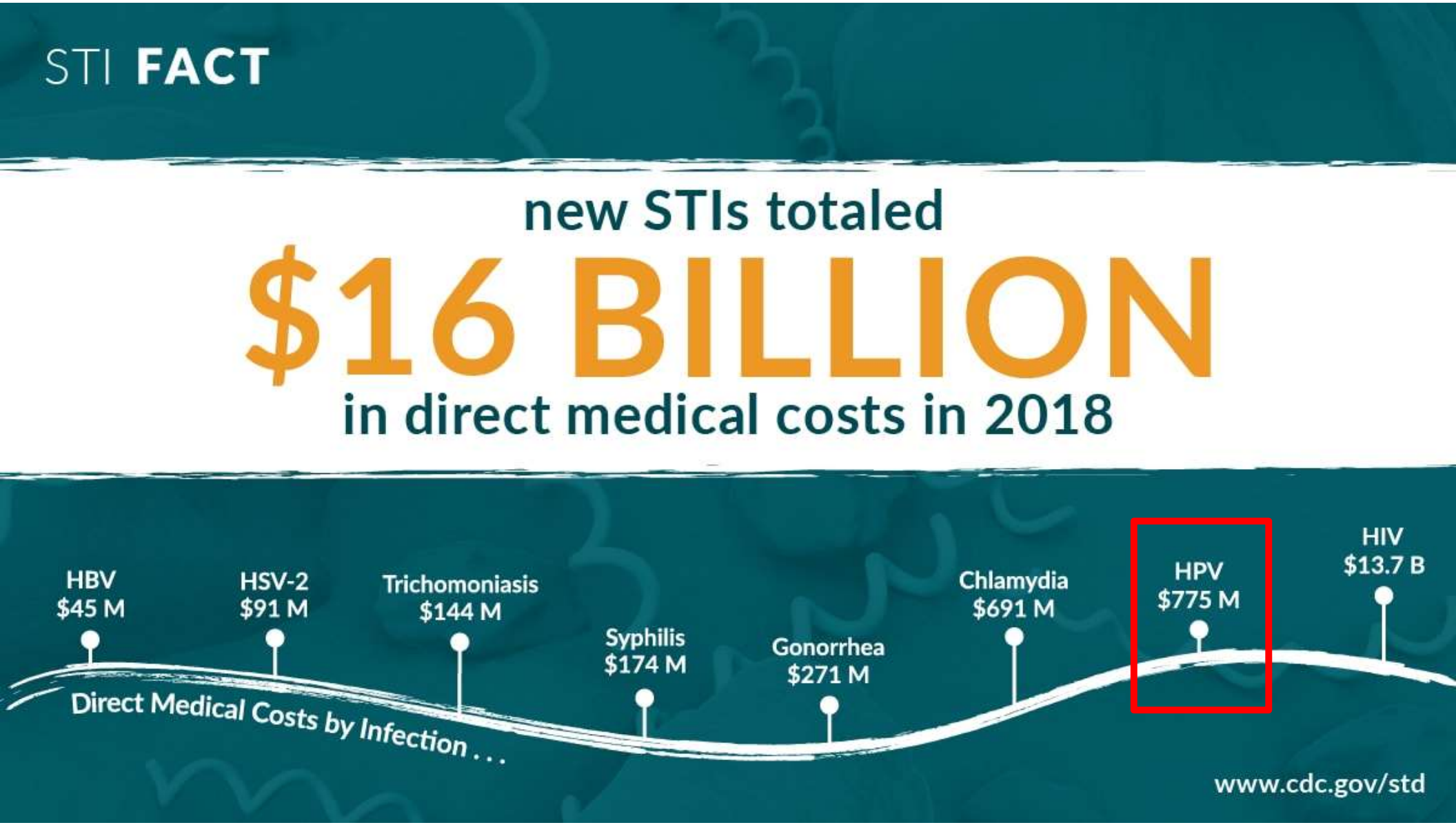
Epidemiology and Pathology



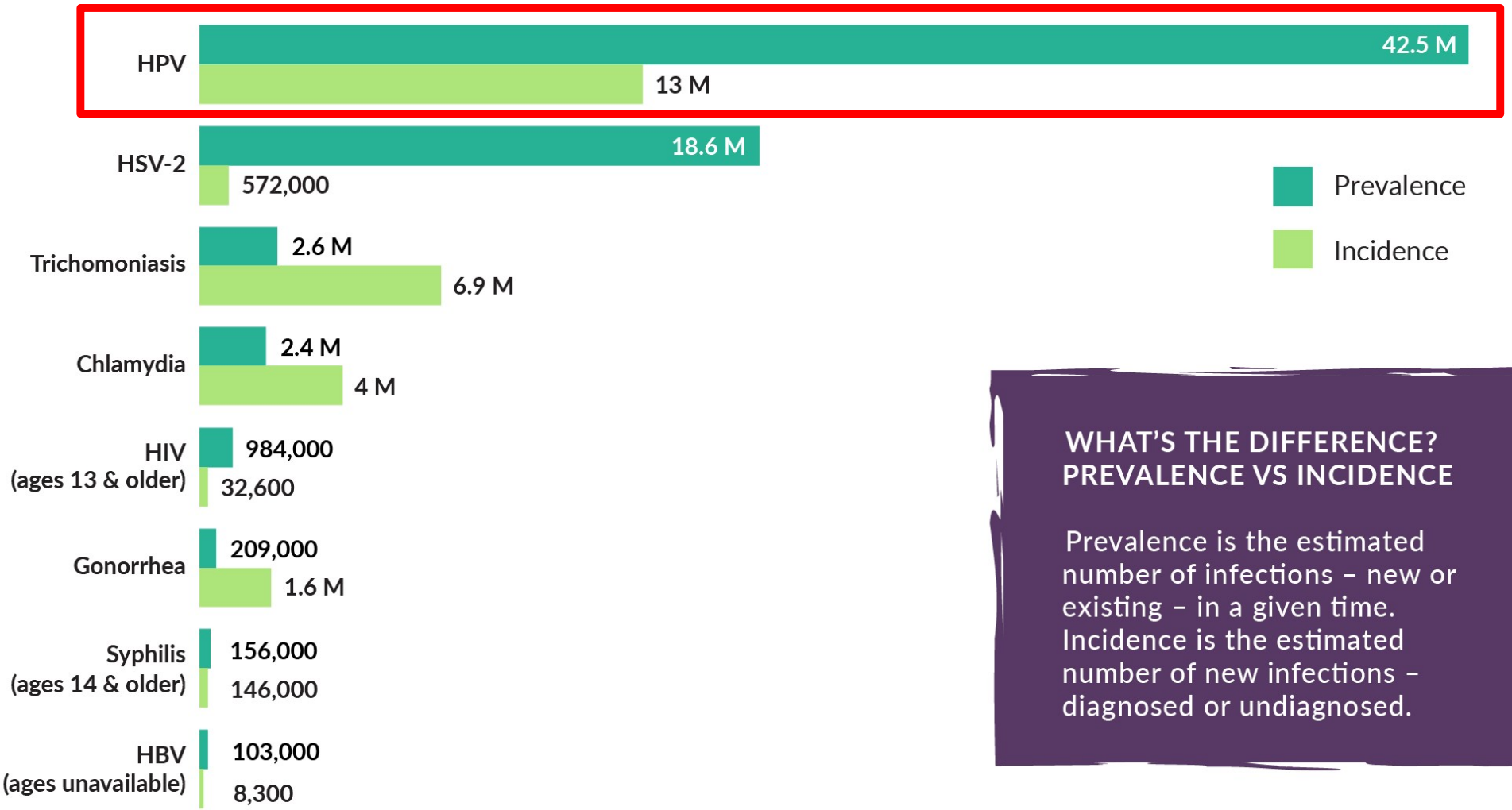
STIs Are Common



CDC, 2024


STI FACT
new STIs totaled
$16 BILLION
in direct medical costs in 2018
HBV
$45 M
HSV-2
$91 M
Trichomoniasis
$144 M
Syphilis
$174 M
Gonorrhea
$271 M
Chlamydia
$691 M
HPV
$775 M
HIV
$13.7 B
Direct Medical Costs by Infection . . .
www.cdc.gov/std

STI Prevalence and Incidence in the US



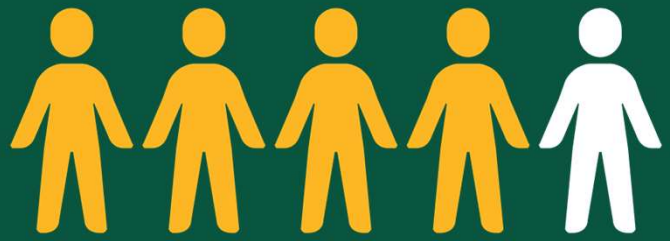
WHAT'S THE DIFFERENCE? PREVALENCE VS INCIDENCE

Prevalence is the estimated number of infections – new or existing – in a given time. Incidence is the estimated number of new infections – diagnosed or undiagnosed.

*Bars are for illustration only; not to scale, due to wide range in number of infections. Estimates for adults and adolescents ages 15+ unless otherwise stated. HIV and HBV data only represent sexually acquired infections.

CDC, 2024

HPV is the MOST common STI worldwide.



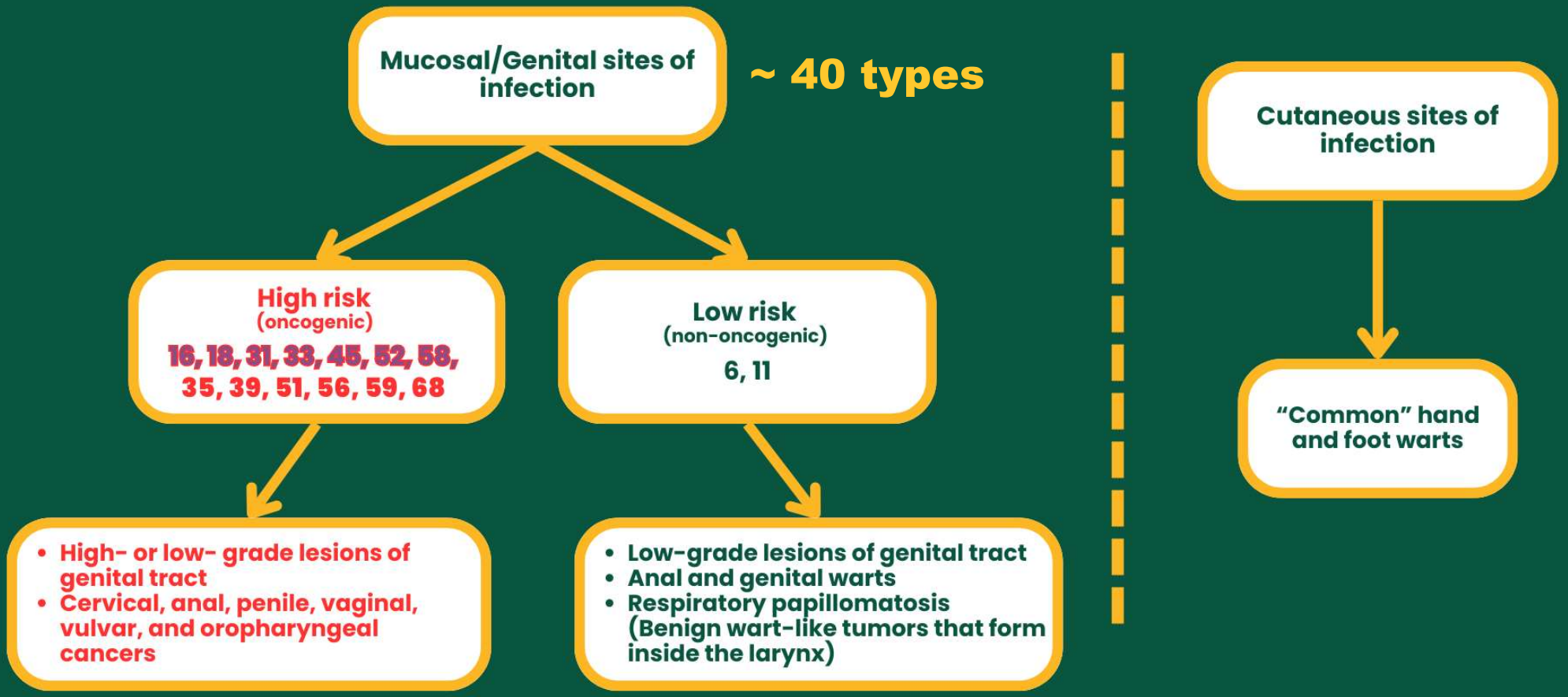
- **85%** of people will get an HPV infection in their lifetime.
- **Almost every unvaccinated person who is sexually active will get HPV at some time in their life.**

90%

- Most HPV infections (9 out of 10) go away on their own within 2 years.
- But sometimes, HPV infections will last longer and can **cause certain types of cancer.**

Sex Transm Dis (Chesson, 2024); WHO, 2024

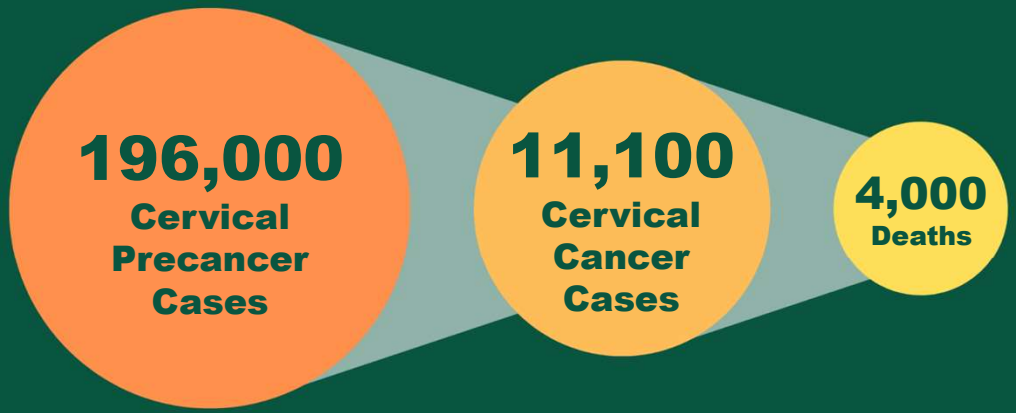
HPV Genotypes and Their Disease Associations



CDC, 2024

>>> 9 in 10

cases of cervical cancer in the U.S. are caused by HPV.



(Every year in the U.S.)

Cervical cancer is the 4th most common cancer in women globally.

Cervical cancer was once the leading cause of cancer deaths among women in the U.S. HPV vaccines and cervical cancer screening have made it one of the most preventable cancers.

CDC, 2024

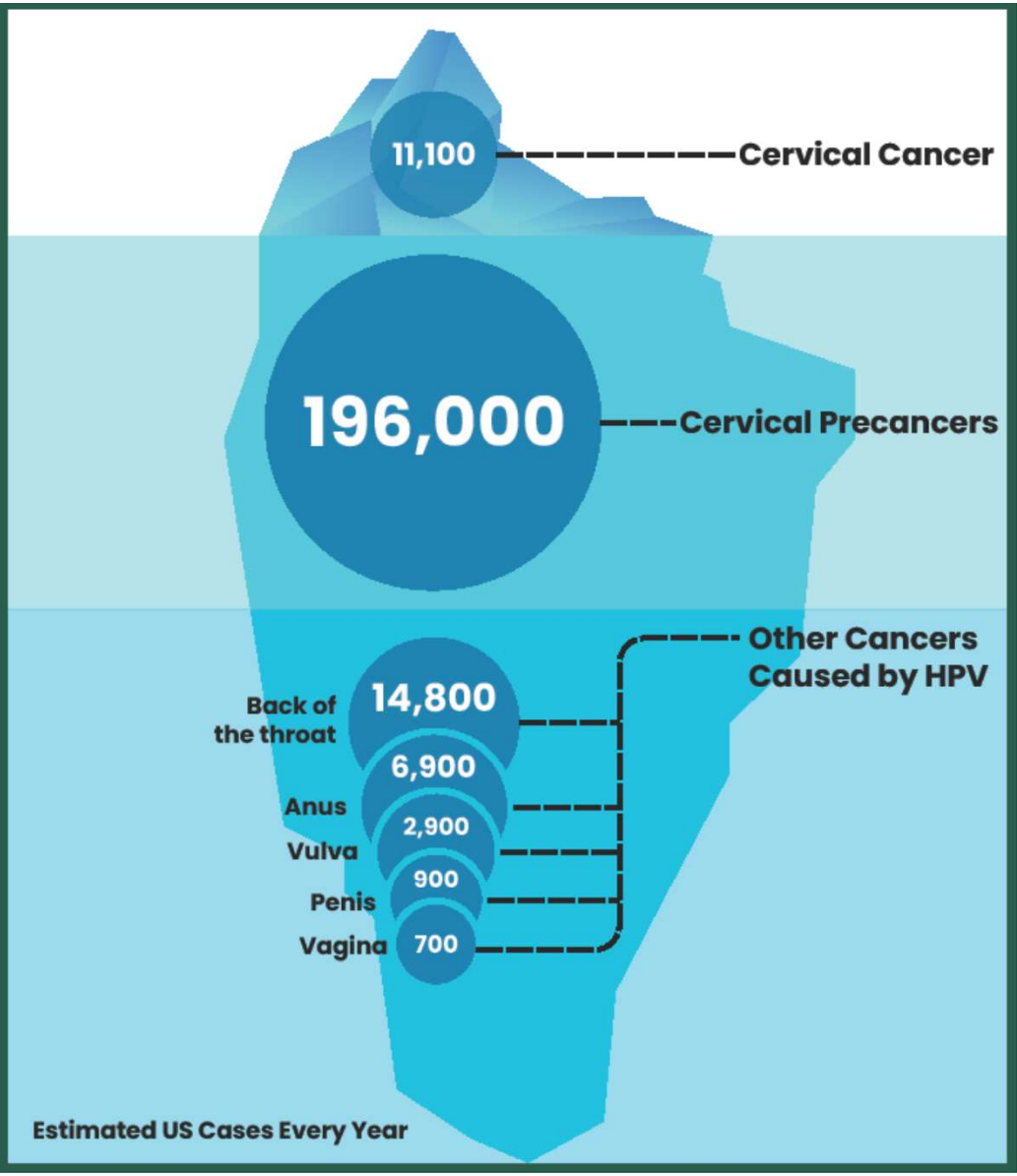
Cervical cancer is just the tip of the iceberg.

Although cervical cancer is the most well-known of the cancers caused by HPV, there are other types of cancer caused by the virus.

90%

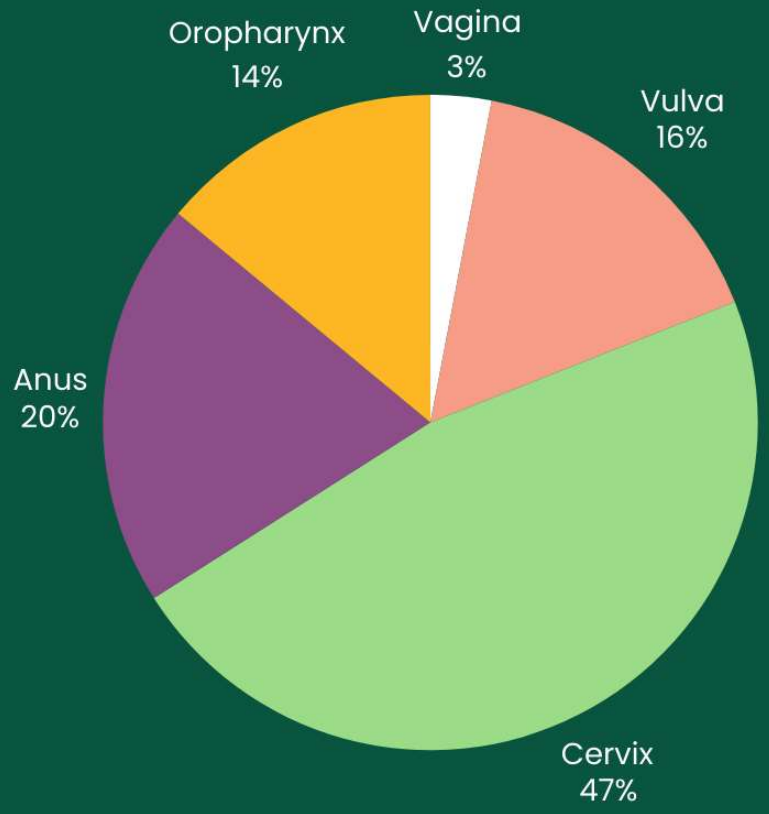
of HPV-related cancers are preventable with **HPV vaccination**.

CDC, 2024

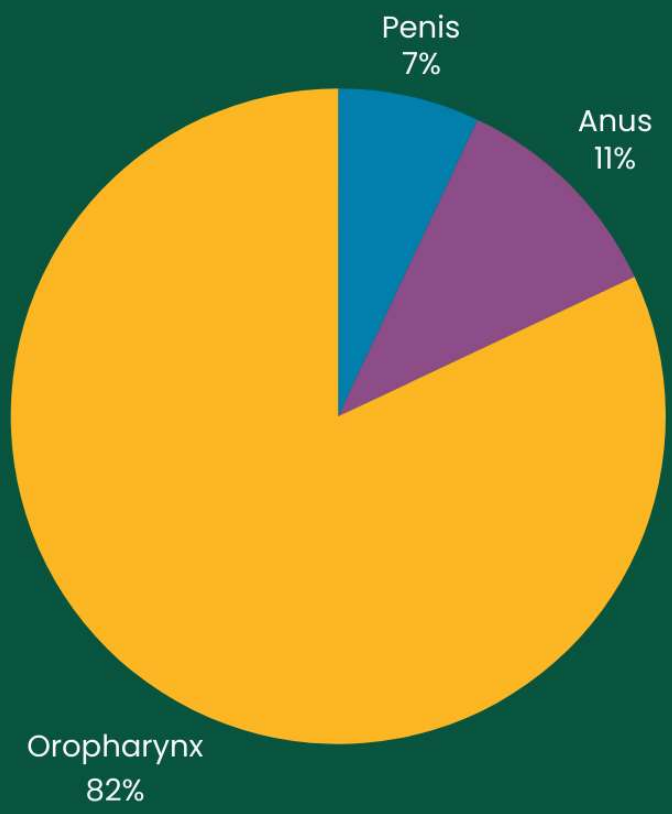


% of New HPV-Associated Cancer Cases Each Year in the U.S. (2015-2019)

Women (n = 26,177)

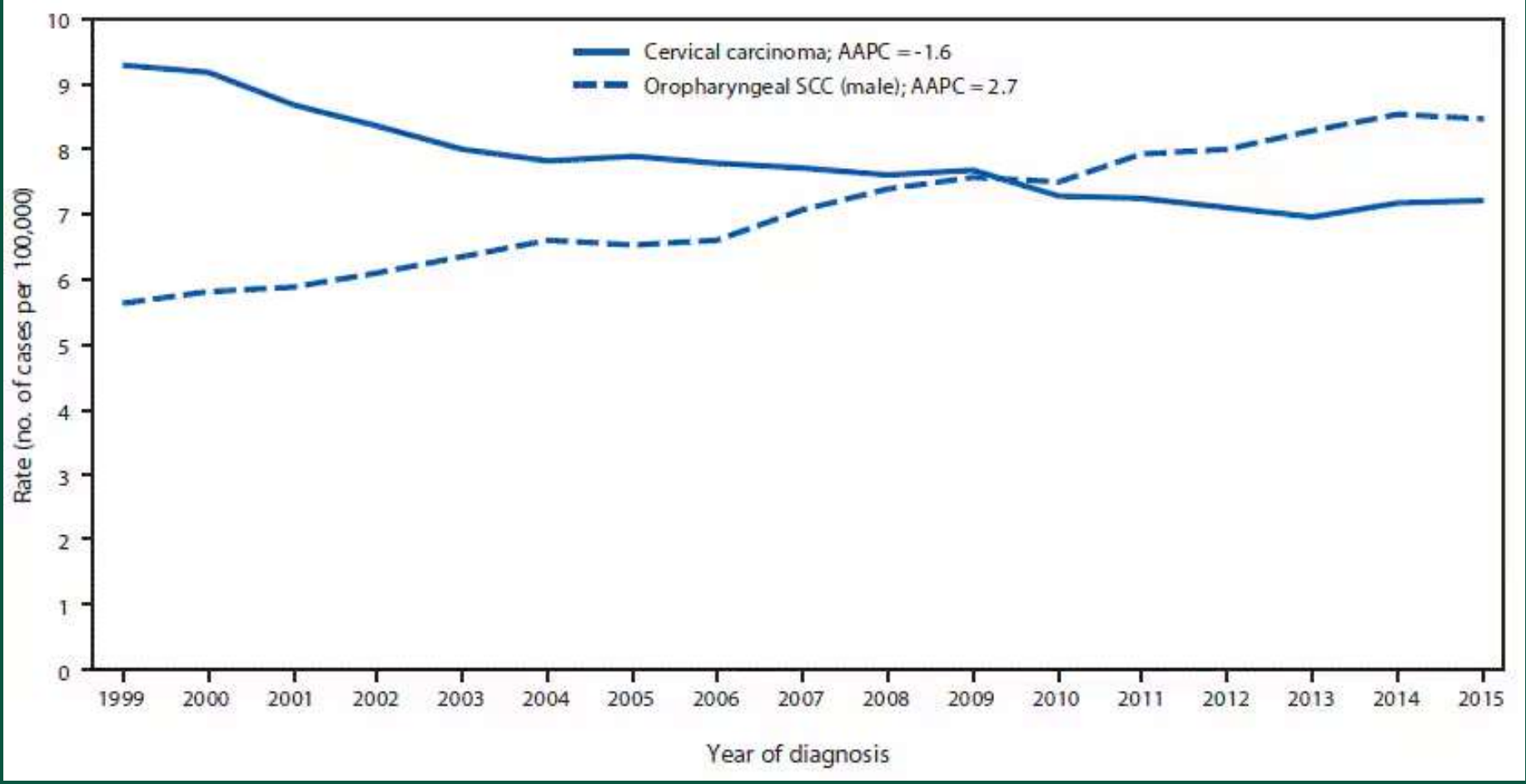


Men (n = 21,022)



CDC, 2024

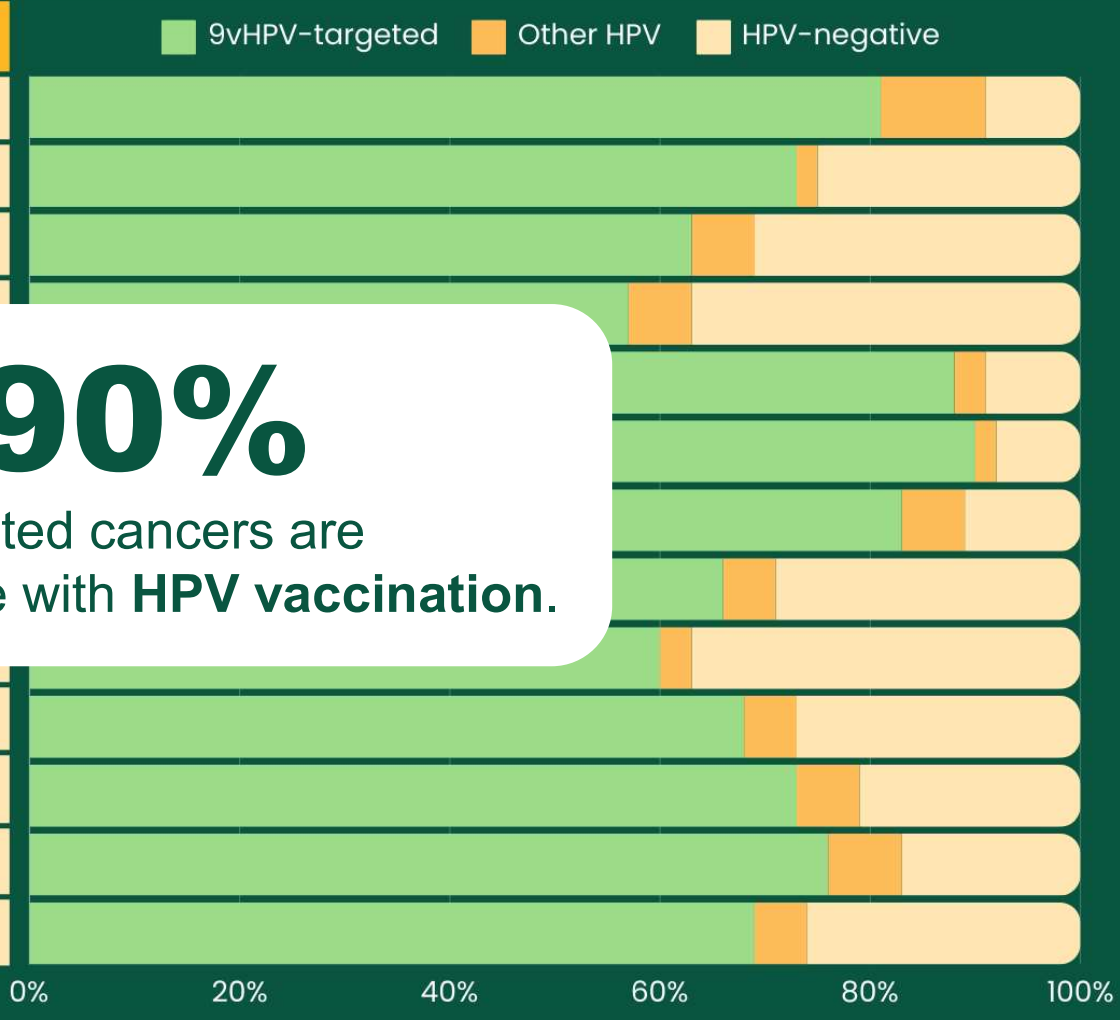
U.S. incidence of cervical cancer (females) and oropharyngeal cancer (males), 1999-2015



MMWR (Van Dyne et al, 2018)

Average annual number and rate of HPV–associated cancers and estimated % cancers attributable to HPV, by HPV type, cancer type, and sex — U.S. 2012–2016

Reported HPV-associated cancer		
Cancer Type	**Total #**	**Rate**
Cervix	12,015	7.2
Vagina	862	0.4
Vulva	4,009	2.1
Penis	1,30	
Anus	6,8	
Female	4,5	
Male	2,2	
Oropharynx	19,(	
Female	3,4(	
Male	15,540	8.5
Total	**43,999**	**12.2**
Female	24,886	13.7
Male	19,113	10.6



90%

of HPV-related cancers are preventable with **HPV vaccination**.

MMWR (Senkomago et al, 2019)

Genital HPV Prevalence in Men

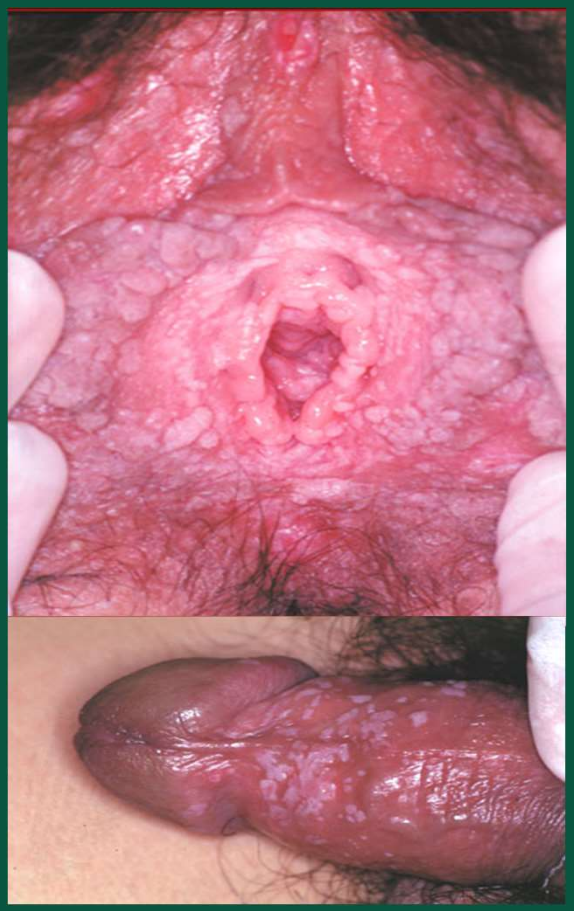
~1 in 3 men over 15 years old are infected with 1+ genital HPV type

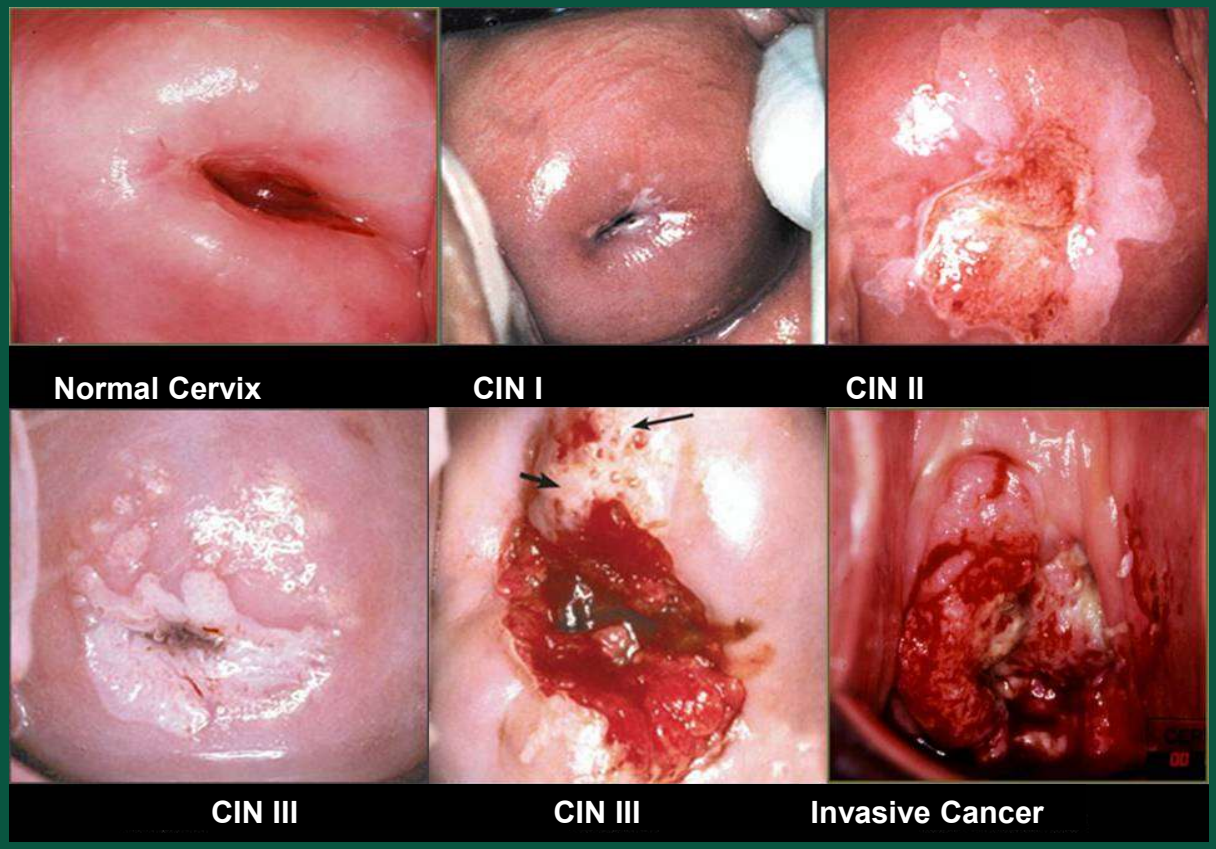
1 in 5 are infected with high-risk HPV types

HPV prevalence highest in young adults, peaking at 25-29 years old

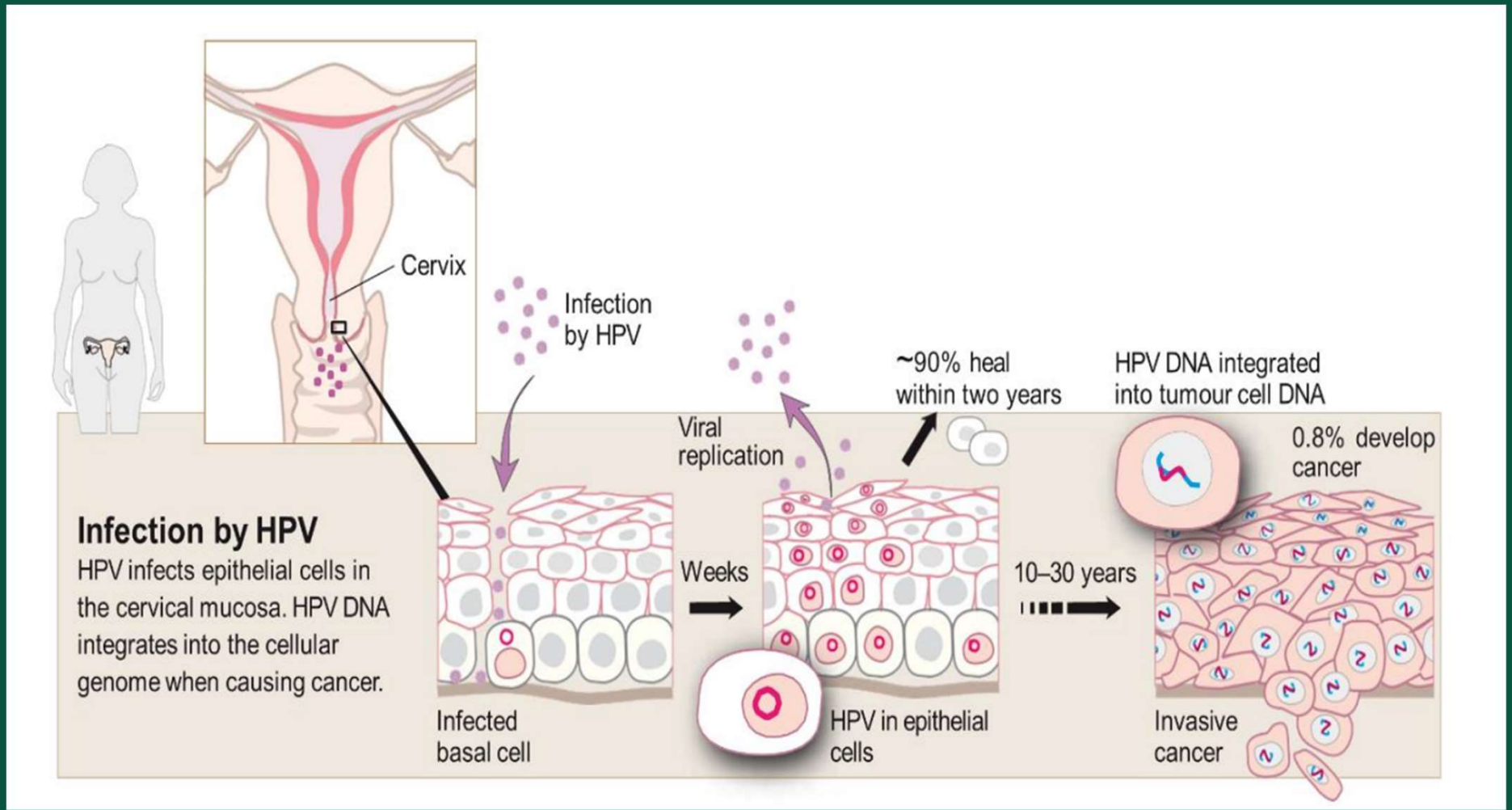
Lancet (Bruni et al, 2023)

HPV - From Warts to Cancer



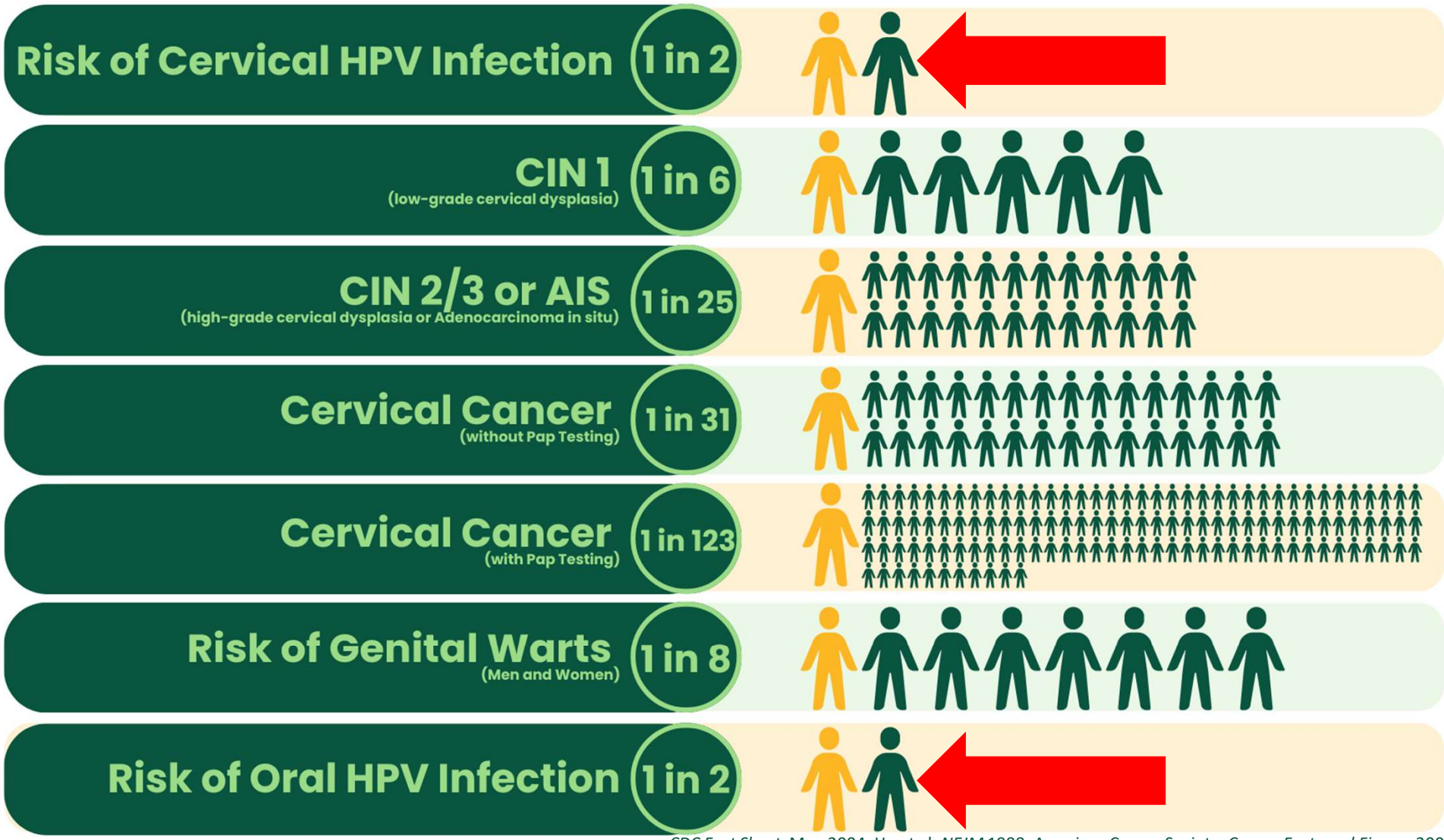


Pathogenesis of HPV Infection



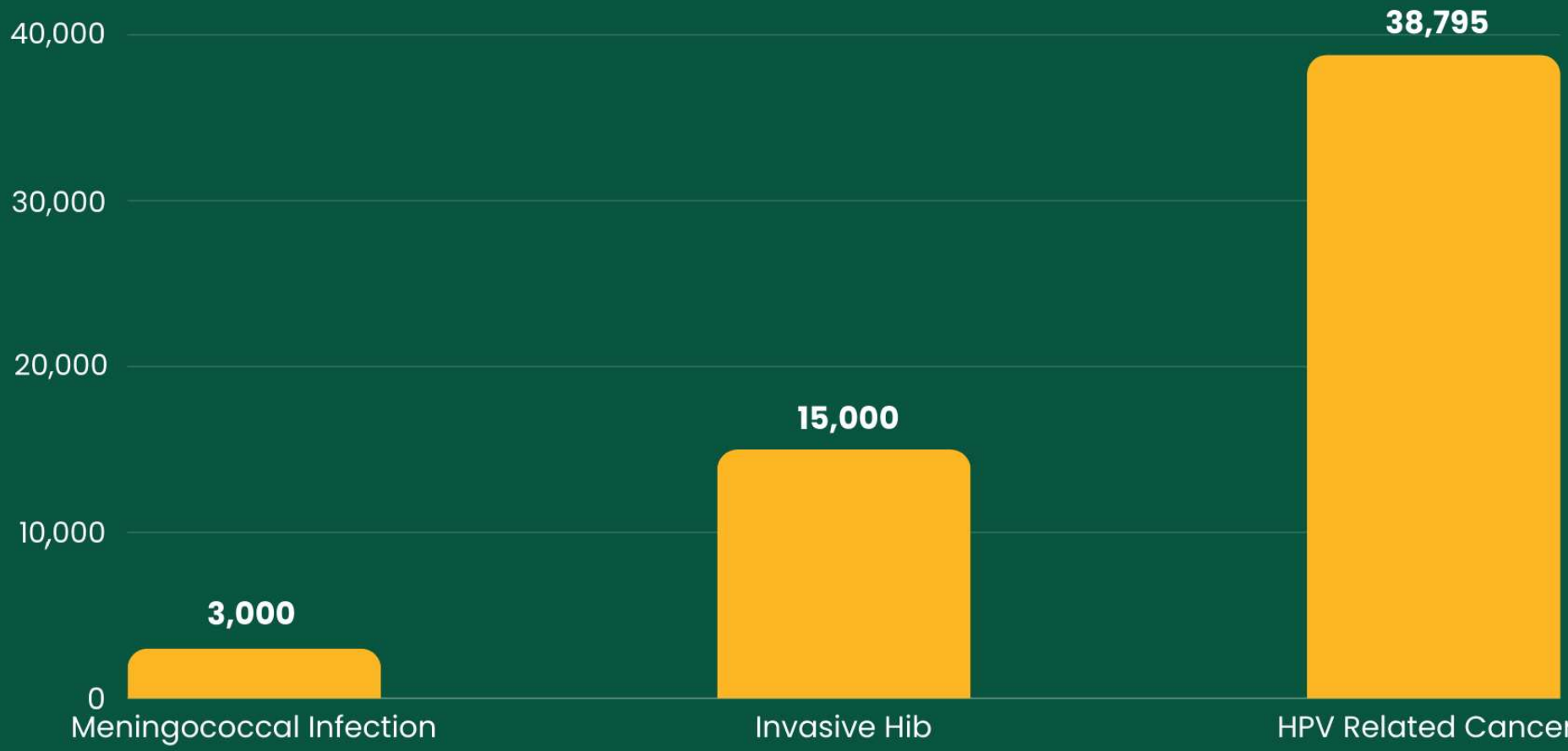
Acta Facultatis Medicae Naissensis (Stark & Zivkovic, 2018)

Lifetime Risk of HPV-Related Pathology



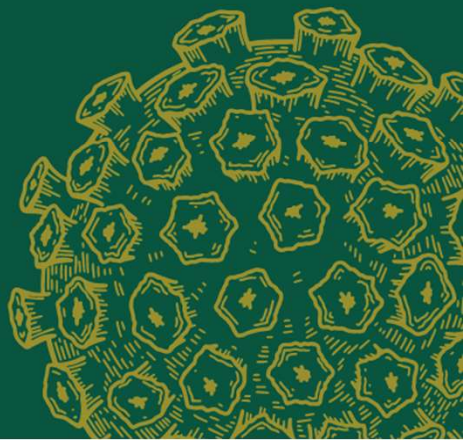
CDC Fact Sheet, May-2004; Ho et al. *NEJM* 1998; American Cancer Society: *Cancer Facts and Figures* 2005.
CIN = Cervical Intraepithelial Neoplasia; AIS = Adenocarcinoma in situ.

Put HPV in Perspective: Incidence of Disease in Pre-Vaccine Era



CDC, 2024

The Vaccine



Evolution of HPV vaccination recommendations – U.S.

2006

Recommendations for girls
Routine: 11 or 12 years, can be started at age 9

Catch-up: through 26 years
3-dose schedule

2011

Recommendations for boys
Routine: 11 or 12 years, can be started at age 9

Catch-up: through 21 years
3-dose schedule

2016

2-dose schedule
if first dose age <15 years

2019

Catch-up: through 26
Shared clinical decision-making: some adults 27 through 45 years

Vaccines Available

- Quadrivalent Vaccine
- Bivalent Vaccine
- 9-valent Vaccine

ACIP Presentation (Markowitz, Oct 23, 2024)

What Does it Cover?

Gardasil 9 is the ONLY vaccine currently available in the U.S.

70% of cervical cancers
90% of genital warts

2006

Quadrivalent HPV vaccine licensed (Gardasil, 4vHPV)

Strains covered: 6, 11, 16, 18

70% of cervical cancers

2009

Bivalent HPV vaccine licensed (Cervarix, 2vHPV)

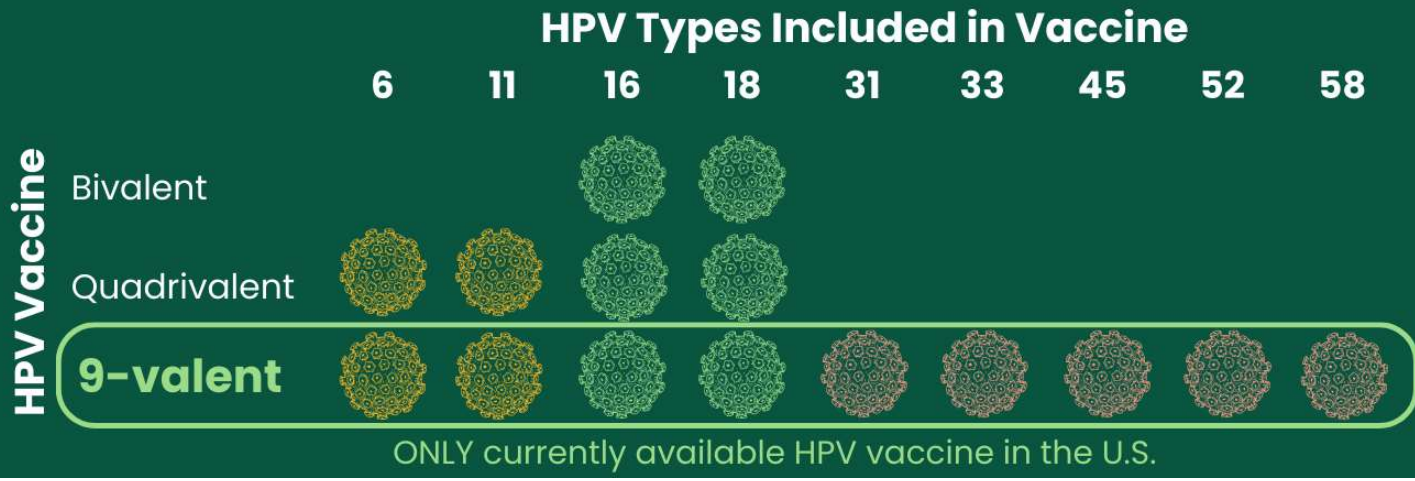
Strains covered: 16, 18

90% of cervical cancers
90% of genital warts

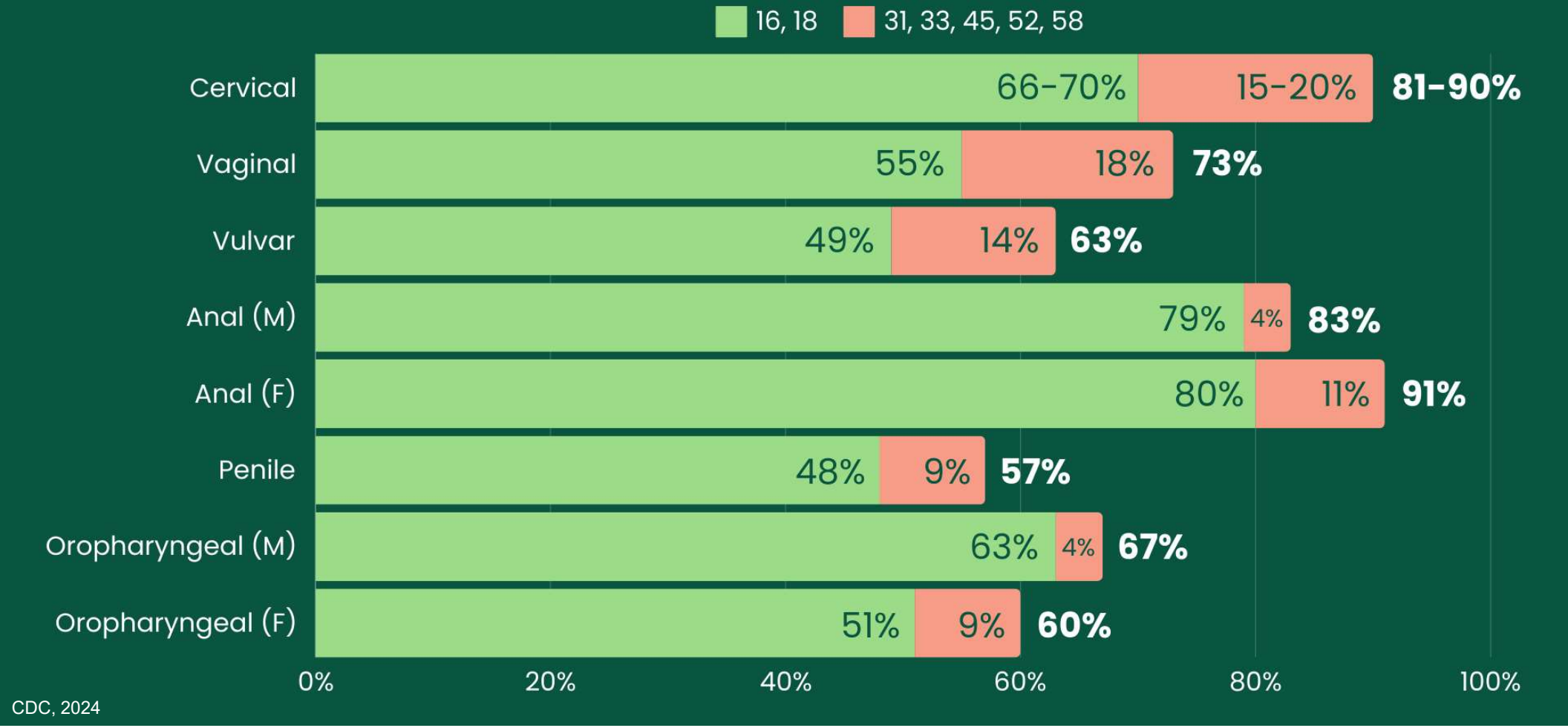
2014

9-valent HPV vaccine licensed (Gardasil 9, 9vHPV)

Strains covered: 6, 11, 16, 18, 31, 33, 45, 52, 58



HPV-Associated Cancers by Serotypes in 9-Valent Vaccine



CDC, 2024

HPV Vaccine: Who Gets it and When

9 – 26 years: routinely recommended at 11-12 years (ACIP – can be given down to age 9 years) or starting at 9 years (AAP). Catch-up vaccination recommended for everyone through 26 years.

Adults >26 years: shared clinical decision-making for some people 27-45 years. HPV vaccines are not licensed for >45 years.

Administration: 2 doses if started <15 years; 3 doses if after. No prevaccination testing.

Cervical cancer screening: all routine screening guidelines should be followed

Special populations and medical conditions:

- Pregnancy: delay until after pregnancy; pregnancy testing not needed before vaccination.
- Breastfeeding: safe to receive

MMWR (Meites et al, 2019)

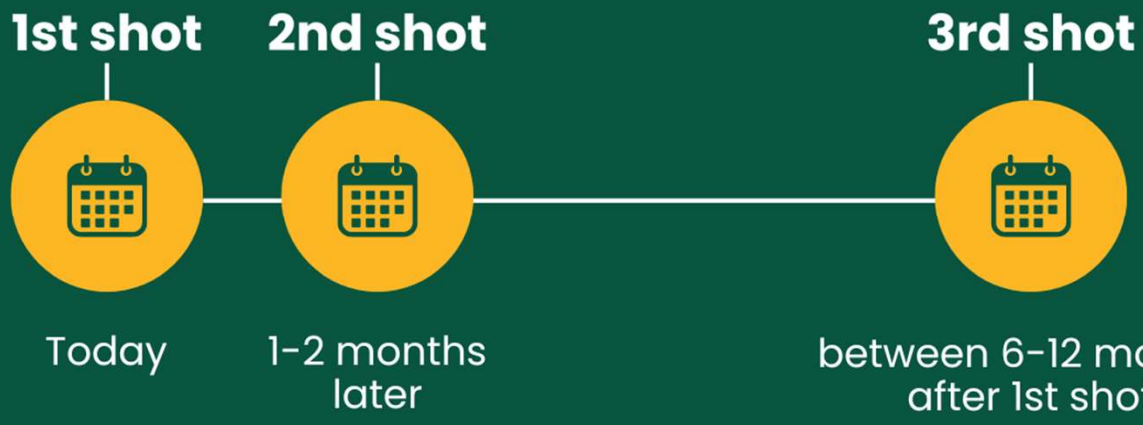
HPV Vaccine: Who Gets it and When

2-dose series

2 doses if started <15 years to complete the vaccine series.

3-dose series

3 doses required to complete the series if series is started *after* a patient's *15th birthday*



MMWR (Meites et al, 2016)

Centers for Disease Control and Prevention
CDC 24/7: Saving Lives, Protecting People™

Morbidity and Mortality Weekly Report (*MMWR*)

BOX. Considerations for shared clinical decision-making regarding human papillomavirus (HPV) vaccination of adults aged 27 through 45 years

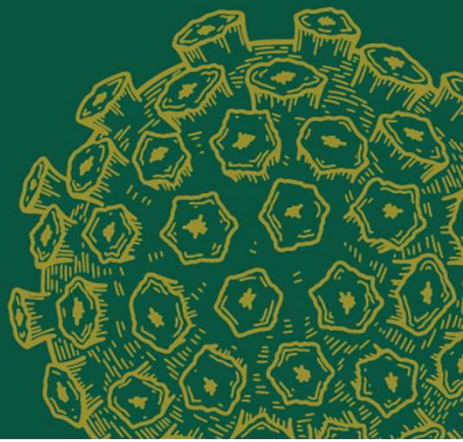
Return

Ideally, HPV vaccination should be given in early adolescence because vaccination is most effective before exposure to HPV through sexual activity. For adults aged 27 through 45 years who are not adequately vaccinated,* clinicians can consider discussing HPV vaccination with persons who are most likely to benefit. HPV vaccination does not need to be discussed with most adults aged >26 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.
- 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.

* Dosing schedules, intervals, and definitions of persons considered adequately vaccinated have not changed.

Vaccine Efficacy



Efficacy of the quadrivalent and 9-valent HPV vaccines against clinical endpoints among patients aged 16-26

Clinical endpoint	Vaccine		Placebo		Vaccine efficacy % (95% CI)
	# of people	# of cases	# of people	# of cases	
Cervical Cancer: HPV 16/18-related CIN 2/3 OR AIS	8,493	2	8,464	112	~98% (93.5, 99.8)
Vulvar Cancer: HPV 6/11/16/18-related VIN 2/3	7,772	0	7744	10	100% (55.5, 100)
Vaginal Cancer: HPV 6/11/16/18-related VaIN 2/3	7,772	0	7,899	9	100% (49.5, 100)
Anal Cancer in Males: HPV 6/11/16/18-related AIN 2/3	194	3	208	13	~75% (8.8-95.4)

Clinical endpoint	Gardasil 9		Gardasil		Vaccine efficacy % (95% CI)
	# of people	# of cases	# of people	# of cases	
HPV 31/33/45/52/59-related CIN 2/3, AIS, VIN 2/3, VaIN 2/3	6,016	1	6,017	30	~97% (80.9, 99.8)

Merck, 2024

HPV Vaccine Efficacy – cervical, vaginal, vulvar disease

Vaccine	Efficacy in HPV-naive populations	Overall Population
Bivalent	99%	61%
Quadrivalent	97-100%	44-62%
9-Valent	97%	

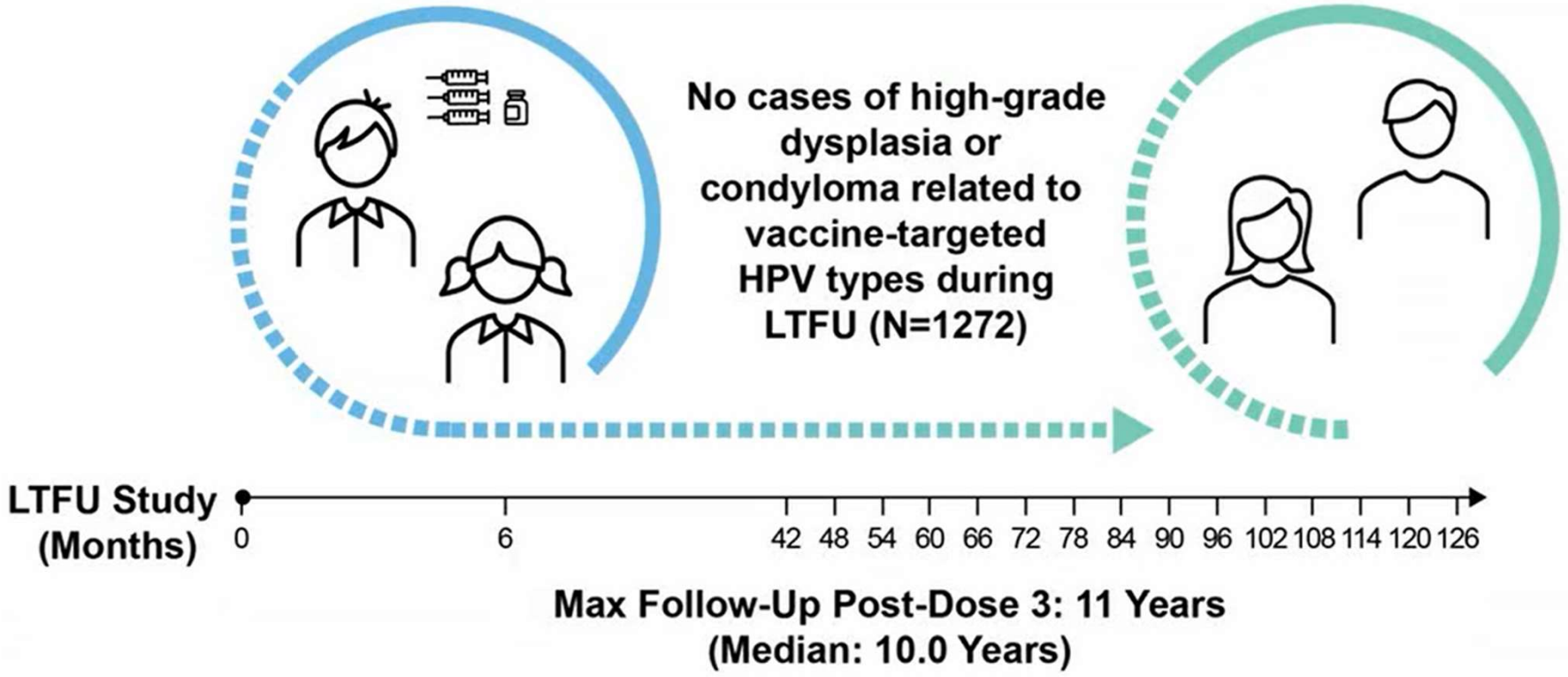
N Engl J Med (Garland et al, 2007); N Engl J Med (FUTURE II Study Group, 2007); N Engl J Med (Joura et al, 2015); Lehtinen M, et al, Lancet Oncol (Lehtinen et al, 2012)

TAKE HOME MESSAGE

Just like putting on a bike helmet BEFORE going on a bike ride to protect against head injury...

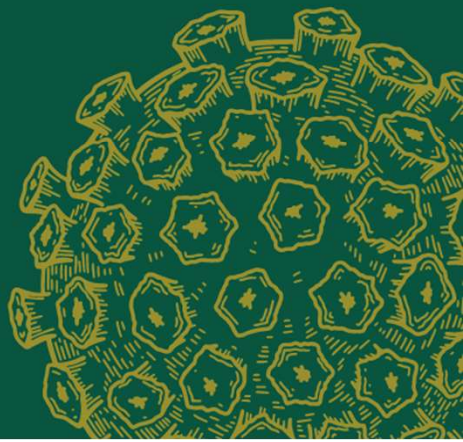
...HPV vaccination is INCREDIBLY effective if given BEFORE exposure to the virus.

9vHPV vaccine immunogenicity and effectiveness ~10 years after 3 doses of 9vHPV vaccination – boys and girls 9-15 years old

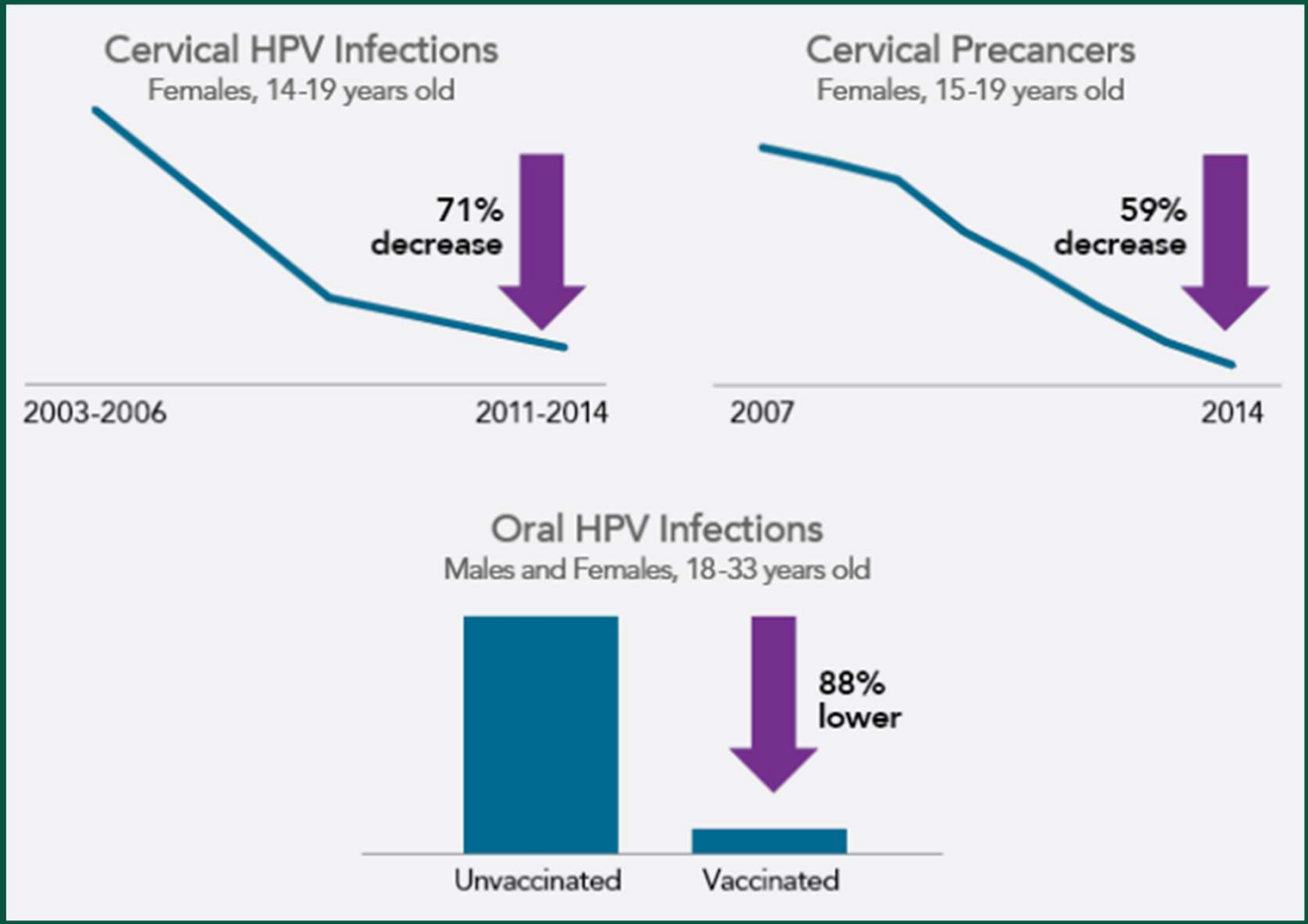


Pediatrics (Restrepo et al, 2023)

What does the real-world data tell us?



Prevalence of Cervical HPV Infection, Cervical Precancers, and Oral HPV Infection in the HPV Vaccine Era



President's Cancer Panel, 2018

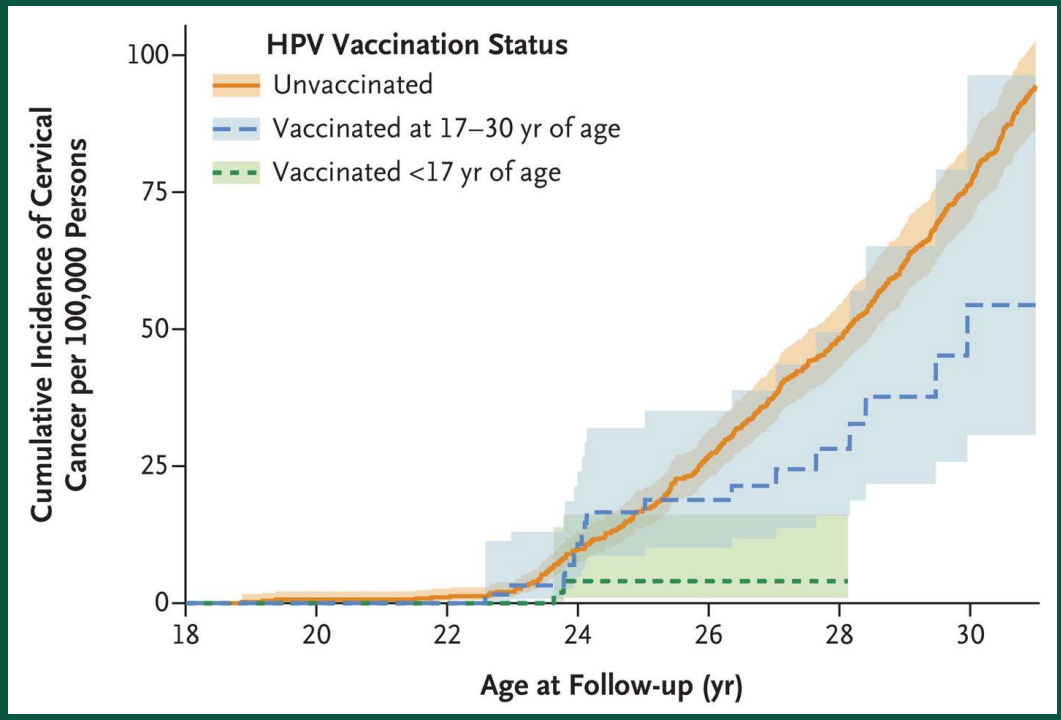
HPV vaccination associated with a substantially reduced risk of invasive cervical cancer in Sweden

88%

Reduced risk of invasive cervical if vaccinated <17 year olds

53%

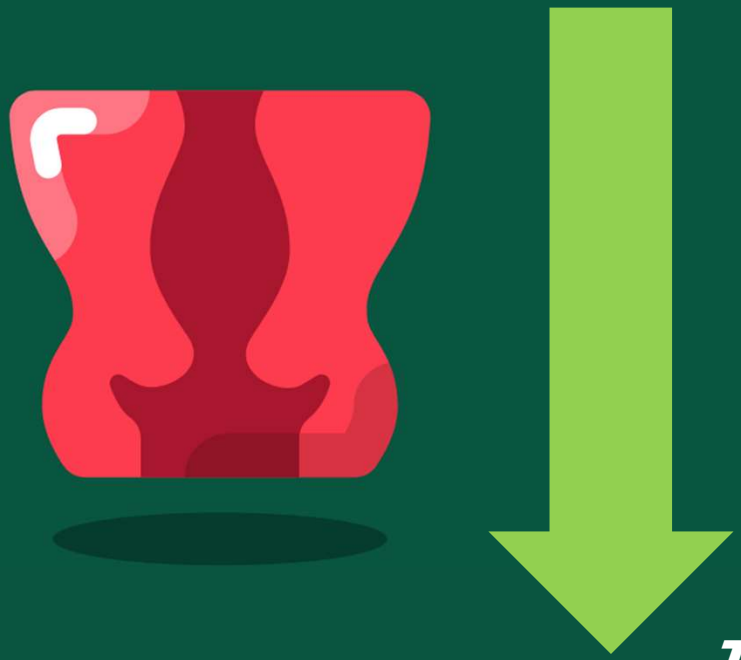
Reduced risk of invasive cervical if vaccinated 17-30 year olds



Study looked at ~1.7M Swedish girls and women 10-30 year olds from 2006-2017

NEJM (Lei et al., 2020)

HPV vaccine reduced the incidence of cervical cancer in England by...



39% in those who received an HPV vaccine between 16-18 years old

62% in those who received an HPV vaccine between 14-16 years old

90% in those who received an HPV vaccine between 12-13 years old

The vaccine is most effective when given between the ages of 11 and 13 when someone is less likely to have been exposed to HPV.

Lancet (Falcaro et al., 2021)

An observational study published in early 2024 looking at data out of Scotland found NO invasive cervical cancer cases documented in women vaccinated against HPV at age 12-13 years old.

JNCI (Palmer et al., 2024)

Early real-world evidence suggests:

54% Lower odds of developing HPV-related cancers among boys
(especially head and neck cancers)

30% Lower odds of developing HPV-related cancers among girls
(cervical cancers and any HPV-related cancer)

These results add to the evidence of HPV vaccine's real-world effectiveness in preventing several types of cancer and precancerous changes caused by HPV.

Journal of Clinical Oncology (DeKloe et al, 2024)

Recent HPV Research – Fall 2024:

Cross-sectional study of 54.7 million participants from Texas

Findings:

HPV cancer rates are highest in counties with low vaccination rates.

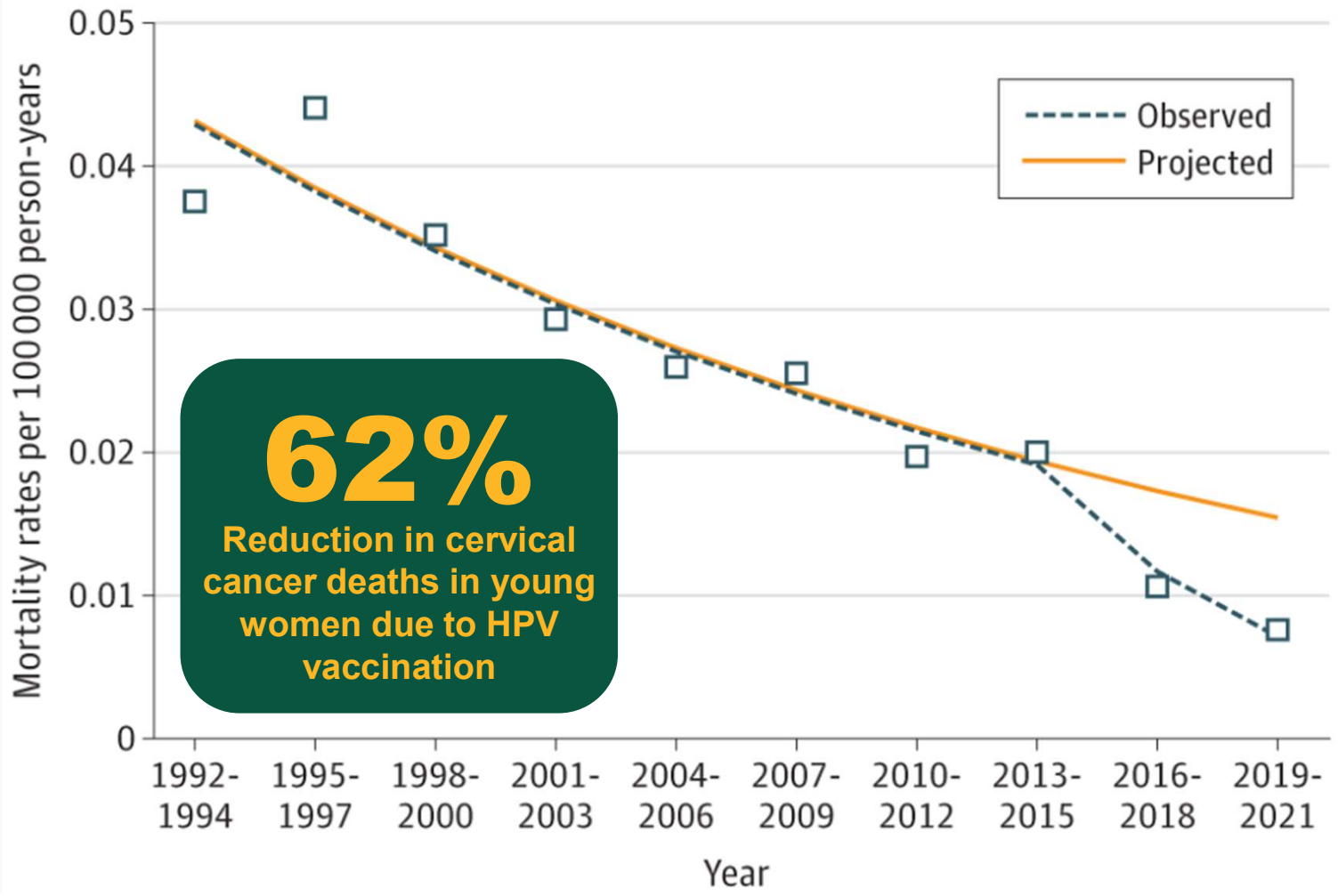
Study based on samples from 205 adult male volunteers who attended a single clinic for an initial fertility assessment or problems of the urinary tract between 2018 and 2021

Findings:

19% tested positive for HPV, and of those who were infected, none had been vaccinated against the virus.

JAMA (Adekanmbi et al., 2024); Frontiers (Oliveria et al, 2024)

HPV vaccinations are associated with reduced cervical cancer mortality in young women



JAMA (Dorali et al, 2024)

NEW: ACIP HPV Vaccines Work Group

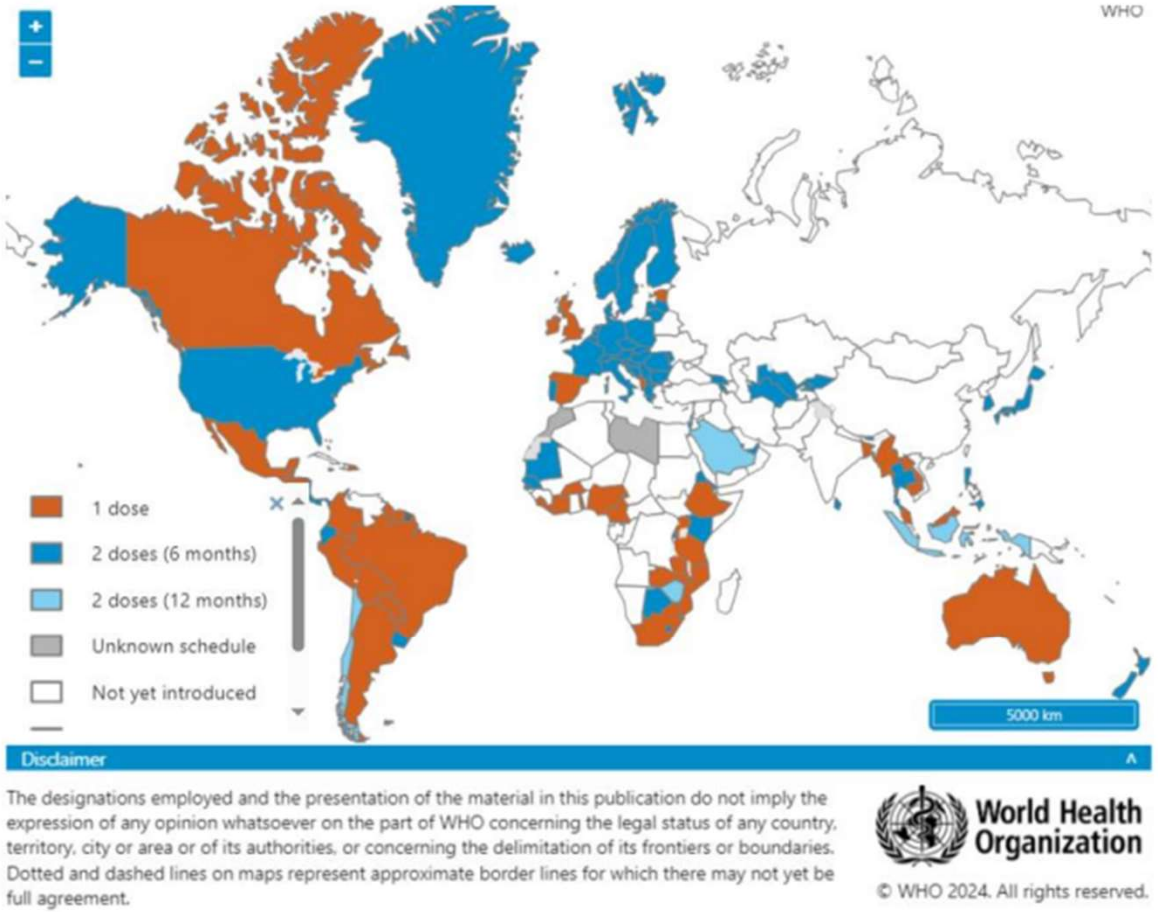
- Work group purpose: The Human Papillomavirus (HPV) Vaccines Work Group reviews and evaluates data on HPV disease, epidemiology, and vaccine and develops possible modifications to policy for ACIP's consideration.
- Topics under discussion by the work group:
  - Reducing the number of vaccine doses in the recommended HPV vaccination series
  - Wording of the age for routine vaccination
  - Guidance regarding persons in the "shared clinical decision-making" age range

CDC, 2024; ACIP Meeting (Brooks, Oct 23, 2024)

Recommended HPV vaccine schedules in 9–14-year-olds, by country

Doses-interval	No. of countries
1 dose	58
2 doses (12 months)	5
2 doses (6 months	76
Not yet introduced	50
Unknown schedule	5

WHO 2022 recommendations:
2 doses for persons aged 9 years and older, with option for single-dose HPV vaccination through age 20 years, except those immunocompromised



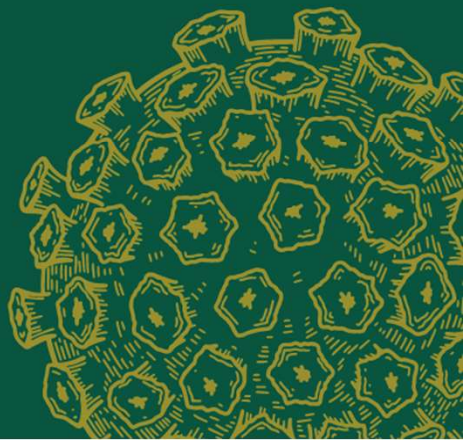
Date: October 2024

Summary of data on vaccination with a reduced number of doses:

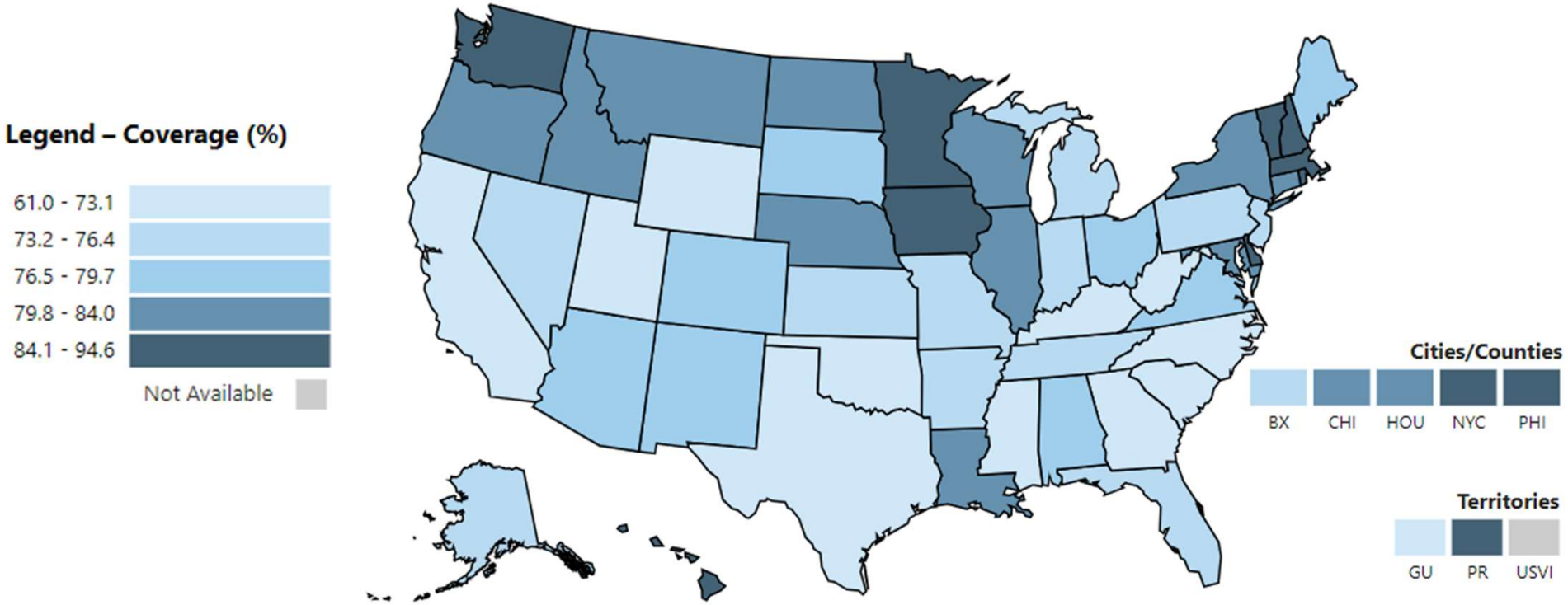
- HPV vaccines were first studied and licensed in a 3-dose schedule in persons aged 9–26 years and later in a 2-dose schedule in persons aged 9–14 years.
- Data are available on single-dose HPV vaccination, including from a randomized controlled trial with 3 years of follow-up, showing high efficacy against incident persistent infection.
- Long term follow-up suggests protection for >10 years with a single dose.
- WHO 2022 updated recommendations.
- Countries are considering new or updated HPV vaccination policy and an increasing number have recommended single-dose HPV vaccination.
- Further data on 1 and 2 doses will be available over the next year.

ACIP Presentation (Markowitz, Oct 23, 2024)

HPV Vaccination Rates

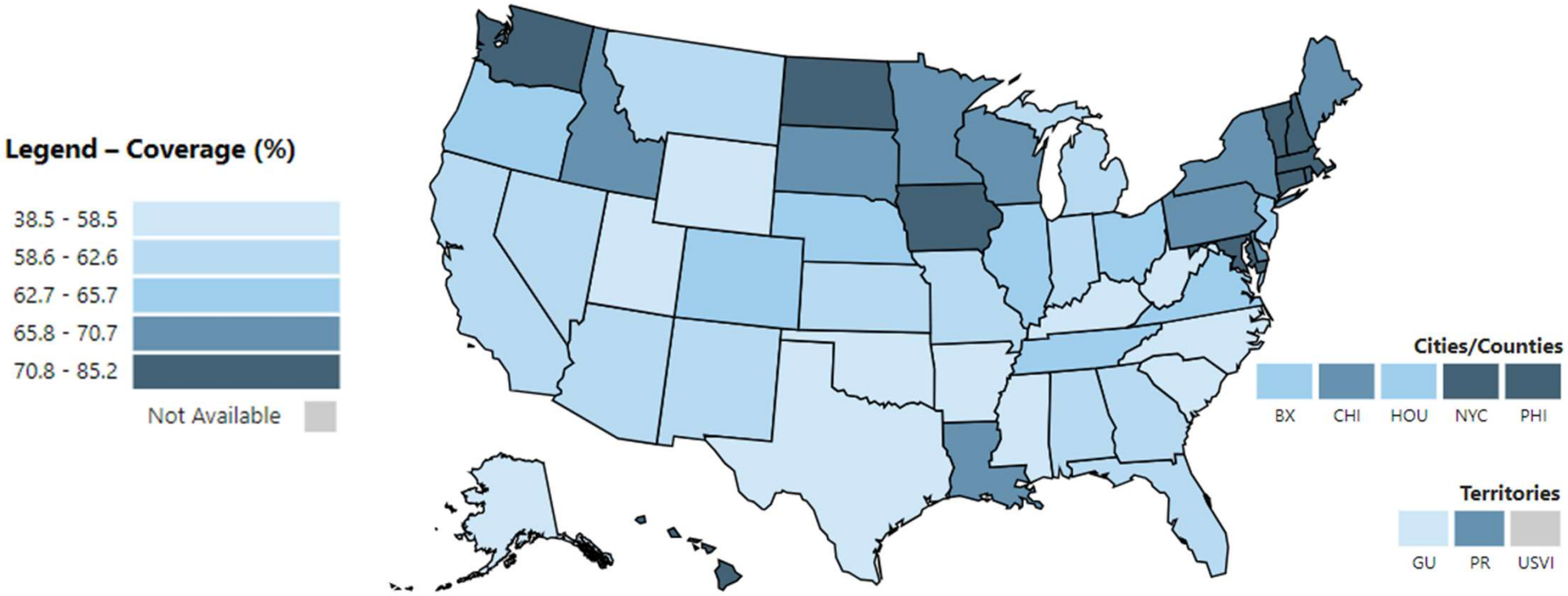


≥1 Dose of HPV Vaccination Coverage among Adolescents Age 13-17 years, 2022, NIS-Teen



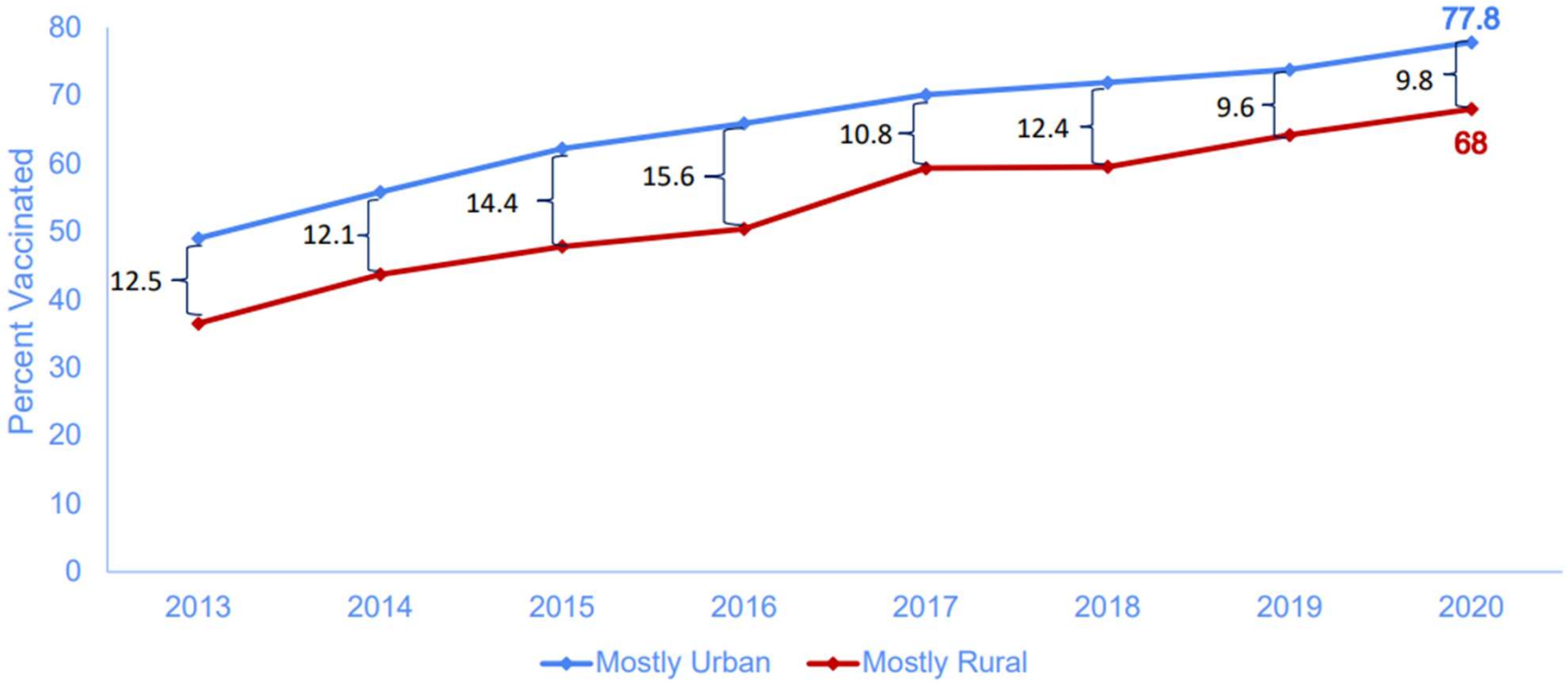
CDC TeenVaxView

Up-to-Date HPV Vaccination Coverage among Adolescents Age 13-17 years, 2022, NIS-Teen



CDC TeenVaxView

≥1 HPV vaccination coverage in **rural areas** is consistently lower



Source: https://www.cdc.gov/vaccines/imz-managers/coverage/teenvaxview/index.html

HPV Vaccine Coverage in U.S., 9-17 years

Various groups support moving HPV vaccine initiation age to 9 years, to improve coverage

In 2022, CDC MMWR showed no increase in vaccine rates for 13-17 years (first time ever)

2022 National Health Interview Survey data

- > 1/3 of children 9-17 years received ≥ 1 HPV vaccine
- Percentage of children that received ≥ 1 dose increased with age, varied by sex and race
- Those with private insurance more likely to receive a dose
  - Private insurance 41.5%
  - Medicaid 37%; other government coverage 30.2%
  - No insurance 20.7%

Parents remain hesitant about HPV vaccine; reframing discussion around cancer prevention could improve uptake

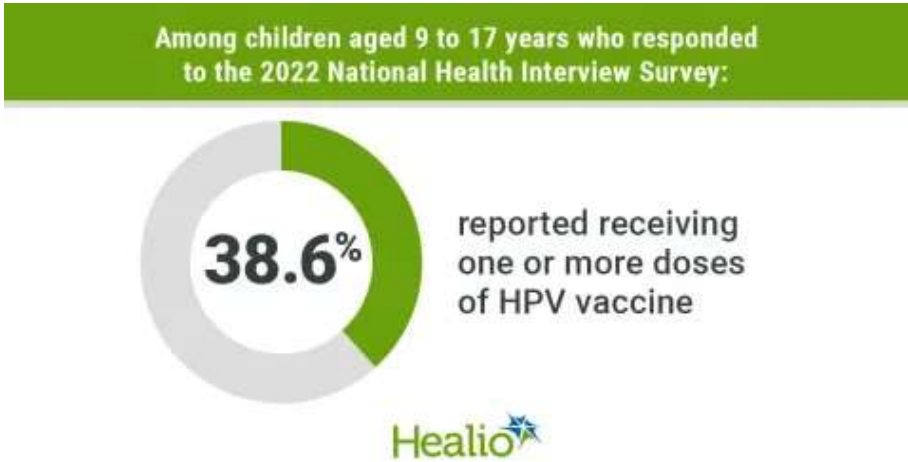
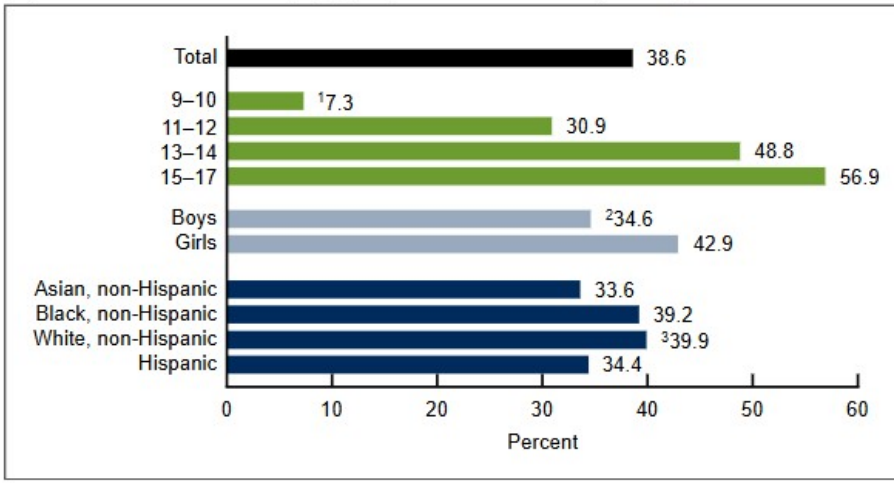


Figure 1. Percentage of children ages 9–17 years who have received one or more human papillomavirus vaccine doses, by age group, sex, and race and Hispanic origin: United States, 2022



Data derived from Villarroel MA, et al. NCHS Data Brief. 2024;doi:10.15620/cdc:145593

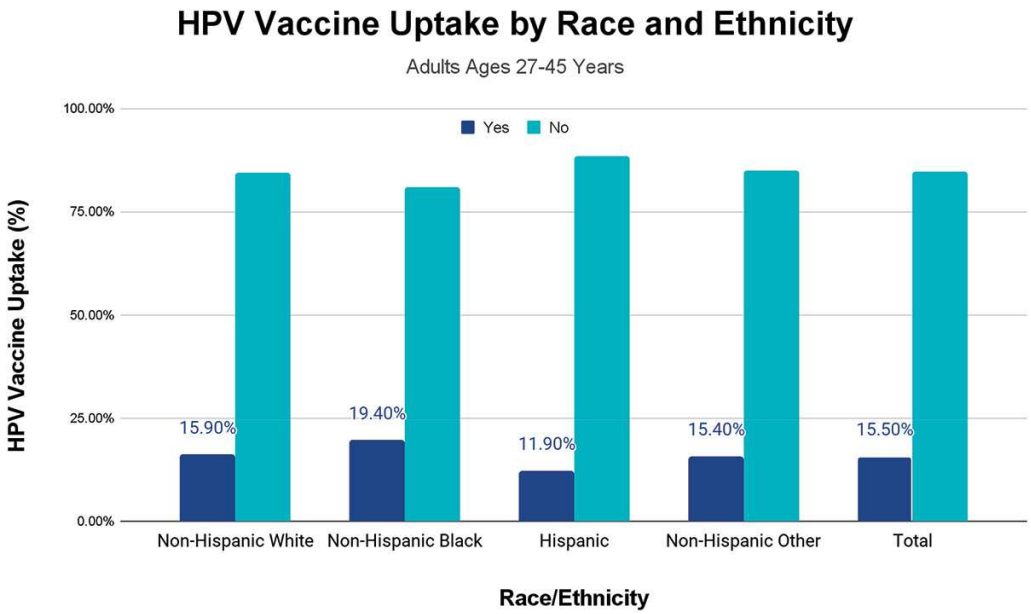
HPV Vaccine Coverage in U.S., 27-45 years

In 2018, FDA expanded age range to adults 27-45 years

Only 16% of U.S. adults 27-45 have received an HPV vaccine

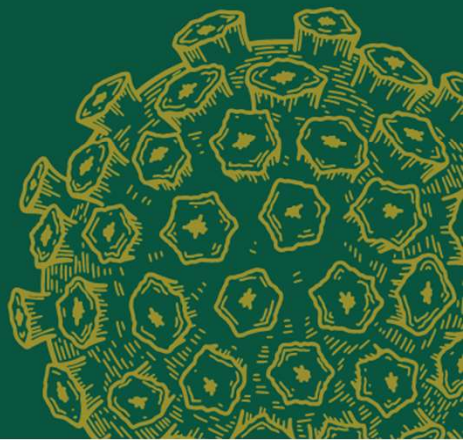
- Women 3x as likely to be vaccinated
- Lower rates in men, Hispanic, less education

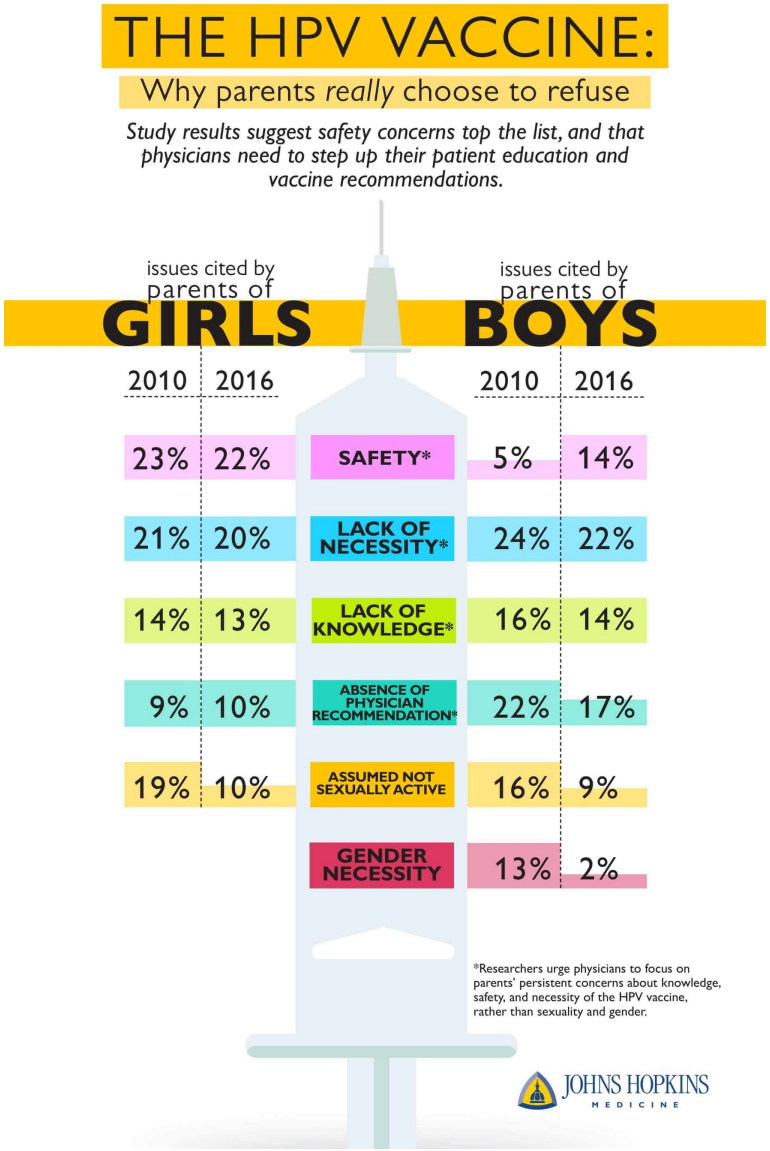
Low uptake in this demographic is concerning for cancer prevention efforts



Human Vaccines & Immunotherapeutics (Rincon et al, 2024)

Barriers to Vaccination





Top reasons why parents refuse the HPV vaccine for their children.

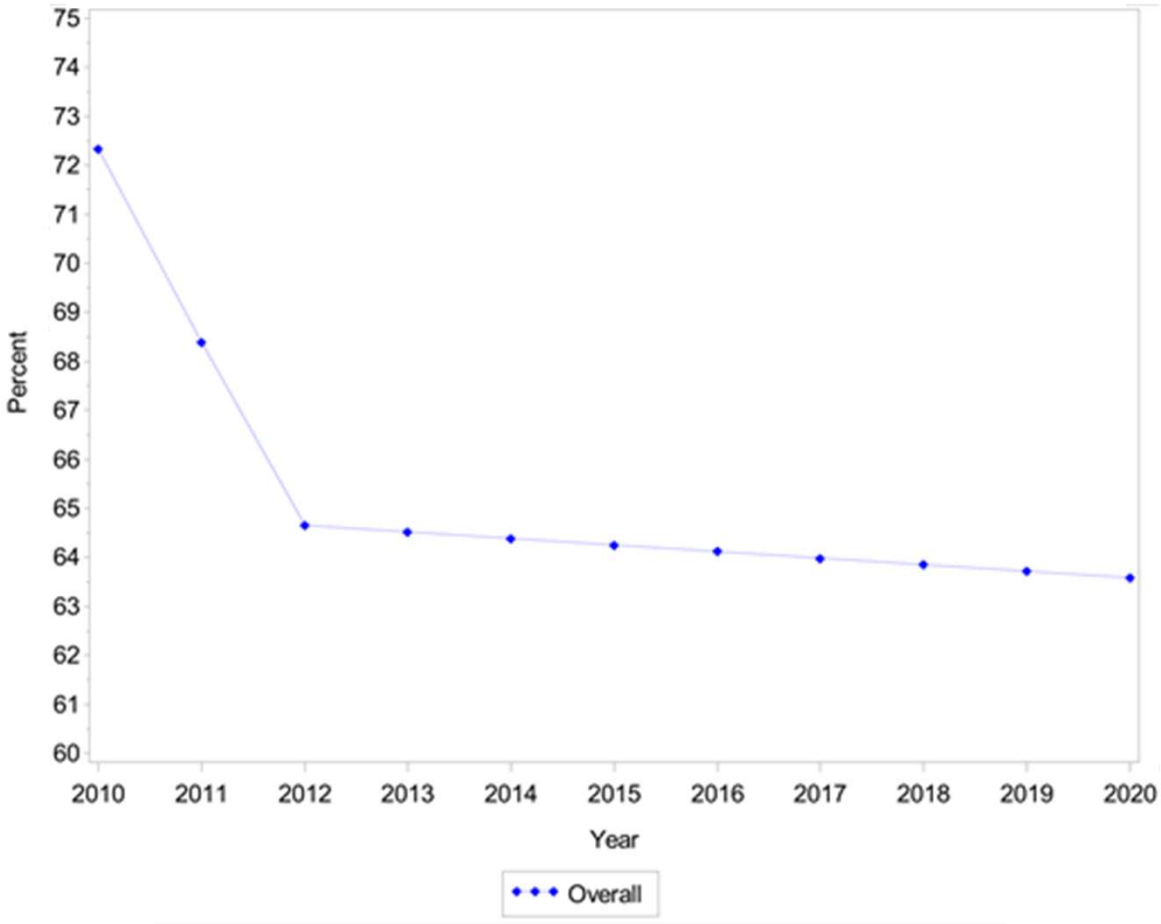
Pediatrics (Brewer et al, 2016)

Trends in parental/ guardian HPV vaccine hesitancy

HPV vaccine hesitancy decreased by 5.5% annually between 2010-2012

Pediatrics (Boakye et al, 2023)

Average % change in HPV vaccine hesitancy, NIS-Teen 2010-2020

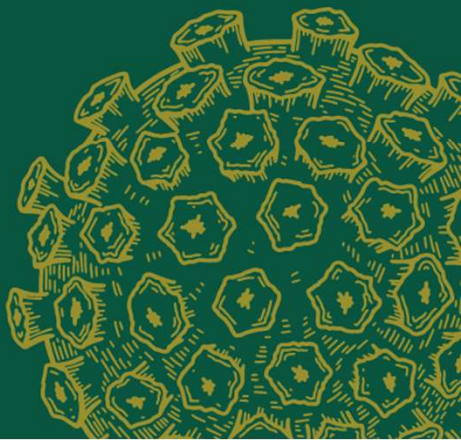


Is there a rise in HPV vaccine hesitancy post-COVID-19?

Data suggests **MAYBE.**

Hum Vaccin Immunother. (Ryan et al, 2023); Vaccine (Brady et al, 2024)

Communicating about HPV Vaccination



Addressing vaccine hesitancy: One size does not fit all

Communication Strategies by Motivation to Act and Level of Resistance

Presumption

Motivational Interviewing & Empathy

High Motivation to Act
Low Resistance

Some Motivation to Act
Some Resistance

Low Motivation to Act
High Resistance

Presumption of Vaccination

Strong provider recommendations are correlated with increased vaccine acceptance versus participatory communication.

"I see that Michael is 11. That means he is due for vaccines against meningitis, HPV cancers, and whooping cough."	VS	"Are we doing shots today?"
Presumptive		**Participatory**

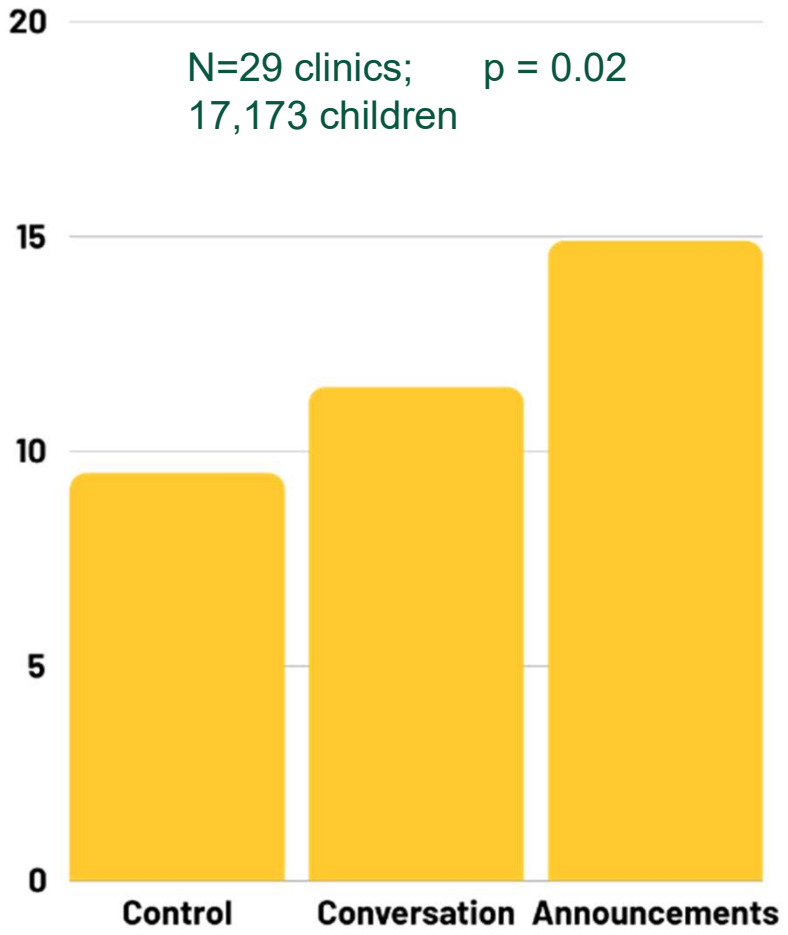
10X Studies show that parents who receive a clear recommendation for their children to get HPV vaccine have around 10 times higher odds of getting their children vaccinated.

The Journal of Pediatrics (William et al, 2020); Int J Environ Res Public Health (Nowak, 2018); Vaccine (Gilkey et al, 2016); Pediatrics (Brewer et al, 2017)

Improving HPV Vaccine Acceptance: Announcement vs. Conversation

Announcement [presumption] resulted in greater vaccine acceptance compared to conversation [participatory].

Pediatrics (Brewer et al, 2016)



Parents are less concerned than we think

Parent and provider perspectives on immunization: Are providers overestimating parental concerns?

Providers underestimated the importance of vaccines to parents in every category

	N = 401	*N* = 105	
Child Health	9.5 (0–10)	9.3 (4–10)	<0.001
Meningitis[b]	9.4 (0–10)	9.2 (5–10)	0.002
Hepatitis[b]	9.5 (0–10)	8.7 (3–10)	<0.001
Rotavirus[b]	9.0 (0–10)	8.4 (2–10)	0.535
Pertussis[b]	9.5 (0–10)	9.3 (0–10)	0.006
Influenza	9.3 (0–10)	7.0 (1–10)	<0.001
HPV	9.3 (0–10)	5.2 (0–10)	<0.001
Adolescent vaccines[c]	9.2 (0–10)	7.8 (4–10)	<0.001

Advantages of the Presumptive Method

It works!

Presumptive approach improves vaccine acceptance.

Similar approach to making other medical recommendations

The more confident you are, the more confident the patient is likely to be.

Saves time

Most patients and families are highly accepting of vaccines.

Based upon the information we just covered, is this a 👎 or a 👍?

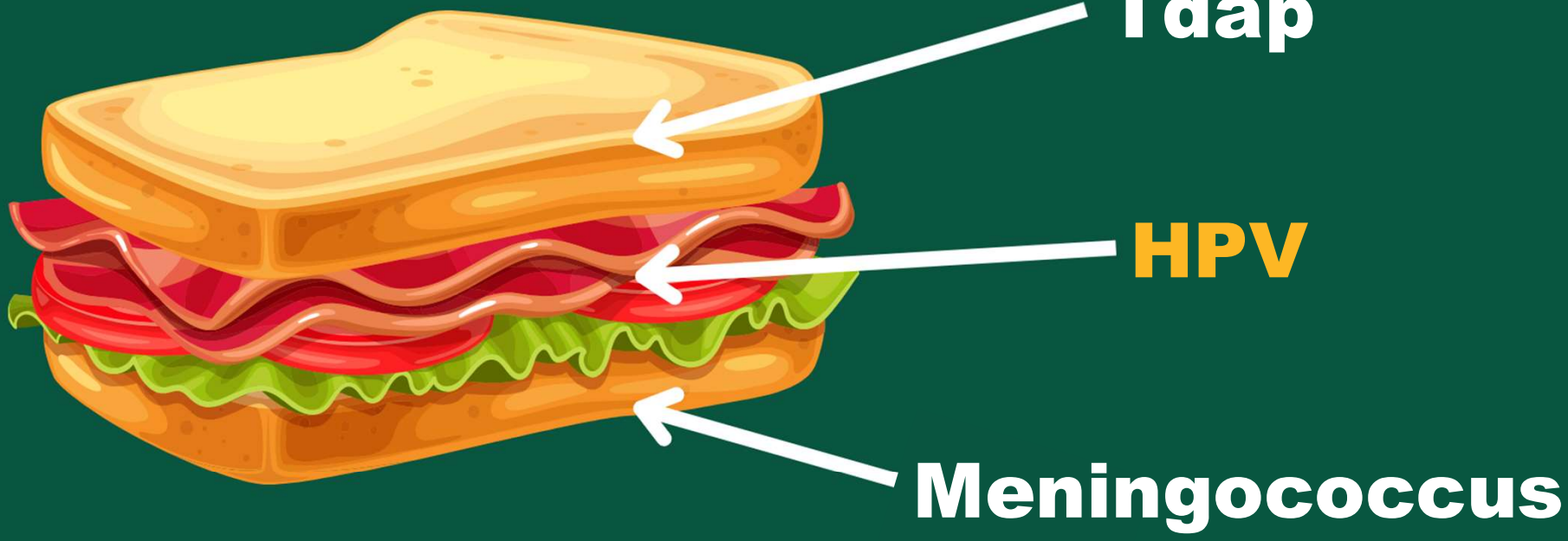
Since Anders just turned 11, he needs a tetanus booster and a meningitis shot, which are required for 7th grade. He can also have the HPV vaccine if you want him to have that too.

Based upon the information we just covered, is this a 👎 or a 👍?

Since Anders just turned 11, he needs a tetanus booster and a meningitis shot, which are required for 7th grade. He can also have the HPV vaccine if you want him to have that too.

We will take the tetanus and meningitis vaccines, but we will skip that other one. Three shots is a lot.

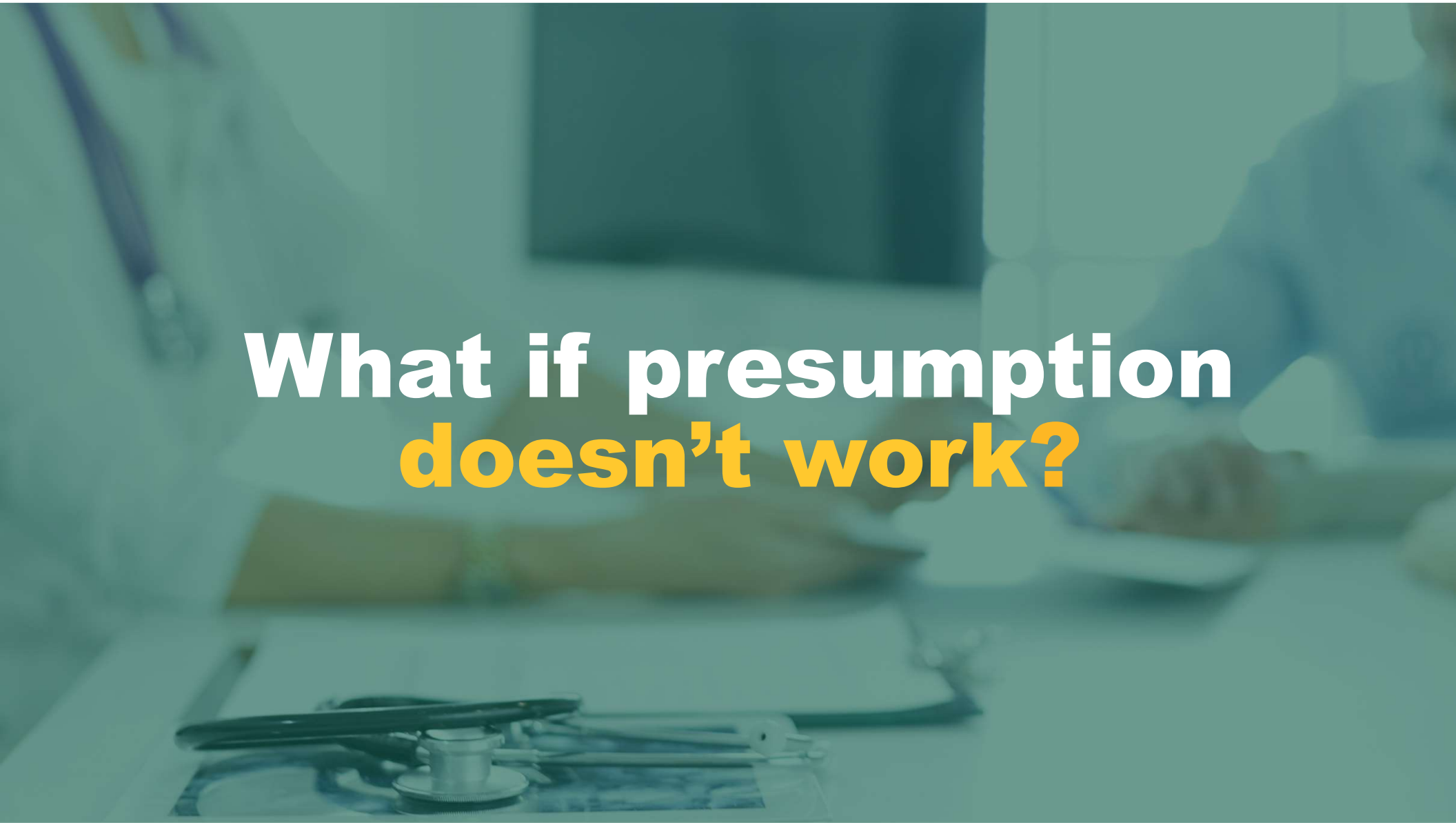
Normalize HPV Vaccination: “Sandwich”



Based upon the information we just covered, is this a 👎 or a 👍?

Andres is 11, so he is due for his tetanus booster, HPV, and meningitis vaccines today. Do you have any questions?

No, that sounds good!


What if presumption
doesn’t work?

Analyzing Strategies by Motivation to Act and Level of Resistance

Presumption

Motivational Interviewing & Empathy

High Motivation to Act
Low Resistance

Some Motivation to Act
Some Resistance

Low Motivation to Act
High Resistance

MI Communication Techniques

Open Ended Questions *"You aren't sure about the HPV vaccine today. What worries you?"*	**Reflect Back** *"You are really worried about the ingredients in vaccines."*	**Honor Ambivalence** *"So, you don't want her to get cervical cancer, but you are also worried about the long-term effects of this vaccine. Many parents feel that way."*
Ask Permission to Share *"Can I share some information that I think might ease your mind?"*	**Make a Strong Recommendation** *"My own children have received the vaccine, and I recommend it to all of my patients."*	**Support Autonomy** *"She is your child, and this is your decision."*

SCALING QUESTIONS

"On a scale of 0 to 10, how important is it for you to get the vaccine today?"

- "Why did you say 5 and not a lower number, like 4?"
- "What would it take to get you to a higher number, like 6?"

Sharing Information Using EPE

ELICIT	PROVIDE	ELICIT
Elicit knowledge and/or needs from the patient • Question with empathy • Learn what the patient has tried/already knows	**Provide information after asking permission** • Stay neutral • Validate feelings • Debunk myths without reinforcing them	**Elicit patient's response** • Reflect on discussion • Emphasize autonomy
“ • What are your specific concerns? • What have you heard? • What would you most like to know?	• May I make a suggestion? • This may not fit for you, but some people find … • Would you be interested in some resources?	• What are your thoughts on that? • How do you think that would work for you? ”

CASE STUDY #1

Great to see you, Julie! I see we have Carly in for a sports physical today. As a part of today's visit, Carly is due for her Tdap, HPV, and meningococcal vaccines. Any questions?

You know, I am just not sure about Carly getting the HPV vaccine. I have done some research online and I'm worried about how safe it is. I read it may cause something called POI which could impact Carly's ability to have kids!

You aren't the first parent that has come to me with this concern. Can I share some information with you?

Sure.

CASE STUDY #1: The Facts!

HPV vaccine has been around for 15+ years.

- Extensive safety testing occurs before any vaccine is licensed by the FDA in the U.S., including HPV vaccination! Gardasil 9 was approved for use and licensed in 2014. Clinical trials looked at 15,000+ men and women indicated that the vaccine was safe and the benefits outweigh any risk.
- 130+ million doses of HPV vaccine have been distributed since they were licensed.
- 160+ studies have shown that HPV vaccines have a favorable safety profile.

HPV vaccine safety will *continue to be monitored.*

- Systems like VAERS, VSD, and CISA work together to provide timely data on vaccine safety in our country on vaccines that licensed and recommended for use.

Acknowledge common side effects of HPV vaccination.

- Pain, redness, or swelling in the arm where the shot was given are common.
- Side effects are generally self-limiting. Put into perspective: HPV vaccination is *cancer prevention.*

CDC, 2024

CASE STUDY #1: The Facts!

Case Report

Journal of Investigative Medicine High Impact Case Reports
October-December 2014: 1–12

DOI: 10.1177/2324709614556129
sagepub.com

Adolescent Premature Ovarian Insufficiency Following Human Papillomavirus Vaccination: A Case Series Seen in General Practice

Deirdre Therese Little, MBBS, DRANZCOG
Harvey Rodrick Grenville Ward, Bsc(M
FCOG(SA), MMed (O&G), FRANZ

ANECDOTAL CASE STUDY

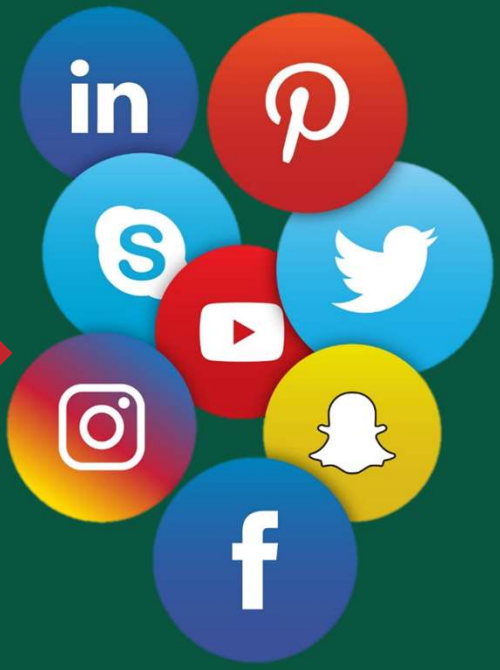
Abstract

Three young women ... following quadriva... vaccination pre... ...n Wales, Australia. The... and 18 ye... ...rs prior to the onset of ovarian decline. Vaccinations had been administe... ...outh Wales and the 3 girls lived in different towns in that state. Each had been p... ... treat menstrual cycle abnormalities prior to investigation and diagnosis. Vaccine rese... ...histology report of tested rats but does present a testicular histology report. Enduring ovari... ...of function following vaccination is unresearched in preclinical studies, clinical and postlicensure st... ...ing surveillance does not accurately represent diagnoses in adverse event notifications and can neither r... ...notified cases nor compare incident statistics with vaccine course administration rates. The potential significanc... ...case series of adolescents with idiopathic premature ovarian insufficiency following HPV vaccination presenting to a general practice warrants further research. Preservation of reproductive health is a primary concern in the recipient target group. Since this group includes all prepubertal and pubertal young women, demonstration of ongoing, uncompromised safety for the ovary is urgently required. This matter needs to be resolved for the purposes of population health and public vaccine confidence.

Keywords

premature ovarian failure, amenorrhea, human papillomavirus vaccination, ovarian insufficiency, menopause

Gains attention that does not correspond to the articles scientific significance



Misinformation shared on social media

What is primary ovarian insufficiency (POI)?

Also known as “premature menopause,” this is a condition in which a woman’s ovaries stop functioning before age 40. Causes of primary ovarian insufficiency include:

- Genetics
- Chemicals in the environment
- Cancer treatments
- Cigarette smoking
- Autoimmune disorders
- Some viral infections

However, in many cases it’s not possible to determine the cause. CDC and FDA have not found any proof that HPV vaccines cause POI.

CDC, 2024; UpToDate, 2024

How have the CDC & FDA addressed the concerns of HPV vaccines causing POI?

- As part of ongoing safety monitoring of HPV vaccines, CDC has reviewed reports of POI to VAERS following both Gardasil 9 and Gardasil vaccination
- CDC has also conducted additional safety research on HPV vaccine in the Vaccine Safety Datalink.

Let's take a look at the research…

CDC, 2024

"With more than 12 years of HPV vaccine safety monitoring and research from the United States and other countries, we have robust data showing the HPV vaccines are safe. With regard to concerns about HPV vaccination and fertility in women, CDC and FDA have not found any convincing evidence that HPV vaccines cause primary ovarian insufficiency (POI).

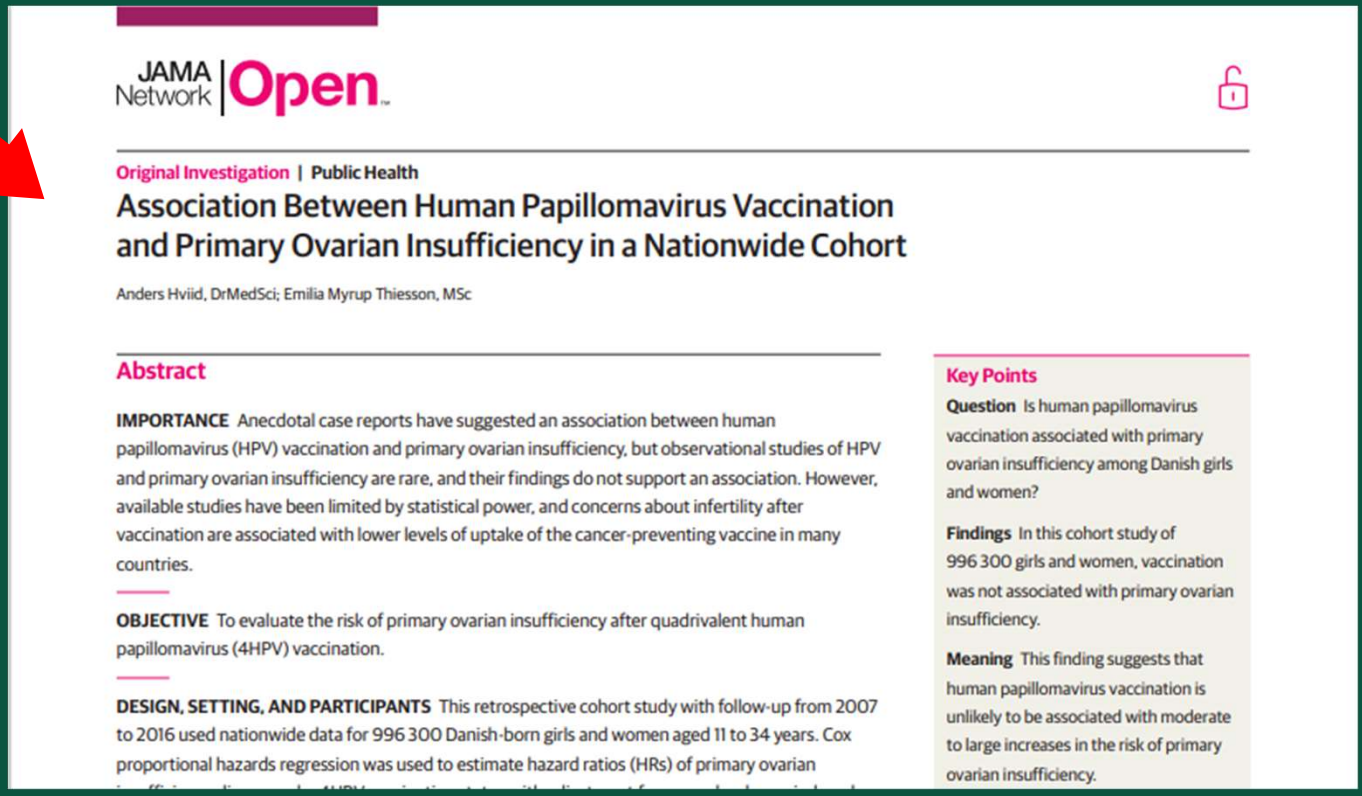
Also known as "premature menopause," POI is a condition in which a woman's ovaries stop functioning before age 40. Causes of POI include genetics, chemicals in the environment, cancer treatments, smoking cigarettes, autoimmune disorders, and some viral infections.

A 2018 study from CDC's Vaccine Safety Datalink that included nearly 200,000 women did not find an increased risk of POI following HPV vaccination."

-Frank Destefano, Director, Immunization Safety Office, CDC
(quote from 2019)

Research in other countries

In 2021, a retrospective cohort study was published in JAMA looking at a nationwide dataset of ~1M Danish-born girls/women aged 11-34. ***No association was found between HPV vaccination and primary ovarian insufficiency.***



JAMA Network | Open

Original Investigation | Public Health

Association Between Human Papillomavirus Vaccination and Primary Ovarian Insufficiency in a Nationwide Cohort

Anders Hviid, DrMedSci; Emilia Myrup Thiesson, MSc

Abstract

IMPORTANCE Anecdotal case reports have suggested an association between human papillomavirus (HPV) vaccination and primary ovarian insufficiency, but observational studies of HPV and primary ovarian insufficiency are rare, and their findings do not support an association. However, available studies have been limited by statistical power, and concerns about infertility after vaccination are associated with lower levels of uptake of the cancer-preventing vaccine in many countries.

OBJECTIVE To evaluate the risk of primary ovarian insufficiency after quadrivalent human papillomavirus (4HPV) vaccination.

DESIGN, SETTING, AND PARTICIPANTS This retrospective cohort study with follow-up from 2007 to 2016 used nationwide data for 996 300 Danish-born girls and women aged 11 to 34 years. Cox proportional hazards regression was used to estimate hazard ratios (HRs) of primary ovarian

Key Points

Question Is human papillomavirus vaccination associated with primary ovarian insufficiency among Danish girls and women?

Findings In this cohort study of 996 300 girls and women, vaccination was not associated with primary ovarian insufficiency.

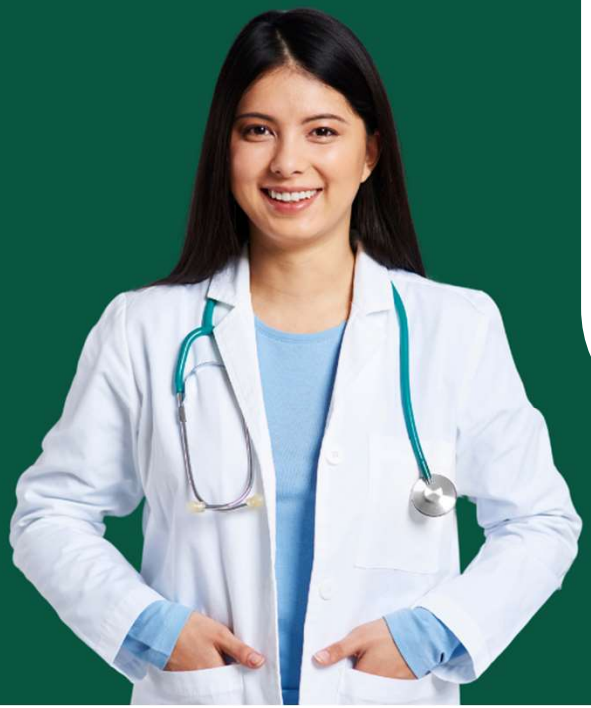
Meaning This finding suggests that human papillomavirus vaccination is unlikely to be associated with moderate to large increases in the risk of primary ovarian insufficiency.

World Health Organization

The Global Advisory Committee on Vaccine Safety (GACVS) concluded that the available data do not support an association between HPV vaccination and infertility or POI. The current safety profile continues to be extremely favorable, as discussed at 7 previous GACVS meetings, and consistent with the pre-licensure safety profile.

Extract from GACVS meeting of 4-5 December 2019, published in the WHO Weekly Epidemiological Record of 24 January 2020

CASE STUDY #1



HPV vaccines have been around a long time now, over 15 years! And during this time, over a hundred million doses of HPV vaccines have been distributed in the U.S. We have very promising and reassuring data that these vaccines provide long-lasting protection and that they are very safe. The rumor that this vaccine causes infertility still makes the rounds on social media. What I hear you saying is that you are concerned this vaccine may cause infertility, and specifically Primary Ovarian Insufficiency or POI?

Yes.

CASE STUDY #1

As part of ongoing safety monitoring of HPV vaccines, researchers have taken a look at the risk of POI following both Gardasil 9 and Gardasil vaccination – many studies looking at hundreds of thousands of girls ***have found no link between HPV vaccination and infertility or POI.*** Some of my patients do experience some soreness, swelling, and redness at where the shot was given. But, this is common and should get better in a day or two. AND do you want to know what is absolutely linked to infertility? ***HPV cancers***. The fact that they can cause issues with having children is unquestioned in the medical world. I vaccinated my own daughter against HPV, and I highly recommend Carly get vaccinated, too. What stands out to you about what I shared?

CASE STUDY #1

No, that makes sense, and I guess I hadn't really realized that HPV vaccination had been around that long. I really appreciate you taking the time to talk to us about it. Your recommendations are important to us. But, I think we are going to take some time to think about it.

Of course. Can I send some resources home with you to take a look at? I think HPV vaccination is an important part of keeping Carly healthy. Can we re-address this at our next appointment?

Absolutely.

CASE STUDY #2

Hi Diego! Thanks for bringing Lenny in for his well-child visit today. As a part of today's visit – great news! We can protect Lenny against flu and start the HPV vaccine series. Any questions?

Wow, HPV? Isn't he a bit young for that vaccine? He's only 9!

That's a great question, and you aren't my first parent to say that. Do you mind if I tell you more about why we should consider starting this vaccine at 9?

I guess so.

CASE STUDY #2: The Facts!

Starting early may improve on-time series completion.

- Increasing the number of adolescents who begin the HPV vaccine series at age 9 may lead to improved cancer prevention by maximizing the number of people protected through on-time vaccination.

Increase cancer prevention among next generation.

- The most recent NIS-Teen showed uptake of Tdap vaccine was 89% and the first dose of MenACWY was 87%. HPV rates remain significantly behind these vaccines, with initiation at 68% and completion at 51%.

No known downside to earlier initiation.

- Begin the conversation now, as attendance at well visits decreases in older adolescents.
- Opportunity to complete the series before other adolescent vaccines are due.
- Implementing HPV vaccination at the earliest opportunity produces a strong immune response.

AAP News (O'Leary & Nyquist, 2019); HPV Round Table Evidence Summary, 2024; Hum Vaccin Immunother (Perkins et al, 2023); Hum Vaccin Immunother (Saxena, 2023)

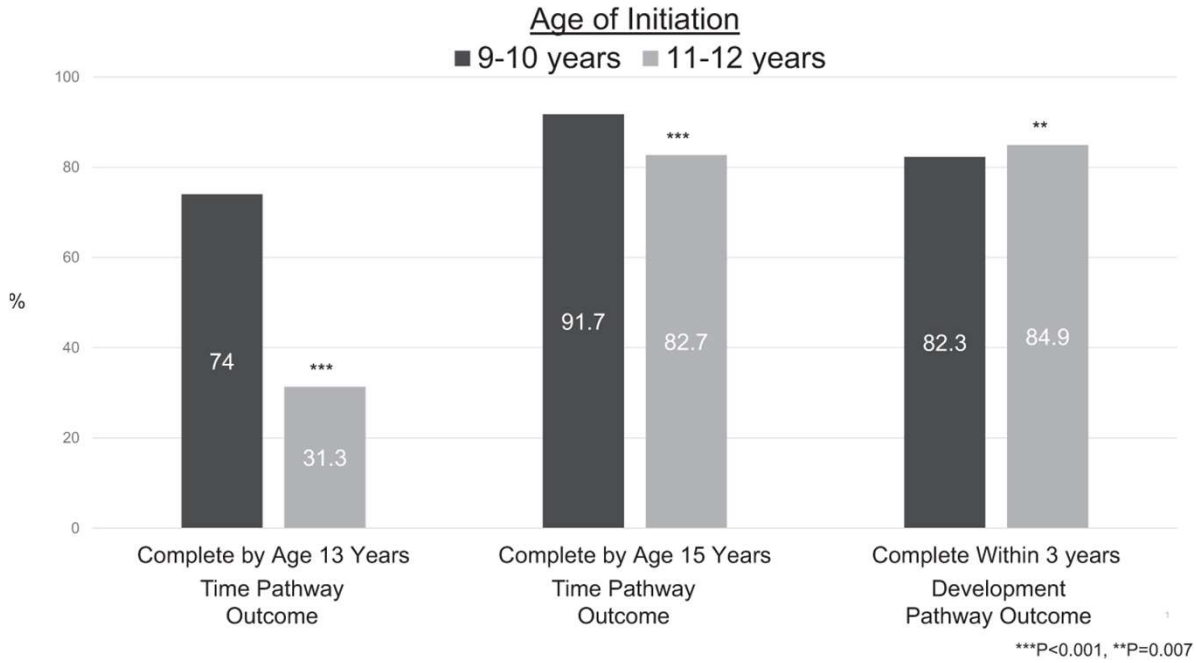
CASE STUDY #2: The Facts!

Early initiators (started at 9/10) were:

- **Much more likely** to complete by age 13 years
- More likely to complete by age 15 years

BUT:

- Only 8% were early initiators (82% at age 11-12)
- Self-selection of patients and providers



Moving routine HPV vaccination to ages 9 to 10 may improve vaccination coverage rates in early and mid-adolescence.

Pediatrics (Goodman et al, 2023); ACIP Meeting (Brewer, Oct 23, 2024)

CASE STUDY #2: The Facts!

Initiation HPV vaccination at age 9-10 is recommended by:

(with some nuanced difference)

American Academy of Pediatrics

DEDICATED TO THE HEALTH OF ALL CHILDREN®

CDC ACIP

CENTERS FOR DISEASE CONTROL AND PREVENTION

American Cancer Society®

CASE STUDY #2

We start to HPV vaccination around 9 because this vaccine is really all about cancer *prevention*, protecting Lenny long before he will have contact with the virus. Starting Lenny now also means we are more likely to finish the series and provide that protection Lenny needs. What stands out to you about what I shared?

I guess my wife and I didn't think about starting HPV this early. We haven't really prepped Lenny for it for today.

CASE STUDY #2

I can appreciate your concerns. On a scale of 0 to 10, how confident are you in vaccinating Lenny against HPV today?

Hmm, maybe a 5?

Great, you said 5. What would get you to a 7 or 8?

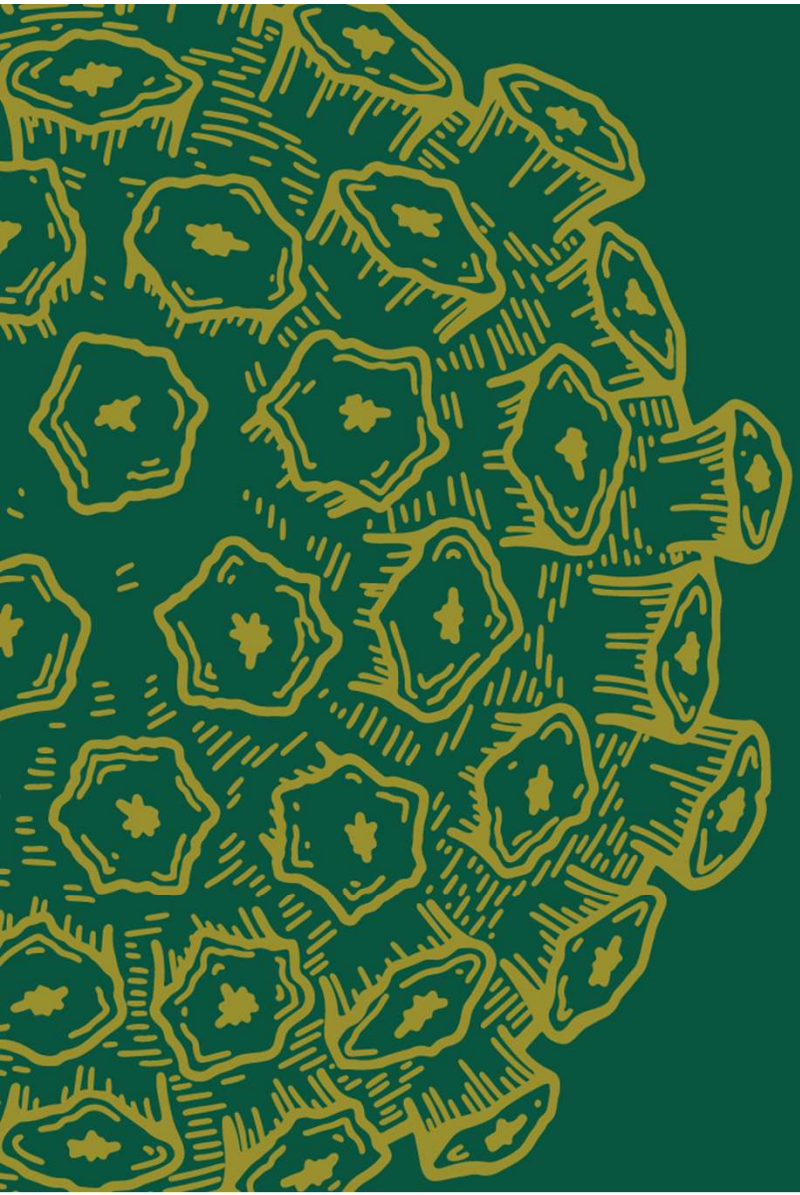
I guess more details on why Lenny really needs it now versus at 11 or 12…

CASE STUDY #2

Absolutely. Mind if I provide you with some additional details [Diego nods]. We know that giving this vaccine at 9 or 10 also produces stronger protection than giving it later in adolescence. Also – if we start this series before 15, Lenny only needs two doses to be up-to-date! This also means less shots at his next well child at age 11. What would you like to do? I highly recommend HPV vaccination to all my patients and recommend we get Lenny started today!

Ok, let's do it.

Great! I will have the nurse come in and get that taken care of for you and get him schedule for his second dose!



Summary

1. *HPV infection is a major public health threat.*
2. *HPV vaccines are safe and effective.*
3. *HPV vaccination rates are suboptimal – however your recommendations can make an impact and improve HPV vaccination rates and reduce missed opportunities.*
4. *HPV vaccination initiation at age 9-10 years is promising – MORE DATA COMING SOON!*

Questions?

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