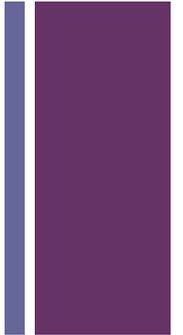


Prevention of HPV infection through vaccination

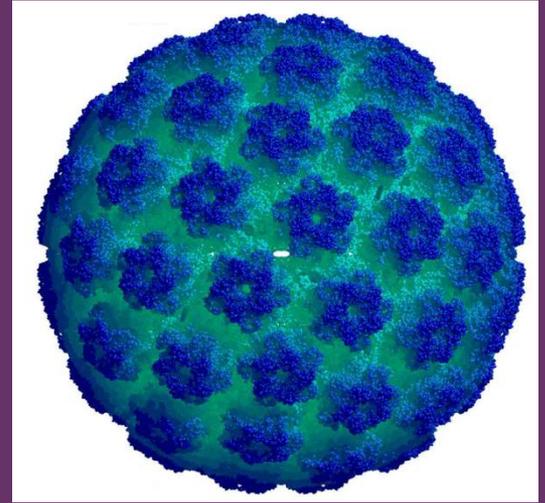
Manika Suryadevara, MD

May 21, 2015

+ Objectives



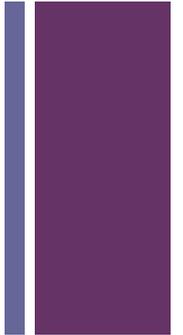
- Describe epidemiology of HPV infection
- Discuss HPV vaccines and updated recommendations
- Review HPV vaccine coverage rates
- Understand factors associated with increased vaccine uptake
- Discuss interventions to optimize HPV vaccination



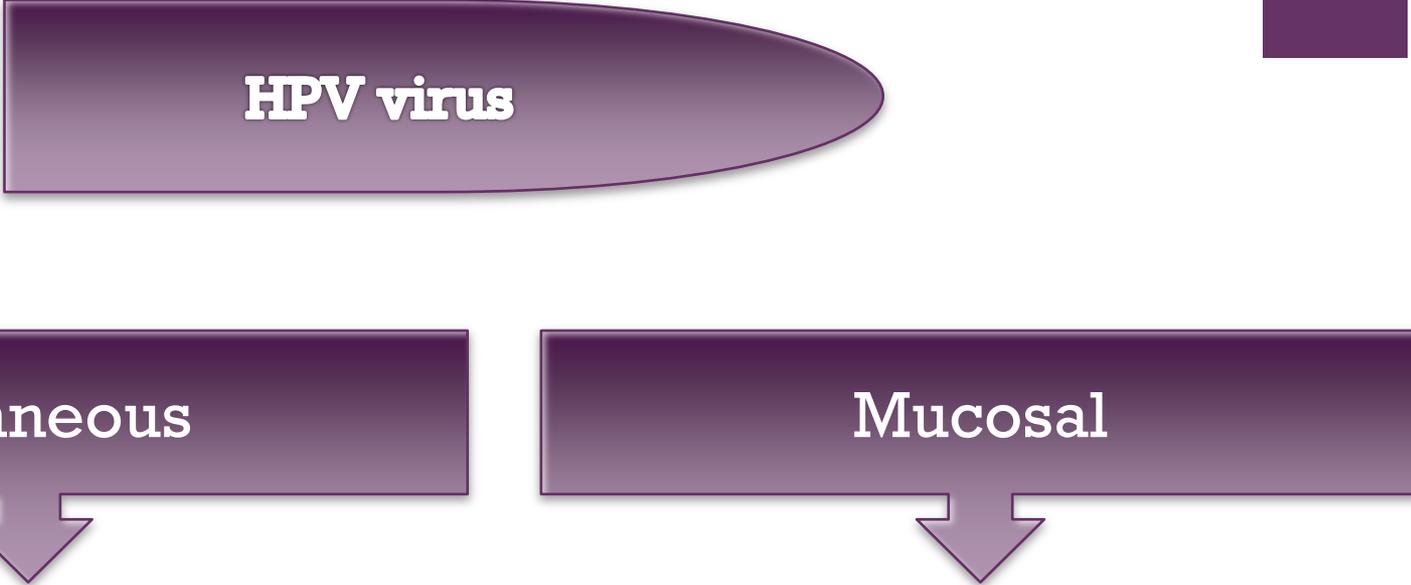
+

HPV background

+ HPV virus



- Double stranded DNA virus
- > 120 HPV types
- Types infect specific epithelium
- Transmission occurs through direct contact



HPV virus

The diagram illustrates the classification of HPV virus. At the top is a purple arrow-shaped box pointing to the right, labeled "HPV virus". Below this, two purple rectangular boxes are positioned side-by-side. The left box is labeled "Cutaneous" and has a downward-pointing purple arrow below it. The right box is labeled "Mucosal" and also has a downward-pointing purple arrow below it. A small purple square is located in the top right corner of the image.

Cutaneous

Mucosal

HPV virus

Cutaneous

Palmar warts

Plantar warts



HPV virus

Mucosal

Genital warts

**Respiratory
papillomatosis**

Low risk

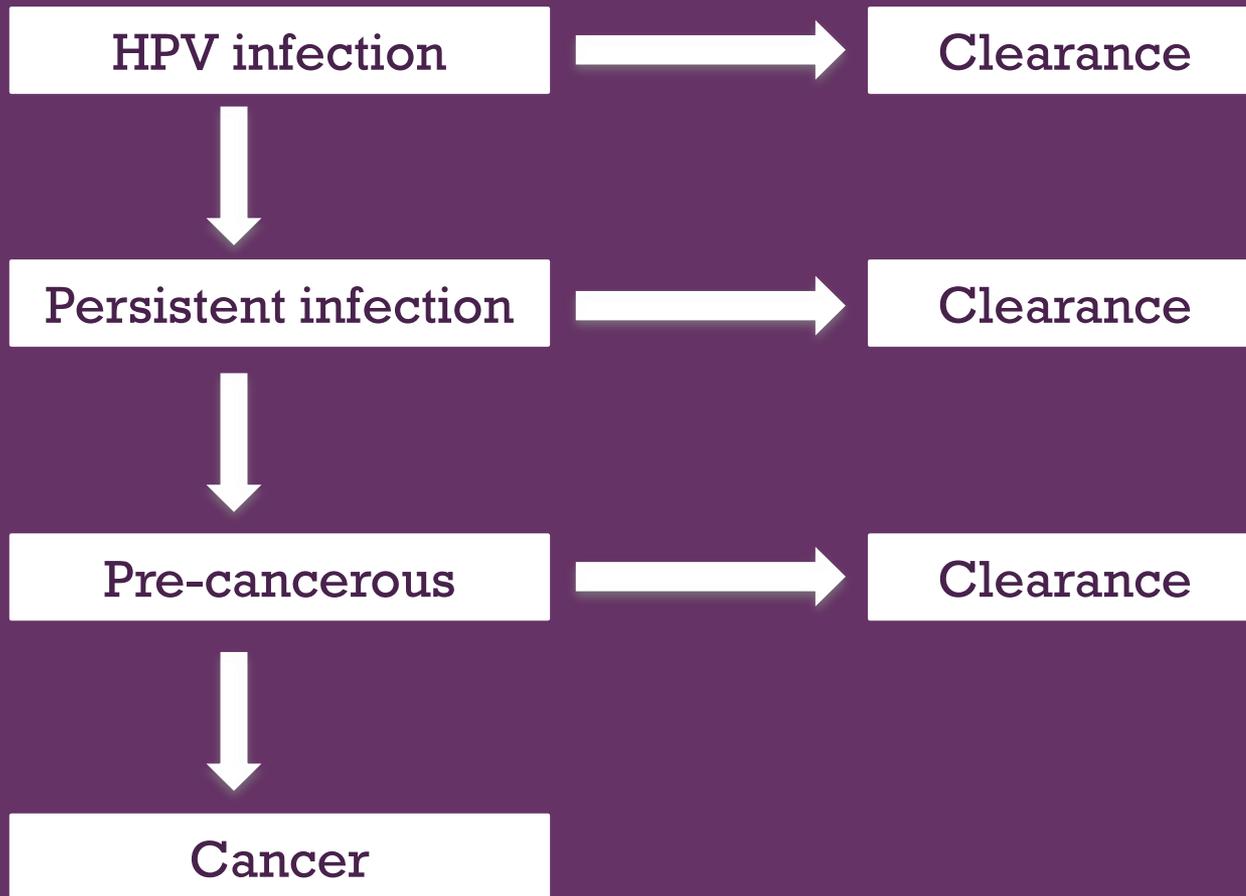
Genitourinary cancer

Oropharyngeal cancer

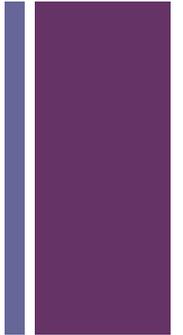
High risk



Natural history of HPV infection



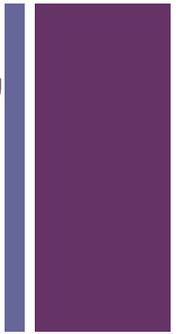
+ Epidemiology – HPV infection



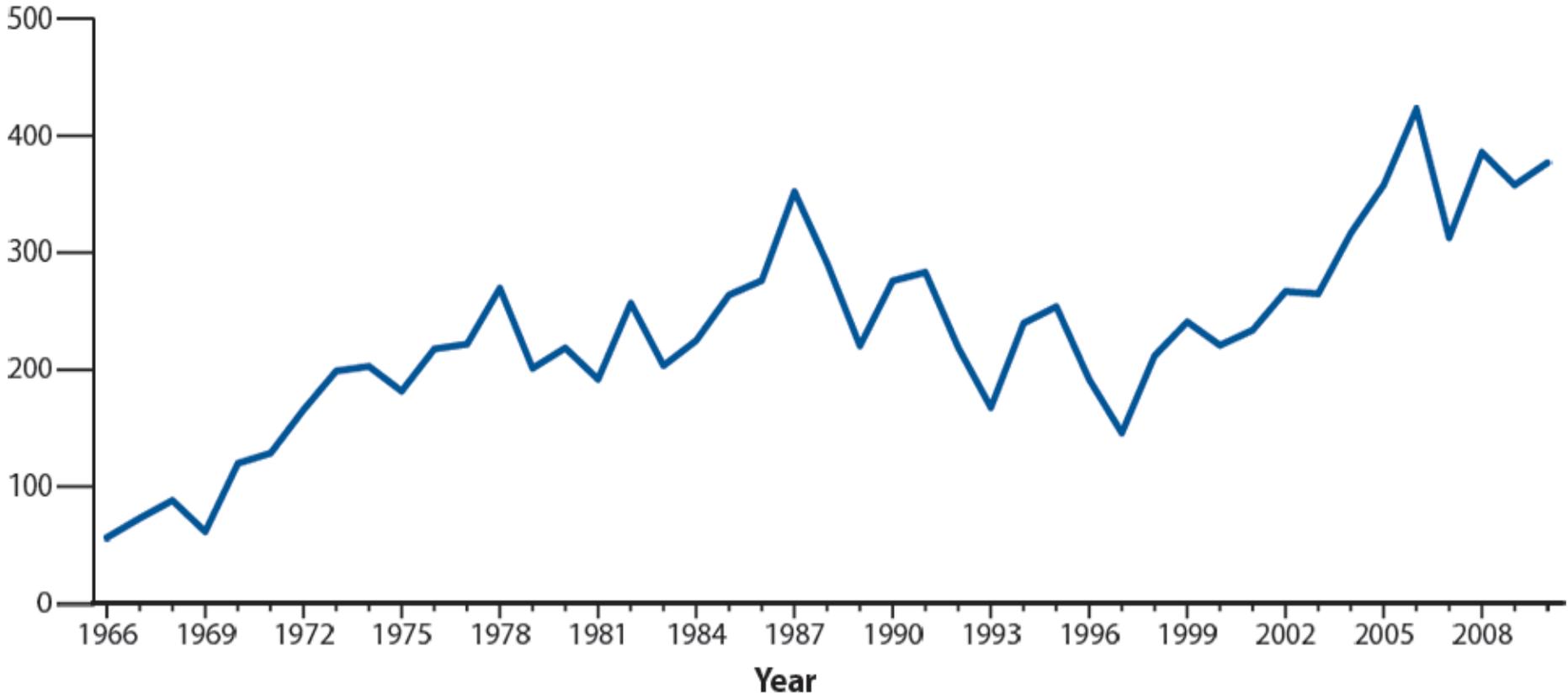
- HPV genital infections in US – most common STI
 - ~79 million people infected
 - ~ 14 million new infections/year
 - ½ in persons aged 15 and 24 years
- The lifetime risk of developing genital HPV infection > 50%
- Genital HPV acquired soon after sexual debut
 - 40% are infected within 2 years
- ~80% of sexually active women will be infected by age 50



Genital Warts—Initial Visits to Physicians' Offices, United States, 1966–2010

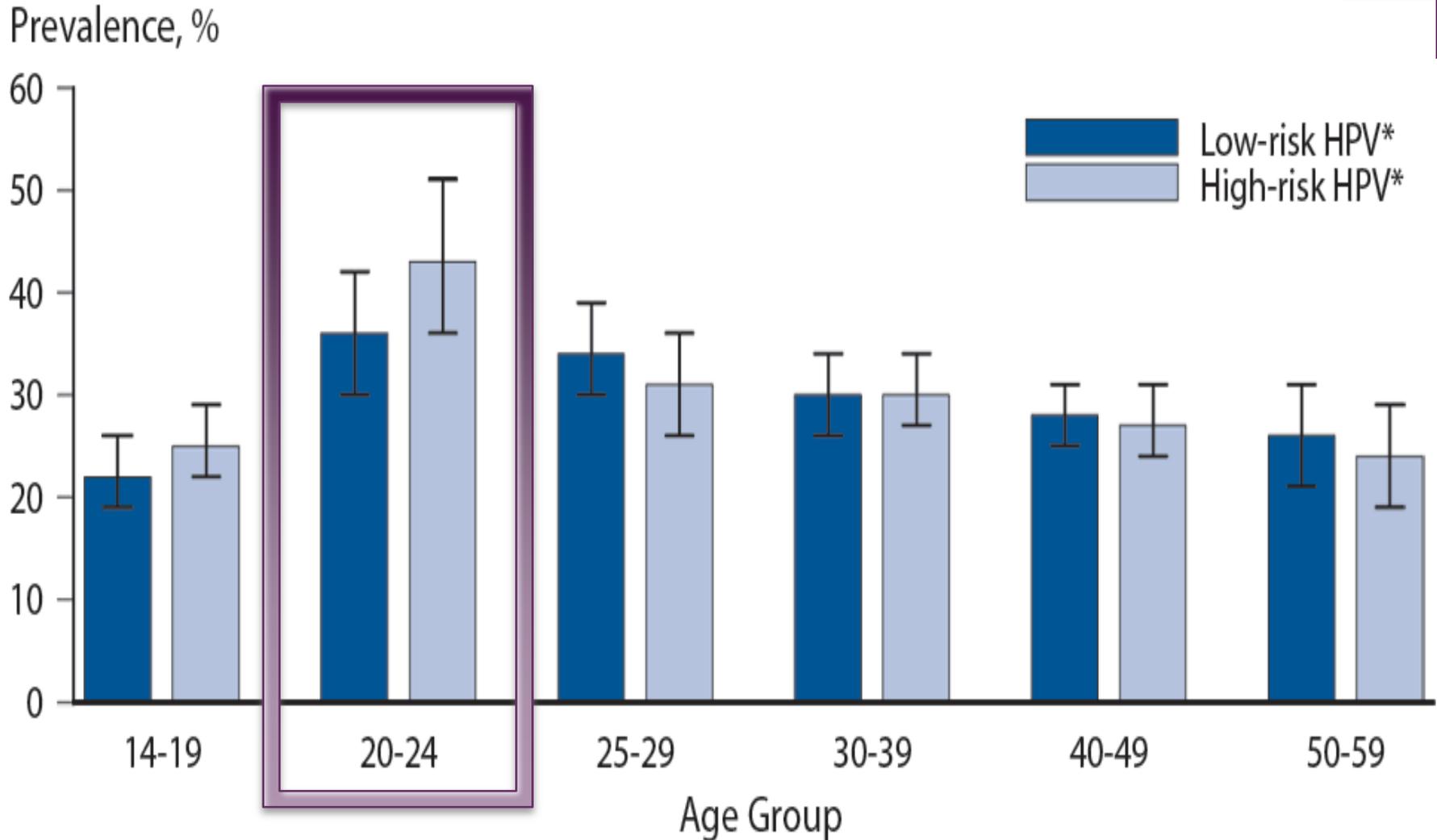


Visits (in thousands)



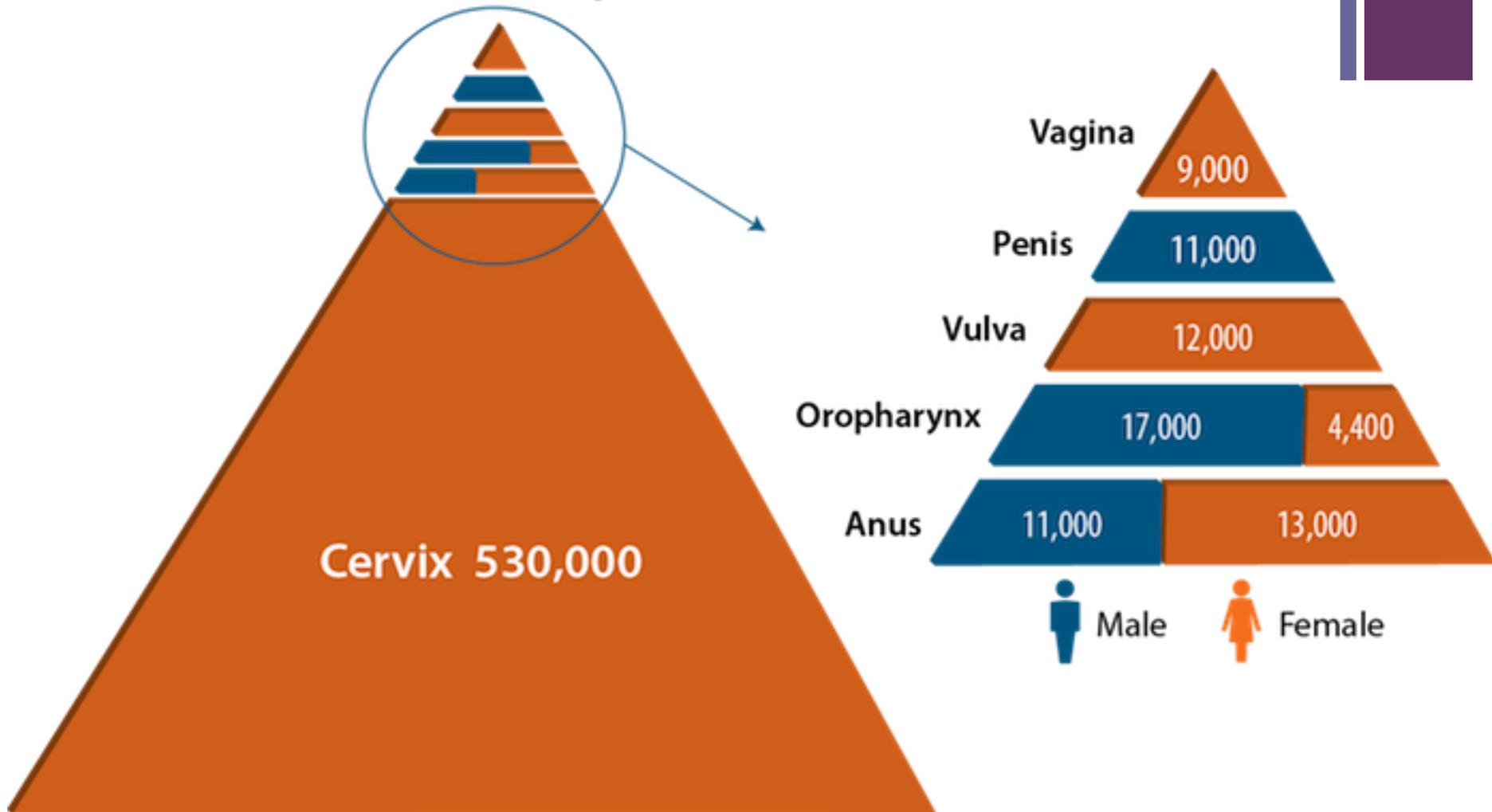
<http://www.cdc.gov/std/stats10/other.htm>

✦ Human Papillomavirus — Cervicovaginal Prevalence of High-risk and Low-risk Types Among Women Aged 14–59 Years by Age Group, 2003–2006



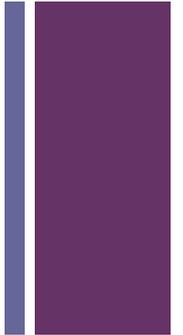
+ HPV-associated cancer burden worldwide

Numbers of Cancers Caused by HPV Worldwide Each Year

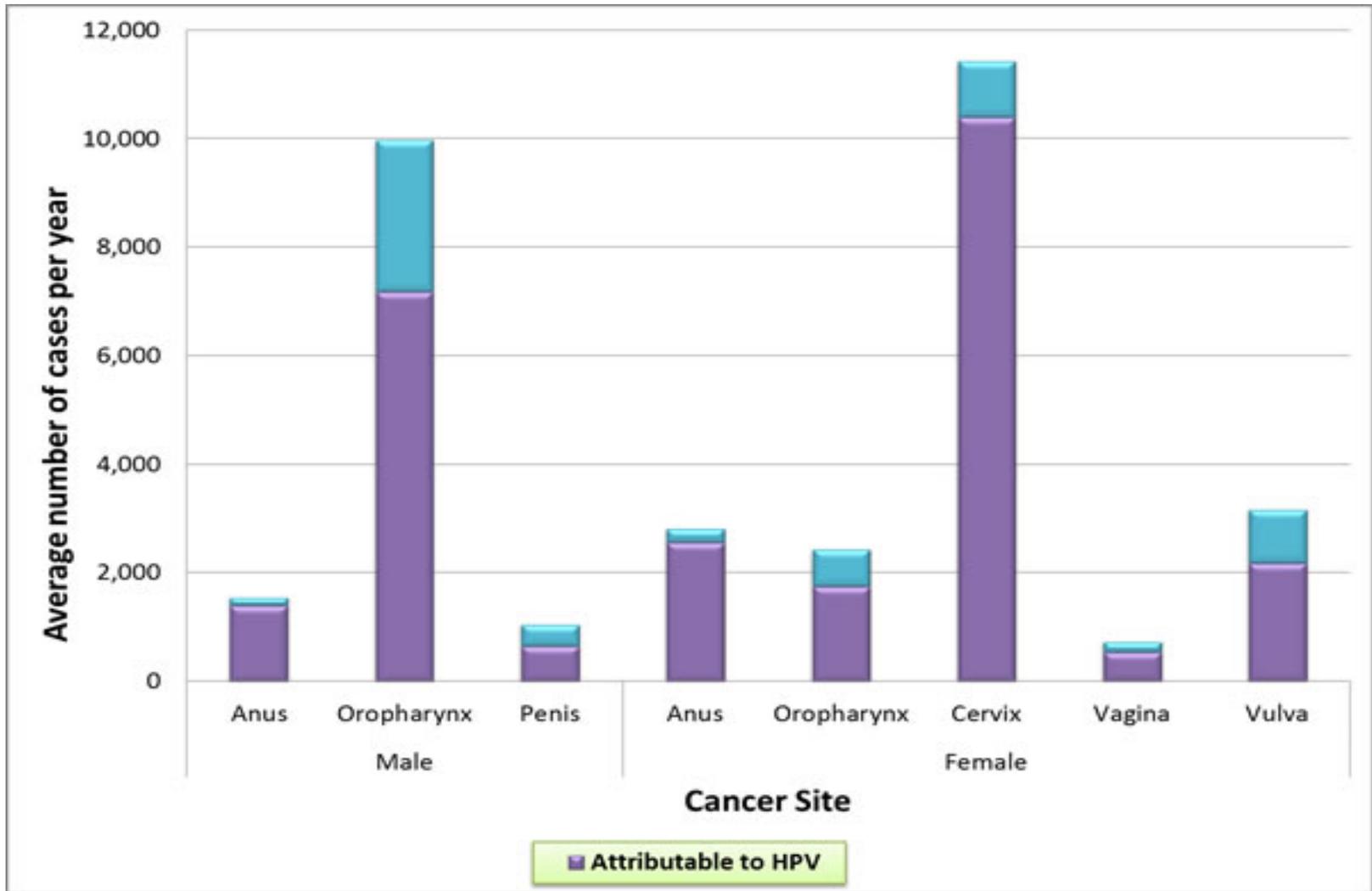


Global burden of cancers attributable to infections in 2008: a review and synthetic analysis. *Lancet Oncol.* 2012;13(6):607-15

+ HPV-associated cancers



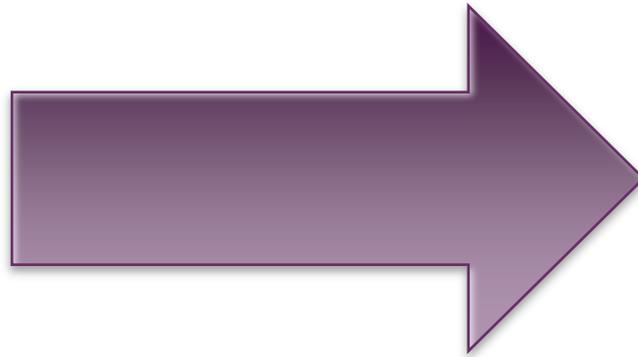
- >33,000 HPV-associated cancers occur in the US each year
- >6,000 deaths due to HPV-associated cancers in the US each year
- Cervical cancer
 - second leading cause of cancer death in women worldwide
 - Almost all is HPV-associated
 - US – African americans and Hispanics highest rate
 - ~4000 females die annually



Data from 2006-2010, represents 94.8% of US population
<http://www.cdc.gov/cancer/hpv/statistics/cases.htm>



**HPV
infection**

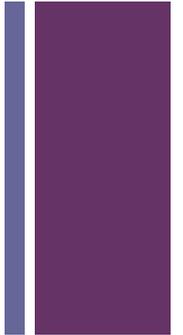


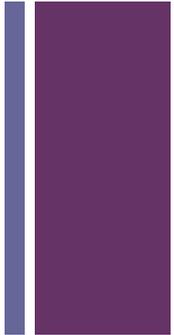
**GU
cancers**

**OP
cancers**

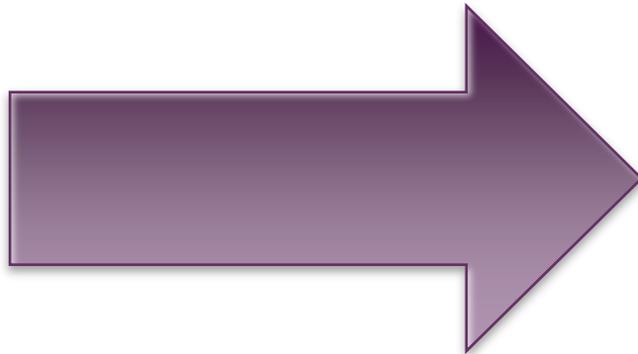
**Genital
warts**

**Respiratory
papillomas**





HPV
VACCINE



~~GU
cancers~~

~~OP
cancers~~

~~Genital
warts~~

~~Respiratory
papillomas~~

If there were a vaccine against cancer, wouldn't you get it for your kids?

Talk to the doctor about vaccinating your 11–12 year old sons and daughters against HPV.

www.cdc.gov/vaccines/teens

HPV vaccine is cancer prevention.

Centers for Disease Control and Prevention
Missouri Department of Health and Senior Services

The advertisement features a young woman with long dark hair looking upwards and to the right. The background is split into a red left side and a white right side with a red border. Logos for the CDC and Missouri Department of Health and Senior Services are at the bottom.

+

HPV vaccine for cancer prevention

+ HPV vaccines

HPV2

- 16, 18

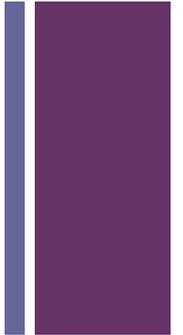
HPV4

- 6, 11, 16, 18

HPV9

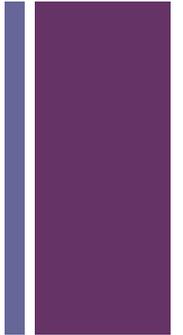
- 6, 11, 16, 18, 31, 33, 45, 52, 58

+ HPV vaccines



- Rationale for vaccinating at 11-12 years
 - Age of sexual debut in the US
 - Most effective when administered prior to infection
 - Higher antibody titers when compared to older adolescents
 - Health care visit when other adolescent vaccines are given

+ HPV vaccine recommendation



- 2006 -- HPV4 licensed and recommended
 - 11-12 year old females
 - Unvaccinated 13-26 year old females

- 2009
 - HPV2 licensed for use in females, either vaccine can be used
 - HPV4 licensed for use in males

- 2011 -- HPV4 recommended
 - 11-12 year old males
 - 13-21 year old males
 - 22-26 year old males may be immunized if high risk

+ HPV vaccine recommendation

- January 2015 → FDA approval of HPV9 for use in
 - 9-26 year old females
 - 9-15 year old males
- February 2015 → ACIP recommendations updated to include:
 - Use of HPV2, HPV4, or HPV9 for females
 - at 11-12 year old visit through 26 years
 - Use of HPV4 or HPV9 for males
 - at 11-12 year old visit through 21 years

+ HPV vaccine recommendation

HPV dose	Recommended interval	Minimum interval
Dose 1	Day 0	
Dose 2	1-2 months after dose 1	4 weeks after dose 1
Dose 3	6 months after dose 1	12 weeks after dose 2

+ HPV vaccine recommendation notes

- If vaccine series is interrupted → no need to restart
- If previous HPV vaccine product unknown or unavailable (during transition to HPV9)...
 - HPV 2 HPV4 or HPV9 can be used to complete series for female
 - HPV4 or HPV9 can be used to complete series for male
- Not recommended for use in pregnant women
 - If found to be pregnant after initiating series → delay until completion of pregnancy
 - If vaccine given during pregnancy → no intervention needed

+ HPV vaccine effectiveness

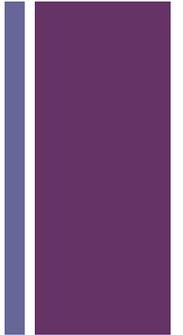
Outcome	Vaccine	Sex	Vaccine efficacy
Cervical precancer	HPV2, HPV4	Females	> 93%
Vaginal/vulvar precancer	HPV4	Females	100%
Anal precancer	HPV4	Males	75%
Anogenital warts	HPV4	Females	99%
		Males	89%
Combined disease	HPV9	Females and males	97%

+ Vaccine effectiveness

Drolet M et al. Lancet Inf Dis. 2015; 15: 565-80

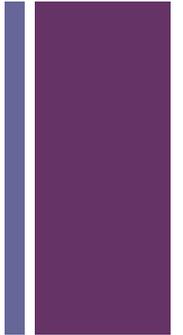
- In countries with female vaccine coverage $\geq 50\%$
 - Reduction in HPV 16 and 18 infection by 68%
 - Anogenital warts by 61% in females
 - Reduction in anogenital warts in males \rightarrow herd effect

- In countries with female vaccine coverage $< 50\%$
 - Reduction in HPV 16 and 18 infection
 - Reduction in anogenital warts in females
 - No herd effect observed



+ Vaccine safety

- June 2006 through March 2014
- 67 million doses HPV4 given in US
- VAERS – 25,176 adverse reporting events after HPV vaccine
 - 22,867 in females
- Most common –
 - Injection site reactions, dizziness, syncope, nausea, headache
- ACIP and CDC recommend
 - Administer vaccine while patient seated
 - Patient should sit for 15 minutes after vaccine



HPV CANCER PREVENTION

1 HPV VACCINE IS CANCER PREVENTION
 HPV vaccine protects against HPV types that most commonly cause anal, cervical, oropharyngeal, penile, vaginal, and vulvar cancers.

Every year in the U.S., 27,000 people get cancer caused by HPV. That's 1 person every 20 minutes of every day, all year long.

Most of these cancers can be prevented by HPV vaccine.

2 HPV VACCINE IS RECOMMENDED AT THE SAME TIME AS OTHER TEEN VACCINES

Preteens need three vaccines at 11 or 12. They protect against whooping cough, cancers caused by HPV, and meningitis. vaccines for your 11-12 year olds: Tdap, HPV, Meningococcal

3 HPV VACCINE IS BEST AT 11-12 YEARS

Preteens have a higher immune response to HPV vaccine than older teens.

While there is very little risk of exposure to HPV before age 13, the risk of exposure increases thereafter.

Parents and healthcare professionals are the key to protecting adolescents from HPV cancers.

VACCINATE YOUR 11-12 YEAR OLDS.

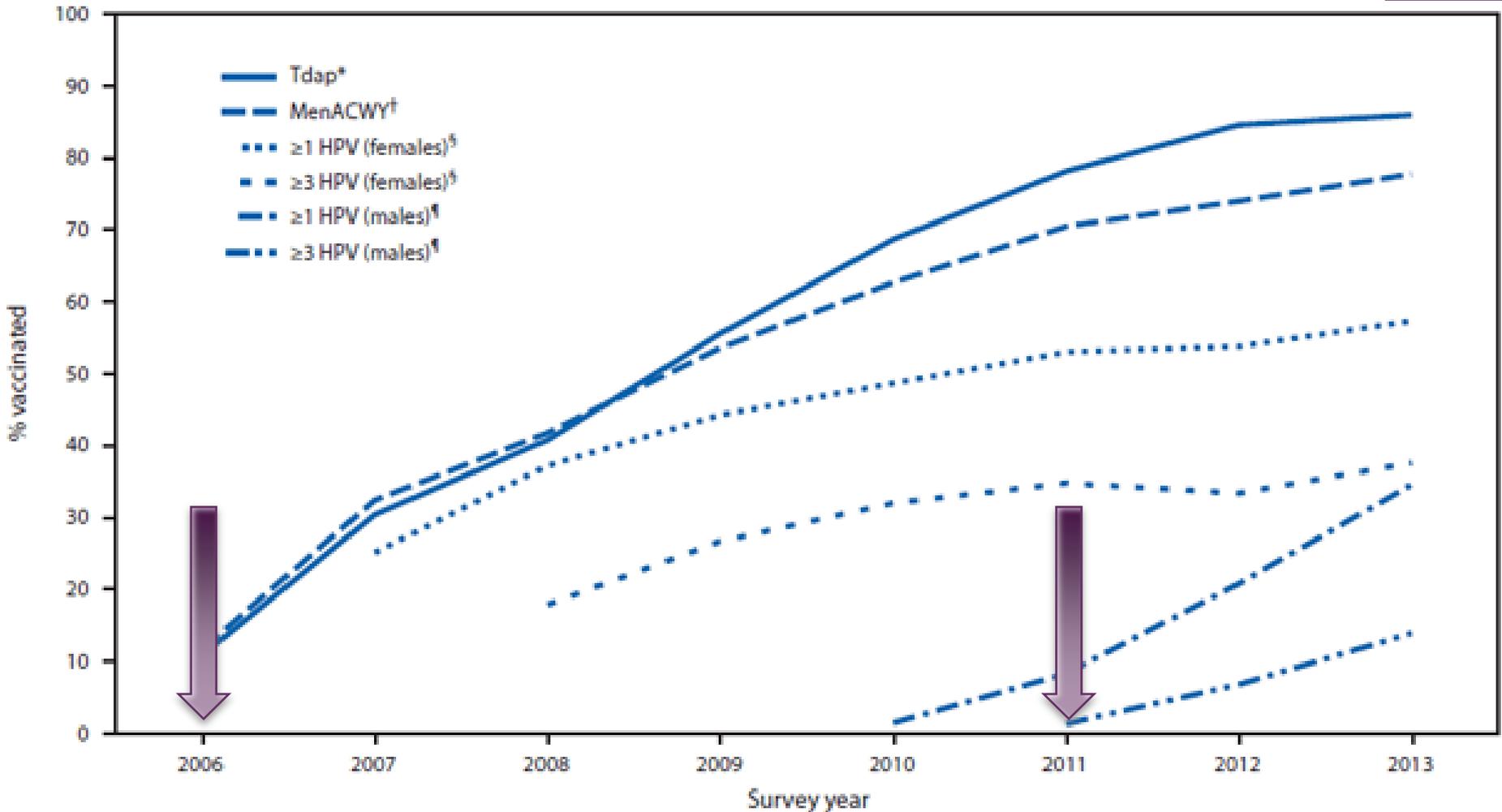
www.cdc.gov/vaccines/teens



HPV vaccine coverage

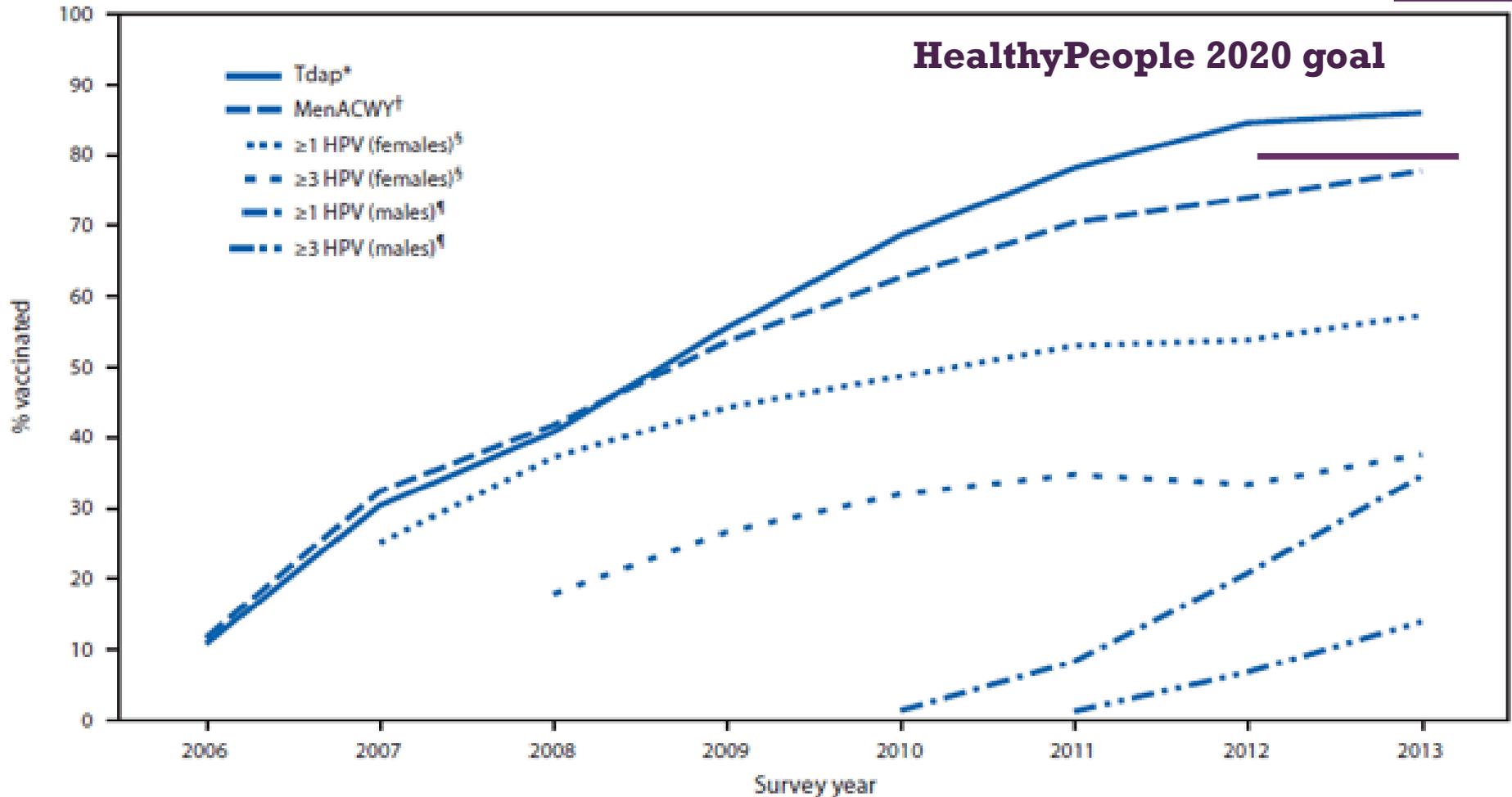


Estimated vaccination coverage with selected vaccines and doses among adolescents 13-17 years by survey year – NIS-teen, US 2006-2013





Estimated vaccination coverage with selected vaccines and doses among adolescents 13-17 years by survey year – NIS-teen, US 2006-2013

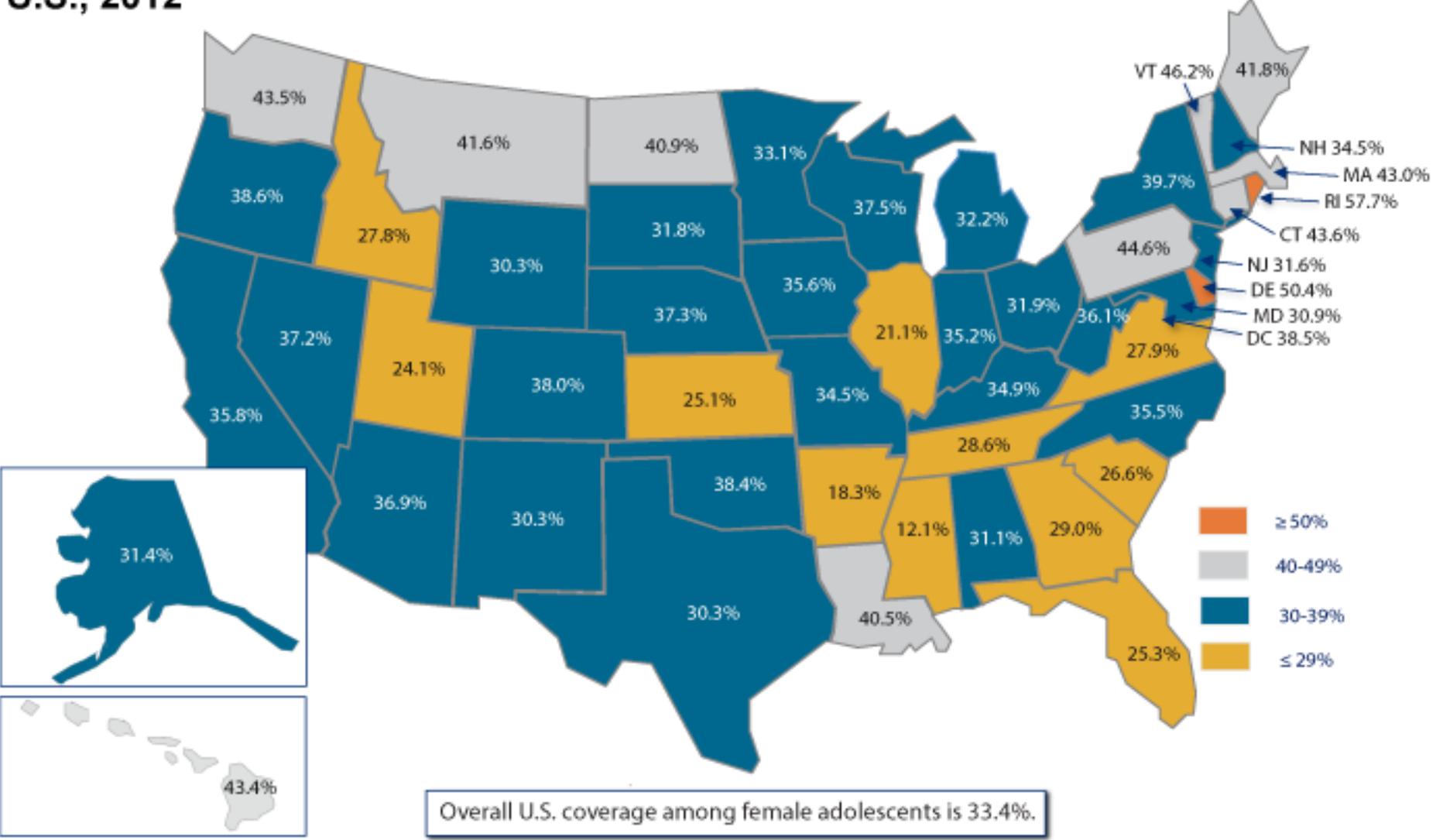


Vaccine	US (%)	NYS (%)
≥1 HPV – females	57.3	60.1
≥2 HPV – females	47.7	55.3
≥3 HPV –females	37.6	45.6
≥1 HPV – males	34.6	33.8
≥2 HPV – males	23.5	25.1
≥3 HPV –males	13.9	12.5

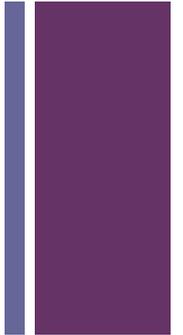


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≥2 HPV – males	23.5	25.1
≥3 HPV –males	13.9	12.5

Percentage of 13- to 17-Year-Old Girls Completing HPV Vaccine Series, U.S., 2012



+ HPV vaccination coverage



- If vaccination coverage was at 80%
 - Additional 53,000 cases of cervical cancer prevented during lifetime of those <12 years
- Each year that coverage does not increase
 - Additional 4,400 women will develop cervical cancer



Life threatening disease

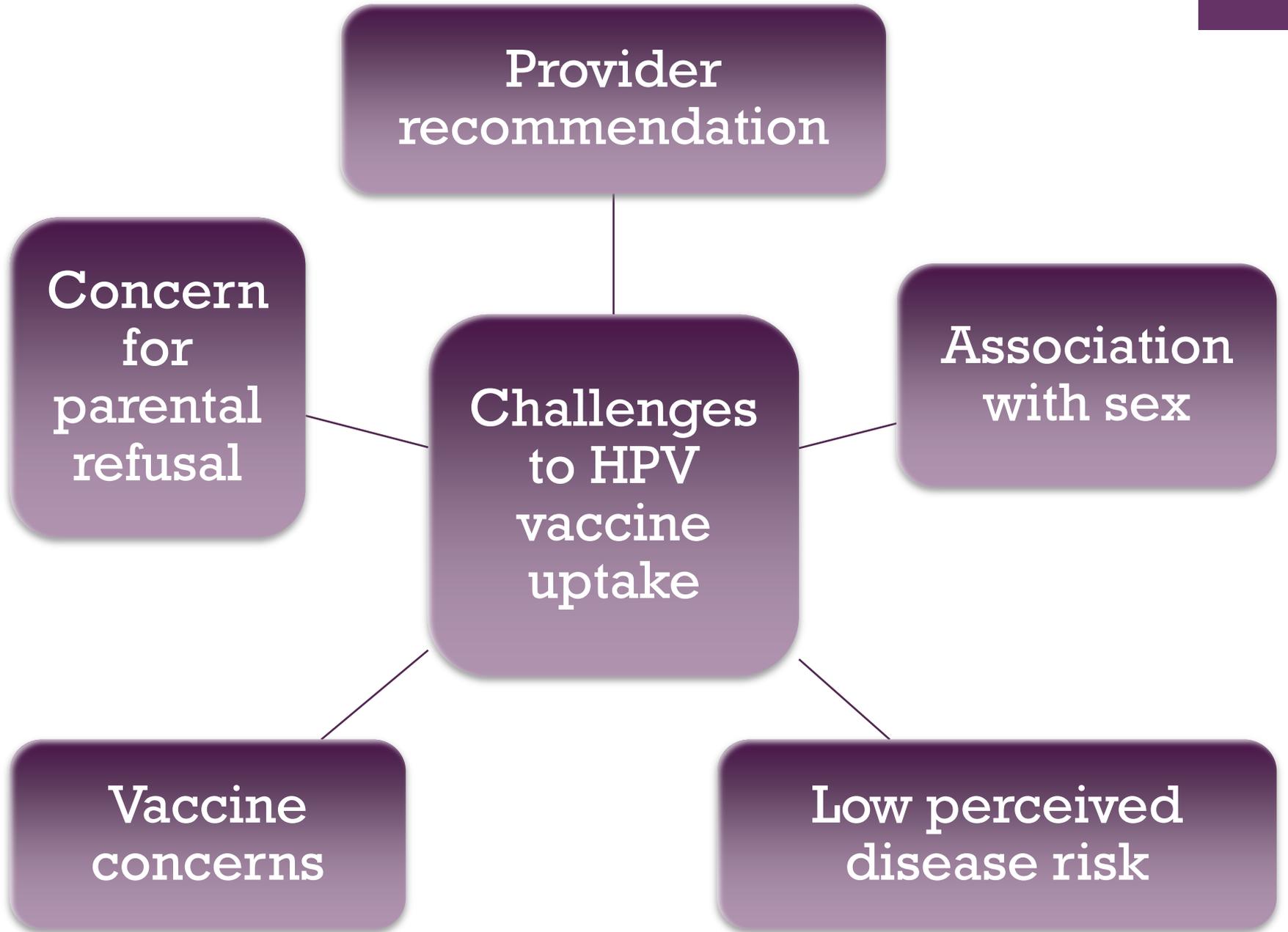
Effective vaccine

Very low vaccine uptake





Challenges in HPV vaccine uptake





Provider vaccine attitudes



Provider vaccine recommendation



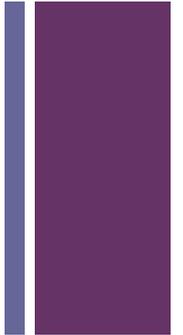
Parental vaccine acceptance



HPV vaccine acceptance

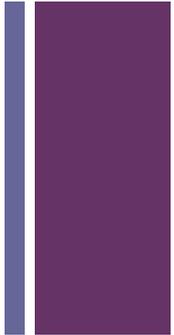


+ HPV vaccine attitudes



Factors associated with vaccine acceptance	Parent	Provider
Perception of disease severity	X	X
Belief that HPV vaccine prevents cancer	X	X
Patient is an older adolescent	X	X
Strong provider recommendation	X	

+ HPV vaccine acceptance



Factors associated with vaccine acceptance	Parent	Provider
Perception of disease severity	X	X

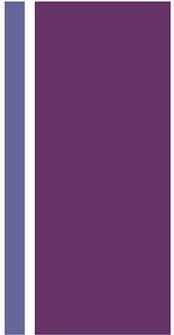
“I don’t get as scared of cervical cancer, just because...the Pap test is another screening method...and it’s not like HPV is going to kill the boys”

“Now, HPV, the truth is that a significant portion of young women will get HPV, but a very large percentage of them will also clear HPV and not actually go on to have cervical cancer. So it's one of those vaccines where I think it's a good idea, but...I don't really twist their arm or anything.”

BMC Pediatr. 2011; 11: 74

Perkins et al. Pediatrics. 2014; 134: e666-e674

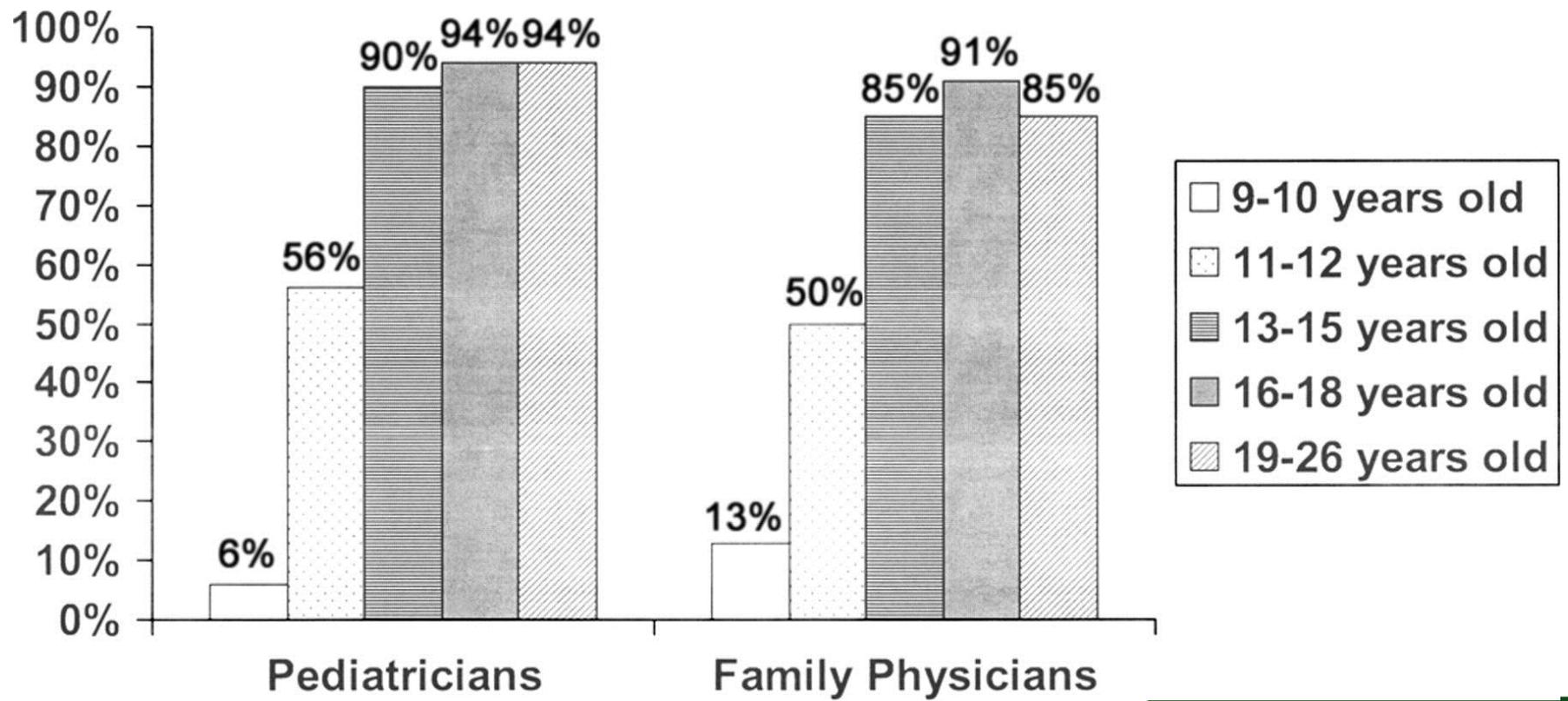
+ HPV vaccine acceptance



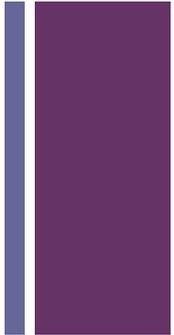
Factors associated with vaccine acceptance	Parent	Provider
Belief that HPV vaccine prevents cancer	X	X

788 adolescents from high school through graduate school → belief in vaccine preventing cancer was significantly associated with vaccine series completion

Factors associated with vaccine acceptance	Parent	Provider
Patient is an older adolescent	X	X



+ HPV vaccine acceptance



Factors associated with vaccine acceptance	Parent	Provider
Strong provider recommendation	X	

Associated with increased vaccine acceptance

Vaccine discussion initiation

Maintaining recommendation even with initial parental resistance

+ HPV vaccine acceptance

Factors associated with vaccine acceptance	Parent	Provider
Strong provider recommendation	X	

Providers recommend HPV vaccine in 1 of 2 ways
presenting HPV vaccine as routine as the other adolescent vaccines
presenting HPV vaccine as optional, highlighting risks and benefits

McRee AL, et al. J Pediatr Health Care. 2014; 28: 541-549

-- 76% of health care providers report recommending HPV vaccine to girls at ages 11-12 years most of the time

-- 46% of health care providers do so for boys

-- More than half of the providers prefer to offer HPV vaccine as an optional vaccine for girls (62%) and boys (69%) ages 11 to 12 years

+ HPV vaccine acceptance

Factors associated with vaccine acceptance	Parent	Provider
Strong provider recommendation	X	

“I do explain that it is optional, it’s not like you have to get it for school or anything like that”

“He said it was optional, we could talk about it later, and the others were not optional”

“When the doctor said it to me, it wasn’t like your daughter should have this, it was like this is an option. It’s like do you want tea or coffee”

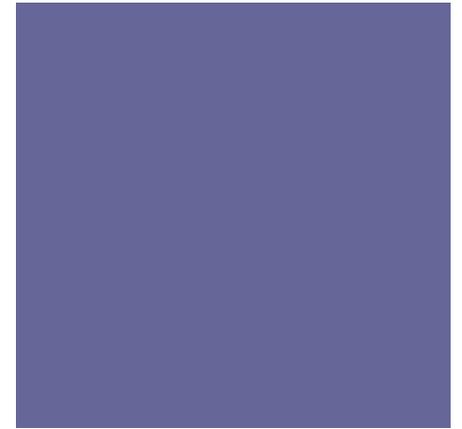
BMC Pediatr. 2011; 11: 74

Perkins et al. Pediatrics. 2014; 134: e666-e674

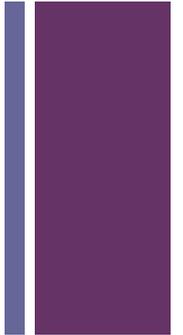
Offering vaccine vs recommending vaccine



HPV vaccine hesitancy

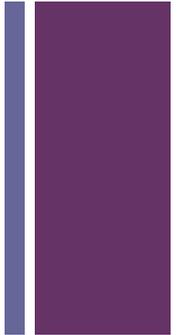


+ HPV vaccine attitudes



Factors associated with HPV vaccine hesitancy	Parent	Provider
Lack of provider recommendation	X	
Low perceived disease risk among adolescents	X	X
Vaccine safety concerns	X	X
Having to associate HPV vaccine with sexual activity	X	X
Concerns for parental refusal		X

+ HPV vaccine attitudes

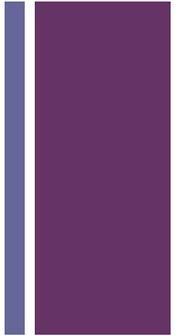


Factors associated with HPV vaccine hesitancy	Parent	Provider
Lack of provider recommendation	X	

Lack of provider recommendation is the single most commonly cited reason for parents not vaccinating their adolescents

788 adolescents high school through graduate school – lack of provider recommendation was significantly associated with non-vaccination

+ HPV vaccine attitudes



Factors associated with HPV vaccine hesitancy	Parent	Provider
Low perceived disease risk among adolescents	X	X

“It is probably more likely that they would die from meningococcal meningitis than die from cervical cancer”

2011 – 751 cases of meningococcal disease, reported case fatality rate ~10%

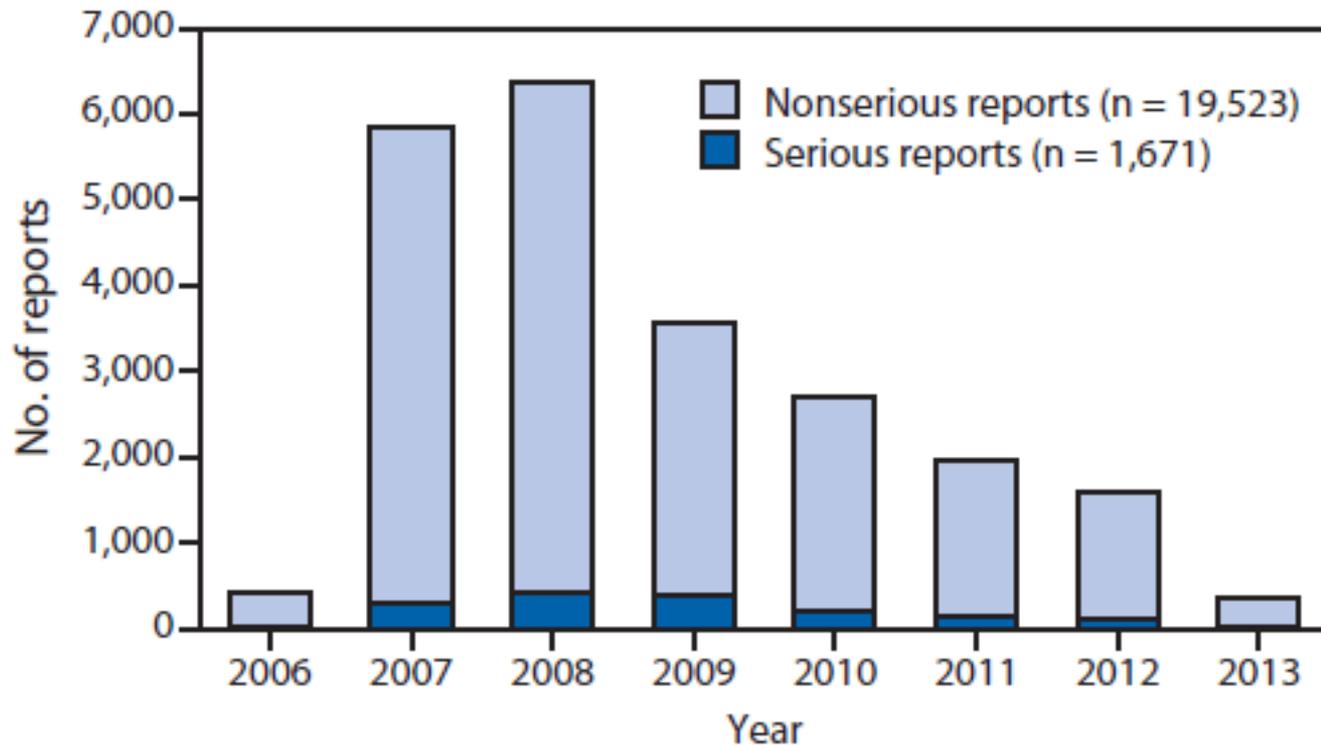
2011 – 12,000 women were diagnosed with cervical cancer
-- 4,000 women died from cervical cancer

BMC Pediatr. 2011; 11: 74

Perkins et al. Pediatrics. 2014; 134: e666-e674

+ HPV vaccine attitudes

Factors associated with HPV vaccine hesitancy	Parent	Provider
Vaccine safety concerns	X	X



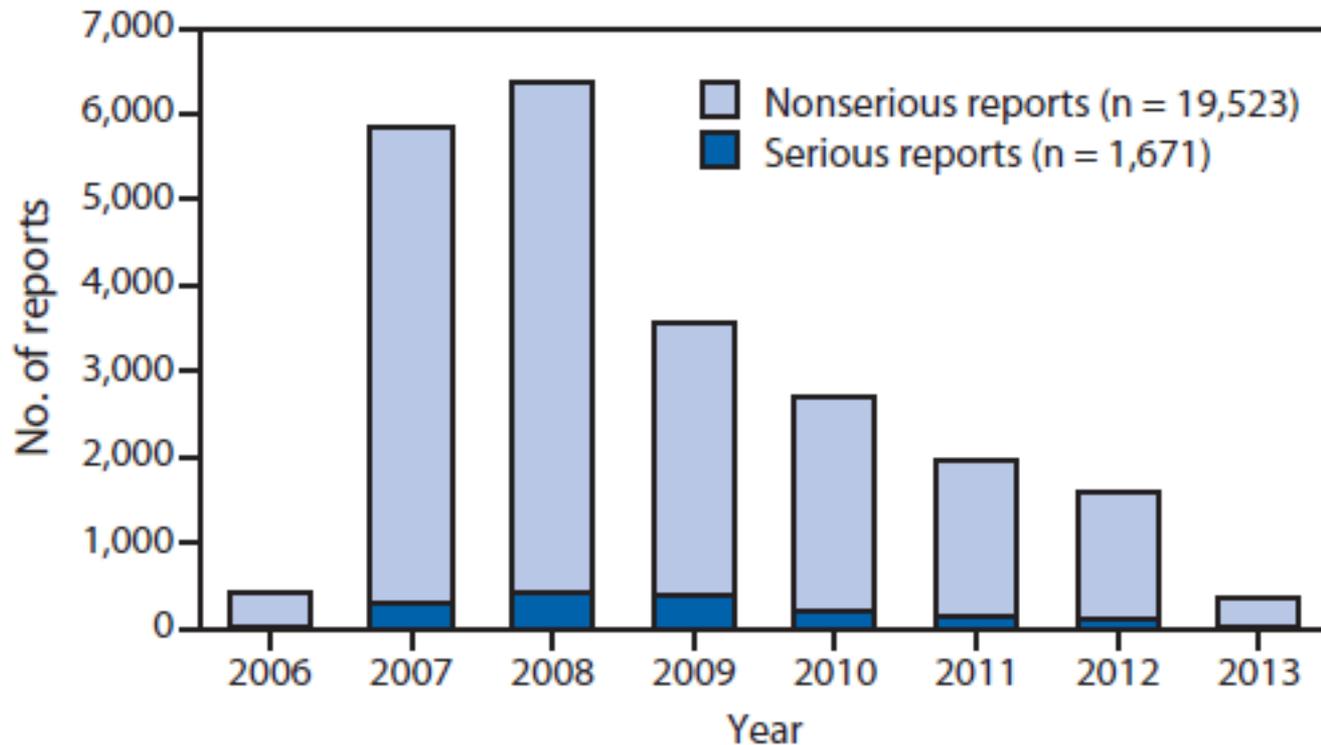
+ HPV vaccine attitudes

Factors associated with HPV vaccine hesitancy	Parent	Provider
Vaccine safety concerns	X	X



+ HPV vaccine attitudes

Factors associated with HPV vaccine hesitancy	Parent	Provider
Vaccine safety concerns	X	X



<http://www.cdc.gov/mmwr/preview/mmwrhtml/mm6229a4.htm>

+ HPV vaccine attitudes

Factors associated with HPV vaccine hesitancy	Parent	Provider
Having to associate HPV vaccine with sexual activity	X	X

Providers who believe it is necessary to discuss sexuality before recommending HPV vaccine

- Less likely to provide strong recommendation

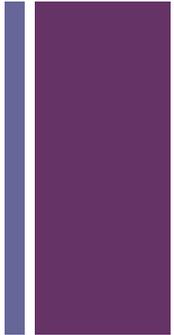
- Less likely to recommend HPV vaccine to younger adolescents

Surveyed AAP providers (NY NJ OH PA) from 2012-2014

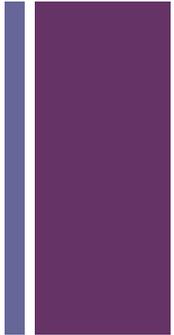
- 4% believed that administering HPV vaccine to adolescents will increase the likelihood of unprotected sexual activity in their patients

“If there is any real need to be giving it at 11 because they’re sexually active, then we have a much bigger problem than HPV”

“I rarely give it at 11 or 12. I most commonly give it in 8th to 10th grade range when sexual activity would put them at risk, rather than just age.”



+ HPV vaccine attitudes



Factors associated with HPV vaccine hesitancy	Parent	Provider
Concerns for parental refusal		X

54% of providers not strongly recommending HPV vaccine to 11-12 year olds believed that parents of this age group are more likely to refuse vaccine

Daley MF. Pediatrics. 2010; 126:425

Providers had lower odds of recommending HPV vaccine to 11 to 12 year olds if they report parents responded more frequently with requests to delay or refuse vaccine

McRee A. J Pediatr Health Care. 2014; 28: 541-549

“At the 11 year old visit, I anticipate that they are not going to do it and I talk to them about it”

Perkins et al. Pediatrics. 2014; 134: e666-e674



+ Improving adolescent HPV
vaccine coverage rates



How to improve vaccine coverage?

What we know

- HPV vaccine is safe and effective in cancer prevention
- Strong provider vaccine recommendation → increased vaccine acceptance
- Lack of provider recommendation main reason cited for non-vaccination
- Associating HPV with sex reduces the likelihood of vaccination in 11 and 12 year olds

What can we do?

- Provide strong vaccine recommendation at all eligible visits to reduce missed opportunities
- De-emphasize the association between HPV vaccine and sex
- Provide information regarding disease severity and vaccine safety and efficacy



How to improve vaccine coverage?

What can we do?

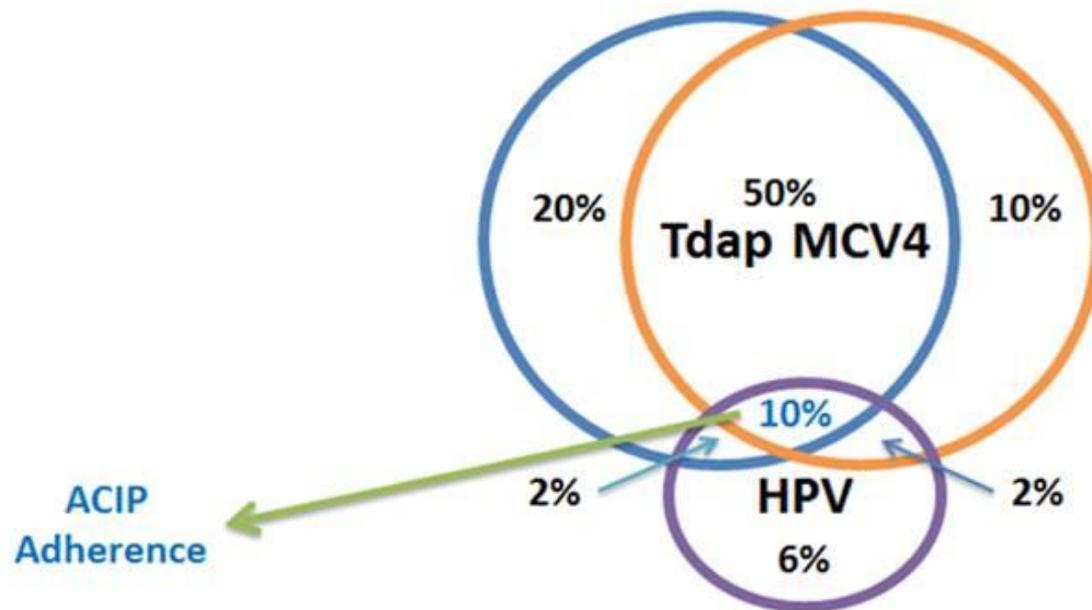
- **Provide strong vaccine recommendation at all eligible visits to reduce missed opportunities**
- De-emphasize the association between HPV vaccine and sex
- Provide information regarding disease severity and vaccine safety and efficacy

Wong et al. *J Adolesc Health*. 2013; 53: 492-7

Retrospective study found missed opportunity

- 82% MCV4
- 85% Tdap
- 82% HPV first dose, females

Figure 1: Vaccines given during the first vaccination visit among privately insured preteens in the US, 2010-12 (N = 1,245,336)

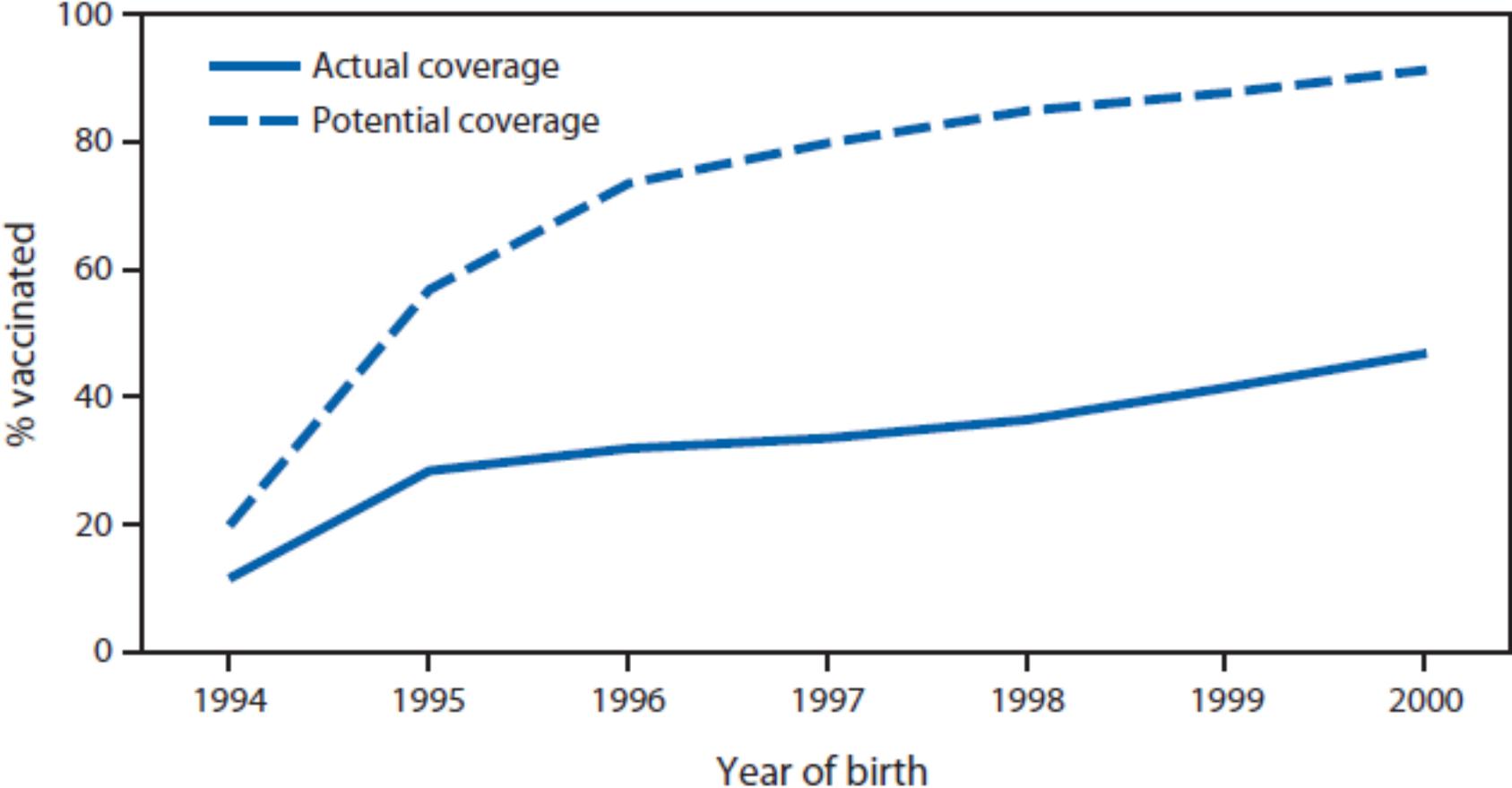


$$1 = P(\text{HPV only}) + P(\text{Tdap only}) + P(\text{MCV4 only}) + P(\text{HPV U Tdap}) + P(\text{HPV U MCV4}) + P(\text{Tdap U MCV4}) + P(\text{HPV U Tdap U MCV4})$$

Borse NN et al. Missed opportunities to adhere to the ACIP vaccine initiation schedule among privately insured preteens in the United States, 2010-2012. Poster presentation. IDWeek 2014



FIGURE. Actual and potentially achievable vaccination coverage with ≥ 1 dose of human papillomavirus (HPV) vaccine if missed vaccination opportunities had been eliminated among girls by age 13 years,* by birth cohort (1994–2000) —2007–2013 combined





How to improve vaccine coverage?

What can we do?

- De-emphasize the association between HPV vaccine and sex



HPV vaccine

is **CANCER PREVENTION.**

www.cdc.gov/vaccines/teens



U.S. Department of Health and Human Services
Centers for Disease Control and Prevention

GARDASIL
 (Human Papillomavirus Quadrivalent
 [Types 6, 11, 16, and 18] Vaccine, Recombinant)

Your **SON** or **DAUGHTER** could be

oneless
 person affected by HPV disease.

PARENTS:
 Why GARDASIL for your son or daughter?
 Find Out

**DON'T GET
 SCREWED
 BY CANCER**
 Get immunized against HPV



You can
CLOSE the DOOR
 to cancer.



TRUST US

*We're going to be ONE LESS
 Who WON'T get the
 HPV Vaccine*



*Studies have shown that 70% of new HPV infections clear within one year, and as many as 91% clear within two years.

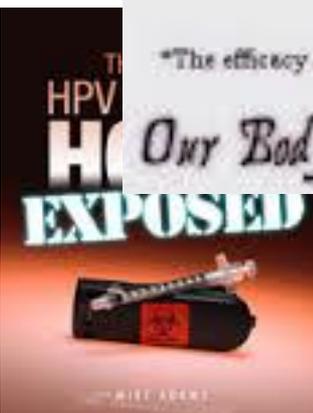
*Medical research is very clear that people who go on to get cancer are chronically selenium deficient.

*The vaccine itself may contribute to an increase in cancer, fetal abnormalities and miscarriage.

*The vaccine contains 225 mcg of Aluminum, a neurotoxin.

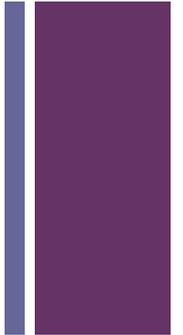
*The efficacy of the vaccine has not been proven. Nor long-term side-effects.

*Our Body * Our Future * Our Choice*





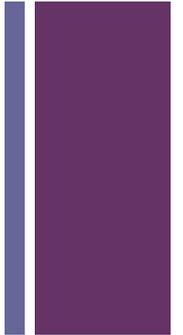
In summary...



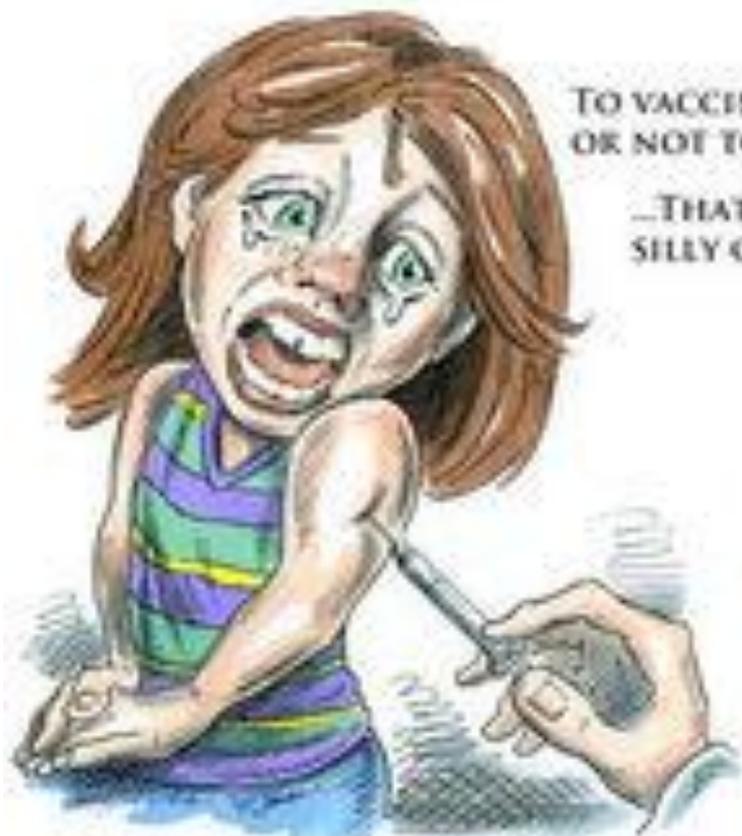
- HPV is associated with > 33,000 cancers and >6,000 deaths in the US each year
- HPV9 protects against 80% of HPV-associated cancers and is safe and effective
- HPV vaccine is recommended for adolescents starting at 11-12 years of age to protect prior to sexual debut, and to result in higher antibody titers when compared to immunized older adolescents
- Delay in vaccination results in increased nonvaccination
- Strong provider vaccine recommendation associated with increased vaccine acceptance and uptake



How can we improve adolescent HPV vaccination?



- Determine adolescent HPV vaccine coverage in the practice
- Educate providers regarding the importance of
 - HPV vaccine as cancer prevention
 - Strong vaccine recommendation despite parental resistance
 - Recommendation of HPV vaccine to eligible adolescents at well child, acute, and follow up visits to reduce missed opportunities
- Provide families with information regarding HPV disease severity, vaccine safety and efficacy
 - CDC tools, AAP tools, NYSDOH tools
- Vaccine tracking and provider feedback



TO VACCINATE,
OR NOT TO VACCINATE?

...THAT IS A
SILLY QUESTION.



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