

You Are the Key to New HPV Cancer Prevention

**Understanding the Burden of HPV Disease and the
Importance of the HPV Vaccine Recommendation**

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Financial Disclosure

- I have no conflict or interest with the manufacturer of any product mentioned in this course

Off-Label Disclosure

- I will discuss HPV vaccine in a manner that conflicts with the HPV package insert from the Food and Drug Administration (FDA)

Objectives

- Following this presentation the learner should be able to:
- Communicate the burden of HPV disease to their patients
- Schedule the HPV vaccination series according to Advisory Committee on Immunization Practices recommendations
- Anticipate the concerns of patients and parents with respect to this vaccine

Understanding the Burden

HPV INFECTION & DISEASE

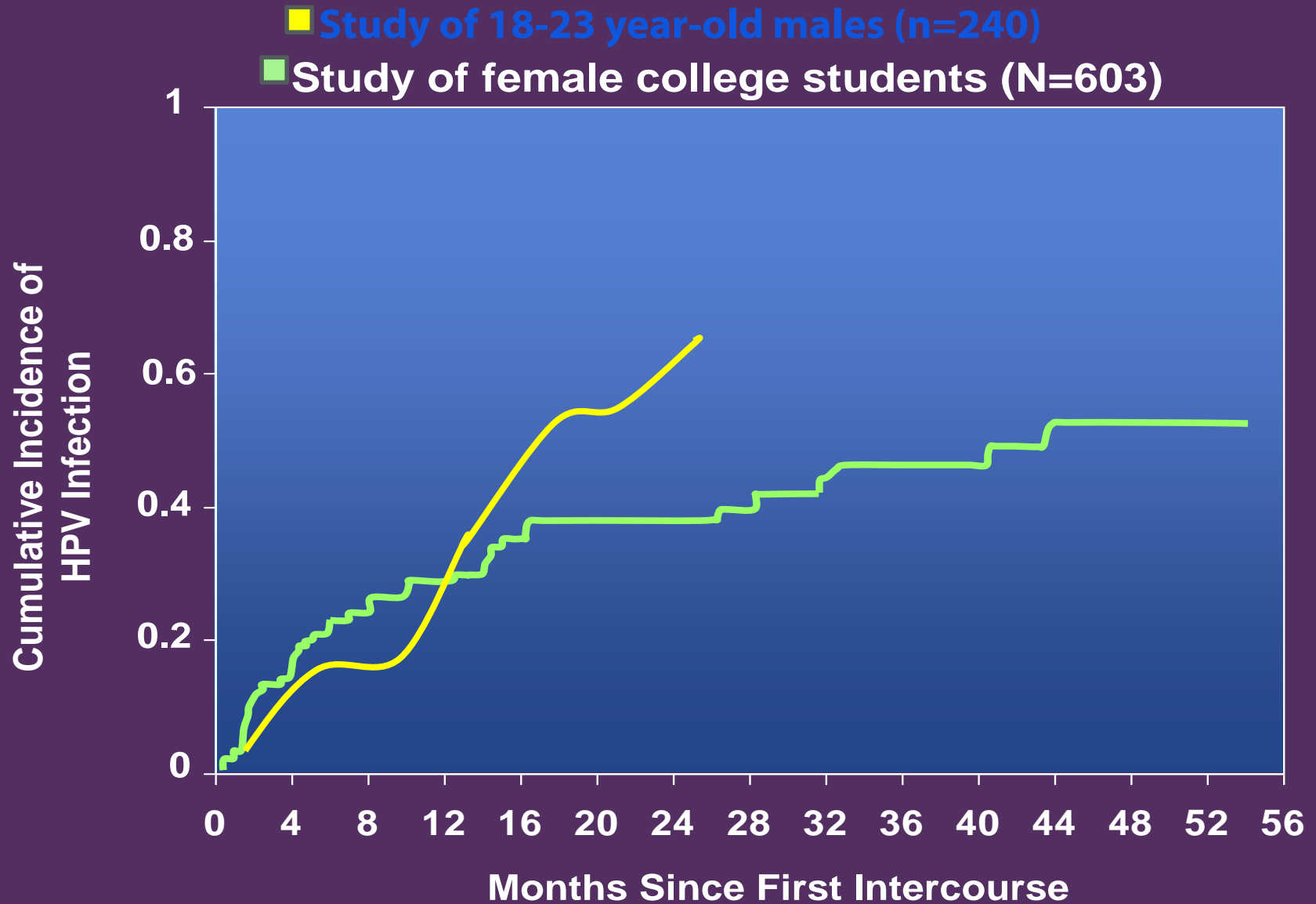
HPV Infection

- Almost females and males will be infected with at least one type of HPV at some point in their lives
 - Estimated 79 million Americans currently infected
 - 14 million new infections/year in the US
 - HPV infection is most common in people in their teens and early 20s
- Most people will never know that they have been infected

HPV Transmission

- HPV exposure can occur with any type of intimate sexual contact
- Intercourse is not necessary to become infected
- Nearly 50% of high school students have already engaged in sexual (vaginal-penile) intercourse
 - 1/3 of 9th graders and 2/3 of 12th graders have engaged in sexual intercourse
 - 24% of high school seniors have had sexual intercourse with 4 or more partners

Rapid Acquisition of HPV Following Sexual Debut



From Winer RL, Lee S-K, Hughes JP, Adam DE, Kiviat NB, Koutsky LA. Genital human papillomavirus infection: incidence and risk factors in a cohort of female university students. *Am J Epidemiol.* 2003;157:218–226. Reprinted with the permission of Oxford University Press.

HPV is Found in Virgins

- Study examined the frequency of vaginal HPV and the association with non-coital sexual behavior in longitudinally followed cohort of adolescent women without prior vaginal intercourse
- HPV was detected in 46% of women prior to first vaginal sex
- 70% of these women reported non-coital behaviors that may in part explain genital transmission

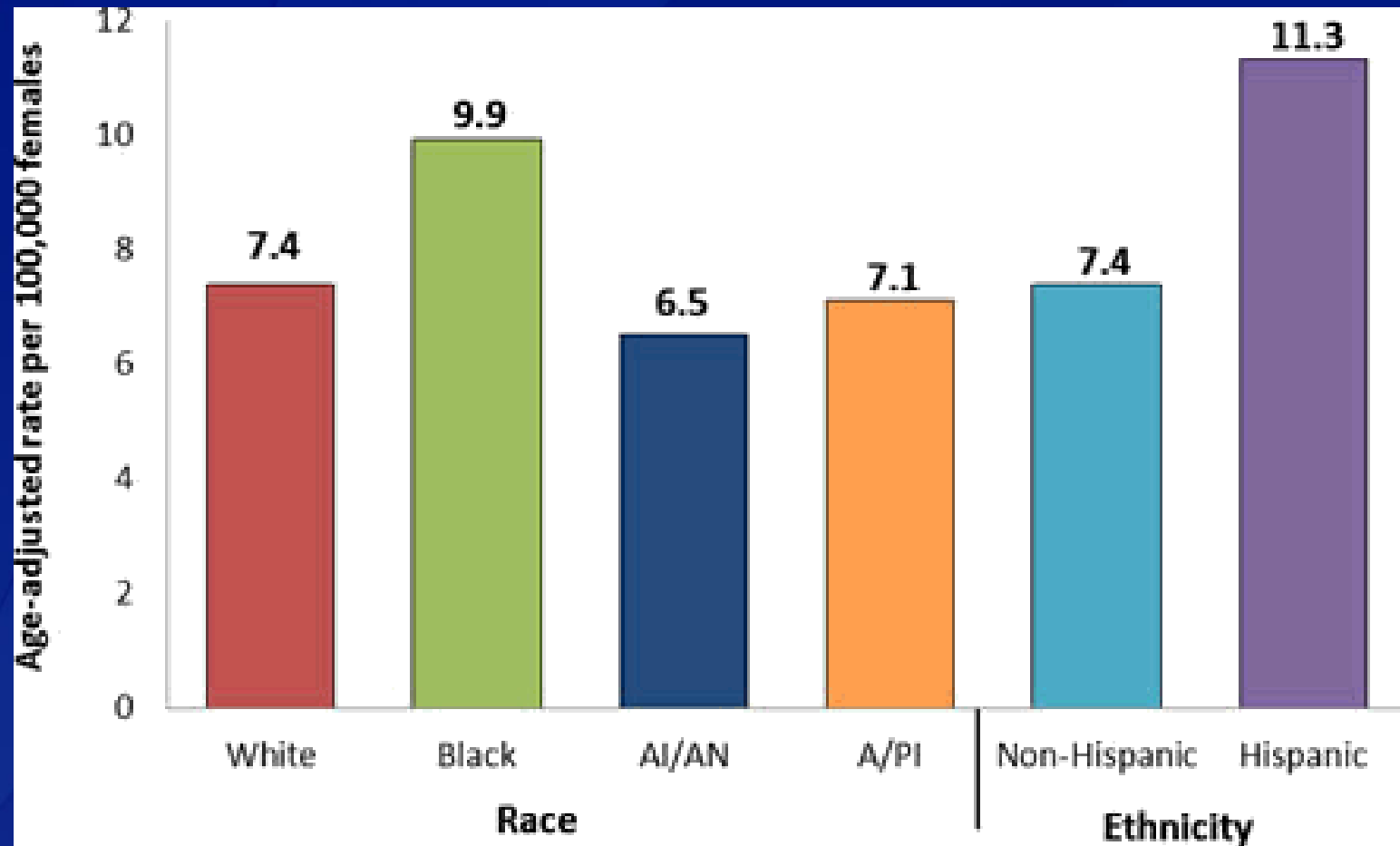
Human Papillomavirus (HPV) Disease

- ❑ **More than 100 types**
- ❑ **Established cause of cervical and other anogenital cancers**

Cervical Cancer

- Cervical cancer is the most common HPV-associated cancer among women
 - 500,000+ new cases and 275,000 attributable deaths world-wide in 2008
 - 12,000+ new cases and 4,000 attributable deaths in 2011 in the U.S.
- 25.9% cervical cancers occur in women who are between the ages of 35 and 44
 - 14% between 20 and 34
 - 23.9% between 45 and 54

HPV-Associated Cervical Cancer Rates by Race and Ethnicity, United States, 2004–2008

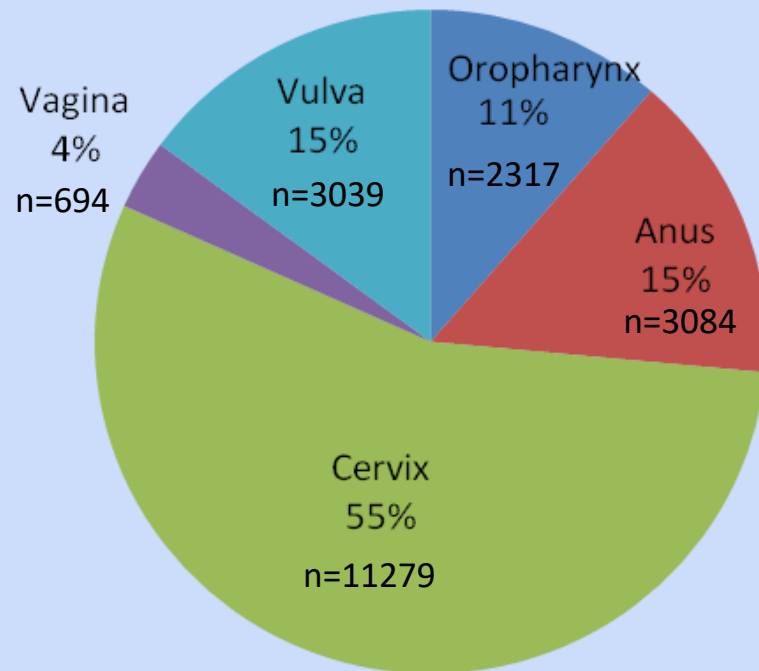


Annual Report to the Nation on the Status of Cancer: HPV-Associated Cancers

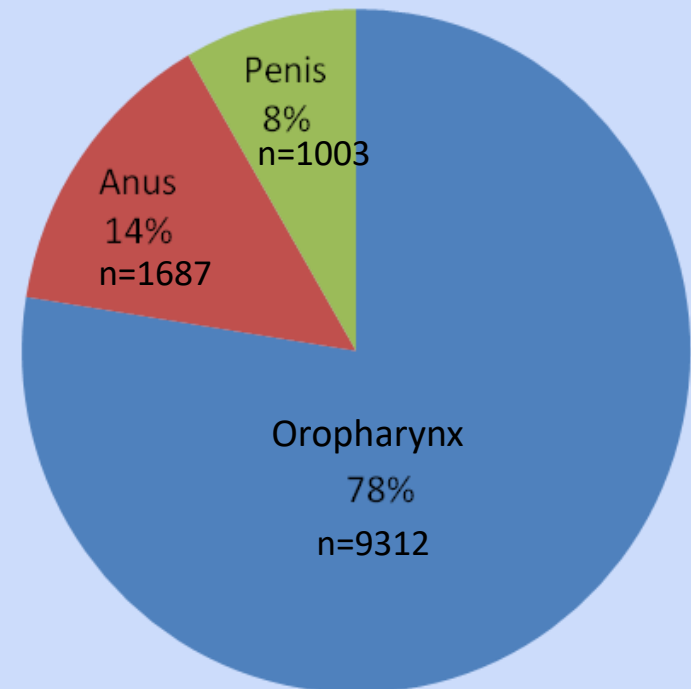
- From 2000 to 2009, oral cancer rates increased
 - 4.9% for Native American men
 - 3.9% for white men
 - 1.7% for white women
 - 1% for Asian men
- Anal cancer rates doubled from 1975 to 2009
- Vulvar cancer rates rose for white and African-American women
- Penile cancer rates increased among Asian men

Average Number of New HPV-Associated Cancers by Sex, in the United States, 2005-2009

Women (N=20,413)



Men (N=12,002)



HPV-Associated Oropharyngeal Cancers

- Prevalence increased from 16.3% (1984-89) to 71.7% (2000-04)
- Population-level incidence of HPV-positive cancers increased by 225% while HPV-negative cancers declined by 50%

If trends continue, the annual number of HPV-positive oropharyngeal cancers is expected to surpass the annual number of cervical cancers by the year 2020

Complications related to current methods of cervical cancer treatment/prevention

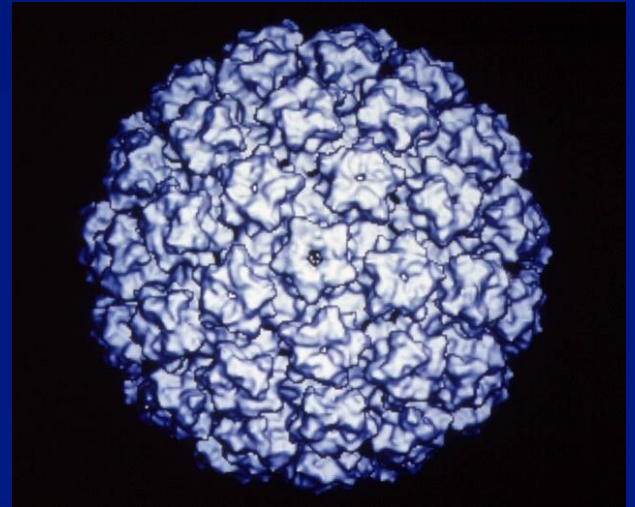
- Infertility due to treatment of cervical cancer by hysterectomy
- Cervical conization and loop electrosurgical excision procedure (LEEP) procedures associated with adverse obstetric morbidity
- Subsequent pregnancies are at risk of
 - Perinatal mortality
 - Severe and extreme preterm delivery (<32 or <28 weeks)
 - Severe and extreme low birth weight (< 2000g or 1500g)

These outcomes have a considerable impact—not only on the mothers and infants concerned—but also on the cost of neonatal intensive care

HPV VACCINE

HPV Prophylactic 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



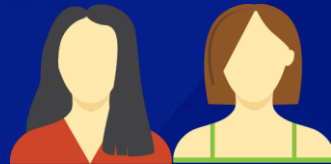
HPV VLP

HPV Associated Disease

TYPE

WOMEN

MEN



16/18

70% of cervical cancers
70% of anal/genital
cancers

70% of anal cancers

6/11

90% of genital warts
90% of RRP* lesions

90% if genital warts
90% of RRP lesions

Transmission to women

* RRP = recurrent respiratory papillomatosis

HPV Vaccines

Vaccine	HPV types	Gender	FDA Approved Ages
HPV4 (Gardasil, Merck)	16 and 18 (high risk) 6 and 11 (low risk)	females AND males	9 through 26 years
HPV2 (Cervarix, GSK)	16 and 18 (high risk)	females	10 through 25 years

HPV Vaccine



Quadrivalent/HPV4 (Gardasil)	Name	Bivalent/HPV2 (Cervarix)
Merck	Manufacturer	GlaxoSmithKline
Hypersensitivity to yeast	Contraindications	Hypersensitivity to latex (latex only contained in pre-filled syringes, not single-dose vials)
3 dose series: 0, 2, 6 months	Schedule (IM)	3 dose series: 0, 1, 6 months

Efficacy: Human Papillomavirus Vaccines

- ❑ High efficacy without evidence of infection with vaccine HPV types**
- ❑ No evidence that the vaccine had efficacy against existing disease or infection**
- ❑ Prior infection with one HPV type did not diminish efficacy of the vaccine against other vaccine HPV types**
- ❑ HPV4 reduces the risk of anal cancers and genital warts in males**

ACIP Recommendation and AAP Guidelines for HPV Vaccine

- Routine HPV vaccination recommended for both males and females ages 11-12 years
- Catch-up ages 13-21 years for males; 13-26 for females
- Permissive use ages 9-10 years for both males and females; 22-26 for males

Recommendation for Females

- Either bivalent HPV vaccine (Cervarix) or quadrivalent HPV vaccine (Gardasil) recommended for girls at age 11 or 12 years for prevention of cervical cancer and precancer
 - Also for girls 13 through 26 who haven't started or completed series
 - Only quadrivalent HPV vaccine (Gardasil) also for prevention of vaginal, vulvar, and anal cancers, as well as genital warts.

Recommendation for Males

- Quadrivalent HPV vaccine (Gardasil) recommended for boys at age 11 or 12 years for prevention of anal cancer and genital warts
 - Also for boys 13 through 21 who haven't started or completed series
 - Young men, 22 through 26 years of age, may get the vaccine
 - Teen boys and young men through age 26 who identify as gay or bisexual and haven't started or completed series should be vaccinated

HPV Vaccination Schedule

- ❑ **Recommended schedule is 0, 1-2, 6 months**
 - Following the recommended schedule is preferred
- ❑ **Minimum intervals**
 - 4 weeks between doses 1 and 2*
 - 12 weeks between doses 2 and 3
 - 24 weeks between doses 1 and 3
- ❑ **The vaccination series can be started as young as 9 years of age at the clinician's discretion**

* Off-label ACIP recommendation- HPV4 only

HPV Vaccine Safety

- The most common adverse events reported were considered mild
- For serious adverse events reported, no unusual pattern or clustering that would suggest that the events were caused by the HPV vaccine
- These findings are similar to the safety reviews of MCV4 and Tdap vaccines
- 57 million doses of HPV vaccine distributed in US since 2006

HPV Vaccine Safety Data Sources

- Post-licensure safety data (VAERS)¹
- Post-licensure observational comparative studies (VSD)²
- Ongoing monitoring by CDC and FDA
- Post-licensure commitments from manufacturers
 - Vaccine in pregnancy registries
 - Long term follow-up in Nordic countries
- Official reviews
 - WHO's Global Advisory Committee on Vaccine Safety³
 - Institute of Medicine's report on adverse effects and vaccines, 2011⁴

¹Vaccine Adverse Events Reporting System, <http://vaers.hhs.gov/index>

²Vaccine Safety Datalink, <http://www.cdc.gov/vaccinesafety/Activities/VSD.html>

³http://www.who.int/vaccine_safety/Jun_2009/en/

⁴<http://www.iom.edu/Reports/2011/Adverse-Effects-of-Vaccines-Evidence-and-Causality.aspx>

HPV Vaccine Contraindications and Precautions

❑ **Contraindication**

- Severe allergic reaction to a vaccine component or following a prior dose
- FYI - HPV2 prefilled syringe contains latex

❑ **Precaution**

- Moderate or severe acute illnesses (defer until symptoms improve)

HPV Vaccination During Pregnancy

- ❑ Initiation of the vaccine series should be delayed until after completion of pregnancy**
- ❑ If a woman is found to be pregnant after initiating the vaccination series, remaining doses should be delayed until after the pregnancy**
- ❑ If a vaccine dose has been administered during pregnancy, there is no indication for intervention**
- ❑ Women vaccinated during pregnancy should be reported to the respective manufacturer**
 - Telephone numbers are in the package insert

HPV Vaccine Impact: HPV Prevalence Studies

- NHANES Study
 - National Health and Nutrition Examination Survey (NHANES) data used to compare HPV prevalence before the start of the HPV vaccination program with prevalence from the first four years after vaccine introduction
 - In 14-19 year olds, vaccine-type HPV prevalence decreased 56 percent, from 11.5 percent in 2003-2006 to 5.1 percent in 2007-2010
 - Other age groups did not show a statistically significant difference over time
 - The research showed that vaccine effectiveness for prevention of infection was an estimated 82 percent

HPV Vaccine Impact: HPV Prevalence Studies, Continued

- Clinic-Based Studies
 - Significant decrease from 24.0% to 5.3% in HPV vaccine type prevalence in at-risk sexually active females 14-17 years of age attending 3 urban primary care clinics from 1999-2005, compared to a similar group of women who attended the same 3 clinics in 2010
 - Significant declines in vaccine type HPV prevalence in both vaccinated and unvaccinated women aged 13-26 years who attended primary care clinics from 2009-2010 compared to those from the pre-vaccine period (2006-2007)

HPV Vaccine Impact: Genital Warts Studies

- Ecologic analysis used health claims data to examine trends in anogenital warts from 2003-2010 among a large group of private health insurance enrollees
 - The study found significant declines after 2007 in females aged 15-19 year (38% decrease from 2.9/1000 PY in 2006 to 1.8/1000 PY in 2010)
 - Smaller declines were observed among those 21-30 years but not in those over 30 years
- A similar study evaluated genital wart trends in males and females attending public family planning clinics and found
 - Significant decrease of 35% (.94% to .61%) in females under 21 years of age and a 19% decrease in males less than 21 years
 - No decreases were reported in the older males or females

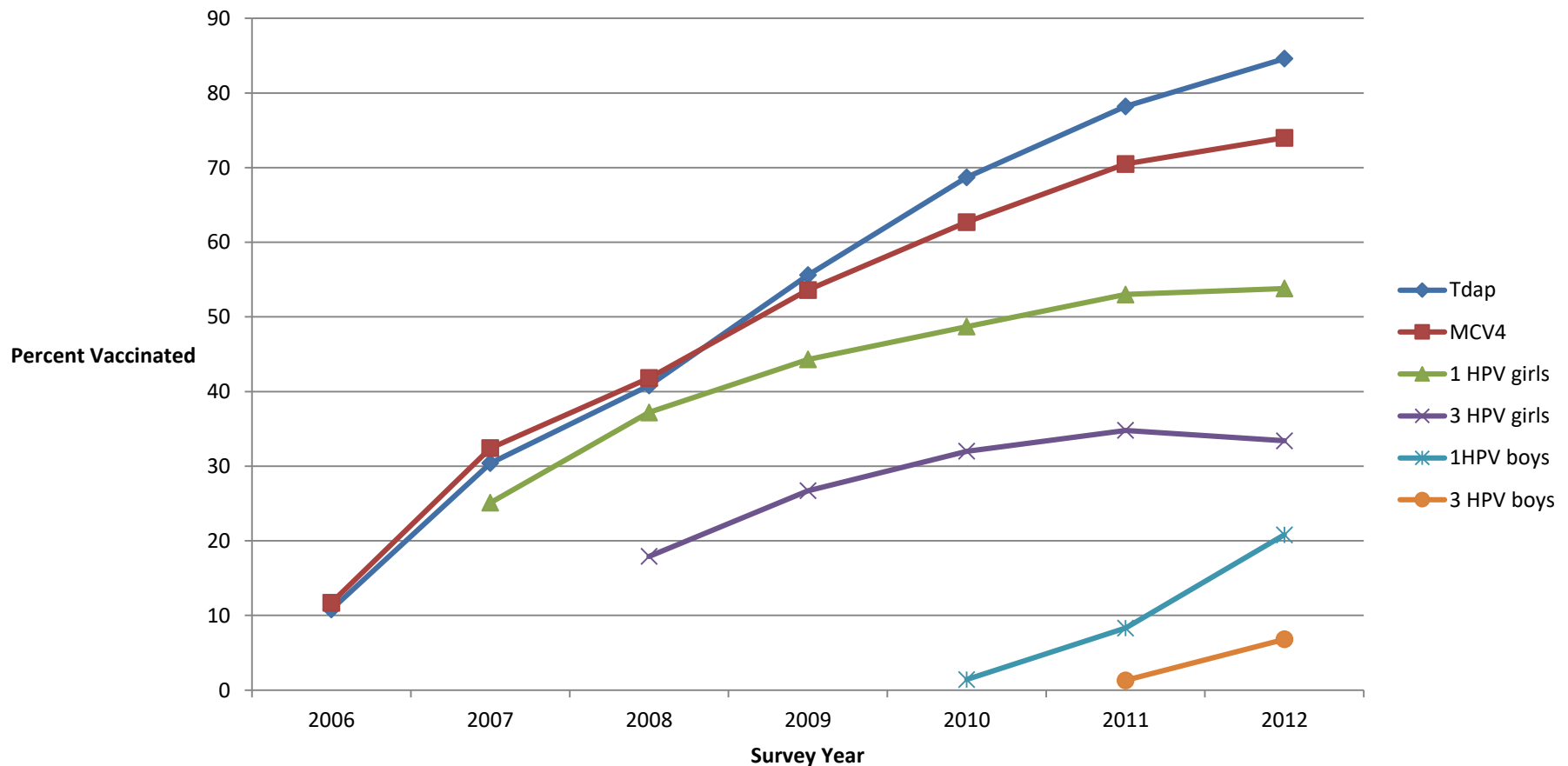
HPV Vaccine Impact: High HPV Vaccine Coverage in Australia

- 80% of school-age girls in Australia are fully vaccinated
- High-grade cervical lesions have declined in women less than 18 years of age
- For vaccine-eligible females, the proportion of genital warts cases declined dramatically by 93%
- Genital warts have declined by 82% among males of the same age, indicating herd immunity

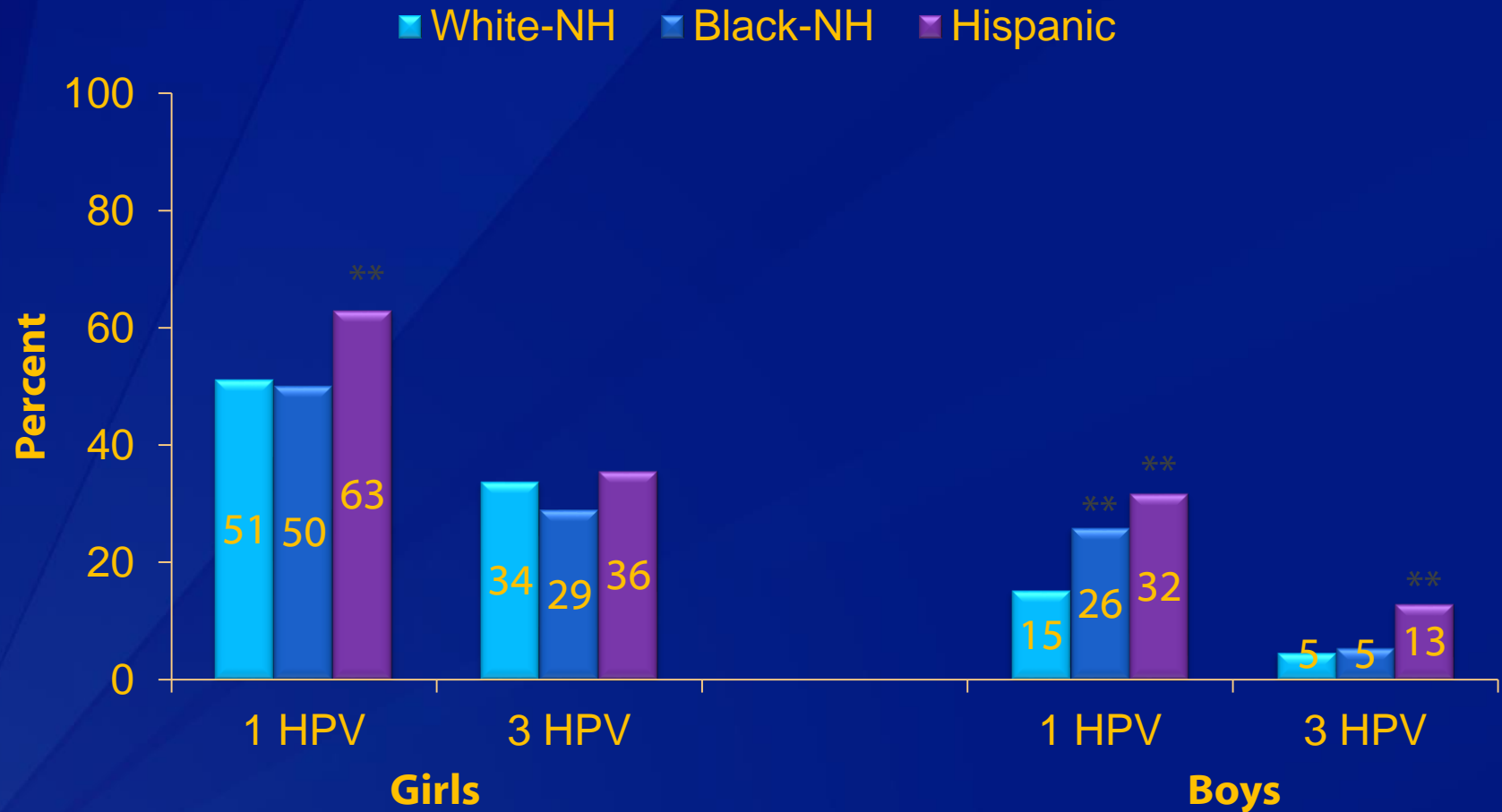
Garland et al, Prev Med 2011

Ali et al, BMJ 2013

National Estimated Vaccination Coverage Levels among Adolescents 13-17 Years, National Immunization Survey-Teen, 2006-2012



HPV Vaccination Estimates among Adolescents 13-17 Years by Race/Ethnicity, NIS-Teen 2012



** Statistically different ($P < 0.05$) from White-NH.

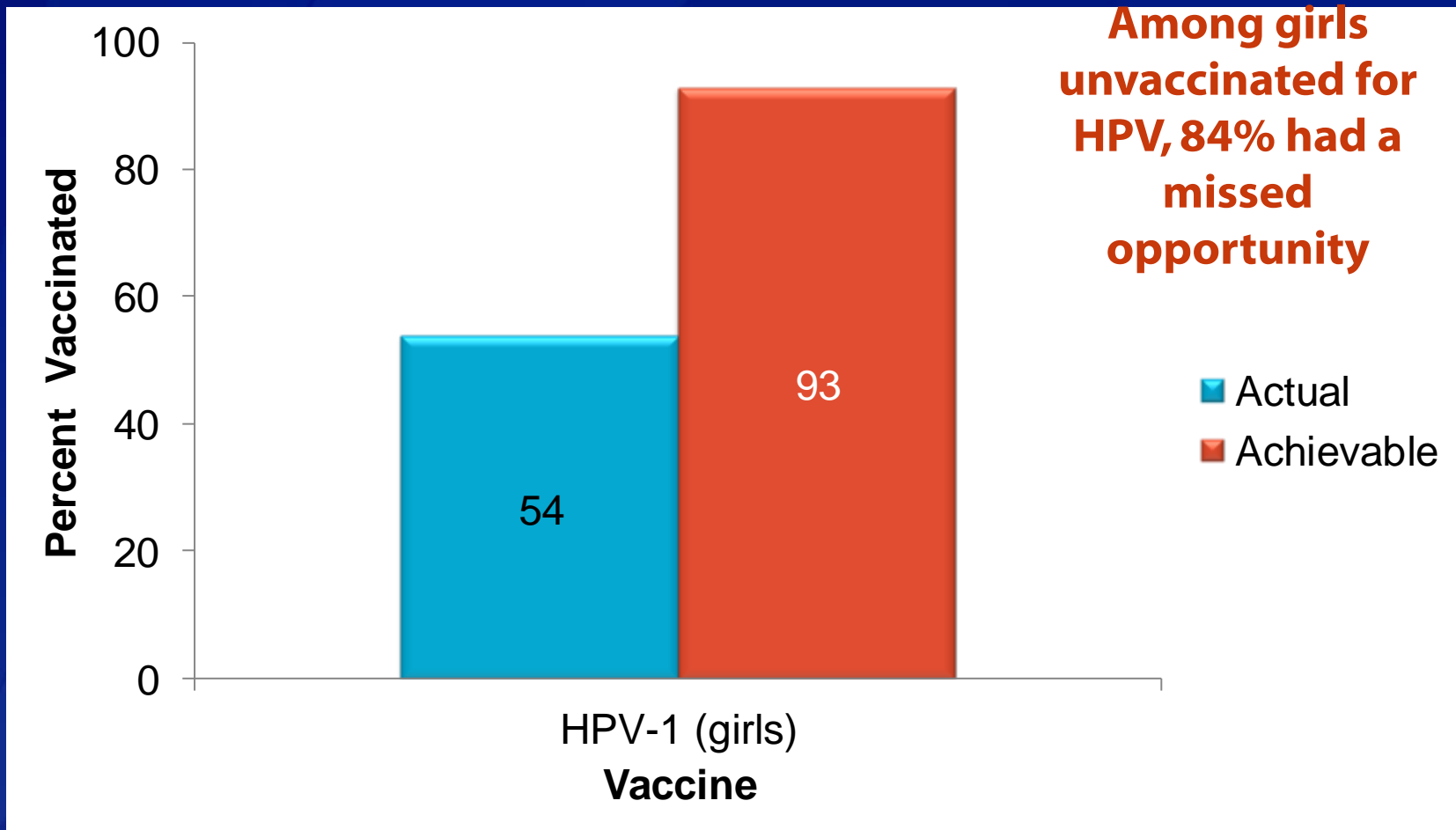
Why We Need to Do Better in HPV Vaccination of 12 year olds

- **Currently 26 million girls <13 yo in the US; If none of these girls are vaccinated then:**
 - **168,400 will develop cervical cancer and**
 - **54,100 will die from it**
- **Vaccinating 30% would prevent 45,500 of these cases and 14,600 deaths**
- **Vaccinating 80% would prevent 98,800 cases and 31,700 deaths**

Why We Need to Do Better in HPV Vaccination of 12 year olds

- ❑ For each year we stay at 30% coverage instead of achieving 80%, 4,400 future cervical cancer cases and 1400 cervical cancer deaths will occur.

Actual and Achievable Vaccination Coverage if Missed Opportunities Were Eliminated: Adolescents 13-17 Years, NIS-Teen 2012



Missed opportunity: Encounter when some, but not all ACIP-recommended vaccines are given.

HPV-1: Receipt of at least one dose of HPV.

Avoid Missed Opportunities

- HPV vaccine can safely be given at the same time as the other recommended adolescent vaccines
- Provide HPV vaccine during routine sports, or camp physicals
- Review immunization record even at acute care visits
- Encourage parents to keep accurate vaccination records and to review the immunization schedule
- Systems interventions depend on clinician commitment- determine what would work best for YOUR practice

The Perfect Storm

- Why is HPV vaccine different?
 - HPV vaccine issues sensationalized by popular media
 - Different reasons for why some girls and boys don't get the first shot and why some don't finish all 3 shots
 - Parents think sexuality instead of cancer prevention
 - Some clinicians aren't giving strong recommendations
 - Parents have questions that are seen as hesitation by some doctors
 - Phased girls-then-boys recommendations initially confusing to parents
 - Systems interventions to improve coverage rates depend on clinician commitment

Talking about HPV vaccine

FRAMING THE CONVERSATION

Tips and Time-savers for Talking with Parents about HPV Vaccine

Recommend the HPV vaccine series the same way you recommend the other adolescent vaccines. For example, you can say “Your child needs these shots today,” and name all of the vaccines recommended for the child’s age.

Parents may be interested in vaccinating, yet still have questions. Taking the time to listen to parents’ questions helps you save time and give an effective response. CDC research shows these straightforward messages work with parents when discussing HPV vaccine—and are easy for you or your staff to deliver.



CDC RESEARCH SHOWS:

The “HPV vaccine is cancer prevention” message resonates strongly with parents. In addition, studies show that a strong recommendation from you is the single best predictor of vaccination.

TRY SAYING:

HPV vaccine is very important because it prevents cancer. I want your child to be protected from cancer. That’s why I’m recommending that your daughter/son receive the first dose of HPV vaccine today.

CDC RESEARCH SHOWS:

Disease prevalence is not understood, and parents are unclear about what the vaccine actually protects against.

TRY SAYING:

HPV can cause cancers of the cervix, vagina, and vulva in women, cancer of the penis in men, and cancers of the anus and the mouth or throat in both women and men. There are about 26,000 of these cancers each year—and most could be prevented with HPV vaccine. There are also many more precancerous conditions requiring treatment that can have lasting effects.

CDC RESEARCH SHOWS:

Parents want a concrete reason to understand the recommendation that 11–12 year olds receive HPV vaccine.

TRY SAYING:

We’re vaccinating today so your child will have the best protection possible long before the start of any kind of sexual activity. We vaccinate people well before they are exposed to an infection, as is the case with measles and the other recommended childhood vaccines. Similarly, we want to vaccinate children well before they get exposed to HPV.

CDC RESEARCH SHOWS:

Parents may be concerned that vaccinating may be perceived by the child as permission to have sex.

TRY SAYING:

Research has shown that getting the HPV vaccine does not make kids more likely to be sexually active or start having sex at a younger age.

CDC RESEARCH SHOWS:

Parents might believe their child won’t be exposed to HPV because they aren’t sexually active or may not be for a long time.

TRY SAYING:

HPV is so common that almost everyone will be infected at some point. It is estimated that 79 million Americans are currently infected with

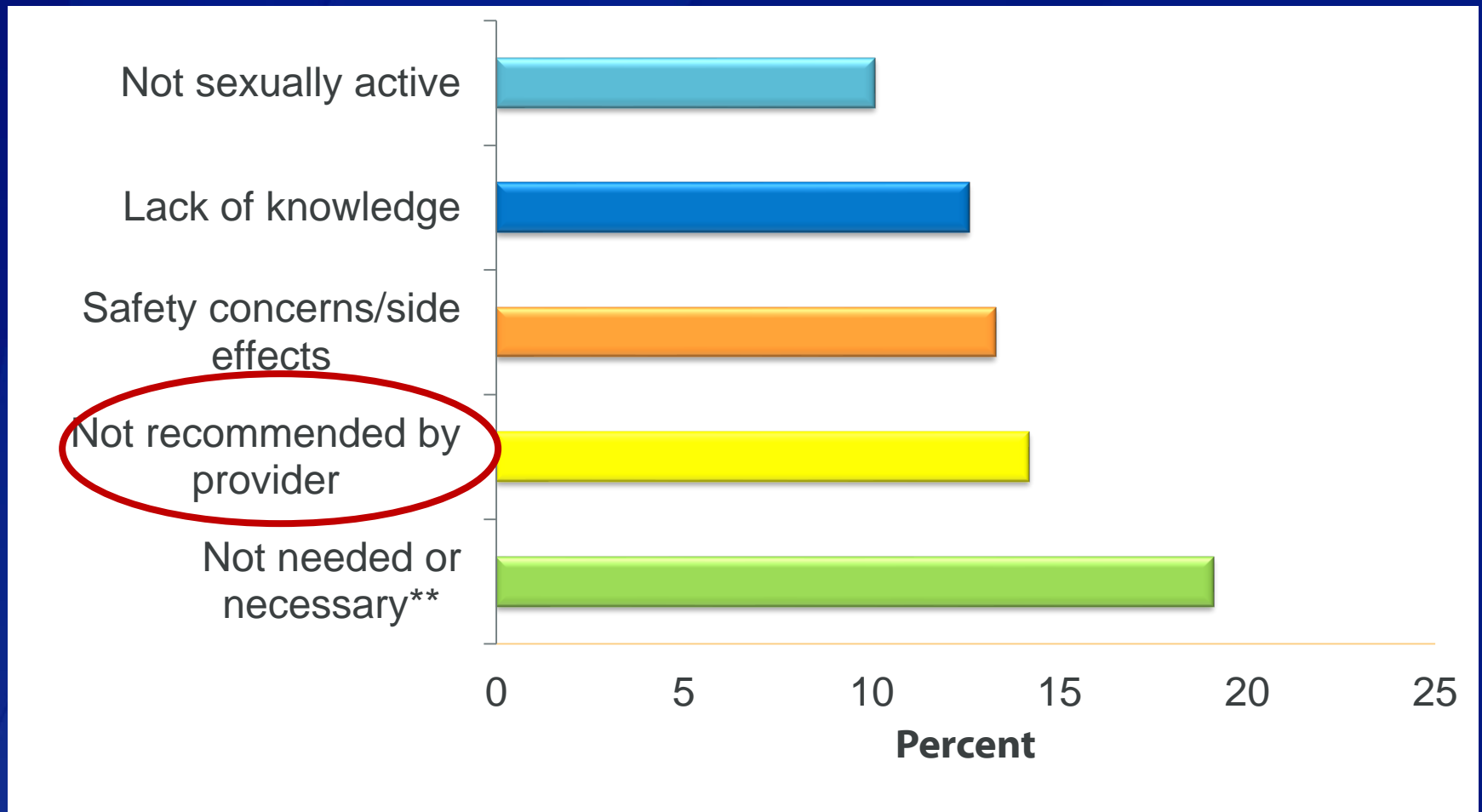
What's in a Recommendation?

- Studies consistently show that a strong recommendation from you is the single best predictor of vaccination
 - In focus groups and surveys with moms, having a doctor recommend or not recommend the vaccine was an important factor in parents' decision to vaccinate their child with the HPV vaccine
 - Not receiving a recommendation for HPV vaccine was listed a barrier by mothers

Just Another Adolescent Vaccine

- Successful recommendations group all of the adolescent vaccines
 - Recommend the HPV vaccine series the same way you recommend the other adolescent vaccines
 - Moms in focus groups who had not received a doctor's recommendation stated that they questioned why they had not been told or *if the vaccine was truly necessary*
 - Many parents responded that they trusted their child's doctor and would get the vaccine for their child as long as they received a recommendation from the doctor

Top 5 Reasons for not Vaccinating Daughter, among Parents with no Intention to Vaccinate in the next 12 months, NIS-Teen 2012



* Not mutually exclusive.

** Did not know much about HPV or HPV vaccine.

Try Saying:

Your child needs three shots today: HPV vaccine, meningococcal vaccine and Tdap vaccine.

You child will get three shots today that will protect him/her from the cancers caused by HPV, as well as to prevent tetanus, diphtheria, pertussis and meningitis.

An Anti-cancer Vaccine

- The “HPV vaccine is cancer prevention” message resonates strongly with parents
 - In focus groups and online panels, mothers wanted more information on the types of HPV cancers
 - In focus groups mothers stated they were influenced to vaccinate their child because HPV vaccine prevents cancer, they had a family history of cervical cancers, and/or because they had a personal experience with cervical cancer

But She's too Young!

- Parents might believe their child won't be exposed to HPV because they aren't sexually active or may not be for a long time
 - In focus groups, some moms couldn't understand how their child could become infected even if they waited until marriage to have sex
 - Some moms stated that they didn't think HPV infection was very common because they had never heard that it was or didn't know anyone who had an HPV infection or HPV disease

Try Saying:

Even if your child waits until marriage to have sex or only has one partner in the future, he/she could still be exposed if his/her future partner has engaged in any type of sexual activity with another person.

We don't wait until exposure occurs to give any other routinely recommended vaccine. HPV vaccine is also given when kids are 11 or 12 years old because it produces a better immune response at that age. That's why it is so important to start the shots now and finish them in the next 6 months.

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Thank You

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CDC-INFO Website www.cdc.gov/info

Website: www.cdc.gov/vaccines

