

Human Papilloma Virus:

A Quick Taste of Cancer Prevention from an Oral Health Perspective

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Objectives

- **H**one our understanding of the role of HPV and its links to oral cancer.
- **P**revent the spread of HPV infections and cancers.
- **V**erbalize why HPV surveillance and prevention are important.

What makes HPV such a hot topic?

ADA Council on Scientific Affairs:

***Statement on Human Papillomavirus and Squamous Cell
Carcinomas of the Oropharynx***

“The rising incidence of oropharyngeal cancer (specifically oropharyngeal squamous cell carcinoma) associated with HPV is a significant concern for the health care community.”

ADA

American
Dental
Association®

What makes HPV such a hot topic?

- Over the past 25 years
 - HPV infection has become firmly established as an etiologic risk factor for **cancers of the oropharynx**
 - Specifically of the tonsils & base of the tongue
 - Recent study:
 - ↑ – 225% increase in HPV-positive oropharyngeal cancers during 1988 to 2004
 - ↓ – 50% decrease of HPV negative cancers over the same period

What makes HPV such a hot topic?

- According to the *ADA Council on Scientific Affairs*:

“Dental care providers are encouraged to educate themselves and their patients about the relationship between HPV and oropharyngeal cancer, especially the growing prevalence of these cancers in younger non-smokers and non-drinkers. . .”

More Questions than Answers for the Medical and Dental Communities?

- Does kissing transfer Human Papilloma Virus making other people susceptible to oral cancer?
 - How much of a deep passionate kiss do you need to transfer HPV?
 - How would you even begin to test this assumption?
- Is a child at risk if the mother is positive?
- Can HPV be transferred if a mother tastes her baby's food before giving it to her child?
- Is an HPV positive person more at risk if using tobacco & alcohol together?
 - Is one more of a risk than the other?
 - Is a person who is genetically susceptible to cancer more affected by this trio?
- Is HPV an entity that can be harbored for years and then reappear?
 - Do you recheck positive patients again and at what intervals?
 - Do you check entire families for HPV, and if so how often?



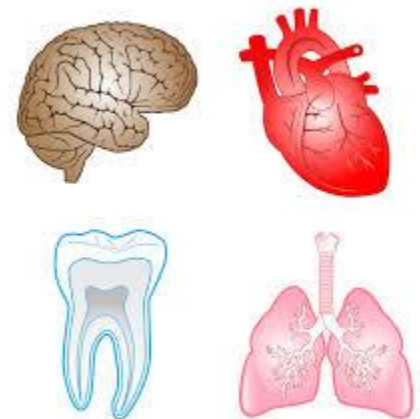
More Questions than Answers for the Medical and Dental Communities?

- Do you test all patients for HPV, or just some high-risk groups?
 - Do you check adolescents who may or may not admit to sexual activity?
 - Do you talk to the parent first without even asking? What would be the reaction of parents?
 - Adolescents and even much older adults do not consider oral sex to be “true” sex, so how crucial is phrasing and communication?
- Who should talk with patients about the illness or test results?
 - How confidential is the information?
- Do you test patients for HPV who have had previous oral cancer at every appointment?
 - What is the accuracy of testing?
- Does the constant bleaching of teeth affect the oral tissues in some individuals? (as practiced by many under the age of 40)
 - Does HPV affect this tissue before or after bleaching?
- Does gastro esophageal reflux disease and frequent heartburn make oropharyngeal tissues more susceptible to HPV in some individuals
 - Possibly those with a genetic predisposition?



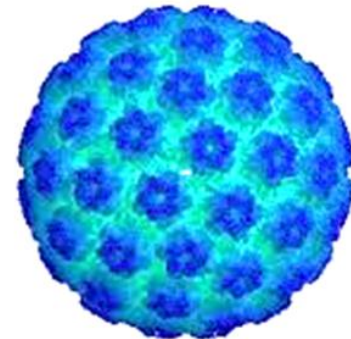
More Questions than Answers for the Medical and Dental Communities?

- With regard to HPV
 - Are you now being asked to counsel patients about sexual practices and personal medical information?
 - If you do provide this counseling, what are the long-term ramifications?



What is Human Papilloma Virus (HPV)?

- HPV is a very common virus that spreads between people when they have sexual contact with another person
- HPV infection can cause cervical cancer in women (and penile cancer in men)
- HPV causes anal, **oropharyngeal and throat cancers**, and genital warts in both men and women

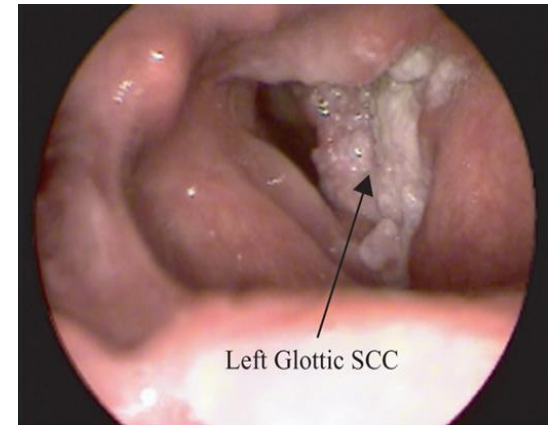


Human Papilloma Virus

- **Most common sexually transmitted viral infection in the US**
- There are nearly 200 different strains of HPV
 - Most are harmless and not cancer causing
 - 9 are known to cause cancers
 - HPV 16 most likely to cause oral cancers
 - also associated with cervical, anal, and penile cancers
 - Additional 6 suspected of causing cancers
- You can have HPV without ever knowing it
 - No obvious signs or symptoms
 - Body often clears it before detection

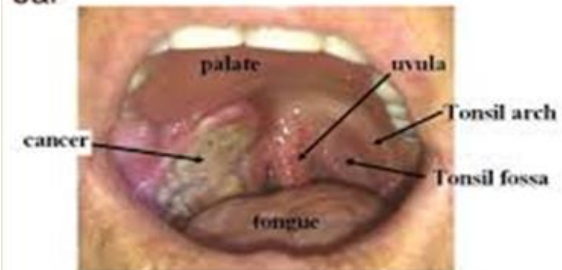
Oropharyngeal Squamous Cell Carcinoma

- 95% of laryngeal cancer
- ~11,000 new cases diagnosed in US annually
- Risk Factors
 - Chronic HPV (RR~230)
 - Tobacco & alcohol (RR>100)
 - Tobacco abuse (RR~14-35)
 - Excess ETOH use (RR~16)
 - Infrequent F/V (RR~2.7)



Source: Usatine RP, Smith HA, Mayeaux EJ, Chumley HS: The Color Atlas of Family Medicine, Second Edition: www.accessmedicine.com
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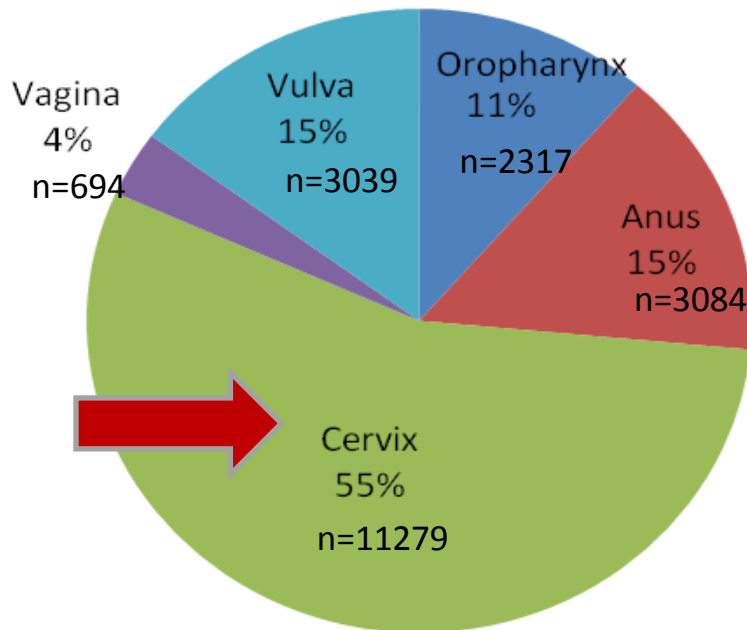
Typical **smoking** related oropharynx cancer, presented with months of throat pain radiating into ear



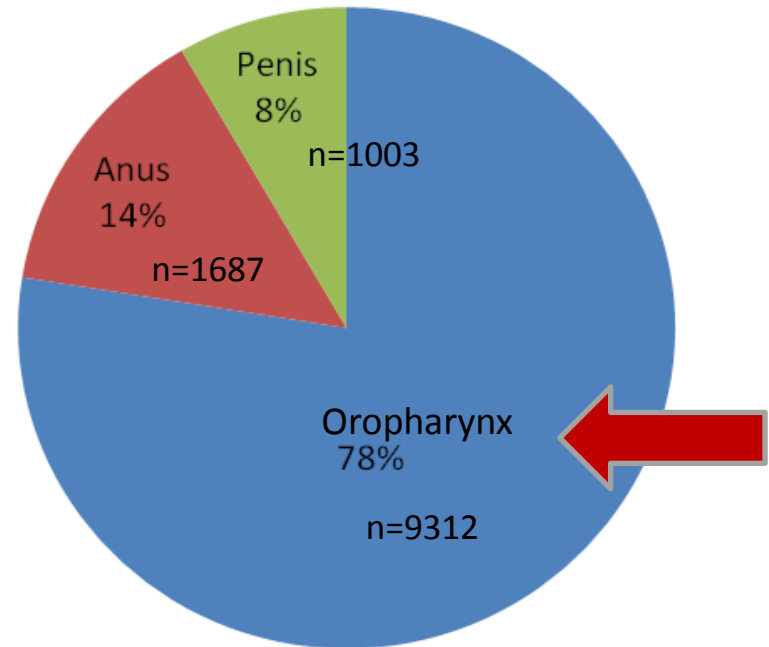
<http://accessmedicine.mhmedical.com.ezproxy.mcphs.edu/content.aspx?bookid=685§ionid=45361075>
www.slideshare.net/2Fdoctorbobm/2Fviruses-and-cancer

Average Number of Newly Diagnosed HPV-Associated Cancers by Sex, in the United States (2005-2009)

Women (N=20,413)

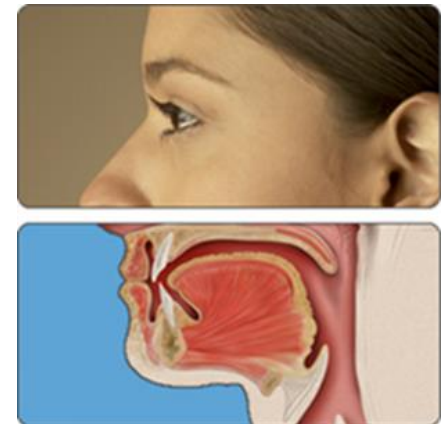


Men (N=12,002)



Oral Cancer Signs and Symptoms

- Oral ulcer/sore without healing over 2-3 weeks
- Difficult or painful swallowing
- Pain when chewing
- Persistent sore throat or hoarse voice
- Swelling or lump in the mouth
- Persistent painless lump in the neck
- Numb feeling in the mouth or lips
- Constant coughing
- Persisting one-sided earache



Human Papilloma Virus

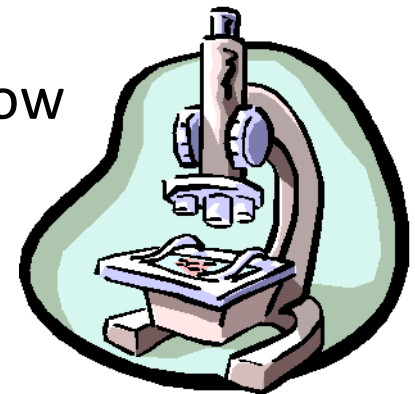
- Leading cause of oropharyngeal cancers
 - HPV 16 is most responsible
 - Affects both males and females
 - Accounts for a very small number of front of the mouth, oral cavity cancers
 - Found primarily posteriorly
 - base of the tongue
 - back of the throat
 - tonsils
 - tonsillar crypts/pillars



#ADAM

How do people get oral HPV?

- Few studies have looked at how people get oral HPV
- Some show conflicting results
- Oral HPV may be passed during oral sex
 - Mouth-to-genital or mouth-to-anus contact
 - Open-mouthed (“French”) kissing
 - Likelihood of getting HPV from kissing or having oral sex with someone who has HPV is unknown
 - Long time sexual partners probably tend to share genital HPV
- More research is needed to understand exactly how people get/give oral HPV infections



Human Papilloma Virus Testing

- Oral HPV testing in both men and women is problematic
 - Commercial tests available in the dental community
 - of unclear value
 - positive testing does not prove persistence of the infection
- There are no visible oral signs of initial HPV infection
- There are also no well established genital tests for men
- For women :
 - Routine HPV/Pap testing recommended during cervical exams



Human Papilloma Virus



- Most people clear the virus naturally
 - Never knowing they were exposed or had it
- If test positive for HPV
 - No sure way to know when they were infected with HPV
 - Who gave it to them
 - Does not mean that someone is having sex outside of their current relationship
 - With higher risk/cancer causing strains, cancer may not develop
- HPV is believed to have long periods of dormancy
 - Causing negative test results
 - Before it is detected or develops into a cancer

HPV Infection

- Most American females and males will be infected at some point in their lives with at least one type
 - Current estimate is 79 million
 - 14 million new infections yearly
 - Most common in teens and early 20's
- **Most people will never know they have been infected**

Reprinted with permission from: www.cdc.gov &
Jemal et al. J Natl Cancer Inst 2013;105:175-201



Photo from [Preparing your family.com](http://Preparingyourfamily.com)

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



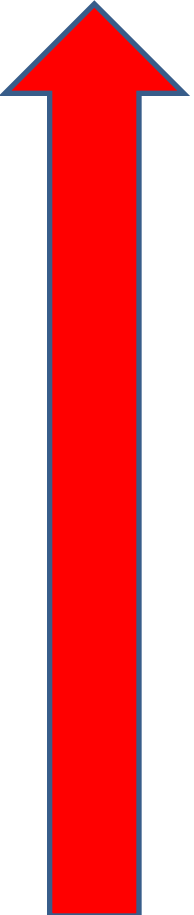
HPV is found in virgins too!

- Study of adolescent women without prior vaginal intercourse examined the frequency of vaginal HPV and the association with non-coital sexual behavior
 - 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

HPV & Cervical Cancer

- **Cervical cancer is the most common HPV-associated cancer among women**
 - 500,000+ new cases and 275,000 attributable deaths world-wide (2008)
 - 12,000+ new cases and 4,000 attributable deaths in the U.S. (2011)
- 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 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%
 - More oropharyngeal cancers that were previously thought to be caused by tobacco and/or alcohol use are now identified as HPV-related cancers

Economic Impact Related to HPV-Associated Disease, 2010

Event	Cost (\$ billions)
Cervical cancer screening*	6.6
Cervical cancer	0.4
Other anogenital cancers	0.2
Oropharyngeal cancer	0.3
Anogenital warts	0.3
RRP**	0.2
TOTAL	8.0

*Cervical cancer screening costs: ~ 80% routine screening, ~20% follow-up

**RRP costs: ~ 70% juvenile-onset, ~ 30% adult-onset

Reprinted with permission from:

www.cdc.gov/vaccines/youarethekey

What are the numbers?

- There are currently 26 million girls <13 yo
- If none of these girls are vaccinated then:
 - 168,400 will develop cervical cancer
 - 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

What are the numbers?

For **each year** we stay at **30%** coverage
instead of achieving **80%**,
there will be an additional:

- 4,400 future cervical cancer cases
- 1,400 cervical cancer deaths nationally



What are the numbers locally?

- Attention is being focused on the continued low rates of HPV vaccination throughout the country
- By extrapolation, **New Hampshire** will have:
 - 19 cervical cancer cases per year
 - 6 cervical cancer deaths per year
 - New Hampshire is NO exception:
 - **Currently, only 34.5% of females 13 to 17 years of age have completed the 3 series dose**

Complications of HPV Infection

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



News Flash!

Photo from picstopin.com

***This is no longer just a
women's healthcare
issue!***

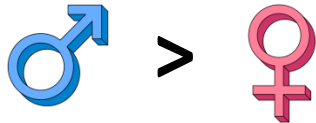
Human Papilloma Virus

- The fastest growing segment of the oropharyngeal cancer population:
 - Otherwise healthy
 - non-smokers in the 25-50 age range
- Most at risk population:
 - White, smoking/drinking males, ages 30 to 64
 - ~2.5x more likely than females
 - Increased #'s of sexual partners



Oral HPV Numbers

- Estimated = 2.1+ million infected in the US
- Prevalence = 7% of population (14 to 69 yo)



- HPV 16 incidence = 1% of population (14-69 yo)
- 90% of HPV positive Oral Squamous Cell Carcinomas linked to HPV type 16



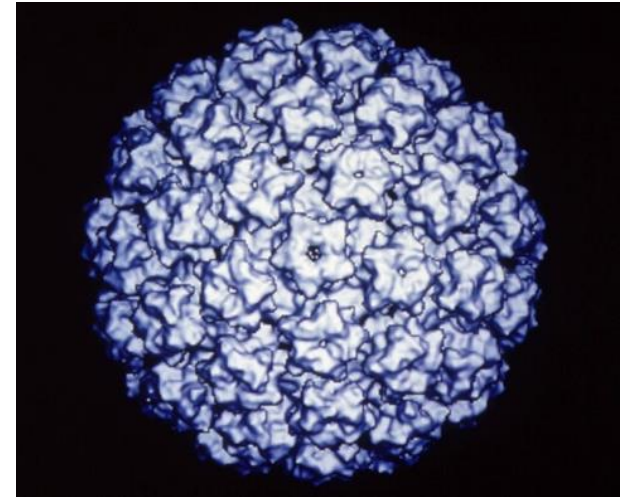
$$\begin{array}{l} 5 \div 2 \frac{3}{4} \\ 14^8 \\ 3.14^{300,000} \\ \sqrt{9} \end{array}$$

Talking Tips. . .

- “Persistent HPV infection 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.”

HPV Prophylactic Vaccines

- Made from recombinant L1 capsid proteins that form “virus-like” particles
- These “virus-like” particles **CAN NOT** cause infection with HPV or cause cancer
- **HPV vaccines produce a better immune response than HPV infection**
 - Vaccines produce higher levels of neutralizing antibodies
 - Inactivated so the vaccine can be administered to immuno-compromised individuals





So how can we help reduce the rate and complications of HPV infection?

Photo from blogs.adobe.com

- Give a strong recommendation and **good screening**
 - How often do you get a chance to prevent cancer?
- Start the conversation early
 - Give info & vaccinate before sexual experimentation begins
 - Preteens exhibit a better antibody response
- Offer a personal story
 - Patients/Parents typically trust advice from their provider
- Welcome questions from parents and teens
 - Especially about safety
 - Remind them that HPV vaccine is safe
 - Vaccination is **NOT** associated with increased sexual activity

Can HPV vaccines prevent oral HPV and oropharyngeal cancers?

- It is possible that HPV vaccines might prevent oropharyngeal cancers, since vaccines prevent initial infection with HPV types that cause oropharyngeal cancers
- Current HPV vaccines were specifically developed to prevent cervical and other less common genital cancers
- Whether HPV vaccines specifically prevent oropharyngeal cancers has not been studied

Available HPV Vaccines

Name	Bivalent 2vHPV (Cervarix)	Quadrivalent 4vHPV (Gardasil)	9-Valent 9vHPV (Gardasil 9)
L1 major capsid protein, virus like particle types	16 , 18	6, 11, 16 , 18	6, 11, 16 , 18, 31, 33, 45, 52, 58
Licensed for	Females 9-25 years	Females 9-26 years Males 9-26 years	Females 9-26 years Males 9-15 years*
Schedule (IM)	3 dose series	3 dose series	3 dose series
Manufacturer	GlaxoSmithKline	Merck	Merck

ACIP recommended use of 9vHPV in the currently recommended age groups

- At the time of the first application to the FDA, 9vHPV trials in males 16-26 years had not been completed
- Immunogenicity data for males 16-26, reviewed by ACIP has been submitted to the FDA



ACIP Recommendation and AAP Guidelines for HPV Vaccine



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

* CDC Advisory Committee on Immunization Practices

* American Academy of Pediatrics

HPV Vaccination

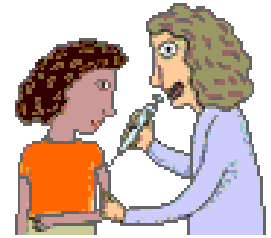




- There is no cure for the HPV virus
- Original vaccine clinical trials focused on cervical cancers
- The FDA restricts from advertising off-label effects
- However, since vaccines prevent cancer causing HPV strains, it's not much of a scientific leap to extrapolate that
 - **“if you can't get the virus, you can't get the things the virus might cause”**
- The scientific/medical/dental communities strongly recommend vaccinating to protect from cancers associated with HPV
- **Quite Simply, this is an Anti-Cancer Vaccine**

Talking Tips. . .

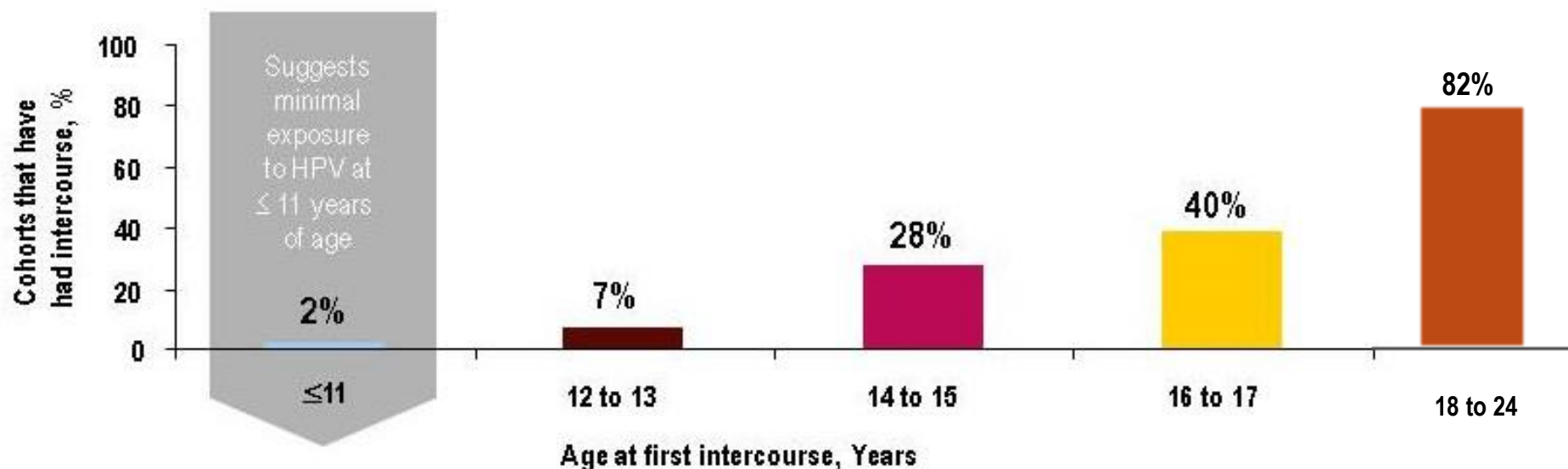
- “HPV vaccine is very important because it prevents cancer.”
- “I want your child to be protected from cancer.”
- “That’s why I’m recommending that your daughter/son receive the first dose of the HPV vaccine series today.”

HPV Vaccine Safety



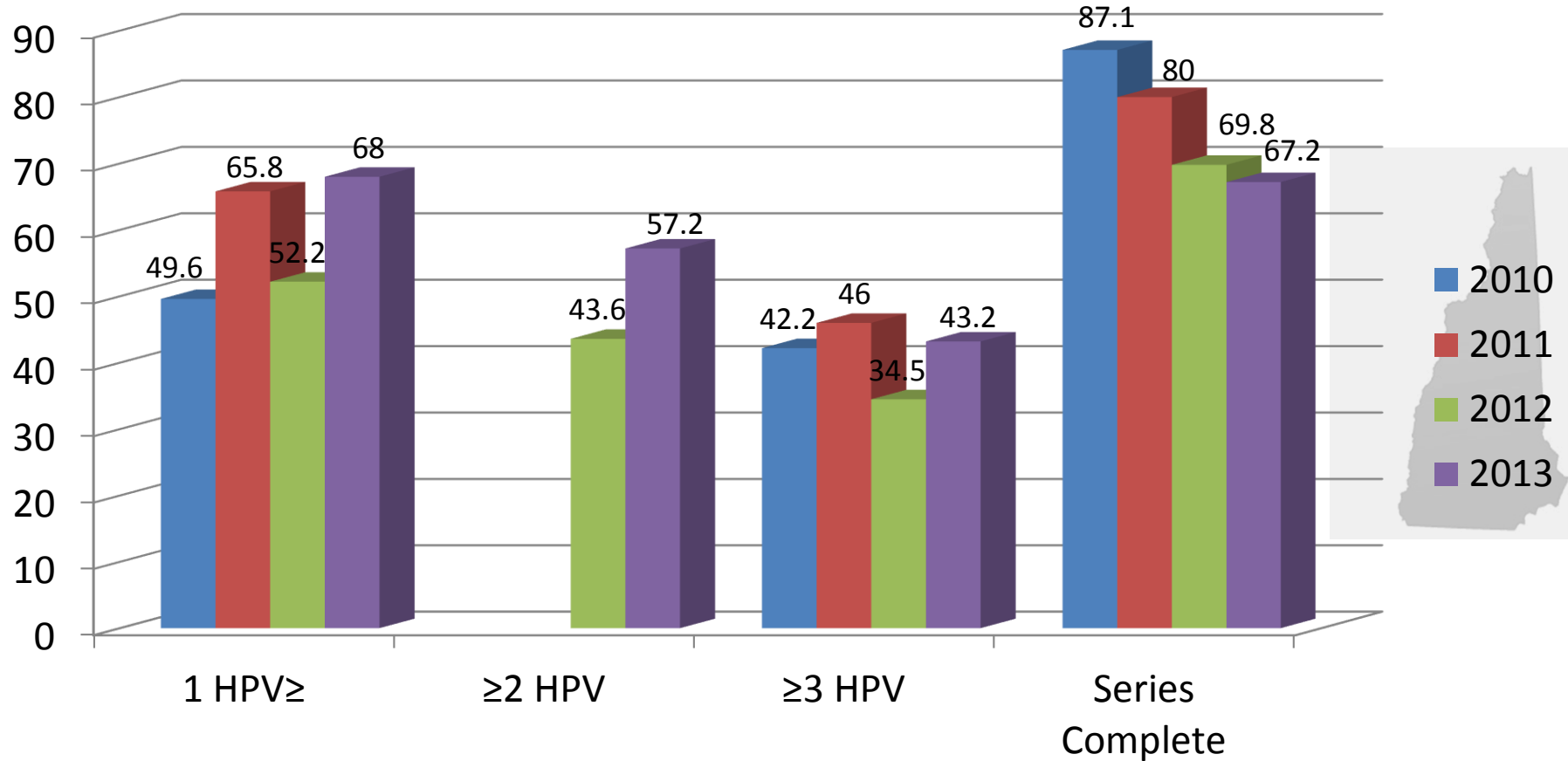
- In general, the most common adverse events reported are considered mild
- For serious adverse events reported, there is no unusual pattern or clustering suggesting that the events were caused by the HPV vaccine
- These findings are similar to the safety reviews of MCV4 and Tdap vaccines in adolescents
- 57 million doses of HPV vaccine have been distributed in the US since 2006 
- More than 175 million distributed worldwide 

Rationale for vaccinating early: Protect prior to HPV exposure



Adapted from Henry J. Kaiser Family Foundation

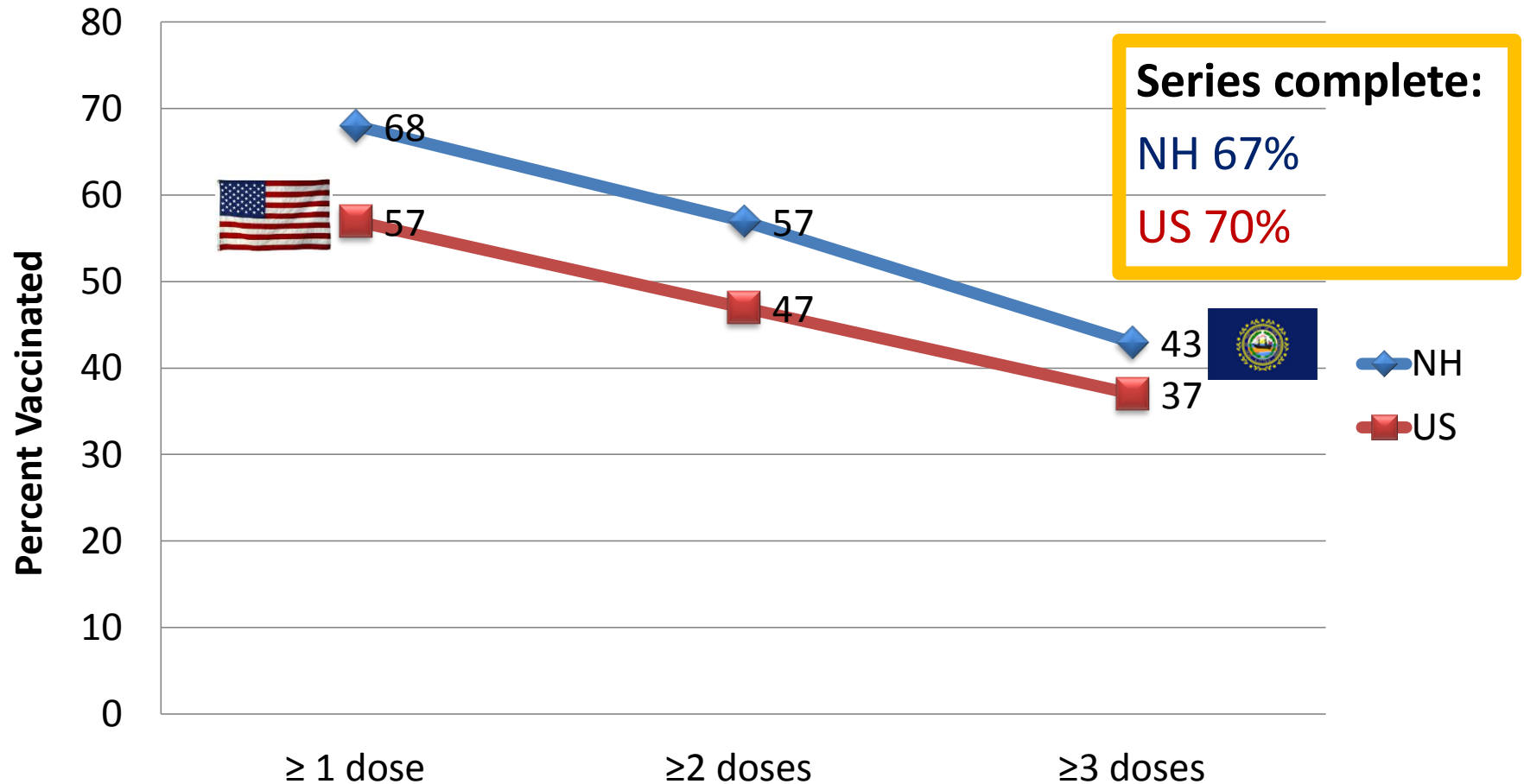
HPV Vaccine in NH Teen Females (13-17 yo)



* Series Complete: Percent of females who received 3 doses among those who had at least 1 HPV dose and at least 24 weeks between the first dose and the interview date.

National Immunization Survey 2013, (Teen, 13-17 years) United States, NH results.

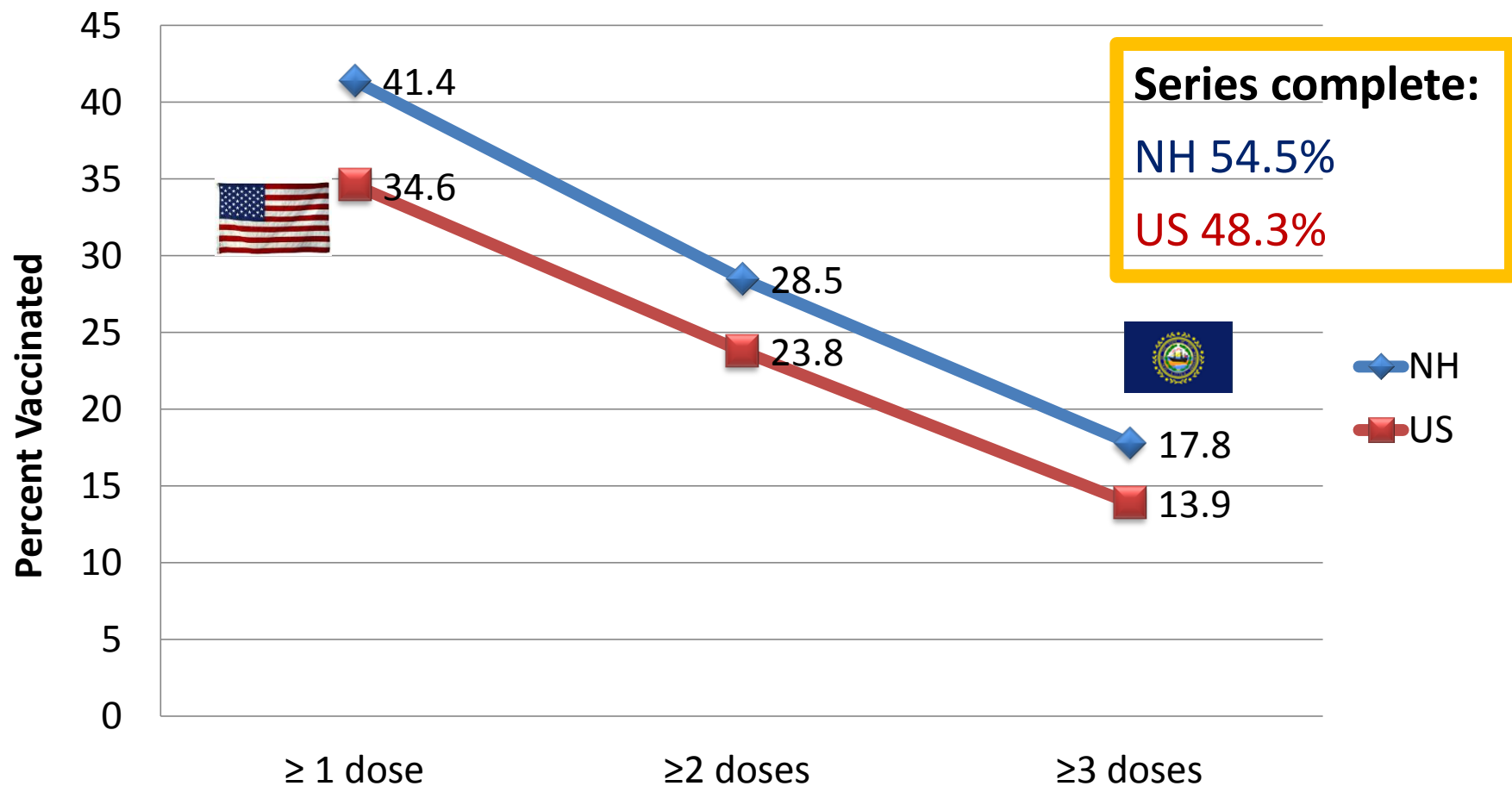
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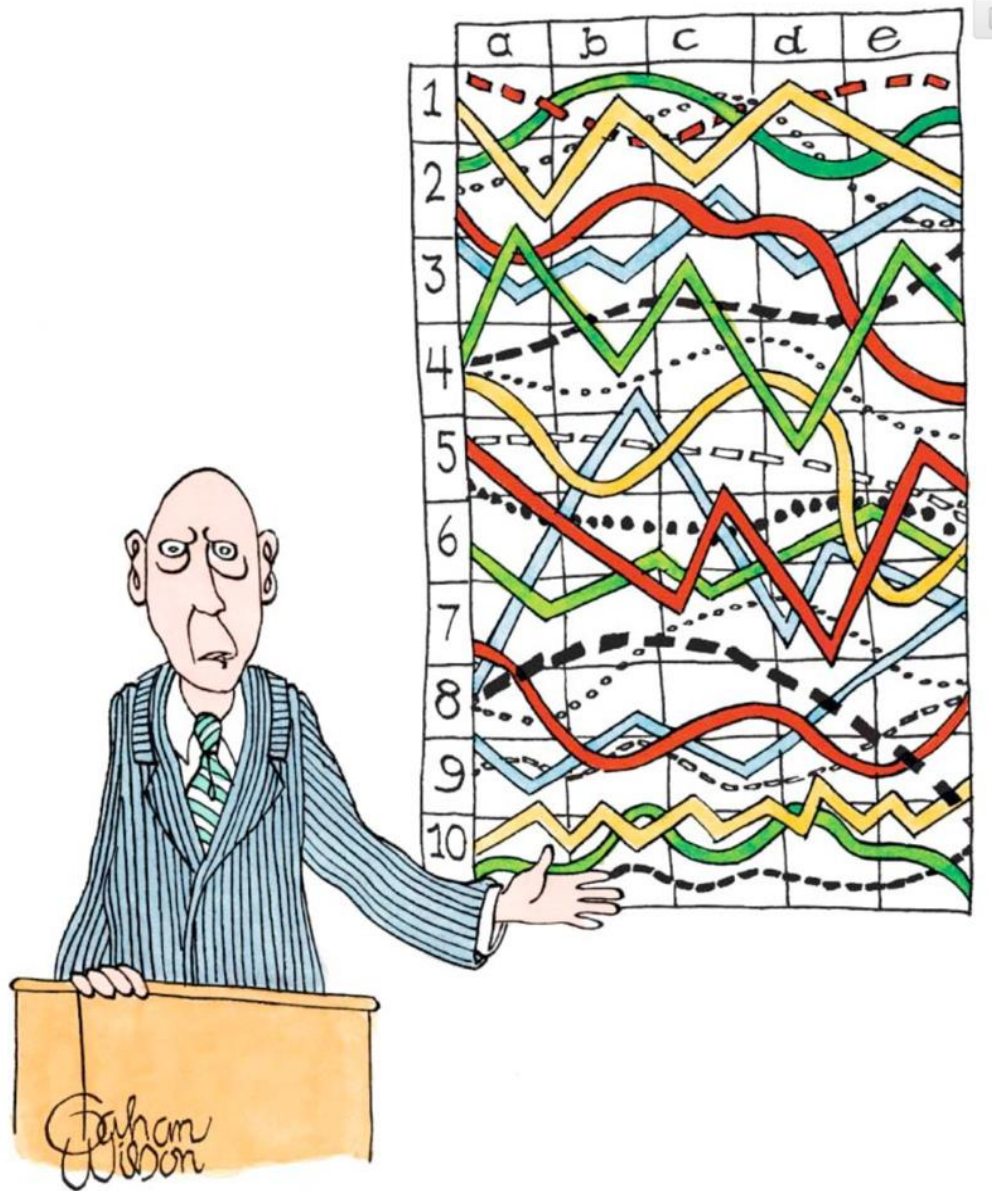
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HPV Vaccine in Teen Males (13-17 years old)



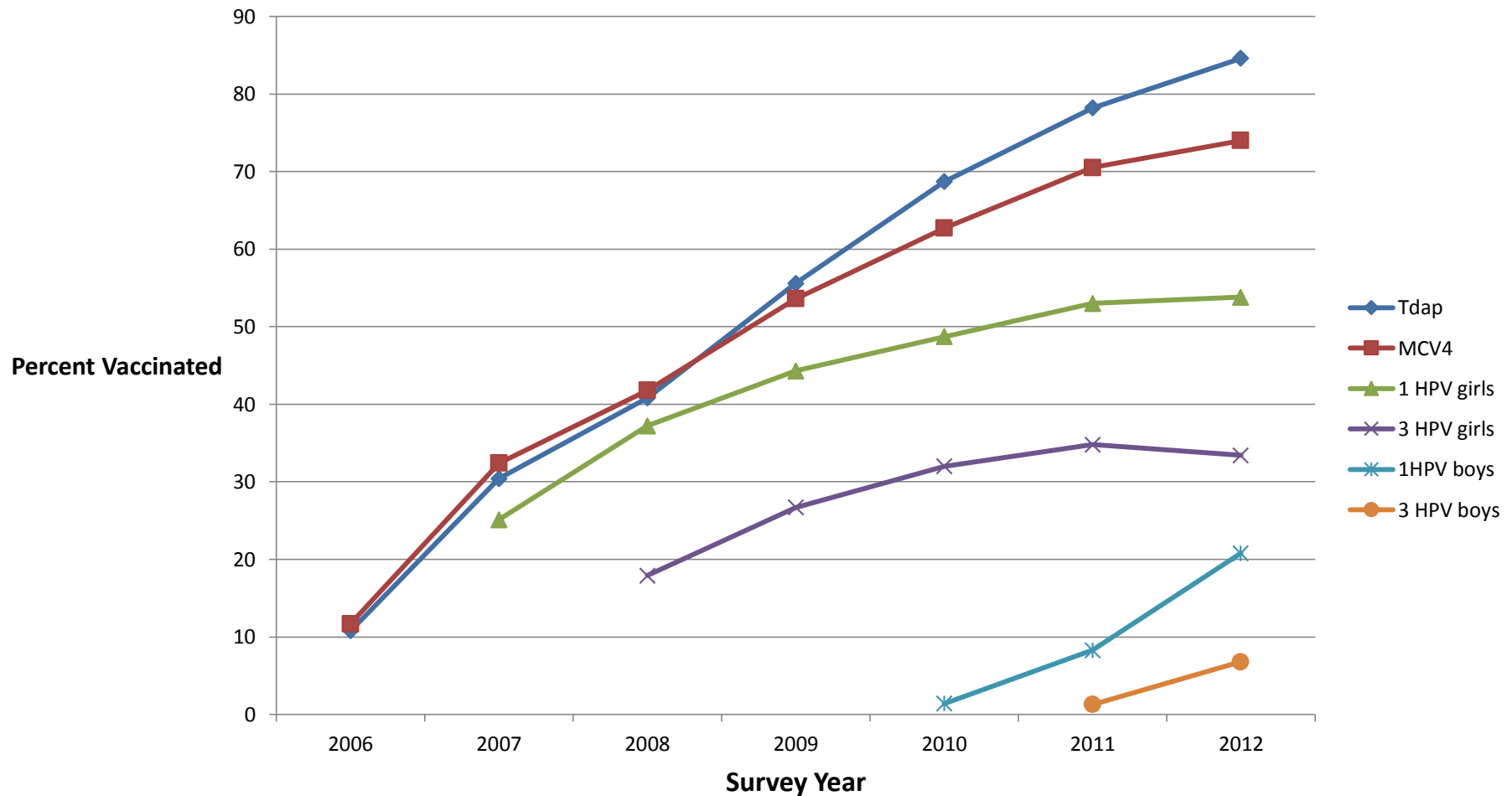
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National Immunization Survey 2013, (Teen, 13-17 years) United States, NH results.



*"I'll pause for a moment so you can
let this information sink in."*

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



“HPV coverage remains a problem”

(Anne Schuchat, MD, Asst. Surgeon General)



- ➡ 1st dose, girls 13-17 = 57%
- ➡ Trails other recommended childhood vaccines by 20-25%
- ➡ Currently 4 of 10 girls have not started series
- ➡ Intimidating 3 dose schedule
- ➡ Ongoing clinical trial testing 2-dose schedule for 9-valent vaccine (undergoing ACIP review)



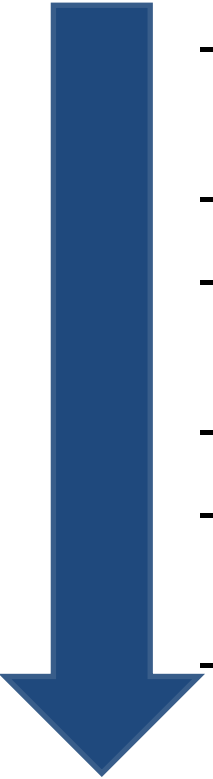
The Need for HPV Prevention

- Currently only 4 in 10 female American teenagers receive the HPV vaccine
- in Europe, the rate is closer to 8 in 10
- the U.S. has been reluctant to catch up for several reasons:
 - some insurance providers don't cover the vaccine (not an issue in New Hampshire)
 - **people like to think that adolescents aren't having sex, and therefore don't need it**



photo from www.redbubble.com

Dramatic Results in Post-Market “Real-World” Surveillance

- 
- Despite only 33% of girls in US receiving 3 doses
 - 56% reduction in adolescent girls in prevalence of strains 6, 11, 16 & 18 (National Health & Nutrition Examination Study)
 - 77% reduction in **Australia** (w/in 3 years of 3 doses)
 - 75% reduction in low-grade cervical abnormalities in **Australian** girls younger than 18 yo (3 doses)
 - 45% reduction in genital warts in Danish girls (16-17 yo)
 - 36% reduction in genital warts in US girls (15-19 yo) (**despite low immunization rates**)
 - 88% reduction in genital warts in **Australian** females less than 21 years old



So how do we effectively deliver the facts and discuss Human Papilloma Virus with patients?



Why aren't more teens vaccinated against HPV?

- CDC Researchers reviewed 55 relevant articles appearing in 2009 or later:
 - **Patients cite needing more information**
 - Concerns about effects on sexual behavior
 - Patients believe that their that are at low risk of HPV infection
 - Social influences
 - Irregular preventive care
 - Vaccine cost



photo from www.vmh.com

Why the need to educate?

- Some patients believe that they/their children won't be exposed to HPV because they aren't sexually active or may not be for a long time
 - “In focus groups, some patients **couldn't understand how they could become infected** even if they waited until marriage to have sex.”
 - “Some patients 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.**”



Complications of HPV Infection

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



News Flash!

Photo from picstopin.com

***This is no longer just a
women's healthcare
issue!***

Avoid missed opportunities

- Review immunization records & educate at every visit
 - Acute/well child visits, **dental visits**, sports/camp physicals
- HPV vaccine is safely given with the other recommended adolescent vaccines
 - Best recommendation is one that bundles all indicated adolescent vaccines
- Determine what works best for your practice
 - Have a well-coordinated strategy
 - In medical practices, schedule next HPV vaccine visit before patients leave the office or clinic
 - Utilize reminder/recall strategies to ensure return for remaining doses

What makes HPV such a hot topic?

“The rising incidence of oropharyngeal cancer (specifically oropharyngeal squamous cell carcinoma) associated with HPV is a significant concern for the health care community.”

ADA Council on Scientific Affairs:

***Statement on Human Papillomavirus and Squamous Cell
Carcinomas of the Oropharynx***



Conclusions about HPV Vaccination

- **W**elcome ?'s from patients, teens and parents
- **E**ducate that almost everyone gets HPV infection

MUST EMPHASIZE THAT HPV IS NOT JUST FOR

WE MUST EMPHASIZE THAT HPV IS NOT JUST FOR

- **G**ive strong recommendations & concrete reasons for getting HPV vaccine
- **I**nform patients that HPV causes a variety of cancers in women and men
- **R**emind patients that HPV vaccine is for cancer prevention
- **L**isten carefully to patient concerns
- **S**ee that oropharyngeal HPV is a growing problem

Thank you!

