HPV vaccination is cancer prevention

DON’T WAIT TO VACCINATE

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Presenter Disclosure Information
Rebecca Perkins

I, Rebecca Perkins, have been asked to disclose any significant relationships with commercial entities that are either providing financial support for this program or whose products or services are mentioned during my presentations.

- I have no relationships to disclose.

I may discuss the use of vaccines in a manner not approved by the U.S. Food and Drug Administration.

- But in accordance with ACIP recommendations.
Objectives

- Describe the burden of HPV-related disease
- Explain that the HPV vaccine is safe and effective
- Discuss Massachusetts HPV vaccination uptake
- Review strategies for effectively communicating the importance of HPV vaccination
What is HPV?

- A virus that infects human skin and mucosal surfaces
- Transmitted easily by touching
- Classified as a carcinogen
- Most females and males will be infected with at least one type of mucosal HPV at some point in their lives
Every year in the United States
3 million Americans seek medical care for HPV
27,000 people are diagnosed with a cancer caused by HPV

That’s 1 case every 20 minutes
Why do we vaccinate?

- To prevent HPV infections
- To prevent HPV-associated cancers
- Because screening is not available/recommended for many HPV related cancers
Average number of new cancers probably caused by HPV, by sex, United States 2006-2010

Women (n = 17,600)

- Oropharynx: 10%
- Vulva: 13%
- Anus: 15%
- Cervix: 59%
- Vagina: 3%

Men (n = 9,300)

- Oropharynx: 77%
- Anus: 15%
- Penis: 8%

CDC, United States Cancer Statistics (USCS), 2006-2010
HPV-Associated Cervical Cancer Incidence Rates by State, United States, 2006-2010

10,000+ Cases and 4,000+ Deaths Every Year

www.cdc.gov/cancer/npcr
Treatment of cervical precancerous lesions can lead to increased risk of preterm delivery

- 330,000 women undergo cone/LEEP procedures every year
- LEEP/HPV infection associated with obstetric morbidity
  - Preterm delivery
  - Preterm rupture of membranes
  - Low birth weight
  - Long term developmental outcomes, neonatal intensive care costs
Why do we want to protect boys from HPV?

- Oropharyngeal cancers more common in men
  - No screening test for oropharyngeal cancers
- Genital warts
- Anal cancer
- Penile cancer
The incidence of oropharyngeal cancers increased in the past 20 years.

During this time:

- Smoking and alcohol-related cancers decreased by 50%.
- HPV-related cancers increased by 225%.
Oropharyngeal Cancer

11,000 cases annually, 7,000 in men
Will be more common than cervical cancer by 2020
Rise in incidence and changing patient demographics due to HPV

http://www.ghorayeb.com/OropharyngealCarcinoma.html
RISK OF HPV ACQUISITION

Almost everyone will be exposed to HPV

Many infections will clear on their own, others may persist and some will reactivate decades after initial exposure
HPV transmission

Most females and males will be infected with at least one type of mucosal HPV at some point in their lives.

Most common route is sexual intercourse:
- genital-genital, anal-genital, oral-genital, manual-genital

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 can be transmitted without "having sex"

- 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 has been detected in women prior to first vaginal sex. The percentage ranges from 9 to 46%, depending on the study.
- 70% of these women reported non-coital behaviors that may in part explain genital transmission.

Shew, J Infect Dis. 2012
Rapid acquisition of HPV following sexual debut

- Study of 18-23 year-old males (n=240)
- Study of female college students (N=603)

Cumulative Incidence of HPV Infection

Months Since First Intercourse

Rationale for vaccinating early:
Protection prior to exposure to HPV

Teen Sexual Activity
Adolescence is a time of rapid change.

% of adolescents who have had sex by each age

- Female
- Male

www.guttmacher.org
HPV may never go away

- 700 women aged 35-60
- Only 13% of incident infections attributed to new sexual partners
- 85% of incident infections occurred during periods of abstinence or monogamy

*Early vaccination can prevent initial infection*
Recommendations, Safety, Impact, & Coverage Rates

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 Virus-Like Particle
Updated ACIP Recommendations

Age

- Routine vaccination at age 11 or 12 years*
- Vaccination recommended through age 26 for females and through age 21 for males not previously vaccinated
- Vaccination recommended for men through age 26 who have sex with men (MSM) or are immunocompromised (including persons HIV-infected)

Formulation by gender (assuming availability)

<table>
<thead>
<tr>
<th></th>
<th>9vHPV</th>
<th>4vHPV</th>
<th>2vHPV</th>
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</thead>
<tbody>
<tr>
<td>Females</td>
<td>✔</td>
<td>✔</td>
<td>✔</td>
</tr>
<tr>
<td>Males</td>
<td>✔</td>
<td>✔</td>
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*vaccination series can be started at 9 years of age
MMWR 2015;64:300-4
9-valent HPV Vaccine Trials

- **Efficacy**
  - ~97% protection against HPV 31, 33, 45, 52, 58-related outcomes
  - Similar protection against HPV 6, 11, 16, 18-related disease

- **Non-inferior immunogenicity**
  - For HPV 6, 11, 16, 18 compared with 4vHPV in 16–26 and 9–15 years
  - For all 9 HPV vaccine types in adolescent females and males compared to adult females and in adult males compared to adult females

- **Concomitant use**
  - No impact on immunogenicity or safety administered concomitantly with MCV4 (Menactra) and Tdap (Adacel)

- **Safety**
  - Similar safety profile, but slightly higher injection site reactions
  - Safety update from the 10-21-15 ACIP meeting. No signals seen for 4vHPV or 9vHPV vaccines.

Overall improvement in cancer prevention for 9-valent vaccine over quadrivalent and bivalent: 14% for females, 4% for males
Clinician questions

Do I need to restart the series if a dose is late?
No, just ensure the recommended minimum intervals are met.

Can I vaccinate someone over age 26?
Vaccination is safe, but disease may not be reduced. Insurance is unlikely to reimburse.

How long does immunity last?
At least 10 years, studies are ongoing.

Should I vaccinate after an abnormal Pap?
Yes, they will be protected from HPV types they don’t already have, and have a 30% lower risk of recurrence of they do go on to develop dysplasia.
Parents and adolescents want to know...

**IS IT SAFE?**

**DOES IT WORK?**

**WILL IT CHANGE MY CHILD’S BEHAVIOR?**
HPV VACCINE SAFETY
HPV Vaccination Is Safe, Effective, and Provides Lasting Protection

atitis is SAFE

- Benefits of HPV vaccination far outweigh any potential risks
- Safety studies findings for HPV vaccination similar to safety reviews of MCV4 and Tdap vaccination

HPV Vaccine WORKS

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

HPV Vaccine LASTS

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

HPV vaccine long-term safety data

No increased risk of:

- 2011 - allergic reactions, anaphylaxis, Guillain–Barré Syndrome, stroke, blood clots, appendicitis, or seizures (than unvaccinated or who received other vaccines)
- 2013 – (almost 1 million girls) blood clots or AEs related to the immune & CNS
- 2014 – (>1 million women) venous thromboembolism or blood clots
- 2012 and 2014 – (2 studies) autoimmune disorders
- 2015 – Multiple sclerosis or other demyelinating diseases
- 2015 - POTS or CRPS (European Medical Review)

2012 - vaccine may be associated with skin infections where the shot is given during the two weeks after vaccination and fainting on the day the shot is received

HPV VACCINE EFFECTIVENESS
HPV vaccine impact: US

Prevalence of vaccine type HPV decreased 56%

Markowitz, et al. JID 2013 *weighted prevalence
Genital warts among females by age group, CA Family PACT 2007-2010

Bauer, et al AJPH 2012
Vaccine effectiveness in Massachusetts

- 1,662 patients aged <27 years presenting to referral colposcopy clinic 2007-2014
- Vaccinated women had
  - 53% lower odds of presenting with high-grade cytology
  - 36% lower odds of presenting with cervical intraepithelial neoplasia 2 or 3 or worse
Near-disappearance of genital warts in Australia following introduction of HPV vaccination

*70% vaccination rate for females only

93% reduction in girls <21
82% reduction in boys <21
Higher effectiveness with vaccination at younger ages

% Reduction in cervical dysplasia 5 years after vaccination, by age at vaccination

- Any high-grade histology
- CIN3/AIS
- CIN2
- CIN1

Gertig DM, BMC Med 2013
Without vaccination, annual burden of genital HPV-related disease in U.S. females:

- 4,000 cervical cancer deaths
- 10,846 new cases of cervical cancer
- 330,000 new cases of HSIL: CIN2/3 (high grade cervical dysplasia)
- 1 million new cases of genital warts
- 1.4 million new cases of LSIL: CIN1 (low grade cervical dysplasia)
- 3 million cases and $8 billion

References:
American Cancer Society. 2008; Schiffman Arch Pathol Lab Med. 2003; Koshiol Sex Transm Dis. 2004; Insinga, Pharmacoeconomics, 2005
Extrapolating the prior pyramid with projections of vaccine efficacy based on Australian data

Cervical cancer

46% reduction in CIN2/3 requiring LEEP
75% if vaccination by age 14

92% reduction in genital warts

35% reduction in CIN1

Impact of HPV vaccine on oral HPV infection

7,466 women 18-25 years of age randomized to receive HPV or hepatitis A (control) vaccine

- 5,840 gave oral specimens at the end of the 4-year study

- Control vaccine group: 15 HPV 16/18 infections
- HPV vaccine group: 1 HPV 16/18 infections

**Estimated vaccine efficacy against oral HPV infection:** 93.3%

Herrero R, et al. Reduced prevalence of oral human papillomavirus (HPV) 4 years after bivalent HPV vaccination in a randomized clinical trial in Costa Rica. PLOS ONE 2013;8:e68329
In summary:
HPV exposure is ubiquitous
HPV causes many cancers
HPV vaccine is safe
HPV vaccine is effective

WHY ISN’T EVERYONE VACCINATED YET?
Adolescent Vaccination Coverage
United States, 2006-2014

Survey Year

Percent Vaccinated

Revised APD Definition

- Tdap
- MCV4
- 1 HPV girls
- 3 HPV girls
- 1 HPV boys
- 3 HPV boys
Impact of Eliminating Missed Opportunities by Age 13 Years in Girls Born in 2000

Missed opportunity: Healthcare encounter when some, but not all ACIP-recommended vaccines are given. HPV-1: Receipt of at least one dose of HPV. MMWR. 63(29);620-624.
A WORD ON SEXUAL PROFILING: DON’T DO IT

- 80% of people will be exposed to HPV
- You can’t predict who or when
- Delays intended to be temporary may become permanent
Each adolescent visit may be the last chance to vaccinate!

- 30% of adolescents never present for preventive care
- 1 in 15 adolescent visits is for preventive care
- Preventive visits decline after age 13
- Early adolescents (11-14 years old) had 3 times more preventive visits than late adolescents

*Use sick and well visits to vaccinate*

You can reassure parents that HPV vaccination does *not* change sexual behavior

- 3 large studies including >200,000 girls & young women
- HPV vaccination NOT associated with
  - Being sexually active
  - Number of sexual partners
  - Receiving counseling on contraceptives
  - Testing for or diagnoses of sexually transmitted infections

Bednarczyk RA, *Pediatrics* 2012;130:798
Jena AB, *JAMA Intern Med, 2015*
Quality of Physician Communication about HPV Vaccine: Findings from a National Survey

Cross-sectional, online survey in 2014

Eligibility criteria
- Pediatric or family medicine specialty
- Provider of preventive care to patients ages 11-17

National sample (n=776)
- 53% pediatrics specialty
- 68% male
- 55% ≥20 years in practice
### What Is a “Strong” Recommendation?

<table>
<thead>
<tr>
<th>Quality measure</th>
<th>Definition</th>
<th>%</th>
</tr>
</thead>
<tbody>
<tr>
<td>Timeliness</td>
<td>Recommend for <strong>girls</strong> by target age</td>
<td>74%</td>
</tr>
<tr>
<td></td>
<td>Recommend for <strong>boys</strong> by target age</td>
<td>61%</td>
</tr>
<tr>
<td>Strength of endorsement</td>
<td>Say vaccine is very important</td>
<td>73%</td>
</tr>
<tr>
<td>Consistency</td>
<td>Deliver routine vs risk-based recommendations</td>
<td>41%</td>
</tr>
<tr>
<td>Urgency</td>
<td>Recommend same-day vaccination</td>
<td>51%</td>
</tr>
</tbody>
</table>

Gilkey et al., *CEBP*, 2015
Evidence-based effective recommendation

Effective framing

- “Today your child is due for 3 vaccines: Tdap, HPV, and meningococcal.”

- HPV is framed as important

- Many parents just say yes—because they trust you!

Making your job harder

- “Today your child is due for the Tdap and meningococcal vaccines. We should also talk about the HPV vaccine…”

- HPV is framed as “something different”

- Parents sense confusion and your job gets harder

Effective framing works at least 10 times better!

Opel DJ, Pediatrics, 2013
Why does framing makes a difference

**Ineffective first discussion**

**Provider:** Meghan and Mark are due for some shots today: Tdap and the meningococcal vaccine. There is also the HPV vaccine...

- Vaccine perceived as different, optional, unimportant

**Effective first discussion**

**Provider:** Meghan and Mark are due for some shots today: HPV, meningococcal vaccine, and Tdap.

- Presumption of vaccine uptake
- Vaccination perceived as normative, important

**Addressing catch-up population**

**Provider:** I see that Meghan and Mark haven’t gotten their HPV vaccines yet. We should definitely start that today!

- Presumption of vaccine uptake, conveys message of importance

Perkins et al, Pediatrics, 2014
Clinicians Underestimate the Value Parents Place on HPV Vaccine

Parents top 5 reasons for not vaccinating their daughters and sons, NIS-Teen 2013

- Not sexually active
- Not recommended
- Safety concerns
- Not needed
- Lack of knowledge

* Not mutually exclusive.
** Did not know much about HPV or HPV vaccine.
Addressing the top 5 concerns in 45 seconds

**Provider:** Meghan and Mark are due for their HPV vaccine.

**Parent:** Why do they need an HPV vaccine?

**Provider:** The HPV vaccine will help protect them from cancer caused by HPV infection. We know that HPV infection is dangerous—27,000 people in the US get cancer from HPV every year. And we know that the HPV vaccine is safe—over 100 million doses have been given and there haven’t been any serious side effects.

**Parent:** I don’t think they need that yet...

**Provider:** Vaccines only work if they’re given before exposure—we never wait until a child is at risk to give any recommended vaccines. HPV vaccine is also given as early as possible because it produces a better immune response in younger adolescents. That’s why it is so important to start the shots now and finish all 3 of them in the next 6 months.
Resources

For more information, including free resources for providers and patients:


cdc.gov/vaccines/teens