You are the Key to HPV Cancer Prevention
Understanding the Burden of HPV Disease, the Importance of the HPV Vaccine Recommendation, and Communicating about HPV Vaccination

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Disclosure

None

Objectives

1. Describe the burden of HPV disease.
2. Define the importance of HPV vaccination for cancer prevention.
3. Explain the rationale for vaccinating youth at ages 11 or 12.
4. List the recommendations for administering the HPV vaccine to girls and to boys.
5. Provide useful and compelling information about HPV vaccine to parents to aid in making the decision to vaccinate.
6. Locate resources relevant to current immunization practice.
Understanding the Burden

HPV INFECTION & DISEASE

HPV Types Differ in their Disease Associations

- 40 Types
  - Mucosal sites of infection
  - Cutaneous sites of infection

- 80 Types
  - High risk (oncogenic) HPV 16, 18 most common
  - Low risk (non-oncogenic) HPV 6, 11 most common

HPV Infection

- Most females and males will be infected with at least one type of mucosal 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

Every year in the United States 27,000 people are diagnosed with a cancer caused by HPV

That’s 1 case every 20 minutes

Cancers Caused by HPV, U.S.

<table>
<thead>
<tr>
<th>Cancer site</th>
<th>Average number of cancers per year probably caused by HPV†</th>
<th>Percentage per year</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Male</td>
<td>Female</td>
</tr>
<tr>
<td>Anus</td>
<td>1,400</td>
<td>2,600</td>
</tr>
<tr>
<td>Cervix</td>
<td>0</td>
<td>10,400</td>
</tr>
<tr>
<td>Oropharynx</td>
<td>7,200</td>
<td>1,800</td>
</tr>
<tr>
<td>Penis</td>
<td>700</td>
<td>0</td>
</tr>
<tr>
<td>Vagina</td>
<td>0</td>
<td>600</td>
</tr>
<tr>
<td>Vulva</td>
<td>0</td>
<td>2,200</td>
</tr>
<tr>
<td>TOTAL</td>
<td>9,300</td>
<td>17,600</td>
</tr>
</tbody>
</table>

CDC, United States Cancer Statistics (USCS), 2006-2010

New Cancers Caused by HPV per Year

United States 2006-2010

CDC, United States Cancer Statistics (USCS), 2006-2010
Cervical Cancer

- Cervical cancer is the most common HPV-associated cancer among women
  - 500,000+ new cases and 275,000 attributable deaths worldwide in 2008
  - 11,000+ new cases and 4,000 attributable deaths in 2011 in the U.S.
- 37% cervical cancers occur in women who are between the ages of 20 and 44
  - 13% (or nearly 1 in 8) between 20 and 34
  - 24% (or nearly 1 in 4) between 35 and 44


HPV-Associated Cervical Cancer Incidence Rates by State, United States, 2006-2010


Watson et al. MMWR 2012;61:258-261.
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)

Nearly 3 million cases and $7 billion

American Cancer Society, 2008; Schiffman Arch Pathol Lab Med. 2003; Koshiol Int J Epi, 2001

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


Evidence-Based HPV Disease Prevention

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

HPV Vaccines Currently Licensed in U.S.

<table>
<thead>
<tr>
<th></th>
<th>Bivalent 2vHPV (Cervarix)</th>
<th>Quadrivalent 4vHPV (Gardasil)</th>
<th>9-Valent 9vHPV (Gardasil 9)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Manufacturer</td>
<td>GlaxoSmithKline</td>
<td>Merck</td>
<td>Merck</td>
</tr>
<tr>
<td>HPV Types Included</td>
<td>16, 18</td>
<td>6, 11, 16, 18</td>
<td>6, 11, 16, 18, 31, 33, 45, 52, 58</td>
</tr>
<tr>
<td>Contraindications</td>
<td>Hypersensitivity to latex*</td>
<td>Hypersensitivity to yeast</td>
<td>Hypersensitivity to yeast</td>
</tr>
<tr>
<td>Dose Schedule</td>
<td>3 dose series: 0, 1, 6 months</td>
<td>3 dose series: 0, 2, 6 months</td>
<td>3 dose series: 0, 2, 6 months</td>
</tr>
</tbody>
</table>

* May be present in tip of pre-filled syringes

HPV Vaccine Comparison

HPV Types Included in Vaccine

- Bivalent 2vHPV (Cervarix)
- Quadrivalent 4vHPV (Gardasil)
- 9-Valent 9vHPV (Gardasil 9)

HPV Types Cause:
- These HPV Types Cause:
  - Genital warts
  - ~66% of Cervical Cancers
  - ~25% of Cervical Cancers
HPV Vaccine Recommendation

Girls & Boys can start HPV vaccination at age 9
Preteens should finish HPV vaccine series by 13<sup>th</sup> birthday

Plus girls 13-26 years old who haven’t started or finished HPV vaccine series
Plus boys 13-21 years old who haven’t started or finished HPV vaccine series

HPV Vaccination is Routinely Recommended

- HPV vaccination is recommended for both females and males ages 11-12 years
- HPV vaccine series should be completed before the 13<sup>th</sup> birthday

Routine immunization for 11- and 12-year-olds includes HPV vaccination.
Clinicians should recommend HPV vaccine on the same day and in the same way as the other vaccines for preteens.

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>
</tr>
</thead>
<tbody>
<tr>
<td>Females</td>
<td>✔</td>
<td>✔</td>
<td>✔</td>
</tr>
<tr>
<td>Males</td>
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<td>✔</td>
<td>✔</td>
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*vaccination series can be started at 9 years of age
MMWR 2015;64:300-4
Updated ACIP Recommendations: Formulations

- 2vHPV, 4vHPV and 9vHPV all protect against HPV 16 and 18, types that cause about 66% of cervical cancers and the majority of other HPV-attributable cancers in the United States.
- 9vHPV targets five additional cancer causing types, which account for about 15% of cervical cancers.
- 4vHPV and 9vHPV also protect against HPV 6 and 11, types that cause genital warts.

Updated ACIP Recommendations: Interchangeability

If vaccination providers do not know, or do not have available the HPV vaccine product previously administered, or are in settings transitioning to 9vHPV:

For protection against HPV 16 and 18,
- Females: Any HPV vaccine product may be used to continue or complete the series
- Males: 4vHPV or 9vHPV may be used to continue or complete the series

ACIP Recommendations: Timing of the Series

- 2vHPV, 4vHPV and 9vHPV are each administered in a 3-dose schedule
  - Interval between doses 1 → 2: 1-2 months
  - Interval between doses 1 → 3: 6 months
- If the vaccine schedule is interrupted, the series does not need to be restarted
HPV Vaccination Is Safe, Effective, and Provides Lasting Protection

- **HPV Vaccine 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


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HPV VACCINE SAFETY

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The Journey of Your Child’s Vaccine

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HOW A VACCINE’S SAFETY CONTINUES TO BE MONITORED

- FDA and CDC closely monitor vaccine safety after the public begins using the vaccine.

VACCINE ADVERSE EVENT REPORTING SYSTEM

- VAERS collects and analyzes reports of adverse events that happen after vaccination. Reports are submitted by parents, including parents of children with autism.

VACCINE SAFETY Databank

- Network of healthcare professionals and researchers share information on vaccine safety.

For more information, visit: [cdc.gov/vaccines/parents/infographics/journey-of-child-vaccine.html](http://cdc.gov/vaccines/parents/infographics/journey-of-child-vaccine.html)
VAERS: HPV Vaccine Safety Monitoring

- Ongoing safety monitoring has shown most reports are non-serious
- Among the 7.6% of reports coded as “serious,” most frequently cited possible side effects are headache, nausea, vomiting, and fever
- Syncope (fainting) continues to be reported following vaccination among adolescents
- Adherence to a 15-minute observation period after vaccination is encouraged

VSD Rapid Cycle Analysis (RCA), 4vHPV

- RCA allows VSD to detect adverse events following vaccination in near real time
- After approx. 600,000 HPV4 doses among females, no significant risk for any of the pre-specified adverse events after vaccination (including GBS, seizures, syncope, appendicitis, stroke, venous thromboembolism, and allergic reactions)

Ongoing HPV Safety Activities at CDC

- Review of reports to VAERS to search for unusual adverse events or changing patterns of adverse events
- VSD addressing HPV vaccine safety in special populations:
  - Safety of 4vHPV among males
  - Inadvertent 4vHPV vaccination during pregnancy
- VSD addressing HPV vaccine safety concerns that may arise from case reports and/or the media
Non-CDC HPV Vaccine Safety Activities

- 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 Safety
  - Institute of Medicine’s report on adverse effects and vaccines, 2011

Key Findings – CDC and Non-CDC

- Venous thromboembolism (VTE)
  - Study evaluating the risk of VTE in vaccinated persons age 9-26 years
  - Found no increased risk of VTE following 4vHPV
- Autoimmune and neurologic conditions
  - Study addressing concerns about autoimmune and neurologic disease following 4vHPV vaccination.
  - Found no association between 4vHPV vaccination and 16 autoimmune conditions
- Injection site reactions and syncope
  - 4vHPV vaccination 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
  - No major safety concerns found

IOM Review: Syncope & Anaphylaxis

- IOM reviewed possible associations between 8 vaccines and adverse health events. Key findings:
  - Evidence “favors acceptance” of a causal relationship between HPV vaccine and anaphylaxis (rare)
  - Evidence “convincingly supports” a causal relationship between the injection of a vaccine and syncope
- Inadequate evidence was found for causal relationships between HPV vaccination and 12 other specific health events studied

9vHPV Vaccine Safety

- Seven pre-licensure studies including 15,000 males and females
- Generally well tolerated
  - Adverse event profile similar to that of 4vHPV across age, gender, race, and ethnicity
  - More injection-site reactions expected among those who receive 9vHPV

HPV VACCINE IMPACT

Monitoring Impact of HPV Vaccine Programs on HPV-Associated Outcomes

HPV vaccine impact monitoring

- Post licensure evaluations are important to evaluate real world effectiveness of vaccines
- Population impact against early and mid outcomes have been reported:
  - Genital warts
    - Australia, New Zealand, Denmark, Sweden, Germany, Quebec, US
  - HPV prevalence
    - Australia, Norway, Denmark, Sweden, UK, US
  - Cervical lesions
    - Australia, British Columbia, Denmark, Sweden, US
NHANES HPV Prevalence Studies

- National Health and Nutrition Examination Survey (NHANES) data used to compare HPV prevalence
- Before the start of the HPV vaccination program (2003-2006) &
  - From the first 4 years after vaccine introduction (2007-2010)
- Results
  - In 14-19 year olds, vaccine-type HPV prevalence decreased 56%
    (11.5% in 2003-2006 to 5.1% in 2007-2010)
  - Other age groups did not show a statistically significant difference over time

Vaccine effectiveness for prevention of infection was an estimated 82%


Anogenital wart prevalence, female private insurance enrollees, U.S., 2003-2010

Impact of HPV vaccination in Australia

Proportion of Australian born females and males diagnosed as having genital warts at first visit, by age group, 2004-11


Flagg, et al. AJP 2013
Systematic Review and Meta-Analysis: Population-Level Impact of HPV Vaccination

- Review of 20 studies in 9 high income countries
- In countries with >50% coverage, among 13-19 yr olds
  - HPV 16/18 prevalence decreased at least 68%
  - Anogenital warts decreased by ~61%
- Evidence of herd effects
- Some evidence of cross protection against other types

Drolet et al. Lancet Infect Dis 2015

Challenges in Monitoring HPV Vaccine Impact on Cervical Lesions

- Detected through cervical cancer screening
- Changing screening recommendations
- Lack of cervical cancer screening registries in some countries
- Incomplete linkages with vaccination registries

HPV Vaccine Duration of Immunity

- Studies suggest that vaccine protection is long-lasting; no evidence of waning immunity
  - Available evidence indicates protection for at least 8-10 years
- Multiple cohort studies are in progress to monitor the duration of immunity
HPV Vaccine Three-Dose Coverage

Among Girls in High-Income Countries

United States

HPV VACCINE COVERAGE

Adolescent Vaccination Coverage
United States, 2006-2014

HPV Vaccine Series Initiation among Girls Aged 13-17 years, by State, NIS-Teen, 2014
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.

FRAMING THE CONVERSATION

Talking about HPV vaccine
Clinicians Underestimate the Value Parents Place on HPV Vaccine

<table>
<thead>
<tr>
<th>Vaccine</th>
<th>Parent's Median Value</th>
<th>Provider's Median Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Meningitis</td>
<td>9.4</td>
<td>9.2</td>
</tr>
<tr>
<td>Hepatitis</td>
<td>9.5</td>
<td>9.2</td>
</tr>
<tr>
<td>Pertussis</td>
<td>9.5</td>
<td>9.3</td>
</tr>
<tr>
<td>Influenza</td>
<td>9.3</td>
<td>7.0</td>
</tr>
<tr>
<td>HPV</td>
<td>9.3</td>
<td>5.2</td>
</tr>
<tr>
<td>Adolescent</td>
<td>9.3</td>
<td>7.8</td>
</tr>
</tbody>
</table>

Adapted from Healy et al. Vaccine. 2014;32(579-584).

Give a Strong Recommendation to Receive HPV Vaccine at Ages 11 or 12

- A strong recommendation from you is the main reason parents decide to vaccinate
- Many moms in focus groups stated that they trust their child’s doctor and would get the vaccine for their child as long as they received a recommendation from the doctor

Talking to parents about HPV VACCINE

- Make a Bundled Recommendation
  - Recommend HPV vaccine the same way and at the same time as other vaccines. A strong recommendation from you is the main reason parents decide to vaccinate.
  - ‘Your child needs these vaccines for protection against meningitis, Hepatitis, and Pertussis.’
  - Parenting HPV vaccine is easier prevention helps parents make the decision to vaccinate. Parents don’t want to talk about the vaccine until they feel ‘sexually or not sexual transmission.’

- Address Parents’ Questions
  - Help them understand why the vaccine is needed at age 11 or 12, let them know that like any other vaccine, they want their children protected as long as exposure.
  - Emphasize your personal belief in the effectiveness of HPV vaccine to help parents feel secure in their decision. Let them know you have discussed it with the children in your life.
### Make an Effective Recommendation

- **Same way:** Effective recommendations group all of the adolescent vaccines
  Recommend HPV vaccination the *same way* you recommend Tdap & meningococcal vaccines.

- **Same day:** Recommend HPV vaccine *today*
  Recommend HPV vaccination the *same day* you recommend Tdap & meningococcal vaccines.

Unpublished CDC data, 2013.

### If a parent were hesitant...

<table>
<thead>
<tr>
<th>Ask</th>
<th>Clarify &amp; restate their concerns to make sure you understand</th>
</tr>
</thead>
<tbody>
<tr>
<td>Acknowledge</td>
<td>• Emphasize it is the parents’ decision.</td>
</tr>
<tr>
<td></td>
<td>• Acknowledge risks and conflicting information sources.</td>
</tr>
<tr>
<td></td>
<td>• Applaud them for wanting what is best for their child.</td>
</tr>
<tr>
<td></td>
<td>• Be clear that you are concerned for the health of their child, not just public health safety.</td>
</tr>
<tr>
<td>Advise</td>
<td>• Clarify their concerns to make sure you understand and are answering the question they actually care about.</td>
</tr>
<tr>
<td></td>
<td>• Allow time to discuss the pros and cons of vaccines.</td>
</tr>
<tr>
<td></td>
<td>• Be willing to discuss parents’ ideas.</td>
</tr>
<tr>
<td></td>
<td>• Offer written resources for parents.</td>
</tr>
<tr>
<td></td>
<td>• Tailor your advice using this sheet or CDC’s Tips &amp; Time Savers.</td>
</tr>
<tr>
<td>Remember</td>
<td>• Declination is not final. The conversation can be revisited.</td>
</tr>
<tr>
<td></td>
<td>• Because waiting to vaccinate is the risky choice, many pediatricians ask the parent to sign a Declination Form</td>
</tr>
</tbody>
</table>

### Some Parents Need Reassurance

- **Many parents simply accept this bundled recommendation**

- **Some parents may be interested in vaccinating, yet still have questions. Interpret a question as they need additional reassurance from YOU, the clinician they trust with their child’s health care**

- **Ask parents about their main concern (be sure you are addressing their real concern)**

Unpublished CDC data, 2013.
Clinicians can give a strong and effective HPV vaccine recommendation by announcing:

Sophia is due for three vaccines today. These will help protect her from meningitis, HPV cancers, and pertussis. We’ll give those shots at the end of the visit.

If main concern is “Why does my child need this vaccine” try saying:

HPV vaccine is very important because it prevents cancer.

I know we’d like to protect Maureen from cancer and I’d feel better if she got her first dose of the HPV vaccine series today.

If main concern is “My daughter will wait for marriage/won’t be exposed”, try saying:

HPV is so common that almost everyone will be infected at some time.

When your daughter marries, she could catch HPV from her husband. He might have been infected before he ever met her.
If main concern is “why now, let’s wait until child is older,” try saying:

*HPV vaccine produces a more robust immune response in preteens than in older teens which is why I recommend starting the HPV vaccine series today.*

If main concern is “HPV vaccine will be a green light for sex,” try saying:

*Studies have shown that getting the HPV vaccine doesn’t make kids more likely have sex, or to have sex at a younger age.*

If main concern is “would you give it to your child,” try saying:

*Yes, I gave it to my child (or grandchild, etc) because I think preventing cancer is very important.*
If main concern is “side effects,” try saying:

Vaccines, like any medication, can cause side effects. With HPV vaccine most are mild, primarily pain or redness in the arm. This should go away quickly.

HPV vaccine has not been linked with any serious or long-term side effects.

If main concern is “possible effects on fertility,” try saying:

There is no data to suggest that getting HPV vaccine will have an effect on future fertility.

However, persistent HPV infection can cause cervical cancer and the treatment of cervical cancer can leave women unable to have children.

Even treatment for cervical pre-cancer can put a woman at risk for problems with her cervix during pregnancy causing preterm delivery or problems.

Before leaving the exam room, remind parents when to come back. Try saying:

To work, Robert needs the full HPV vaccine series, so . ..

When you check out, please make sure to make an appointment for about 6 weeks from now for the next shot, and put that appointment on your calendar before you leave the office today!
Increase the number of target patients who come in & leave vaccinated

1. Align office policy with mission – e.g., immunize at every opportunity
2. Align communication with mission
3. Standing orders
4. Prompt the person who is supposed to order the vaccine
   - Nursing personnel
   - EHR
   - Both

**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)**

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<tr>
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*vaccination series can be started at 9 years of age

**MMWR 2015;64:300-4**

**Catch-up Vaccination**

- Remember HPV vaccination:
  - Family Planning and preconception visits
  - Well Woman Visits
  - Postpartum visits (MPW) (OK if breastfeeding)
  - Colposcopy Clinic
  - Teen Clinic
  - STD Clinic visits
  - HIV care
- Sexual health visits – think HPV!
Affordability

- Vaccine for Children (VFC) program / NC Immunization Program (NCIP)
- NC Medicaid (including Pregnancy Medicaid) covers HPV vaccine in 19 and 20 year olds
- FP Program Be Smart Medicaid does not cover HPV vaccine
- Merk Vaccine Patient Assistance Program
  - Call to enroll, apply for each dose, replacement vaccine shipped quarterly

Be sure everyone in the office understands the mission

Human stories often influence people more than statistics. To understand the human stories behind HPV, listen to survivors:

- Shot By Shot
- Unprotected People on www.immunize.org

Standing orders

- Empower non-physician personnel to vaccinate patients (after assessing for specific contraindications) without direct physician involvement
- Practices should have on file preapproved orders to vaccinate
- Templates available for all routine vaccines at www.immunize.org/standing-orders/
- To save physicians time, staff have to be aware of the standing orders and be trained to use it
Review Question #1

HPV vaccine is recommended for the following persons:

A. All adolescents at the 11 to 12 year old visit.
B. Females only at the 13 year old visit.
C. Males only at the 11 to 12 year old visit.
D. Females only at the 11 to 12 year old visit.

Review Question #2

Why should males receive HPV vaccine?

A. Prevention of infection with HPV types 6, 11, 16, 18.
B. Prevention of genital warts caused by HPV types 6 and 11.
C. Prevention of anal cancer caused by HPV types 16 and 18.
D. All of the above.
Review Question #2

Why should males receive HPV vaccine?

A. Prevention of infection with HPV types 6, 11, 16, 18.
B. Prevention of genital warts caused by HPV types 6 and 11.
C. Prevention of anal cancer caused by HPV types 16 and 18.
D. All of the above.

Review Question #3

Which of the following HPV vaccine recommendations for a child aged 11 or 12 years is the most likely to be successful?

A. Ask parent if child is sexually active and then discuss importance of HPV vaccination.
B. Tell parent that their child needs three vaccinations to prevent meningitis, HPV cancers, and pertussis.
C. Tell parent about the vaccinations that are mandatory for school entry and ask if they also want HPV vaccine.
D. Ask parent if they want to get HPV vaccination for their child or wait until the child is older.
Want to know when we have new resources and tools? Send us an email to request our newsletter: PreteenVaccines@cdc.gov

We can help provide speakers for grand rounds and continuing education events, as well.

HPV VACCINE IS CANCER PREVENTION And YOU are the key! #WeCanStopHPV