Public Health Importance of Human Papillomavirus Infection and Disease

Mona Saraiya, MD MPH
Associate Director for Global Cancer
Division of Cancer Prevention and Control
National Center for Chronic Disease Prevention and Health Promotion
Human Papillomaviruses

- **Double-stranded DNA virus**
  - More than 120 closely related viruses
    - Types numbered in order of discovery

- **HPV infection confined to epithelium**
  - Begins in base of epithelium, cells proliferate and are not killed

- **Humoral and cellular immune responses identified**
  - Antibodies detected in less than 70% of females infected
HPV Types Differ in their Disease Associations

~40 Types
- Mucosal/Genital sites of infection
- Cutaneous sites of infection

High risk (oncogenic)
HPV 16, 18

Low risk (non-oncogenic)
HPV 6, 11

Cervical cancer other anogenital & oropharyngeal cancers and cancer precursors
Low grade cervical disease

Genital warts
Laryngeal papillomas
Low grade cervical disease

“Common” hand and foot warts
Overview of HPV Epidemiology and Natural History

- **HPV infection is very prevalent in the population**
  - Almost all sexually active persons will acquire HPV
  - In the US:
    - ~79 million infected
    - 14 million new infections per year

- **Genital HPV is first acquired soon after onset of sexual activity**
  - 40% infected within 2 years

- **Infection is usually transient, asymptomatic**

- **Cancer is a rare outcome**
  - Requires persistent infection with high risk HPV types

Satterwhite CL et al. STD 2013;40:187-93

Hariri S et al. JID 2011;204:566-72
NHANES: National Health and Nutrition Examination Survey
Burden of Disease Caused by Low-Risk HPV

- **Genital Warts**
  - Over 300,000 new cases a year in the US
  - Peak incidence in persons aged 20-29 years
  - Recur 40% of the time and lead to repeat clinical visits, treatments and psychosocial stigma

- **Recurrent respiratory papillomatosis (RRP)**
  - Rare condition in which warts grow in the throat
  - Occur in children (juvenile-onset) and adults (adult-onset)
  - Can result in airway obstruction requiring multiple surgeries
Persistent infection with high-risk types required for progression to precancer and cancer
- Peak incidence of precancers in late 20’s and of cancers in mid to late 40’s
Cervical Cancer Screening
Pap (Papanicolaou) Test

- A test which collects cells from the surface of the cervix and looks for abnormal cells
- Precancer can be detected and treated before cervical cancer develops
- HPV testing added as part of screening, resulting in improved sensitivity while safely allowing for extension of screening intervals
## New Cervical Cancer Screening Guidelines: ACS, USPSTF, ACOG

<table>
<thead>
<tr>
<th></th>
<th>ACS 2012</th>
<th>USPSTF 2012</th>
<th>ACOG 2012</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Age to start</strong></td>
<td>Age 21 years</td>
<td>Age 21 years</td>
<td>Age 21 years</td>
</tr>
<tr>
<td><strong>Women ages 21-29 years</strong></td>
<td>Pap every 3 years</td>
<td>Pap every 3 years</td>
<td>Pap every 3 years</td>
</tr>
<tr>
<td><strong>Women ages 30-65 years</strong></td>
<td>Cotesting every 5 years (preferred) or Every 3 years with Pap alone</td>
<td>Cotesting every 5 years (preferred) or Every 3 years with Pap alone</td>
<td>Cotesting every 5 years (preferred) or Every 3 years with Pap alone</td>
</tr>
<tr>
<td><strong>Screening among fully vaccinated</strong></td>
<td>Same as for non-vaccinated</td>
<td>Not reviewed</td>
<td>Same as for non-vaccinated</td>
</tr>
</tbody>
</table>

*All guidelines recommend that women who have been adequately screened can discontinue Pap at age 65.*

ACS: American Cancer Society  
USPSTF: US Preventive Services Task Force  
ACOG: American College of Obstetricians and Gynecologists
Federally Funded Cancer Registries, 2013

American Samoa; Commonwealth of the Northern Mariana Islands; Federated States of Micronesia; Guam; Republic of Marshall Islands; Republic of Palau

NPCR: National Program of Cancer Registries (CDC)
SEER: Surveillance, Epidemiology, and End Results Program (National Cancer Institute)
Average Number of New HPV-associated Cancers Overall, and by Sex, in the United States, 2005-2009

Total (N=32,415)

- Cervix 35% n=11,279
- Oropharynx 36% n=11,629
- Anus 15% n=4,771
- Vagina 9% n=3,039
- Vulva 2% n=694
- Penis 3% n=1,003

Women (N=20,413)

- Cervix 55% n=11,279
- Oropharynx 11% n=2,317
- Anus 15% n=3,084
- Vagina 15% n=3,039
- Vulva 4% n=694
- Penis 3% n=1,003

Men (N=12,002)

- Cervix 78% n=9,312
- Oropharynx 8% n=1,003
- Anus 14% n=1,687
- Vagina 2% n=694
- Vulva 3% n=1,003


*In addition: Cervical disease and pre-invasive cancers: CIN1,2,3 ~ 1.4 million; AIN3 ~ 4300; VIN3 ~ 27,000, VAIN3 ~ 7600 (CDC, unpublished data)

Y axis scale is different for cervical cancer.

Trends in Oropharyngeal and Anal Cancer by Sex, Race, and Ethnicity in the United States, 2000–2009

Average Annual Percent Change

*statistically significantly different from zero at P<0.05

API: Asian/Pacific Islander
AI/AN: American Indian/Alaskan Native
Percentage of Cervical Cancers Attributed to HPV types, Worldwide

- HPV 16: 60.6%
- HPV 18: 10.2%
- HPV 45: 5.9%
- HPV 33: 3.8%
- HPV 31: 3.7%
- HPV 52: 2.8%
- HPV 58: 2.3%
- HPV 35: 1.9%
- HPV 39: 1.6%
- HPV 51: 1.3%
- HPV 59: 1.1%
- HPV 56: 0.8%

Source: de Sanjose S et al. Lancet Oncol 2010;11:1048-56
### Percentages of HPV DNA-positive Cancers, United States, 1999-2005

<table>
<thead>
<tr>
<th>Cancer</th>
<th>Any HPV %</th>
<th>HPV 16/18 %</th>
</tr>
</thead>
<tbody>
<tr>
<td>Cervix</td>
<td>90</td>
<td>66</td>
</tr>
<tr>
<td>Vaginal</td>
<td>75</td>
<td>55</td>
</tr>
<tr>
<td>Vulvar</td>
<td>69</td>
<td>49</td>
</tr>
<tr>
<td>Anal</td>
<td>91</td>
<td>79</td>
</tr>
<tr>
<td>Penile</td>
<td>63</td>
<td>48</td>
</tr>
<tr>
<td>Oropharyngeal</td>
<td>72</td>
<td>62</td>
</tr>
</tbody>
</table>

HPV attributable cancers = 26,000 cancers
HPV 16/18 attributable cancers= 21,000 cancers

Data presented by Saraiya M, 28th International Papillomavirus Conference 2012, Puerto Rico
### Annual Cost of HPV-associated Disease, in 2010 U.S. Dollars

<table>
<thead>
<tr>
<th>Health outcome</th>
<th>Cost ($ billions)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Cervical cancer screening*</td>
<td>6.6</td>
</tr>
<tr>
<td>Cervical cancer</td>
<td>0.4</td>
</tr>
<tr>
<td>Other anogenital cancers</td>
<td>0.2</td>
</tr>
<tr>
<td>Oropharyngeal cancer</td>
<td>0.3</td>
</tr>
<tr>
<td>Anogenital warts</td>
<td>0.3</td>
</tr>
<tr>
<td>RRP**</td>
<td>0.2</td>
</tr>
<tr>
<td>TOTAL</td>
<td>8.0</td>
</tr>
</tbody>
</table>

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

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

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RRP: recurrent respiratory papillomatosis
Summary

- HPV is a common infection and cause of malignant and non-malignant diseases
  - Causes cancer at a variety of anatomic sites
- Outcomes are burdensome, costly and stigmatizing
- Approximately 26,000 HPV-attributable cancers
  - 21,000 are vaccine preventable
  - Trends for anal and oropharyngeal cancers increasing
  - Racial and ethnic disparities exist
- Cervical cancer screening guidelines
  - Newly harmonized
  - Unchanged for vaccinated individuals, but may change in future
Overview of HPV Vaccines and Impact Monitoring

Eileen F. Dunne, MD, MPH
Medical Officer
Division of STD Prevention
National Center for HIV/AIDS, Viral Hepatitis, STD and TB Prevention
# HPV Vaccines Licensed by FDA

<table>
<thead>
<tr>
<th></th>
<th>Quadrivalent (Gardasil®)</th>
<th>Bivalent (Cervarix®)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Manufacturer</td>
<td>Merck</td>
<td>GlaxoSmithKline</td>
</tr>
<tr>
<td>VLP types</td>
<td>6, 11, 16, 18</td>
<td>16, 18</td>
</tr>
<tr>
<td>Schedule in months from first vaccination</td>
<td>0, 1-2, 6</td>
<td>0, 1-2, 6</td>
</tr>
</tbody>
</table>

**FDA:** Food and Drug Administration  
**VLP:** virus like particle
# HPV Vaccine Efficacy in Randomized Controlled Trials

<table>
<thead>
<tr>
<th>Outcome</th>
<th>Vaccine</th>
<th>Sex</th>
<th>Vaccine Efficacy</th>
</tr>
</thead>
<tbody>
<tr>
<td>Cervical precancer</td>
<td>Bivalent and Quadrivalent</td>
<td>F</td>
<td>&gt;92%</td>
</tr>
<tr>
<td>Vaginal/Vulvar precancer</td>
<td>Quadrivalent</td>
<td>F</td>
<td>100%</td>
</tr>
<tr>
<td>Anal precancer</td>
<td>Quadrivalent</td>
<td>M</td>
<td>75%</td>
</tr>
<tr>
<td>Genital warts</td>
<td>Quadrivalent</td>
<td>F, M</td>
<td>&gt;89%</td>
</tr>
</tbody>
</table>

No evidence of efficacy against existing HPV infection or disease

Evolution of Recommendations for HPV Vaccination in the U.S.

**Quadrivalent Routine**, females 11 or 12 yrs* and 13-26 yrs not previously vaccinated

- **2006**
- **June**

**Quadrivalent or Bivalent Routine**, females 11 or 12 yrs* and 13-26 yrs not previously vaccinated

- **2007**
- **October**

**Quadrivalent May be given**, males 9-26 yrs*

- **2008**

**Quadrivalent Routine**, males 11 or 12 yrs* and 13-21 yrs not previously vaccinated

- **2009**
- **October**

**May be given, 22-26 yrs**

- **2010**
- **2011**
- **2012**

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Quadrivalent (HPV 6,11,16,18) vaccine; Bivalent (HPV 16,18) vaccine

* Can be given starting at 9 years of age

** For MSM and immunocompromised males, quadrivalent HPV vaccine through 26 years of age
Current ACIP HPV Vaccine Recommendations
Females and Males

- **Routine vaccination of females aged 11 or 12 years with 3 doses of either bivalent or quadrivalent HPV vaccine**
  - Also for 13 through 26 year olds who have not been vaccinated previously or who have not completed the 3-dose series

- **Routine vaccination of males aged 11 or 12 years with 3 doses of quadrivalent HPV vaccine**
  - Also for 13 through 21 year olds who have not been vaccinated previously or who have not completed the 3-dose series
  - Gay, bisexual and other men who have sex with men are recommended to receive vaccine through age 26 years

www.cdc.gov/vaccines/pubs/ACIP-list.htm#hpv
ACIP: Advisory Committee on Immunization Practices
## Monitoring of HPV Vaccines

<table>
<thead>
<tr>
<th>Objectives</th>
<th>Methods</th>
<th>Examples</th>
</tr>
</thead>
<tbody>
<tr>
<td>Vaccine Safety</td>
<td>Surveillance and Research</td>
<td>VAERS, VSD, CISA</td>
</tr>
<tr>
<td>Vaccine Impact on Infection and Disease Burden</td>
<td>Surveillance and Research</td>
<td>NHANES, Administrative data HPV-IMPACT, Cancer Registries</td>
</tr>
<tr>
<td>Vaccine Coverage</td>
<td>National Surveys, Registries</td>
<td>NIS-Teen, Immunization Registries</td>
</tr>
<tr>
<td>Behaviors and Attitudes</td>
<td>National Surveys</td>
<td>NSFG, NHANES</td>
</tr>
</tbody>
</table>

VAERS: Vaccine Adverse Event Reporting System  
VSD: Vaccine Safety Datalink  
NHANES: National Health and Nutrition Examination Survey  
NIS-Teen: National Immunization Survey, Teen Component  
NSFG: National Survey of Family Growth
Post-licensure Vaccine Safety Monitoring: Rationale

- High safety standards expected for vaccines
  - Products given to healthy populations for prevention of disease
- Pre-licensure trials are often too small to detect rare events and special populations may not be adequately represented
- Critical to maintain public confidence in immunization, provide timely information
Post-licensure Vaccine Safety Systems

- **Vaccine Adverse Event Reporting System (VAERS)**
  - Collaboration between CDC and FDA
    - National spontaneous reporting system
    - Can detect potential vaccine safety concerns (signals) but not designed to assess causality

- **Vaccine Safety Datalink (VSD)**
  - Collaboration between CDC and 9 managed care organizations
    - ~9.2 million insured members under active surveillance annually
    - Rates, risks estimates calculated
    - Near real time evaluation through Rapid Cycle Analysis (RCA)

- **Clinical Immunization Safety Assessment (CISA)**
  - Collaboration between CDC and 7 academic medical centers
    - For clinically complex vaccine adverse events and research on biologic mechanisms

References:
- Lieu TA et al. Med Care 2007;45:S89-95
Summary of VSD Safety Evaluation of HPV Vaccine

- **Findings from the VSD RCA:**
  - Among 600,588 doses of quadrivalent vaccine administered to females 9-26 years, no significant increased risk for any of the pre-specified adverse events after vaccination:
    - Guillain-Barré syndrome, seizures, syncope, appendicitis, stroke, venous thromboembolism, anaphylaxis and other allergic reactions

- **Total doses of quadrivalent HPV vaccine administered through January 2013 within VSD:**
  - > 2.07 million doses
    - ~270K doses of quadrivalent HPV vaccine given to males
Impact on Biologic Outcomes - What is Vaccine-Preventable?

- **Cancers:** 70% of cervical and ~90% of non-cervical HPV associated cancers are potentially preventable by either vaccine
  - ~21,000 cancer cases each year

- **Cervical Pap test abnormalities:** 30-70% are potentially preventable by either vaccine
  - ~1 million cervical Pap test abnormalities each year

- **Genital warts:** 90% of genital warts preventable by quadrivalent vaccine
  - ~325,000 genital warts cases each year
Monitoring Impact on Biologic Outcomes: Current Activities

- **Surveillance and research to monitor different outcomes**
  - Early, mid, late measures
  - National, regional, state
  - General, other populations

- **Vaccine effectiveness studies**

- **Laboratory evaluations**
  - HPV type-specific prevalence for various outcomes
  - U.S. population, precancers, cancers

- **Challenges**
  - Most outcomes not nationally reportable, many outcomes dependent on cervical cancer screening, varied stakeholder, laboratory testing
## Monitoring Impact on Biologic Outcomes: Current Activities

<table>
<thead>
<tr>
<th>Timeframe</th>
<th>System/study</th>
<th>Outcome</th>
</tr>
</thead>
<tbody>
<tr>
<td>Early</td>
<td>NHANES</td>
<td>HPV type specific prevalence</td>
</tr>
<tr>
<td></td>
<td>Administrative data</td>
<td>Genital warts</td>
</tr>
<tr>
<td>Mid</td>
<td>Select cancer registries</td>
<td>Cervical precancers</td>
</tr>
<tr>
<td></td>
<td>HPV-IMPACT</td>
<td></td>
</tr>
<tr>
<td>Late</td>
<td>Cancer registries</td>
<td>Cervical and other associated cancers</td>
</tr>
</tbody>
</table>

Flagg E et al. AJPH 2013 (in press)  
Hariri S et al. JID 2012;206:1878-86
Proportion of Women Aged <26 Years with Genital Warts, 2004-2010, Australia

Vaccine first introduced in Australia in 2006 (dashed line)

73% decrease in genital warts

Genital Warts, Females 2003-2010 by Age Group, U.S. MarketScan® Database

Vaccine first introduced in United States (dashed line)

Incidence per 1,000 person years

- 15-19
- 20-24
- 25-29
- 30-34
- 35-39

Flagg E et al. AJPH 2013 (in press)
Summary

- **HPV Vaccines**
  - Bivalent and quadrivalent vaccines are safe and effective
  - Potential to prevent large burden of cancers and diseases

- **Monitoring**
  - Ongoing monitoring is important for vaccine program and policy
    - Safety surveillance
    - Biologic outcomes
      - Special evaluations: e.g. effectiveness of less than 3 vaccine doses
  - Early in timeline to measure impact on some biologic outcomes
    - Evidence of impact on genital warts
  - Increasing HPV vaccine coverage important to reduce cancers and diseases
U.S. HPV Vaccination Program: Progress and Challenges

Shannon Stokley, MPH
Acting Associate Director of Science
Immunization Services Division
National Center for Immunization and Respiratory Diseases
Overview

- Describe U.S. vaccination program
- Review HPV vaccination coverage levels
- Summarize factors contributing to less than optimal vaccination coverage
U.S. HPV Vaccination Program

- HPV is one of several vaccines recommended for the adolescent age group ("adolescent platform")
  - Tdap, MCV4, annual influenza
- Majority (83%) of vaccines are administered in primary care provider offices and publicly funded clinics (FQHC, RHC)
  - Vaccines often administered during preventive healthcare visits
- National survey found that 98% of pediatricians and 88% of family physicians stocked and administered HPV vaccine
- Vaccine covered by most private health insurance companies and government insurance programs

Daley M et al. Pediatrics 2010;126:425-33
Tdap: tetanus, diphtheria, and acellular pertussis vaccine
MCV4: quadrivalent meningococcal conjugate vaccine
FQHC: federally qualified health center
RHC: rural health clinic
Vaccines For Children (VFC) Program

- Federal legislation enacted in 1994 to remove cost as a barrier to vaccination
- Provides federally purchased vaccines recommended by ACIP at no cost to eligible children 18 years and younger:
  - Medicaid eligible
  - Uninsured
  - American Indian/Alaska Native descent
  - Underinsured (if vaccinated at an FQHC or RHC)
- In 2011, 39.4% of adolescents 13-17 years of age were eligible for VFC vaccine
- ~44,000 immunization providers enrolled in VFC

\[1^{1} \text{2011 National Immunization Survey-Teen available at http://www.cdc.gov/vaccines/stats-surv/nis/nis-2011-released.htm#nistineen} \]
\[2^{2} \text{2010 VFC Program Management Survey available at: http://www2a.cdc.gov/nip/irar/grantee/vfcprovider10.asp} \]

ACIP: Advisory Committee on Immunization Practices
FQHC: federally qualified health center
RHC: rural health clinic
National Immunization Survey-Teen (NIS-Teen)

- **Annual survey**
  - Implemented in 2006
  - State level estimates available beginning 2008

- **Uses National Immunization Survey (NIS) sample frame methodology**
  - Random digit dial telephone survey
  - National sample of parents of adolescents aged 13-17 years
  - Provider record check for verification of immunizations received

- **All analyses limited to adolescents with provider reported immunization histories**

Additional information about the NIS-Teen available at: http://www.cdc.gov/vaccines/stats-surv/nis/default.htm#nistineen
National Estimated Vaccination Coverage Levels among Adolescents 13-17 Years, NIS-Teen, 2006-2011
Coverage of 1 of More Doses of HPV among Adolescent Girls 13-17 Years by State, NIS-Teen 2011

Note 1: Human Papillomavirus Vaccine, either quadrivalent or bivalent.
Note 2: Includes female adolescents born between January 1993 and February 1999
Vaccination Estimates among Adolescent Girls 13-17 Years by Poverty Status, NIS-Teen 2011

**statistically significant (p<0.05)
Vaccination Estimates among Adolescent Girls 13-17 Years by Race/Ethnicity, NIS-Teen 2011

**statistically significant (p<0.05)
Completion of the HPV Series among Adolescent Girls 13-17 Years by Race/Ethnicity, NIS-Teen 2011

Completion: among the girls who started the series, the proportion that received all 3 doses

- Nationally, 71% of girls that start the HPV series, complete the series
- In contrast, population-wide 3-dose coverage was 35% in 2011

** Statistically different (P<0.05) from White-NH.
NH: non-Hispanic
HPV Vaccination Uptake among Adolescent Boys

- Available data represents vaccination activities prior to implementation of routine recommendation approved in October, 2011
- 8.3% of boys 13-17 years of age have initiated the series
- So far vaccine uptake (coverage) follows the same pattern as observed for girls
  - Higher coverage among boys living below the poverty level
  - Higher coverage among Black and Hispanic boys
  - Based on only one year of data

Challenges in Achieving High Levels of HPV vaccination

- Parental attitudes and vaccine intentions
- Provider attitudes and practices
HPV Vaccine Intentions (in the Next 12 Months) among Parents of Adolescent Girls 13-17 Years of Age, NIS-Teen

NIS-Teen available at http://www.cdc.gov/vaccines/stats-surv/nis/default.htm#nisteen
### Most Common Reasons for Not Vaccinating Daughter, among Parents with No Intention to Vaccinate in the Next 12 Months, NIS-Teen 2011

<table>
<thead>
<tr>
<th>Reason</th>
<th>Percentage</th>
</tr>
</thead>
<tbody>
<tr>
<td>Not needed or necessary</td>
<td>23.2%</td>
</tr>
<tr>
<td>Not sexually active</td>
<td>19.5%</td>
</tr>
<tr>
<td>Safety concern/side effects</td>
<td>19.3%</td>
</tr>
<tr>
<td>Lack of knowledge</td>
<td>15.2%</td>
</tr>
<tr>
<td>No recommendation by provider</td>
<td>9.6%</td>
</tr>
</tbody>
</table>

Response categories are not mutually exclusive

Strength of HPV Vaccine Recommendation for Female Patients, Pediatrics and Family Physicians (N=609)

- **11-12 y.o. females**
  - Strongly recommend: 51%
  - Recommend, but not strongly: 36%
  - Make no recommendation: 8%

- **13-15 y.o. females**
  - Strongly recommend: 79%
  - Recommend, but not strongly: 15%

- **16-18 y.o. females**
  - Strongly recommend: 85%
  - Recommend, but not strongly: 10%

Allison et al. [https://cdc.confex.com/cdc/nic2011/webprogram/Paper25181.html](https://cdc.confex.com/cdc/nic2011/webprogram/Paper25181.html)
HPV Vaccine Communications During the Healthcare Encounter

- HPV vaccine is often presented as ‘optional’ whereas other adolescent vaccines are recommended
- Some expressed mixed or negative opinions about the ‘new vaccine’ and concerns over safety/efficacy
- When parents expressed reluctance, providers were hesitant to engage in discussion
- Some providers shared parents’ views that teen was not at risk for HPV and could delay vaccination until older

Goff S et al. Vaccine 2011;10:7343-9
Hughes C et al. BMC Pediatrics 2011;11:74
Among girls unvaccinated for HPV, 78% had a missed opportunity.
Summary

- HPV vaccination coverage among U.S. adolescent girls is increasing, but slowly
  - Vaccination uptake varies by state
- Efforts are needed to achieve high HPV coverage and subsequent HPV disease prevention:
  - Address provider and parent attitudes towards HPV vaccination
  - Improve communication skills among primary care providers
  - Implement evidence based strategies (e.g. reminder/recall, coverage assessment and feedback) to reduce missed opportunities

Task Force on Community Preventive Services recommendations at http://www.thecommunityguide.org/vaccines/vpd-ajpm-recs.pdf
What Is Needed to Increase HPV Vaccine Coverage?

Amy B. Middleman, MD, MSEd, MPH
Associate Professor of Pediatrics
Baylor College of Medicine
Texas Children’s Hospital
Houston, Texas
Dr. Middleman’s institution receives grants from Novartis and the Society for Adolescent Health and Medicine
Increasing HPV Vaccine Coverage

- **Adolescent platform**
  - A specific time period during which there is an expectation of vaccine completion

- **Public policy strategies**

- **Provider strategies**
  - Practice strategies
  - Provider communication
## ACIP Adolescent Immunization Schedule ("Adolescent Platform")

<table>
<thead>
<tr>
<th>Vaccines</th>
<th>11-12 yrs</th>
<th>13-15 yrs</th>
<th>16-18 yrs</th>
</tr>
</thead>
<tbody>
<tr>
<td>HPV</td>
<td>3-dose series</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Tdap</td>
<td>1 dose</td>
<td></td>
<td></td>
</tr>
<tr>
<td>MCV4</td>
<td>1st dose</td>
<td></td>
<td>booster</td>
</tr>
<tr>
<td>Influenza</td>
<td></td>
<td>Annual immunization</td>
<td></td>
</tr>
</tbody>
</table>

- Range of recommended ages for all children
- Range of recommended ages for catch-up immunization

Tdap: tetanus, diphtheria, and acellular pertussis vaccine
MCV4: meningococcal conjugate vaccine
ACIP: Advisory Committee on Immunization Practices
Building an Adolescent Immunization Platform

- Focuses on disease prevention and health promotion among this age group
- Presents opportunities for improved comprehensive care that includes other health issues (e.g., screening and prevention of risk behaviors)
- Creates parental and provider expectation of adherence to established adolescent vaccine recommendations
Increasing HPV Vaccine Coverage

- Adolescent platform
- Public policy strategies
- Provider strategies
  - Practice strategies
  - Provider communication
Policy Approaches to Support Adolescent Immunization

- State legislative efforts for school requirements and education
- Utilization of alternative immunization sites
- Health insurance reform
Current State Legislation

- **Middle School requirements**
  - Vaccination: Td/Tdap: 41 states; MCV4: 13 states;
  - HPV (vaccination): 2 (DC, VA)
  - HPV (education): 7 states (WA, LA, NC, MI, IA, TX, IN)

- **General state legislation related to HPV vaccine:**
  - Education of parents/general public (n=14 states)

- **Study of state requirements and coverage**
  - School requirements: For Tdap and MCV4 - significantly higher coverage compared with states no requirements
  - Education requirements: for HPV and MCV4, no difference compared with states with no requirements

Alternative Immunization Sites and Potential Benefits

- **Sites**
  - Pharmacies, school-located clinics, city/county clinics, family planning clinics, Ob/Gyn offices and clinics, emergency departments

- **Potential Benefits**
  - Immunize adolescents who lack a medical home AND provide a list of nearby adolescent medical homes
  - Complete multiple-dose regimens
  - Provide access (e.g., expanded hours and closer to home)
  - Safety of vaccination at alternate sites documented
  - Share information with patient’s medical home using IIS

IIS: Immunization Information Systems
D’Heilly SJ et al. Vaccine 2006;24:4024-27
Middle School Parents’ Willingness to Use Alternative Sites

<table>
<thead>
<tr>
<th>Service</th>
<th>Percent</th>
</tr>
</thead>
<tbody>
<tr>
<td>Medical home</td>
<td>65</td>
</tr>
<tr>
<td>ER</td>
<td>6</td>
</tr>
<tr>
<td>Public clinic</td>
<td>32</td>
</tr>
<tr>
<td>Mobile clinic</td>
<td>14</td>
</tr>
<tr>
<td>School</td>
<td>41</td>
</tr>
<tr>
<td>Pharmacy</td>
<td>5</td>
</tr>
</tbody>
</table>

Houston, Texas; 1838 respondents
Middleman AB et al. Vaccine 2010; 28:2674-78
School-Located Vaccination

- **Benefits**
  - Majority of adolescents attend school
  - Potential to vaccinate a large number of adolescents
  - Reach many adolescents who may not have regular access to healthcare

- **Challenges**
  - Adolescent participation may be limited to specific sub-groups
  - Cost to provide vaccination in schools can be quite high
  - Billing different health plans for immunization services
  - Obtaining parental consent

Approximately 6% of all students returned consent forms
Among 8 middle schools, 522 eligible students were immunized:

<table>
<thead>
<tr>
<th>Vaccine</th>
<th>Number Administered</th>
</tr>
</thead>
<tbody>
<tr>
<td>Flu (inactivated and LAIV)</td>
<td>475</td>
</tr>
<tr>
<td>Tdap</td>
<td>328</td>
</tr>
<tr>
<td>MCV4</td>
<td>327</td>
</tr>
<tr>
<td>HPV</td>
<td>410</td>
</tr>
<tr>
<td>Other (HepB, varicella, etc.)</td>
<td>82</td>
</tr>
</tbody>
</table>
Insurance Reforms that Might Impact Vaccine Uptake (Affordable Care Act)

- **First dollar coverage under private insurance**
  - No out of pocket costs for all ACIP routinely recommended vaccines when given by in-network provider
  - In effect September 2010
  - Plans have one year following CDC adoption of new ACIP recommendations to implement

- **Increase in Medicaid reimbursement for vaccine administration fee - time limited**
  - Time period: 2013-2014
  - Before 2013 range: $2.00 - $17.85
  - Proposed fees range: $19.54 - $27.44
Increasing HPV Vaccine Coverage

- Adolescent platform
- Public policy strategies
- Provider strategies
  - Practice strategies
  - Provider communication
Strengthening Immunization in the Medical Home: What Can Providers Do?

- Increase their own knowledge regarding vaccine recommendations and safety of recommended vaccines

- Improve communication with parents
  - Importance of provider recommendation
  - Overall messages
  - Responses to specific concerns

- Initiate practice changes to increase immunization
  - Recall systems
  - Screening tools and standing orders
  - Use of Immunization Information Systems (IIS)
  - Vaccination “quick visits”

Impact of Reminder and Recall on Vaccination Rates among Adolescents

- **Tdap**: 49.5% (干预组) vs. 40.8% (对照组)  (*p<0.05*)
- **MCV4**: 44.3% (干预组) vs. 29.5% (对照组)  (*p<0.05*)
- **HPV-1**: 26.5% (干预组) vs. 15.3% (对照组)  (*p<0.05*)

*Suh C et al. Pediatrics 2012;129:e1437-45*
Key Messages for Parents

- This is a vaccine to prevent CANCER
- The vaccine is SAFE and EFFECTIVE
- The time to give the vaccine is before exposure
- Vaccine is recommended for boys and girls
Guidance for Providers: Improving the “Discussion”

- The discussion regarding mode of HPV transmission should be age appropriate
- Discussion of HPV vaccine might provide an opportunity to discuss sexual health issues, if appropriate
- Vaccination not found to result in increase sexual risk behavior

Bednarczyk RA et al. Pediatrics 2012;130:798-805
Forester AS et al. Vaccine 2012;30:4939-44
Take Home Points

- New immunization recommendations provide enhanced primary prevention opportunities for adolescents
- Public health policies at state and federal levels can be implemented to support adolescent immunization
- Providers can implement communication and quality improvement strategies in the office to improve adolescent immunization rates
Prevention of HPV-associated Disease
Global and Domestic Overview

Lauri Markowitz, MD
Team Lead
Division of STD Prevention
National Center for HIV/AIDS, Viral Hepatitis, STD and TB Prevention
Global Burden of Cervical Cancer

Incidence of cervical cancer per 100,000 females (all ages), age-standardized 2008

80% of cervical cancer deaths occur in developing countries

Countries with HPV Vaccine in their National Immunization Schedules, 2011

- HPV vaccination programs have been introduced into more than 40 countries
- Most are developed countries
- Challenges:
  - Expense of vaccine
  - Competing priorities with other new vaccine introduction
  - Adolescent target age group

No (150 countries or 77%)
Yes (40 countries or 21%)
Yes (Part of the country) (4 countries or 2%)

WHO/IVB database, 194 WHO Member States. Data as of October 2012
International Cervical Cancer Prevention Efforts

- **WHO recommends introduction of HPV vaccination**
  - Part of a comprehensive strategy for cervical cancer prevention

- **Vaccine financing will allow increased HPV vaccine introductions in low resource countries**
  - The Global Alliance on Vaccines and Immunizations (GAVI) will fund HPV vaccine for eligible countries starting in 2013

- **Cervical cancer prevention through other public-private partnerships focusing on cervical cancer screening**
  - Pink Ribbon Red Ribbon®
    (Partners include Susan G. Komen for the Cure, PEPFAR, George W. Bush Foundation, UNAIDS)

WHO. WER No.15, 2009;84:117-32
http://www.gavialliance.org/
Summary

- The substantial burden of HPV-associated disease can be decreased by use of two available safe and effective prophylactic HPV vaccines
- In the United States, vaccine coverage is below target goals
  - Programs are in place to monitor coverage, safety and impact of vaccination
  - Measures can be implemented to improve vaccine uptake
- Progress being made to introduce vaccine in low income countries where most cervical cancer cases and deaths occur