Making Sense of Cervical Cancer Screening and HPV Vaccination Guidelines

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Women’s Health Congress
April 2015

Objectives
At the conclusion of this session, participants will be able to—
- Describe the epidemiology, natural history, and clinical features of cervical cancer.
- Discuss current recommendations and rationale for HPV vaccination and cervical cancer screening in the U.S.
- Identify opportunities for screening and vaccination and share evidence-based practices for clinicians

Conflict of Interest Disclaimer
I have no conflict of interest

Cervical Cancer Is Preventable—
No woman should die of cervical cancer

- More than 4,000 women die of cervical cancer each year.
- As many as 93% of cervical cancers could be prevented by screening and HPV vaccination.
- In 2012, 8 million U.S. women ages 21 to 65 have not been screened for cervical cancer in the last 5 years.

Percentage of Women Who Had Not Been Screened for Cervical Cancer in the Past 5 Years, BRFSS 2012

- 11.4% (8 million) women aged 21–65 had not been screened for cervical cancer in the past 5 years.
- 23.1% of women not screened did not have health insurance.
- 25.5% of women not screened did not have a regular health care provider.
- The proportion of inadequately screened women is higher among older women and Asian/Pacific Islanders.

Cervical Cancer Incidence Rates—United States, 2011

Source: MMWR 2014,63.
Cervical Cancer Deaths—United States, 2011

Screening, Incidence, and Death by State and Region

- **Screening, 2012**
  - Range of not screened by state: 6.9% to 18.7%.
  - South had the lowest percentage overall not screened (12.3%).

- **Incidence rates, 2007–2011**
  - 62,150 cervical cancer cases.
  - Overall 1.9% per year decrease in the United States.
  - South had the highest incidence rate (8.5 per 100,000).

- **Death rates, 2007–2011**
  - 19,969 cervical cancer deaths.
  - Overall death rate did not change in the United States.
  - South had the highest death rate (2.7 per 100,000).


**Cervical Cancer Deaths in the U.S., 1975–2011**

- Widespread use of the Pap test has resulted in dramatic decreases in cancer deaths.
- Death rates did not change from 2007–2011.


**From virus to cancer**


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**Precancerous lesions**

Cervical intraepithelial neoplasia (CIN)

Graded based on proportion of epithelium involved

- **CIN 1**: indicates active HPV infection; high spontaneous resolution: treatment discouraged
- **CIN 2**: most treated, but about 40% resolve over a 6-month period; treatment may be deferred in young women
- **CIN 3**: proximal cancer precursor
- **Adenocarcinoma in situ** (rare)

Source: [ACS, ACOG 2012, USPSTF 2012](http://www.cdc.gov/vitalsigns/cervical-cancer/)

<table>
<thead>
<tr>
<th>Age to start</th>
<th>ACS, ACOG 2012</th>
<th>USPSTF 2012</th>
</tr>
</thead>
<tbody>
<tr>
<td>Women ages 21-29</td>
<td>Cytology every 3 years</td>
<td>Cytology every 3 years</td>
</tr>
<tr>
<td>Women ages 30-65</td>
<td>Cotesting every 3 years (preferred) or Every 3 years with Pap alone</td>
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</tr>
<tr>
<td>Women ages &gt;65</td>
<td>Discontinue after age 65 years with adequate negative screening</td>
<td>Discontinue after age 65 years with adequate negative screening</td>
</tr>
<tr>
<td>Post-Hysterectomy</td>
<td>Discontinue if for benign reason</td>
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Women <21 years
• Current Guideline: begin at age 21 years.
  – Women under the age of 21 should not be screened regardless of the age of sexual initiation or other risk factors.

Why the change?
✓ Cancer is rare in young women
✓ Screening may not prevent cancer in this young population
✓ Overtreatment leads to net harm

Women ages 21-29
• Current Guideline: Screen with cytology alone every 3 years.

Why the change?
✓ Annual screening results in slightly greater cancer risk reduction but twice the number of colposcopies compared to screening every 3 years
✓ No significant difference in cancer reduction between a 2- and 3-year screening interval (lifetime risk 4-6 vs 5-8 per 1000 women) with a 40% increase in number of colposcopies

Women ages 30-65
• Current Guideline: Screen with cytology alone every 3 years or cotesting every 5 years.

Why the Change
✓ Shorter intervals lead to little additional benefit with large increases in harms:
  – additional procedures and assessment
  – treatment of transient lesions
  – procedures may have unwanted side effects, including the potential for cervical incompetence and preterm labor

Women >65 years
• Current guideline: Women over the age of 65 with evidence of adequate negative prior screening and no history of cervical cancer should not be screened.

Why the change?
✓ In well-screened women >65, CIN2+ prevalence is low and cancer is rare
✓ Potential for harms outweigh small potential benefit
✓ Most new HPV infections in women >65 should clear spontaneously

Caveats
• Guidelines do not apply to immunocompromised women (HIV+), those with in utero DES exposure and those with prior CIN 2 or 3 or cervical cancer.
• Vaccinated women are screened the same as unvaccinated women.

Cobas HPV test (14 HR types): FDA approved as a primary screening test beginning at age 25 years

Currently not endorsed by any major guideline group
SGO/ASCCP Guidelines for Primary HPV testing

- Primary HPV is one of 3 options
- Would not recommend before Age 25
- Would not screen sooner than 3 years

What are women doing?

How likely are you to wait 3 years for next Pap test?
Baseline Patient Survey (n=984), 2009

Extending Screening Intervals to 3 years for Patients (Baseline Patient Survey n=984)


Women and New Guidelines

- Women just getting used to newer messages about screening guidelines
- Starting to screen at a later age more palatable
- Getting used to extending screening interval to 3 years and using HPV cotesting
- Distrustful of 5 year interval
  - Older women more than younger women
  - Open to provider recommendations
  - Feel this has to do with cost-savings instead of better care

What are Providers doing?

- Screening starting at age 21 makes sense
  - Harm outweighs benefit
- Screening every 3 years makes sense but slow to increase in practice to every 3 years
  - Practice is highly variable
- Hardly any providers cotesting every 5 years
  - Clinicians and women having a hard time figuring out the purpose and scope of an annual clinic visit
Progress

- From self-report and NM Registry, less women under 21 are getting screened
- Beginning to see movement toward a longer screening interval
- Surveys show that women would accept a longer screening interval if the doctor recommended it
- Kaiser as example of accepting of cotesting

PROGRAMMATIC ISSUES

Affordable Care Act
Four Public Health Pillars

- Preventive services without co-pay
- Policies and programs
- Prevention and Public Health Fund
- National Prevention Strategy

Affordable Care Act
More People Will Have Access to Preventive Services

- Preventive services covered with no cost sharing
  - United States Preventive Services Task Force (USPSTF), Advisory Committee on Immunization Practices (ACIP), Bright Futures, and women’s health guidelines and recommendations
  - Private insurance, Medicare
  - Incentive for states to include in Medicaid
- Annual well-woman visit covered with no cost sharing
  - Movement underway to define core set of elements that would be covered based on evidence
  - HRSA

HHS Coverage Guidelines for Women’s Preventive Services

- Adopted on August 1, 2011
- Used the Institute of Medicine (IOM) report “Clinical Prevention Services for Women: Closing the Gaps” when developing the guidelines
  - Issued July 19, 2011
  - Recommended 8 additional clinical preventive services for women for coverage and adopted by HHS
    - Well woman visits
    - Contraceptive Care

HHS Guidelines for Women’s Preventive Services
Effect on National Breast and Cervical Cancer Early Detection Program (NBCCEDP)

- NBCCEDP practice may differ from HHS requirements for private insurers for cervical cancer screening
  - CDC has limited resources for all the algorithms for management
  - CDC has been providing reimbursement for HPV cotesting
    - Many programs not ready to move to 5 year screening interval
  - CDC may not be providing direct clinical care
The Healthcare Effectiveness Data and Information Set (HEDIS) Measures for 2014

- Non-Recommended Cervical Cancer Screening in Adolescent Females
  - percentage of adolescent females 16–20 years of age unnecessarily screened for cervical cancer
- Cervical Cancer Screening
  - percentage of women 21–64 years of age screened for cervical cancer using either of the following criteria:
    - Women age 21–64 who had cervical cytology performed every 3 years.
    - Women age 30–64 who had cytology/HPV cotesting performed every 5 years.

Federally Qualified Health Care Centers-Best Practices to improve Cervical Cancer Screening

- Emphasis on quality through performance measurement;
- Comprehensive and coordinated care through support for patient navigation;
- Patient-centered care through messaging and informational materials;
- Accessibility through transportation assistance;
- Payment and financing to insure or screen more women; and
- Health information technology implementation.

Treating precancerous lesions:
3 main modalities

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<tr>
<td>Freezing or Laser</td>
<td>Destroying abnormal cervical changes by freezing with a very cold instrument (cryotherapy) or by vaporizing them with a laser beam</td>
</tr>
<tr>
<td>LEEP or Cone biopsy</td>
<td>Removing abnormal cervical changes with a hot wire (LEEP) or with a scalpel (cone biopsy)</td>
</tr>
<tr>
<td>Hysterectomy</td>
<td>Removing the cervix and uterus entirely</td>
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HPV / HPV Vaccine Basics

- 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
  - Cervical cancer
    - Vaginal, vulvar, penile, anal, oropharyngeal, tonsil cavity
  - High-grade precancers — Low-grade cervical disease
- Low-risk (non-oncogenic) HPV 6, 11
- Low-risk (non-oncogenic) HPV 16, 18
- ~80 Types Cutaneous sites of infection
  - Genital warts
  - Laryngeal papillomas
  - “Common” hand and foot warts
  - High-grade precancers — Low-grade cervical disease
Genital HPV Infection

- Most common sexually transmitted infection
- ≈14 million new infections in U.S. each year
- Acquired around sexual debut
  - 40% infected within 2 years
- Most sexually active persons infected at some point
- Infection usually transient, asymptomatic
  - 90% clear or become undetectable within 2 years
- Persistent infection with some types can lead to disease

Evolution of Recommendations for HPV Vaccination in the United States

ACIP Recommendation for HPV Vaccine

- Routine HPV vaccination recommended for both males and females ages 11–12 years
- Catch-up ages 13–21 years for males; 13–26 for females
- May vaccinate at ages 9–10 years for both males and females; 22–26 for males

HPV Vaccine Recommendation for Females

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

HPV Vaccine Recommendation for Males

- Quadrivalent HPV vaccine (Gardasil) recommended for boys at age 11 or 12 years for prevention of anal cancer and genital warts
  - Also for boys 13 through 21 who haven’t started or completed series
  - Young men, 22 through 26 years of age, who identify as gay or bisexual
  - Young men, 22 through 26 years of age, who are immunocompromised

HPV Vaccination Schedule

- ACIP recommended schedule is 0, 1–2, 6 months
  - Following the recommended schedule is preferred
- Minimum intervals
  - 4 weeks between doses 1 and 2
  - 12 weeks between doses 2 and 3
  - 24 weeks between doses 1 and 3
- Administer IM
HPV Vaccine
Duration of Immunity

- The vaccine appears to have good long-term protection duration after a complete 3-dose schedule
- Available evidence indicates protection for at least 8–10 years
  - Multiple cohort studies are in progress to monitor the duration of immunity

Thank You
www.cdc.gov/cancer