How Should We Approach Cervical Cancer Screening and Routine Pelvic Examinations in 2019?

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I have no financial interests in any product I will discuss today.

What’s New for Primary Care?

- USPSTF updated guidelines: added an HPV-alone strategy (August 2018)
- HPV-alone testing with SurePath: FDA-approved (July 2018)
- ACOG: more detailed guidance for screening immuno-compromised women (October 2016)

Objectives

- To understand the latest cervical cancer screening guidelines (updated in 2012, 16, 18)
- To understand areas of existing controversy (with FAQs)
- To understand the current role of the pelvic examination in the context of less-than-annual screening
Background

- ~12,990 cervical cancer cases and 4,120 deaths per year in the US (ACS, 2016)
- ~50-60% of cases occur in never- and poorly-screened women
- High hysterectomy rates in the US account for much protection
- Most effective approach: screen unscreened and poorly-screened women

From virus to cancer

Schiffman and Wright NEJM 2003;348(6):489-490

HPV testing

- Several different tests available
  - Tests for 13 or 14 high-risk types
  - Tests for specific high-risk types (16, 18)
- Tests for low-risk HPV types not clinically useful (do not order these)
- FDA-approved for use with both ThinPrep and SurePath liquid-based cytology (July, 2018)

Primary HPV Testing Alone

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

Current US Recommendations: The Big 3

- US Preventive Services Task Force. August, 2018
- American Cancer Society, American Society for Colposcopy and Cervical Pathology, American Society of Clinical Pathologists (ACS/ASCCP/ASCP) 2012
- American College of Obstetricians and Gynecologists (ACOG) 2016

*Sawaya et al. Ann Int Med 2015*

### 2016 Cervical Cancer Screening Guidelines

<table>
<thead>
<tr>
<th></th>
<th>Under 21 years old</th>
<th>21-29 yrs old</th>
<th>30-65 yrs old</th>
<th>&gt;65 yrs old</th>
<th>Hyst. benign</th>
</tr>
</thead>
<tbody>
<tr>
<td>USPSTF 2012</td>
<td><em>D</em></td>
<td>Cytology</td>
<td>Co-test: every 5 or 3 y</td>
<td>None*</td>
<td>[D]</td>
</tr>
<tr>
<td>Triple A 2012</td>
<td>None</td>
<td>Cytology</td>
<td>Co-test: every 5 or 3 y</td>
<td>None*</td>
<td>None</td>
</tr>
<tr>
<td>ACOG 2016</td>
<td><em>Avoid</em></td>
<td>Cytology</td>
<td>Co-test: every 5 or 3 y</td>
<td>None*</td>
<td>None</td>
</tr>
</tbody>
</table>

* In adequately screened women
* Co-test: cervical cytology plus high risk HPV test (hr-HPV)
* Cytology: cervical cytology (Pap smear) alone

### Draft Recommendation Statement for Cervical Cancer Screening

- hrHPV alone replaces co-testing in women 30-65 y.o.
- hrHPV alone every 5 years, rather than every 3 years

**Rationale**
- Co-testing increases follow-up tests by 2-fold
- Does not increase detection of CIN 3 vs. hrHPV alone
- 5-year interval: best balance of benefits and harms

**2017**

**Characteristics of Cervical Cancer Screening Tests**

- Questions about the strength of evidence supporting the inferiority of co-testing compared with 1st hrHPV testing
- Transition time to hrHPV-alone screening for clinicians, patients

<table>
<thead>
<tr>
<th>Method</th>
<th>Every</th>
<th>If started at 30, reduction in the number of cervical cancer deaths from 1.34 to 3.44</th>
</tr>
</thead>
<tbody>
<tr>
<td>Cytology</td>
<td>3 yrs</td>
<td>0.76 deaths per 1000 women</td>
</tr>
<tr>
<td>hrHPV-only</td>
<td>5 yrs</td>
<td>0.29 deaths per 1000 women</td>
</tr>
<tr>
<td>Co-testing</td>
<td>5 yrs</td>
<td>0.30 deaths per 1000 women</td>
</tr>
</tbody>
</table>
Cervical Cancer Screening

Final Recommendation

[•] Three options for women 30-65 years of age...either
- Primary hrHPV (only) every 5 years, OR
- Co-testing every 5 years, OR
- Cervical cytology alone every 3 years

[•] Women 21-29 years of age: cytology every 3 years

[•] Women < 21 years of age: do not screen

[•] Women > 65, adequately screened in prior 10 yrs, no history of treatment or NED >20 years: do not screen

Recommends women discuss options with clinicians

2018 Cervical Cancer Screening Guidelines

<table>
<thead>
<tr>
<th>Age</th>
<th>Recommendation</th>
</tr>
</thead>
<tbody>
<tr>
<td>&lt; 21 yo</td>
<td>[D] Cytology every 3 yrs</td>
</tr>
<tr>
<td>21-29 y.o.</td>
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<tr>
<td>30-65 y.o.</td>
<td>[D] Cytology every 3 yrs</td>
</tr>
</tbody>
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Co-test: cervical cytology plus high risk HPV test (hrHPV)

Cytology: cervical cytology (Pap smear) alone

Implications: 2018 USPSTF Cervical Cancer Screening Recommendations

- ACOG and ASCCP haven’t changed recommendations yet, but will do so
- Fewer cervical cytology tests, since 1st hrHPV-alone screening option added in women >30 years of age
- More colposcopies, as women >30 years of age move away from cytology alone and toward 1st HPV screening
- Health plans may consider limiting the use of co-tests to surveillance after abnormal cytology or treatment

Age to Begin Screening: Rationale

- Most dysplastic lesions low-grade and transient
- Long progression time of preinvasive lesions to invasive cancer
- Potential adverse effects of treatment (e.g., LEEP, cone biopsy) on pregnancy outcomes
- Many health plans now monitor over-screening of women under 21 as a quality metric
FAQ #1: Should I Screen A 21-year-old Virgin?

• ACOG: “Speculum examinations for cervical cancer screening should begin at age 21 years, irrespective of sexual activity of the patient.”
• USPSTF: begin at 21 “regardless of sexual history”
• Prevalence of HPV among virgins: 1.7% – 0.3% for HPV-16

Am J Epidemiol. 2003 Feb 1;157(3):218-26

FAQ #2: Should I Screen A 40-year-old Virgin?

No official guidance

Recommend discussing benefits and harms of screening and making a plan based on patient preferences and value.

Age to End Screening

• ACS/ASCCP/ASCP (2012): end at age 65 in those with adequate negative prior screening
• ACOG (2016): same
• USPSTF (2012): same

FAQ #3: What Is “Adequate Negative Prior Screening”?

3 consecutive negative cytology results or 2 consecutive negative co-tests within the 10 years before ceasing screening, with the most recent test occurring within the past 5 years
FAQ #4: Should I Re-start Screening In Women Over Age 65 Who Acquire New Partners?

No

as per ACS/ASCCP/ASCP

Ending Screening After Hysterectomy

- ACOG, ACS and USPSTF: screening following total hysterectomy with removal of the cervix for benign disease is not indicated. USPSTF: “D” recommendation
- ACOG (2003): If hysterectomy for CIN 2 or 3, may stop screening after 3 normal tests
- ACOG (2016): Continued routine screening (cytology ever 3 years) recommended for 20 years after treatment.

FAQ #5: How Should I Screen Women Who Only Have (Or Ever Had) Sex With Women?

No differently

Which Women Are Not “Average Risk”?

- Immunocompromised due to HIV-infection
- Exposure to diethylstilbestrol in utero
- Prior CIN 2, 3 or cancer
- Other causes of immunocompromise
  - Major organ transplant
  - Immunosuppressive drugs
  - No guidelines yet for “biologicals”

ACOG Bulletin No. 168, October 2016
FAQ #6: So, How Should I Screen HIV-infected Women?

CDC Panel on Opportunistic Infections

- Begin screening at age of initiation of sexual activity but no later than age 21
- No stopping age
- Women infected with HIV who are aged 30+ can be screened with cytology alone or co-testing
- After 3 consecutive annual normal cytology results OR one negative co-test, can screen every 3 years

Panel on Opportunistic Infections in HIV-Infected Adults and Adolescents, Centers for Disease Control and Prevention, the National Institutes of Health, and the HIV Medicine Association of the Infectious Diseases Society of America

FAQ #7: How Should I Screen Women Who Are Immunocompromised Due To Medications?

ACOG 2016

- Reasonable to extrapolate the recommendations for women with HIV infection with screening starting at age 21 years
- No clear guidance on which medications. Certainly includes women on medications after solid organ transplantation.
- Annual cervical cytology screening is reasonable for women exposed to diethylstilbestrol in utero

FAQ #8: If I am not doing annual cytology, do I still need to perform an annual pelvic exam (external, speculum, bimanual)?

Ovarian Cancer Screening

- Recommends against screening for ovarian cancer in asymptomatic women Grade [D]
- Applies to asymptomatic women who are not known to have a high-risk hereditary cancer syndrome

February 2018
**The SPE Debate: Terms**

- **Screening Pelvic Exam (SPE)**
  - External inspection, speculum and bimanual exam at the time of a WWV in an asymptomatic patient
- **Diagnostic Pelvic Exam**
  - Pelvic exam for the purpose of evaluating symptoms, signs, or other abnormal findings (lab, imaging)
- **Cervical cytology sampling**
  - Speculum used for the purpose cervical sampling

**SPE: American College of Physicians**


- ACP recommends *against* performing SPE in asymptomatic, non-pregnant adult women
- Many clinicians include SPE as part of the WWV, and because it is *low-value care*, it should be omitted

**Why Did ACP Recommend Against SPE?**

- Accuracy for detecting ovarian cancer is low
  - PLCO Trial: More harms than benefits
- No studies have assessed benefit for other conditions (PID, benign conditions, or other gyn cancers)
- Outcomes are not improved
- Harms: unnecessary laparoscopies or laparotomies, fear, anxiety, embarrassment, pain, discomfort
- Adds unnecessary costs

**ACOG Well Woman Task Force**

Obstet Gynecol 2015;126:697–701

**For women age 21 years and older (Qualified)**

- External exam may be performed annually
- Inclusion of speculum exam, bimanual exam, or both, in otherwise healthy women should be a shared, informed decision between patient and provider

*“Qualified” recommendations rely primarily on expert consensus*
Screening Pelvic Exam

- [1] Recommendation
- Current evidence is insufficient to assess the balance of benefits and harms of performing SPE
- “…clinicians are encouraged to consider risk factors for various gynecologic conditions and the patient’s values and preferences, and engage in shared decision making to determine whether to perform a pelvic exam”

Should I Do a Screening Pelvic Exam...

- **ACOG**: We think we know….do it. But discuss it first
- **ACP**: We know….don’t do it
- **USPSTF**: We don’t know, but you may want to discuss it

George Sawaya MD, Oct 2017

SPE: What Do We Tell Patients?

**Active**
- “3 national guidelines: each one is different”
- All 3 agree that there is *no evidence* of benefit
- Evidence of harms: “false alarms” and complications

**Passive**
- It is reasonable to say nothing about the SPE, and only respond to questions or to a request for an exam

Summary

- No cytology screening prior to age 21
- Annual cytology not recommended for most women
- Annual screening is recommended for high-risk women: immunocompromised (HIV+), prior CIN2+, in utero DES exposure
- Co-testing (hrHPV plus cytology) every 5 years may be equivalent to cytology every 3 years for women aged 30-65 years
- HPV testing every 5 years beginning at age 30 years is a new reasonable option
Summary

• Screen HPV vaccinated women same as others
• Screening with (conventional) cytology alone (without HPV testing) every 3 years is still a good option (and perhaps the least complicated); using HPV testing for ASC-US adds additional simplicity
• What we do at ZSFG/UCSF in your syllabus.
• Be aware of limited data on benefits and harms of routine pelvic exams in asymptomatic women

Questions