# Overview

1. Review current 2012 cervical cancer screening guidelines
2. Recent updates cytology management guidelines
3. Screening for oral or anal HPV related disease

## Risk and Benefits of More Screening

<table>
<thead>
<tr>
<th>Benefits</th>
<th>Harms</th>
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<tbody>
<tr>
<td>Decrease cancer rates</td>
<td>Cost</td>
</tr>
<tr>
<td>Increase detection precursor lesions</td>
<td>Too many procedures</td>
</tr>
<tr>
<td>Reduce anxiety of false negative tests</td>
<td>Overtreatment pregnancy risks</td>
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<tr>
<td>Increased anxiety, pain</td>
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## 2012 Screening Guidelines

- **ASCCP/ACS**
  - Q3 years age 21-29
  - Recommend co-testing age 30 and older with 5 year interval or Pap every 3 years.

- **USPSTF**
  - Q3 year screening for ages 21-65
  - May use HPV co-testing to extend interval of screening to 5 years 30 and older
Who gets Annual Screening?

HIV positive/Immune-suppressed
Hx DES exposure in utero

- Not necessarily women with history tobacco, STDs, OCPs, high risk behavior
- No longer women who have been treated for high grade cervical disease

Should you co-test?

- 4 randomized trials, 2 rounds of screening compared co-testing to Pap. Little to no reduction cervical CA incidence.
- Increased CIN3 first round, colposcopy numbers not reported. Decreased cancer second round
- No cost analysis, general increase colpo
- RONCO trial, Lancet 2010;11:249

HPV <age 30

Co-testing extends interval

<table>
<thead>
<tr>
<th></th>
<th>6 year interval</th>
<th>3 year interval</th>
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<tbody>
<tr>
<td>Co-test</td>
<td>0.28%</td>
<td></td>
</tr>
<tr>
<td>HPV only</td>
<td>0.27%</td>
<td></td>
</tr>
<tr>
<td>Pap only</td>
<td>0.97%</td>
<td></td>
</tr>
<tr>
<td>Pap only</td>
<td>0.51%</td>
<td></td>
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Pooled data 24, 295 subjects.
Pap screening in pregnancy

- Only diagnosis that may change management is invasive cancer, route and timing of delivery.
- Management of ASCUS and LSIL same as non pregnant but can defer until postpartum. Therefore HPV triage not necessary.

Paps in Pregnancy

- Hormonal changes to squamous and glandular cells
- Arias-Stella reaction or decidual cells have large nuclei and may appear similar to HSIL
- Abundance immature metaplastic cells similar to HSIL
- Increased inflammatory cells during pregnancy
- * Be sure to label Paps as Pregnant specimens

Colpo in Pregnancy

- Best to wait until 2nd trimester so miscarriage not blamed on procedure
- Lots of metaplasia, mucus, immature metaplasia, decidualization of stroma may all appear high grade.
- Goal is only to rule out invasive disease

2006 ASCCP Consensus Conference Updates

- Published in Obstetrics and Gynecology March 2013
- www.asccp.org
### Recommendation Criteria

<table>
<thead>
<tr>
<th>Follow-up</th>
<th>5 Year Risk CIN3</th>
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<tbody>
<tr>
<td>Colposcopy</td>
<td>&gt;5%</td>
</tr>
<tr>
<td>6-12 Months</td>
<td>2-5%</td>
</tr>
<tr>
<td>5 years</td>
<td>0.1%</td>
</tr>
</tbody>
</table>

### What to do with abnormal cytology and histology results?

- Co-test HPV positive/Pap negative
- Unsatisfactory Paps
- LSIL HPV negative
- Change to ASCUS management
- Women less than 25 years
- Follow-up after colpo and LEEP

### Case #1

30 yo with Unsatisfactory Pap

- Repeat Pap 2-4 months
- Treat specific infections to resolve inflammation if present
- HPV test, if positive then may genotype. If 16/18 positive to Colpo, if not 16/18 then repeat pap.

### Absent EC/TZ

- Age 21-29 Pap every 3 years
- Age 30 or over
  - Repeat Pap 3 years is fine
  - HPV negative routine screen 5 years
  - If HPV positive then either Pap with HPV one year or immediate genotyping 16/18
CASE 2: 35yo with Neg Paps. Co-testing performed Pap Neg HPV Pos

A) Pap and HPV test one year
B) HPV typing
C) Refer to colposcopy

HPV positive/Pap negative >30

- No colposcopy: CIN3 0.8-4.1% 12 months
- Repeat testing current recommendation with colposcopy for persistent positive HPV, weak evidence.
- HPV genotyping for 16/18 with immediate colposcopy based on observational studies and one industry sponsored trial.


Athena Study

- 32,260 Women >30 years
- Negative cytology
- 6.7% HPV positive
- 1.5% were 16/18 positive

<table>
<thead>
<tr>
<th>CIN2+ Absolute risk</th>
<th>HPV 16/18</th>
<th>Other HPV</th>
<th>HPV Neg</th>
</tr>
</thead>
<tbody>
<tr>
<td>11.4%</td>
<td>4.4%</td>
<td>0.8%</td>
<td></td>
</tr>
<tr>
<td>CIN3+</td>
<td>9.8%</td>
<td>2.4%</td>
<td>0.3%</td>
</tr>
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</table>

Khan, JNCI 2005;97:1072-79

Value of Type specific testing

- Cumulative incidence of CIN3 over a 10 year period, as a function of a single HPV test results at enrollment.
Case #3
32 yo with LSIL HPV Neg

A) Colposcopy
B) Repeat Pap 1 yr
C) Repeat Co-test 1 yr

Abnormal Pap HPV negative

* LSIL with HPV negative, repeat co-testing 1 year preferred.
* If co-test is negative negative then repeat at 3 years. Colpo if any other result.

For AGC, ASCH, AIS or HSIL, Colpo no matter what HPV status.

Case #4
26 yo ASCUS pap smear

A) Immediate Colpo
B) HPV Triage
C) Repeat Pap 6 mo
D) Repeat Pap 1 year

ASCUS

* If ASCUS repeat 1 year, if ASCUS again then Colpo. If normal than cytology 3 years
* Preferred- use HPV triage unless under 25 years.
HPV Negative ASCUS Pap

- ASCUS HPV Neg risk CIN3 0.3% 1 year
- ASCUS HPV Pos risk CIN3 14.4% 1 year
- 5 year cumulative risk CIN3 0.85%

(REPEAT PAP 3 YEARS)

ASCUS/LSIL in Pregnancy

- ASCUS pap repeat one year
- HPV negative 3 years screen
- HPV positive - colpo acceptable but 6 weeks postpartum preferred.
- Less than 25 years repeat Pap 1 year.
- LSIL pap
- ASCCP prefer colpo but defer until PP acceptable
- LSIL HPV negative repeat 1 year co-test
- Less than age 25 repeat Pap 1 year
- Cancer risk <1%

Case #5
28 yo with LSIL
Colpo biopsy CIN1

A) HPV test 1 year
B) Pap 12, 24, 36 mo
C) Co-testing 12 mo

CIN1/Neg result after LSIL or ASCUS

- Co-test 12 months, may beginning routine screening 3 years if both negative
- (Pap at 12, 24 months equivalent) Pap only should be done for less than age 25
CIN1/Neg results after HSIL or ASC-H

- Co-test 12 and 24 mo, if negative routine screening in 3 years. Refer to colposcopy if HPV positive or ASCUS or worse
- (Pap 12, 24, 36 month equivalent)
- Also women with CIN1 on ECC can be followed similarly

Following Treatment CIN2,3

- Co-test 12, 24 mo if both negative then co-test 3 years then return to routine screening intervals at least 20 years

False positive Paps <25

- ASCUS or LSIL, annual Pap recommended. After 24 months then ASCUS or greater referred to Colpo. HPV REFLEX NOT RECOMMENDED
- Even if HPV positive then repeat cytology at 12 months. NO IMMEDIATE COLPO
- Negative Pap x 2 return to routine screening

Cancer cases 1.4/100,000
False Positive Pap 55,000/ cancer
USPTF report 2012
Untreated CIN2/CIN3

- Young Women
- Pap and colposcopy every 6 months x 2
- Cotest after colpo neg x2 then routine screen 3 years

CIN1 biopsy < Age 25

- Annual Pap for follow-up
- At 12 mo repeat Colpo only if HSIL or ASH
- At 24 mo repeat Colpo for ASCUS or greater
- Treatment CIN1 in young women unacceptable!

CIN2-3 biopsy < Age 25

- Observation is preferred. Treatment acceptable.
- Treatment recommended for CIN3, Colpo unsatisfactory or ECC positive

Estimate Cancer rates

<table>
<thead>
<tr>
<th>Site</th>
<th>Average #/yr</th>
<th>% HPV related</th>
<th>Range</th>
</tr>
</thead>
<tbody>
<tr>
<td>Cervix</td>
<td>11947</td>
<td>96</td>
<td>95-97</td>
</tr>
<tr>
<td>Vulva</td>
<td>3136</td>
<td>51</td>
<td>37-65</td>
</tr>
<tr>
<td>Vagina</td>
<td>729</td>
<td>51</td>
<td>37-65</td>
</tr>
<tr>
<td>Anus-female</td>
<td>2089</td>
<td>93</td>
<td>66-97</td>
</tr>
<tr>
<td>Anus-male</td>
<td>1678</td>
<td>93</td>
<td>66-97</td>
</tr>
<tr>
<td>Oral-female</td>
<td>2370</td>
<td>63</td>
<td>50-75</td>
</tr>
<tr>
<td>Oral-male</td>
<td>9336</td>
<td>63</td>
<td>50-75</td>
</tr>
</tbody>
</table>

Gillison, Cancer 2008; 113: 3036-46
Screening with Anal Paps?

**Who would we screen**
- HIV positive women
- CIN3
- Vulvar Cancer
- Regular Anal intercourse?

**Screening risks**
- May not prevent cancer
- Treatment premalignant lesions is morbid
- Natural history poorly understood

Risk of progression 10% in 5-10 years primarily limited to immune compromised. Average age 60 compared to 48 for cervical cancer. Screening should start with anoscopy at time of colonoscopy age 50.

Coarse mosaicism + coarse punctation + ulceration
Bx = Ca in situ

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**Oral HPV**

- HPV linked to oropharyngeal squamous cell carcinomas (OSCCs) (~90% due to HPV16)
- Incidence of OSCCs is increasing and expected to surpass that of cervical cancer by 2020


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**Risk factors for Oral Cancer**

- Tobacco
- Alcohol
- HPV
- Immune compromise

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*References:
Autoinnoculation

* In a small study of 25 heterosexual couples, the rate of autoinnoculation (between genitals, anus, hands) in men was comparable to the rate of female-to-male transmission.¹

* In female university students, vaginal HPV infections tended to precede cervical infections.²

¹Hernandez et al. Emerging Infectious Diseases 2008;14:888-94.

Take Home Lessons

* No HPV testing in young women < age 25 or pregnant.

* No immediate colposcopy for ASCUS or LSIL pap less than age 25, also may defer if pregnant

* Post colposcopy and treatment follow-up co-test annual x1 if low grade, x2 for all others

* Only two indications for HPV genotyping, HPV + Pap negative (or Pap Unsatisfactory)