New Pap Guidelines for Midwives: Case Studies 2013

Connie Mao, MD
University of Washington

Overview

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

Risks and Benefits of More Screening

- Benefits
- Decrease cancer rates
- Increase detection precursor lesions
- Reduce anxiety of false negative tests
- Harms
- Cost
- Too many procedures
- Overtreatment pregnancy risks
- Increased anxiety, pain

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

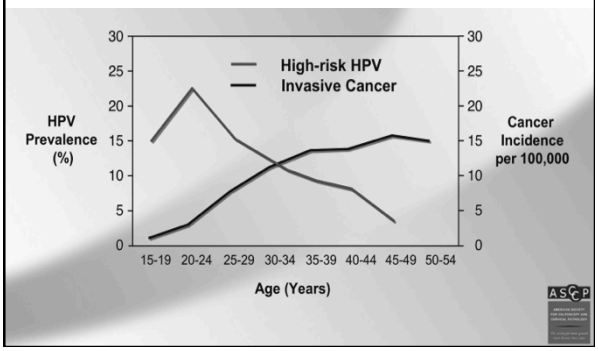
Who gets Annual Screening?

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

HPV <age 30



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, colpo numbers not reported. Decreased cancer second round
* No cost analysis, general increase colpo
* RONCO trial, Lancet 2010;11:249

Co-testing extends interval

* Pooled data 24, 295 subjects.

		Risk of CIN3 or Cancer
Co-test	6 year interval	0.28%
HPV only	6 year interval	0.27%
Pap only	6 year interval	0.97%
Pap only	3 year interval	0.51%

Pap screening in pregnancy

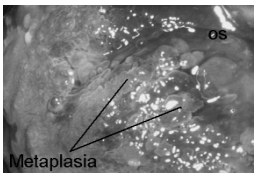
- Only diagnosis that may change management is invasive cancer, route and timing of delivery.
- Management of ASCUS and LSIL same as non pregnant but can defer until postpartum. Therefore HPV triage not necessary.

Paps in Pregnancy

- Hormonal changes to squamous and glandular cells
- Arias-Stella reaction or decidual cells have large nuclei and may appears 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, immagure metaplasia, decidualizaiton 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
- Algorithms in Journal of Lower Genital Tract Disease Release March 22, 2013
- www.asccp.org

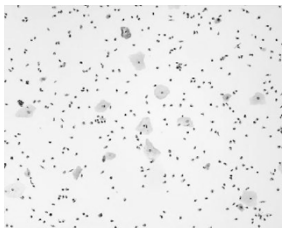
Recommendation Criteria

Follow-up	**5 Year Risk CIN3**
Colposcopy	>5%
6-12 Months	2-5%
5 years	0.1%

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 Unsat PAP



A) Repeat pap 2-4 months

B) Treat specific infections to resolve inflammation if present

C) 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.

Wright, Am J Clin Path 2011. 136(4):578-86.

Athena Study

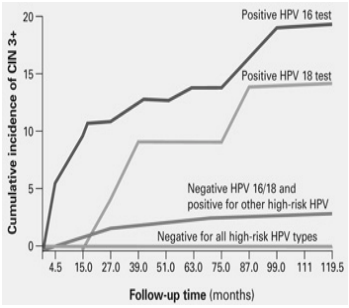
* 32,260 Women >30years
* Negative cytology
* 6.7% HPV positive
  1.5% were 16/18 positive

CIN2+ Absolute risk	HPV 16/18 +	Other HPV +	HPV Neg
	11.4%	4.6%	0.8%
CIN3+			
	9.8%	2.4%	0.3%

* Wright, Am J Clinic Pathol 2011;136:578

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.



Khan, JNCI2005;97:1072-79

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 Pod risk CIN3 14.4%
  (Wright, Am J Clin Path 2011. 136(4):578-86)
- 5 year cumulative risk CIN3 0.85%
  (Katki, Lancet Oncol 2011; 12 (7): 663-72)
- 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

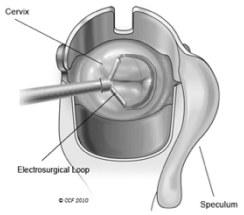
CIN1/Neg result after LSIL or ASCUS

- 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

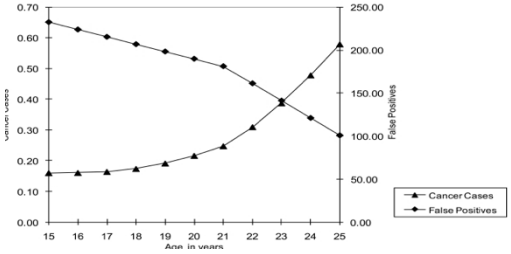
- Co-test 12 and 24 mo, if negative routine screening in 3 years. Refer to colposcopy if HPV positive or ASCUS or worse
- (Pap 12,24,36 month equivalent)
- Also women with CIN1 on ECC can be followed similarly

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

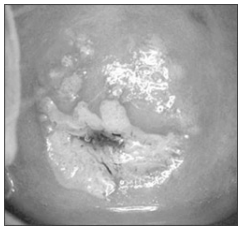


Cancer cases 1.4/100,000
False Positive Pap 55,000/ cancer
USPTF report 2012

Paps < Age 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

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 US 2004-2008

Site	Average #/yr	% HPV related	Range
Cervix	11967	96	95-97
Vulva	3136	51	37-65
Vagina	729	51	37-65
Anus-female	3089	93	86-97
Anus-male	1678	93	86-97
Oral-female	2370	63	50-75
Oral-male	9356	63	50-75

Gillison, Cancer 2008; 113: 3036-46

Screening with Anal Paps?

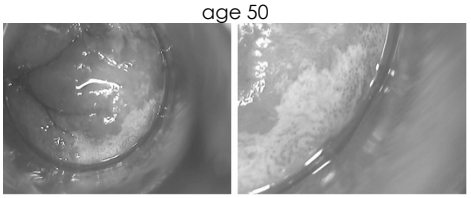
Who would we screen

- 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

Oral HPV

- HPV linked to oropharyngeal squamous cell carcinomas (OSCCs) (~90% due to HPV16)[1]
- Incidence of OSCCs is increasing and expected to surpass that of cervical cancer by 2020[2]

[1]D'Souza et al. N Engl J Med 2007;356(19):1944-56
[2]Chaturvedi et al. J Clin Oncol 2011;29(32):4294-301

Risk factors for Oral Cancer

- Tobacco
- Alcohol
- HPV
- Immune compromise

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]

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

[2]Winer et al. AJE 2003;157:218-26.

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)