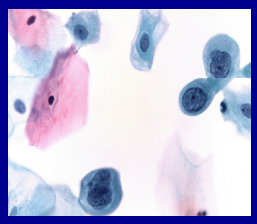
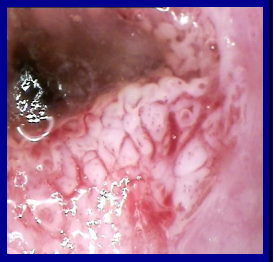
Cervical Cancer Screening Recommendations 2012





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Disclosures

1. Apgar B, Brotzman G, Spitzer M. Integrated Text and Atlas of Colposcopy. Elsevier Publishers, 2004, 2008.

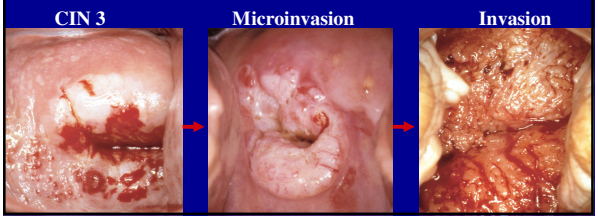
2. Brotzman G, Spitzer M, Apgar B. Colposcopic Image Library on CD. SABK, Inc 2004.

3. ASCCP Executive Committee, Board of Directors. 2007-current.

Goal of cervical cancer prevention

Cervical cancers develop from precursor lesions (CIN 3)

Average of 10 years for a high-grade lesion to progress to invasive cancer



Cervical cancer prevention:
Where have we been and where are we going?

Goal of cervical cancer screening

- Prevention of morbidity and mortality from cancer.
- Prevention works via identification and destruction of cancer precursors.
  - Finding CIN
  - Finding abnormal Pap's
  - Finding HPV

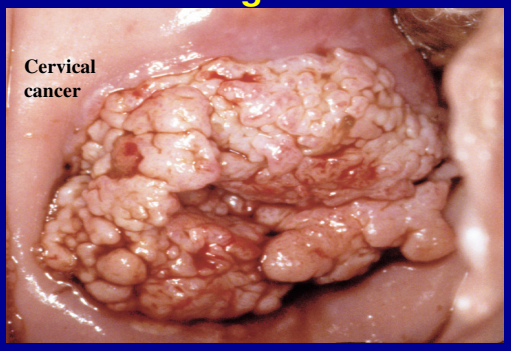
Limits to screening

- ***Attempting to prevent all cervical cancers is unrealistic and harmful.***
  - Cancers in youngest women may not be detectable by screening
  - To achieve total prevention would require high sensitivity screen (e.g. HPV) at frequent intervals (< 1 year) with treatment of equivocal or mostly transient abnormalities
  - *Harms outweigh benefits.*

Potential harms from screening

- Stigma, disrupted relationships, anxiety and distress
- Lost time
- Expense of investigation for lesions destined to regress
- Pain, injury from colposcopy and treatment
- *Adverse pregnancy outcomes*

Carcinogenic risk



Persistent positivity with oncogenic HPV types uncommon but required for progression. HPV 16 uniquely carcinogenic

Natural NZ history study of untreated women with CIN 3

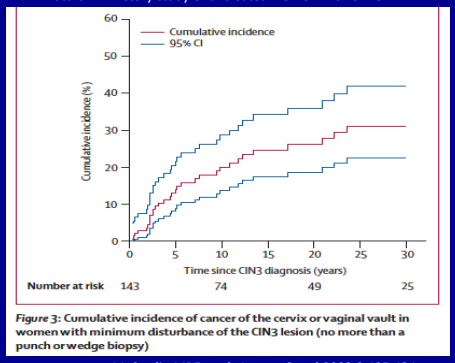
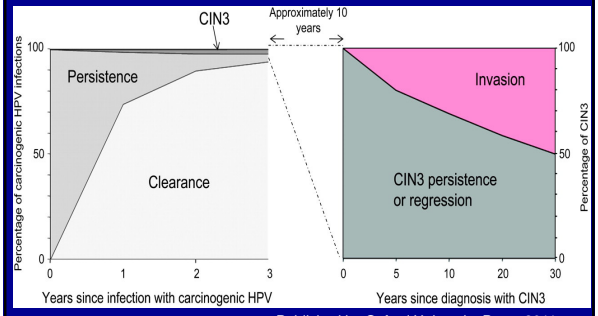


Figure 3: Cumulative incidence of cancer of the cervix or vaginal vault in women with minimum disturbance of the CIN3 lesion (no more than a punch or wedge biopsy)

McCredie MRE et al. Lancet Oncol 2008;9:425-434

Risks of human papillomavirus (HPV) persistence and progression.



Published by Oxford University Press 2011.
Schiffman M et al. J Natl Cancer Inst 2011;103:368-383

Who was involved in framing screening guidelines?

American Cancer Society

ASCCP American Society for Colposcopy and Cervical Pathology

ASCP American Society for Clinical Pathology

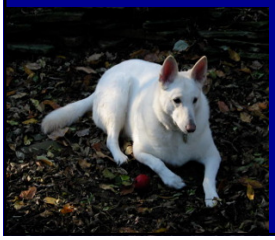
The American College of Obstetricians and Gynecologists 1951 Women's Health Care Physicians

The Guide to Clinical Preventive Services 2010 - 2011

NCCN National Comprehensive Cancer Network

Cervical cancer screening

Special considerations of women who fall outside of the guidelines



2012 Consensus Guidelines
Who should be screened outside of the screening guidelines?

Recommendations NOT intended for women with HIV, immunocompromised state, or *in utero* DES exposure

1. Saslow et al. ACS/ASCCP/ASCP. CA Cancer J Clin 2012; 62: 147-72 and AJCP 2012; 137: 516 – 542.
2. Moyer VA, et al. USPSTF. Ann Int Med 2012; 156: 880-91
3. ACOG Practice Bulletin #131, November 2012
4. NCCN Cervical Cancer Screening Guideline v. 2-2012. www.NCCN.org

2012 Consensus Guidelines
Women with prior HPV Vaccination

Recommended screening practices should not change on the basis of HPV vaccination

Not addressed

1. Saslow et al. ACS/ASCCP/ASCP. CA Cancer J Clin 2012; 62: 147-72 and AJCP 2012; 137: 516 – 542.
2. Moyer VA, et al. USPSTF. Ann Int Med 2012; 156: 880-91
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20 year old G1P1 presents for a Rx for OCPs. She has had annual Pap's (all normal) since her pregnancy at age 16. She has had 7 partners since age 15 and a new partner for 3 months. What would you advise her about cervical cancer screening?

1. No Pap test now but at age 21.
2. Pap test now and annually because of multiple partners.
3. HPV testing now.
4. Pap test and HPV testing at age 21.

2012 Consensus Guidelines
When to begin screening

Women younger than 21 Years: No screening.

1. Saslow et al. ACS/ASCCP/ASCP. CA Cancer J Clin 2012; 62: 147-72 and AJCP 2012; 137: 516 – 542.
2. Moyer VA, et al. USPSTF. Ann Int Med 2012; 156: 880-91
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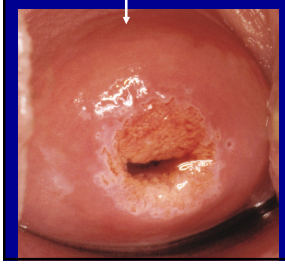
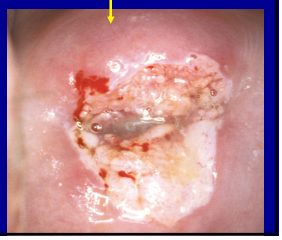
Concepts of HPV infection by age

HPV infections in adolescents and young women.
Benign and reversible disease



HPV infections in adult women

Risk of persistent infection and advanced CIN >> Invasive CA



Rates of Cervical Cancer 2002-2006 SEER Data

Age	Rate/100,000	Incidence
Age 10-14	0	0
Age 15-19	0.1	0
Age 20-24	1.6	0.1
Age 25-29	5.5	0.5
Age 30-34	11.0	1.4
Age 35-39	13.4	2.3
Age 40-44	15.3	3.4
Age 45-49	14.3	4.1

http://seer.cancer.gov
Courtesy T Darragh

Schlecht et al. J Natl Cancer Inst 2003;95:1336;
Moscicki et al. Lancet 2004;364;1678;

The incidence of cervical cancer has not changed in adolescents in the UK over the last 4 decades

Despite increases in screening

Sasieni P et al. BMJ 2009;339:b2968

Risk in young women (age 21-24), not exactly adolescents

- The risk of cervical cancer is 10-fold higher than risk in adolescents (1.4/100,000).
  - *High enough to justify screening.*
    - ~ 55,000 Pap's must be obtained for every cervical cancer diagnosed.
  - *Low enough to allow observation* for minor cytologic abnormalities.

26 year old G3P3 had a Pap 4 years ago while pregnant. She is recently divorced and dating multiple men. Smokes 1ppd. Recent chlamydia. What cervical cancer screening is recommended now?

1. Pap only.
2. Pap and HPV testing (cotesting).
3. HPV only.
4. No screening now.

2012 Consensus Guidelines: Screening Frequency

Age 21-29. Testing with cytology (Pap) alone every 3 years.

- Co-testing should NOT be performed for women under age 30.
- Reflex HPV testing for ASCUS only.

American Cancer Society | ASCP | American Society for Clinical Pathology | NCCN National Comprehensive Cancer Network

1. Saslow et al. ACS/ASCCP/ASCP. CA Cancer J Clin 2012; 62: 147-72 and AJCP 2012; 137: 516 – 542.
2. Moyer VA, et al. USPSTF. Ann Int Med 2012; 156: 880-91
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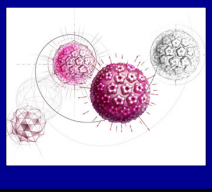
Determining screening intervals

- USPSTF determined benefits and harms of screening at different starting ages and intervals.
  - *Screening every 3 yrs. with Pap's starting at age 21 confers similar # of life-years as annual screening.*
    - *Screening beginning at age 21 at an interval of 3 years = most acceptable balance of benefits/harms (AHRQ 2011)*

What is the rationale for combined screening with HPV testing and Pap (co-testing) in women ≥ 30 years?



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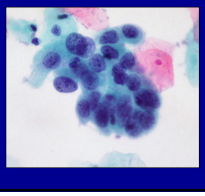
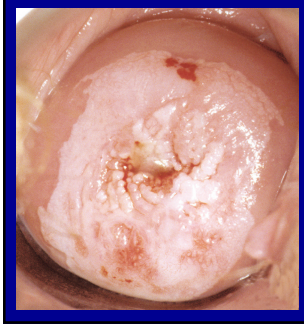


Which one of the following tests provides greater reassurance against CIN 3+ over an extended time?



1. Pap smear

2. HPV testing.

Combined HPV and Pap Testing

The Portland Kaiser Study

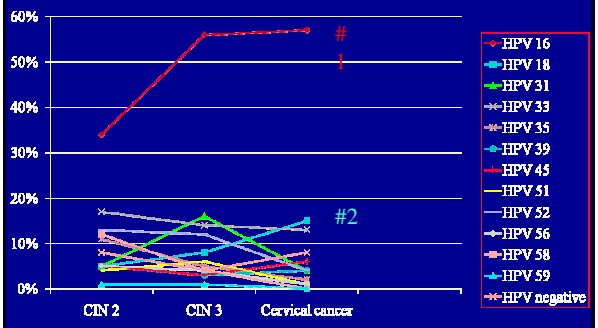
- 20,810 women followed for up to 122 months
- Over 45 mo, incidence of CIN 3+ = 4.54% if HPV+ or Pap ≥ ASC-US. If both negative, incidence = 0.16%

Efficacy to predict CIN3+ within 45 mo.

	Sensitivity	PPV	NPV
Pap + HPV	86.4%	4.54	99.84
Pap alone	49.2%	9.63	99.47
HPV	75.4%	4.40	99.76

Sherman et.al. JNCI 2003;95:46-52

HPV Types in CIN 2, CIN 3 and Cervical Cancer, Iceland, 1990-1994 and 1999-2003



Sigurdsson K et al. Int J Cancer 2007;2682-2687.

Pap test and HPV testing

- HPV DNA detection has a 20-45% greater one time test sensitivity for CIN 3+ than cytology-based methods.
- CIN 2+ found by HPV testing and missed by cytology is clinically important.

Castle et al. Obstet Gynecol 2011;117:650-6.
Ronco et al. Lancet Oncol 2010;11:249-57.
Mayrand et al. NEJM 2007;357:1579-88.
Cuzick et al. Int J Cancer 2006;119:1095-101.

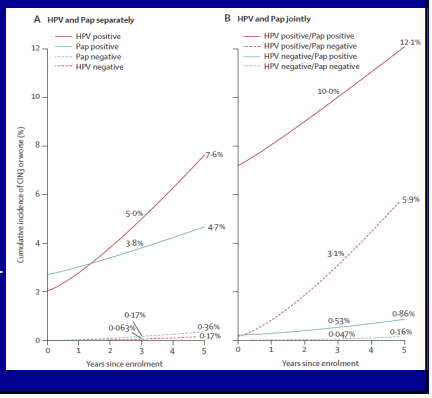
- Negative HPV identifies a very low risk group, whether cytology is negative or not

Kaiser Study

N=331,818 women age > 30 in prospective co-testing study

Katki HA, et al. Lancet Oncol 2011; 12: 663

Cumulative incidence of CIN 3+ according to test modality

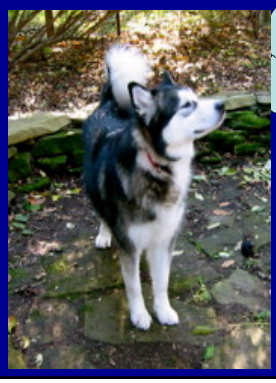


Finding oncogenic HPV types *does not* provide a diagnosis of CIN 3 or cancer

It identifies a group of women in whom CIN 3+ is more likely

Challenges of implementing HPV testing

- 66% of clinicians co-test at a frequency < q 3 years despite lack of benefit.
- Both low and high-risk HPV ordered despite the lack of benefit of low risk testing. (low risk HPV tests have no place in cervical cancer screening)
- Co-testing instead of Pap for women < age 30 (transient HPV does not warrant cotesting)
  - Lee et al. Obstet Gynecol 2011;118:4-13
  - Saraiya et al. Arch Intern Med 2010;170:977-85
  - Castle et al. Obstet Gynecol 2010;116:76-84



Kaiser Permanente Northern California data

- Risk analysis of 1.4 M women from Kaiser
  - 2003: shifted to co-testing; annual Pap's continued to be available.
    - > 1 M women age 30+ with cotesting.
      - 440 cancers
      - 3231 CIN 3+
      - 7581 CIN 2+
  - 400 K women age < 30 with cytology and HPV triage of ASCUS.
    - 26 cancers
    - 1231 CIN 3+
    - 4193 CIN 2+

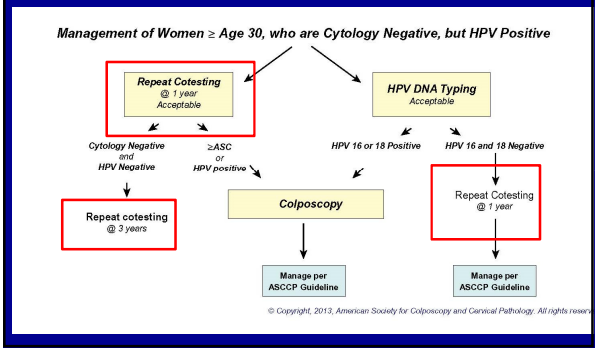
KPNC conclusions

- *5 year risk of CIN 3+ following a negative co-test was comparable to a 3-year risk of CIN 3+ following a negative Pap.*
  - *Assesses cancer risk when high even when CIN 2+ risk is low.*

What are immediate and future (5y) risks after x?

2013 ASCCP mgt guidelines

More use of cotesting to reduce follow-up visits

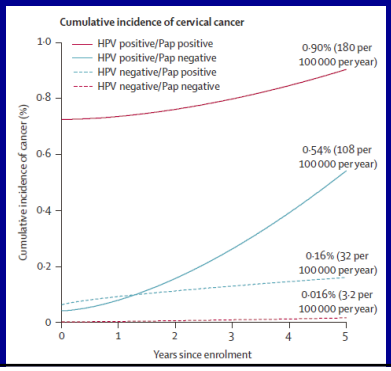


Cumulative Risk Of Invasive Disease Based on Initial Co-Test

Kaiser Study

N=331,818 women > 30 years in prospective co-testing study

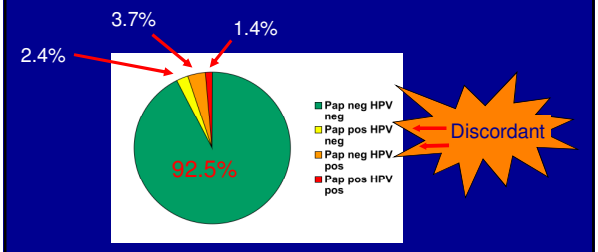
Katki HA, et al. Lancet Oncol 2011; 12: 663



35 year old G1P1 presents after routine co-testing showing a *negative Pap test and positive HPV testing*. She was previously screened with cytology only but has not had screening in 5 years. She's had multiple sexual partners in the past year but before was monogamous for 15 years What is the next step??

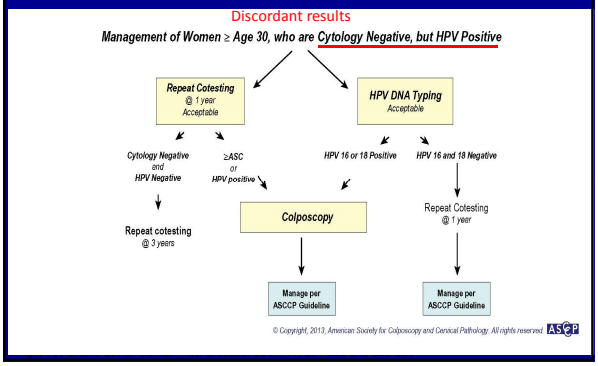
1. Routine screening in 5 years.
2. Immediate colposcopy.
3. Repeat HPV testing in one year.
4. Repeat both cytology and HPV testing (cotesting) in one year.

Proportion of Co-Test Results in 331,061 Kaiser women ≥ 30 years



Katki HA, et al. Lancet Oncol 2012; 12: 663

2013 ASCCP consensus guidelines Women ≥ age 30, Pap -, HPV +



33 year old G2P2 presents for her Pap. No history abnormal Paps. Last Pap 3 years ago. Monogamous.

What is the *preferred* cervical cancer screening ?

1. Pap and if negative, Pap every 3 years.
2. Co-testing and if both negative, cotesting every 5 yrs.
3. No cervical cancer screening is needed today.

2012 Consensus Guidelines: Screening Frequency

Age 30-65. Testing with cytology alone every 3 years or co-testing with cytology and testing for high-risk HPV types every 5 years.

- Co-testing "preferred" and cytology "acceptable" by all but USPSTF.
  - USPSTF says either acceptable.

American Cancer Society | ASCP | American Society for Clinical Pathology | NCCN National Comprehensive Cancer Network

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You are considering stopping cervical cancer screening in a 65 year old woman who has never had an abnormal Pap. She has not had co-testing but had 2 Pap's in the past 10 years with the most recent one 2 years ago.
Is her screening "adequate" enough to stop screening?

1. **Yes**
2. **No**

Adequate screening: ACOG, ASCCP, ACS*

- *Adequate negative prior screening is defined as:*
  - 3 consecutive negative cytology results
    OR
  - 2 consecutive negative co-tests
  - done within the 10 years before stopping screening with the most recent test within 5 years.
    - **USPSTF does not define adequate screening*

2012 Consensus Guidelines: When to stop screening

Women older than 65 Years:

After adequate negative prior screening results.

1. Saslow et al. ACS/ASCCP/ASCP. CA Cancer J Clin 2012; 62: 147-72 and AJCP 2012; 137: 516 – 542.
2. Moyer VA, et al. USPSTF. Ann Int Med 2012; 156: 880-91
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71 year old woman's husband died 5 years ago. She has no hx abnormal Pap's and her last Pap was at age 66. New sexual partner. What would you advise her about cervical cancer screening?

1. **Pap test only now.**
2. **Pap and HPV testing now.**
3. **Pap test 3 years after resuming sexual activity.**
4. **No further Pap test is necessary.**

2012 Consensus Guidelines: When to stop screening

Women older than 65 Years:

Screening should not be resumed for any reason, even if a woman reports having a new sexual partner.

1. Saslow et al. ACS/ASCCP/ASCP. CA Cancer J Clin 2012; 62: 147-72 and AJCP 2012; 137: 516 – 542.
2. Moyer VA, et al. USPSTF. Ann Int Med 2012; 156: 880-91
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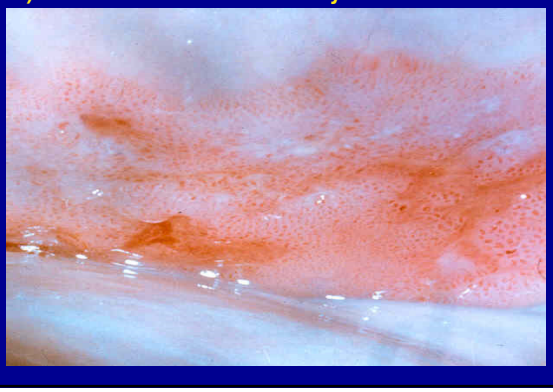
55 year old postmenopausal woman had a LEEP 2 years ago for CIN 3. She recently had a TAH for fibroids. What would you advise her about vaginal cancer screening?

1. **She does not need further Pap tests.**
2. **She should have Pap tests until age 65 and then discontinue.**
3. **She should continue Pap tests for 20 years after her LEEP.**

High grade vaginal intraepithelial neoplasia (VaIN 3) after TAH for CIN 3 in a 55 year old woman



2012 Consensus Guidelines: Women with prior hysterectomy

No screening is necessary. Applies to women without a cervix and without a history of CIN2, CIN3, AIS, or cancer in the past 20 years.

Evidence of adequate negative prior screening is not required (all but USPSTF).

Screening should not be resumed for any reason, including if a woman reports having a new sexual partner.

American Cancer Society | ASCP | American Society for Clinical Pathology | NCCN National Comprehensive Cancer Network

1. Saslow et al. ACS/ASCCP/ASCP. CA Cancer J Clin 2012; 62: 147-72 and AJCP 2012; 137: 516 – 542.
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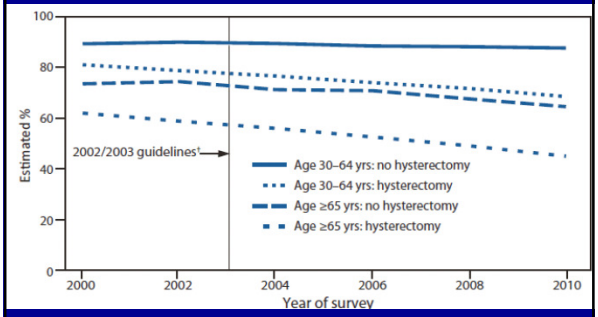
Percentage of women who had a Pap test within 3 years by hysterectomy status and age group



MMWR 2013;61(51):1043-1047

See you soon for management guidelines of abnormal Pap's

Thanks!