ASCCP 2013 Guidelines for Managing Abnormal Cervical Cancer Screening Tests

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Disclosures


3. ASCCP Board of Directors. 2007-current.

Permission obtained from ASCCP to use algorithms
What are we going to talk about today?
Principles of 2013 Management Guidelines

- Preventing all cervical cancer is unrealistic.
  - No screening test has 100% sensitivity.
  - Precursor disease can recur post management/treatment.
  - Risk of persistent oncogenic HPV.
- Women at similar risk for cancer are managed the same.
  - ASC-US, LSIL ("lesser")
  - ASC-H, HSIL, AGC ("greater")

- Potential harms of overzealous management.
  - Pain/bleeding from procedures.
  - Treatment-related pregnancy complications.
“Similar Management of Similar Risks” ensures simplified, consistent management for different test result combinations.

- Can be initial management or follow-up.

Is this “similar management of similar risks”? 
Cervical Intraepithelial Neoplasia (CIN)

CIN 1 (histologic LSIL)
CIN 2 (histologic HSIL)
CIN 3 (histologic HSIL)

You will see less “CIN” as CIN is converted into LSIL and HSIL
Screening targets

- **CIN 3 is a true precancer, 30-50% progress to cancer over 30 years.**
  - Observation is unacceptable since it cannot be predicted which CIN 3’s will invade.

- **CIN 2 is a collection of CIN 3 and CIN 1**
  - 50% regression rate, low risk of invasion
  - Observation acceptable, especially in young women

- **CIN 1 is a transient or stable HPV infection with minimal cancer risk:** *DO NOT TREAT!*
How risk is managed

◆ High risk >>> treat
◆ Low risk >>> observe
◆ Intermediate risk >> manage by level of risk
  ◆ Short interval rescreening.
  ◆ Molecular triage (HPV, genotyping, biomarker)

◆ Definitions of high/low/intermediate risk are arbitrary, based on balancing risks of intervention vs. risks of cancer
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.

3. ACOG Practice Bulletin #131, November 2012
4. NCCN Cervical Cancer Screening Guideline v. 2-2012. www.NCCN.org
Proportion of Co-Test Results in 331,061 Kaiser women ≥ 30 years

- 92.5%
- 3.7%
- 1.4%
- 2.4%

Discordant

35 year old G1P1 has a negative Pap test and positive HPV testing. She was previously screened with Pap's only but has had no screening in 5 years. What is the next step?

1. Cotesting in 1 year.
2. Routine screening (cotesting) in 5 yrs.
3. Immediate colposcopy.
2013 ASCCP management guidelines

Management of Women ≥ Age 30, who are Cytology Negative, but HPV Positive

Repeat Cotesting
@ 1 year
Acceptable

HPV DNA Typing
Acceptable
She returns in one year. Cotesting results show Pap – HPV –
What is the next step?

1. Repeat cotesting in 1 year.
2. Repeat cotesting in 3 years.
3. Pap only in 3 years.
Management of Women ≥ Age 30, who are Cytology Negative, but HPV Positive

- Repeat Cotesting @ 1 year
  Acceptable

- Cytology Negative
  and
  HPV Negative

- Repeat cotesting @ 3 years
She returns in 3 years and her cotesting is Pap - HPV +
What does she do now?

1. Go back and start all over with cotesting in 1 year.

2. Immediate colposcopy.
Management of Women ≥ Age 30, who are Cytology Negative, but HPV Positive

- **Repeat Cotesting @ 1 year Acceptable**
  - Cytology Negative and HPV Negative
  - Repeat cotesting @ 3 years

- **HPV DNA Typing**
  - ≥ASC or HPV positive
  - HPV 16 or 18 Positive
  - HPV 16 and 18 Negative
  - Repeat Cotesting @ 1 year

- **Colposcopy**

- **NO**
  - Manage per ASCCP Guideline
HPV Genotyping

- Both DNA and mRNA tests available
  - Prognostic information seems similar.
- 5 year risk of CIN2+ if HPV 16 + = ~10%
- Risk of CIN2+ is lower if HPV 18, but there is association for adenocarcinoma.

**Bottom line**: ASCCP guidelines show genotyping acceptable without recommending for or against use
  - Allows for clinician discretion and patient choice
42 year old woman is Pap – HPV +
You decide to genotype her and she is
*HPV 16 and 18 negative.*
What is the next step?

1. Cotesting in 1 year.
2. Cotesting in 3 years.
3. Colposcopy.
Management of Women ≥ Age 30, who are Cytology Negative, but HPV Positive

- Repeat Cotesting @ 1 year
  Acceptable

- HPV DNA Typing
  Acceptable

  HPV 16 and 18 Negative

  Repeat Cotesting @ 1 year

  Manage per ASCCP Guideline
Her cotesting in one year is Pap – HPV +. What do you do now?

1. Immediate colposcopy.
2. Repeat cotesting in 1 year.
3. Repeat cotesting in 3 years.
Management of Women ≥ Age 30, who are Cytology Negative, but HPV Positive

Repeat Cotesting
@ 1 year
Acceptable

HPV DNA Typing
Acceptable

HPV 16 and 18 Negative

Repeat Cotesting
@ 1 year

Manage per ASCCP Guideline

Pap -
HPV +

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Management of Women ≥ Age 30, who are Cytology Negative, but HPV Positive

Repeat Cotesting @ 1 year
Acceptable

Cytology Negative and HPV Negative

≥ASC or HPV positive

Repeat cotesting @ 3 years

HPV DNA Typing
Acceptable

HPV 16 or 18 Positive

HPV 16 and 18 Negative

Repeat Cotesting @ 1 year

Colposcopy

Manage per ASCCP Guideline

Manage per ASCCP Guideline

Pap - HPV +
22 year old presents for her first Pap. She has been sexually active since age 17 (3 partners). You decide to do cotesting because she is sexually active. She is Pap negative but HPV +. What do you do now?

- Pap in one year. No HPV testing.
- Pap in 3 years. No HPV testing.
- Cotesting in one year.
- Genotyping now.
2012 Consensus Guidelines: Screening Frequency

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

Co-testing should NOT be performed for women under age 30.

3. ACOG Practice Bulletin #131, November 2012
4. NCCN Cervical Cancer Screening Guideline v. 2-2012. www.NCCN.org
Managing Women 21-24

- Kaiser data
  - 3 cancers noted in 133,947 women ages 21-24

- HPV infection incidence peaks in this age group.

- Likelihood of future pregnancy is high.

- Most CIN2 in this age group will regress.

- Be conservative, conservative, conservative!
22 year old with ASC-US. This is her first Pap. You requested reflex HPV testing. She is HPV +

What is the next step?

1. Colposcopy now.
2. Pap in 1 year.
3. HPV testing in 1 year.
Management of Women Ages 21-24 years with either Atypical Squamous Cells of Undetermined Significance (ASC-US) or Low-grade Squamous Intraepithelial Lesion (LSIL)

Women ages 21-24 years with ASC-US or LSIL

Repeat Cytology @ 12 months Preferred

HPV Positive

Reflex HPV Testing Acceptable for ASC-US only

HPV Negative

Routine Screening

ASC-H, AGC, HSIL

Negative, ASC-US or LSIL

Repeat Cytology @ 12 months

Negative x 2 > ASC

Colposcopy

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23 year old G1P1 has a Pap showing HSIL. Her previous Pap was ASC-H (PCP records) 2 years ago. She did not return until now. What is the next step?

1. Repeat Pap in 1 year.
2. Ask for HPV testing.
3. Ask for genotyping.
4. Immediate colposcopy.
Management of Women Ages 21-24 yrs with Atypical Squamous Cells, Cannot Rule Out High Grade SIL (ASC-H) and High-grade Squamous Intraepithelial Lesion (HSIL)

Colposcopy
(Immediate loop electrosurgical excision is unacceptable)

No CIN2,3

CIN2,3

Two Consecutive Cytology Negative Results and No High-grade Colposcopic Abnormality

Observation with colposcopy & cytology*
@ 6 month intervals for up to 2 years

Other results

HSIL
Persists for 24 months with no CIN2,3 identified

Biopsy

CIN2,3
(If no CIN2,3, continue observation)

Manage per ASCCP Guideline for young women with CIN2,3

Routine Screening

Manage per ASCCP Guideline

Diagnostic Excisional Procedure+

Figure 9

*If colposcopy is adequate and endocervical sampling is negative. Otherwise, a diagnostic excisional procedure is indicated.
+Not if patient is pregnant

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ASC-H and HSIL in Women Ages 21-24

- Precancer risk higher than after ASC-US/LSIL
- 5 year CIN3+ risk
  - 16% after ASC-H
  - 28% after HSIL
- 5 year cancer risk
  - 0% after ASC-H
  - 0% after HSIL

Bottom line: cancer unlikely during extended observation
TREAT women with high risk of developing invasive disease

OBSERVE women who are not at high risk of developing invasive disease and protect them from over-treatment
Treatment in young women

- Treatment can have adverse consequences on future pregnancy.
- CIN 2 can regress – up to 49%.
  - Risk of progression is real but usually takes significant time.
  - Treat if CIN 2 present for 2 years.
- Treatment recommended for CIN 3.
  - Risk of progression is high enough to justify potential risks to future pregnancy.
23 year old presents for a Pap. She had a “slightly bad” Pap during pregnancy at age 18. She does not know the result and did not follow-up. She is referred to colposcopy for HSIL cytology. What is your colposcopic impression?

1. Normal
2. Low grade
3. High grade
4. Cancer
Biopsies showed LSIL (CIN 1) and HSIL (CIN 2). ECC negative. What is the next step?

1. Colposcopy and cytology at 6 and 12 months.
2. LEEP.
3. Cotesting in one year.
Management of Young Women with Biopsy-confirmed Cervical Intraepithelial Neoplasia - Grade 2,3 (CIN2,3) in Special Circumstances

Young Women with CIN2,3

Either treatment or observation is acceptable, provided colposcopy is adequate. When CIN2 is specified, observation is preferred. When CIN3 is specified, or colposcopy is inadequate, treatment is preferred.

**Observation - Colposcopy & Cytology**
@ 6 month intervals for 12 months

2x Cytology Negative and Normal Colposcopy

- Cotest in 1 year
- Both tests negative

- Cotest in 3 years

Colposcopy worsens or High-grade Cytology or Colposcopy persists for 1 year

- Either test abnormal

Repeat Colposcopy/Biopsy Recommended

CIN3 or CIN2,3 persists for 24 months

Treatment Recommended

**Treatment using Excision or Ablation of T-zone**

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HSIL persists for 12 months. The lesion is larger on colposcopy. Biopsy shows CIN 3. What is the next step?

1. Repeat colposcopy and biopsy in 6 months
2. LEEP
3. Cotesting in one year.
Management of Young Women with Biopsy-confirmed Cervical Intraepithelial Neoplasia - Grade 2,3 (CIN2,3) in Special Circumstances

Young Women with CIN2,3

Either treatment or observation is acceptable, provided colposcopy is adequate. When CIN2 is specified, observation is preferred. When CIN3 is specified, or colposcopy is inadequate, treatment is preferred.

Observation - Colposcopy & Cytology
@ 6 month intervals for 12 months

- 2x Cytology Negative and Normal Colposcopy
  - Cotest in 1 year
  - Both tests negative
    - Cotest in 3 years

Treatment using Excision or Ablation of T-zone

- Colposcopy worsens or High-grade Cytology or Colposcopy persists for 1 year
  - Either test abnormal
    - Repeat Colposcopy/Biopsy Recommended

- CIN3 or CIN2,3 persists for 24 months
  - Treatment Recommended

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Let’s discuss adult women now……
Managing ASC-US in adult women

- Up to 2/3 are HPV-associated
- HPV+ more frequent in younger women
  - >60% ages <25 vs. <25% ages 45-55
- More frequent among those with more partners
- HPV triage of ASC-US more cost-effective than repeat cytology

Arbyn M et al Vaccine 2006;24:S3:78-70
Management of Women with Atypical Squamous Cells of Undetermined Significance (ASC-US) on Cytology*

Repeat Cytology
@ 1 year
Acceptable

No colpo

Routine Screening*

Colposcopy
Endocervical sampling preferred in women with no lesions, and those with inadequate colposcopy; it is acceptable for others

Manage per ASCCP Guideline

HPV Testing
Preferred

HPV Positive
(managed the same as women with LSIL)

Repeat Cotesting @ 3 years

HPV Negative

Repeat Cytology
@ 1 year
Acceptable

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*Management options may vary if the woman is pregnant or ages 21-24
*Cytology at 3 year intervals

Figure 4
What has changed in adult women with *ASC-US* from prior guidelines?

- Colposcopy is not immediate option (2006).

- HPV- *ASC-US* insufficient to exit from screening at age 65.
  - Repeat cotesting in one year.
28 year old G1P1 has had 3 normal Pap tests. She now has LSIL. What is the next step?

1. Colposcopy.
2. Reflex HPV testing.
4. Repeat Pap in 1 year.
Management of Women with Low-grade Squamous Intraepithelial Lesions (LSIL)*

**LSIL with negative HPV test**
- Preferred
- Repeat Cotesting @ 1 year
  - Cytology Negative and HPV Negative
    - Repeat Cotesting @ 3 years

**LSIL with no HPV test**
- Acceptable
- Colposcopy
  - ≥ASC or HPV positive
    - No CIN2,3
      - Manage per ASCCP Guideline
  - CIN2,3
    - Manage per ASCCP Guideline

**LSIL with positive HPV test**

*Management options may vary if the woman is pregnant, postmenopausal, or ages 21-24 years (see text)

Figure 6

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Managing ASC-H in adult women

- > 60% are HPV+
  - HPV triage relatively inefficient
  - CIN3+ risk when HPV negative = 3.5% at 5 years
  - CIN3+ risk when HPV+ = 25% at 5 years
Management of Women with Atypical Squamous Cells:
Cannot Exclude High-grade SIL (ASC-H)*

Colposcopy
Regardless of HPV status

No CIN2,3
Manage per ASCCP Guideline

CIN2,3
Manage per ASCCP Guideline

*Management options may vary if the woman is pregnant or ages 21-24 years.

Figure 8
HSIL in adult women

- Immediate CIN3+ risk is 36%
- Risk rises to 47% at 5 years
  - Justifies immediate excision when pregnancy not at issue

- Bottom line: 6% of women ages 30-64 with HSIL have cancer
Management of Women with High-grade Squamous Intraepithelial Lesions (HSIL) *

- Immediate Loop Electrosurgical Excision *
- Or

- Colposcopy (with endocervical assessment)

- No CIN2,3
  - Manage per ASCCP Guideline

- CIN2,3

* Management options may vary if the woman is pregnant, postmenopausal, or ages 21-24
* Not if patient is pregnant or ages 21-24

Figure 10
37 year old had a LEEP for CIN 3. Margins clear. LEEP sample showed CIN 3. What is the next step?

1. Colposcopy and cytology at 6 and 12 months.
2. HPV testing at 12 months.
3. Cotesting at 12 and 24 months.
4. Cotesting in 3 years.
Management of Women with Biopsy-confirmed Cervical Intraepithelial Neoplasia - Grade 2 and 3 (CIN2,3) *

Either Excision† or Ablation of T-zone *

Cotesting at 12 and 24 months

2x Negative Results

Inadequate Colposcopy or Recurrent CIN2,3 or Endocervical sampling is CIN2,3

Diagnostic Excisional Procedure†

Any test abnormal

Colposcopy With endocervical sampling

Repeat cotesting in 3 years

Routine screening

*Management options will vary in special circumstances or if the woman is pregnant or ages 21-24
†If CIN2,3 is identified at the margins of an excisional procedure or post-procedure ECC, cytology and ECC at 4-6mo is preferred, but repeat excision is acceptable and hysterectomy is acceptable if re-excision is not feasible.

Figure 16
Cumulative risk of CIN 2+ following subsequent negative follow-up tests after tx for CIN 2,3 or AIS.

Katki HA et al. JLGTD 2013; 17(5):s78-84.
23 year old G1P1 has had no endocervical cells on 2 recent negative Pap's.

What is the next step?

1. Pap in 1 year.
2. Pap in 3 years.
3. Request HPV testing now.
Cytology NILM* but EC/TZ Absent/Insufficient

Ages 21-29*

HPV negative

HPV testing (Preferred)

HPV unknown

Repeat cytology in 3 years (Acceptable)

Age ≥30 years

HPV positive

HPV negative

Cytology + HPV test in 1 year

HPV unknown

Genotyping

Routine screening

Repeat cytology in 3 years (Acceptable)

Manage per ASCCP Guideline

*Negative for intraepithelial lesion or malignancy
*HPV testing is unacceptable for screening women ages 21-29 years

Figure 2

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The End.....

Thanks!
For More Information

- Explanatory text available at J Lower Genital Tract Dis 2013;17:S1-S27
- Algorithms are available for free download at www.asccp.org/consensus2012
- Algorithm booklets
- ASCCP guidelines app