



## Complete Summary

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### GUIDELINE TITLE

Initial management of abnormal cervical cytology (Pap smear) and HPV testing.

### BIBLIOGRAPHIC SOURCE(S)

Institute for Clinical Systems Improvement (ICSI). Initial management of abnormal cervical cytology (Pap smear) and HPV testing. Bloomington (MN): Institute for Clinical Systems Improvement (ICSI); 2008 Oct. 32 p. [63 references]

### GUIDELINE STATUS

This is the current release of the guideline.

This guideline updates a previous version: Institute for Clinical Systems Improvement (ICSI). Initial management of abnormal cervical cytology (Pap smear) and HPV testing. Bloomington (MN): Institute for Clinical Systems Improvement (ICSI); 2006 Oct. 32 p. [73 references]

## COMPLETE SUMMARY CONTENT

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## SCOPE

### DISEASE/CONDITION(S)

Abnormal cervical cytology (Pap smear)

### GUIDELINE CATEGORY

Diagnosis  
Evaluation

Management  
Treatment

### **CLINICAL SPECIALTY**

Family Practice  
Internal Medicine  
Nursing  
Obstetrics and Gynecology  
Oncology  
Pathology  
Pediatrics

### **INTENDED USERS**

Advanced Practice Nurses  
Allied Health Personnel  
Health Care Providers  
Health Plans  
Hospitals  
Managed Care Organizations  
Nurses  
Physician Assistants  
Physicians

### **GUIDELINE OBJECTIVE(S)**

- To provide recommendations for appropriate clinical follow-up for women who undergo cervical cytologic analysis (Pap smear) and receive an abnormal cervical cytology result
- To provide recommendations regarding colposcopy with endocervical curettage (ECC) or loop electrosurgical excision procedure (LEEP) for women who are diagnosed with a high grade abnormal cervical cytology result
- To reduce the psychological distress and increase the knowledge of women who are notified of a cervical cytology abnormality

### **TARGET POPULATION**

Any adolescent or adult woman who has undergone cervical cytologic analysis (Pap smear) and has received an abnormal result

### **INTERVENTIONS AND PRACTICES CONSIDERED**

1. Patient education regarding cervical cytology (Pap smear) and abnormal results
2. Routine cervical cytology screening
3. Management based on classification of abnormal cytology results. Options include repeat Pap smear, treatment of infections, human papillomavirus (HPV) DNA testing, colposcopy, endocervical curettage (ECC), endometrial biopsy, loop electrosurgical excision procedure (LEEP), and dilation and curettage (D & C)

**Note:** LEEP is not recommended in adolescents since surgical excision may be detrimental to future fertility and cervical competency.

4. Consultation with gynecology or gynecologic oncology, when necessary

#### **MAJOR OUTCOMES CONSIDERED**

- Incidence of abnormal cervical cytology findings
- Risk of cervical and endometrial cancer in women with abnormal cervical cytology
- Sensitivity and specificity of human papillomavirus deoxyribonucleic acid (HPV DNA) testing

## **METHODOLOGY**

#### **METHODS USED TO COLLECT/SELECT EVIDENCE**

Searches of Electronic Databases

#### **DESCRIPTION OF METHODS USED TO COLLECT/SELECT THE EVIDENCE**

A literature search of clinical trials, meta-analysis, and systematic reviews is performed.

#### **NUMBER OF SOURCE DOCUMENTS**

Not stated

#### **METHODS USED TO ASSESS THE QUALITY AND STRENGTH OF THE EVIDENCE**

Weighting According to a Rating Scheme (Scheme Given)

#### **RATING SCHEME FOR THE STRENGTH OF THE EVIDENCE**

##### **Classes of Research Reports:**

A. Primary Reports of New Data Collection:

Class A:

- Randomized, controlled trial

Class B:

- Cohort study

Class C:

- Non-randomized trial with concurrent or historical controls

- Case-control study
- Study of sensitivity and specificity of a diagnostic test
- Population-based descriptive study

Class D:

- Cross-sectional study
- Case series
- Case report

B. Reports that Synthesize or Reflect upon Collections of Primary Reports:

Class M:

- Meta-analysis
- Systematic review
- Decision analysis
- Cost-effectiveness analysis

Class R:

- Consensus statement
- Consensus report
- Narrative review

Class X:

- Medical opinion

## **METHODS USED TO ANALYZE THE EVIDENCE**

Review of Published Meta-Analyses  
Systematic Review

## **DESCRIPTION OF THE METHODS USED TO ANALYZE THE EVIDENCE**

Not stated

## **METHODS USED TO FORMULATE THE RECOMMENDATIONS**

Expert Consensus

## **DESCRIPTION OF METHODS USED TO FORMULATE THE RECOMMENDATIONS**

### **Guideline Development Process**

Each guideline, order set, and protocol is developed by a 6- to 12-member work group that includes physicians, nurses, pharmacists, other healthcare professionals relevant to the topic, along with an Institute for Clinical Systems

Improvement (ICSI) staff facilitator. Ordinarily, one of the physicians will be the leader. Most work group members are recruited from ICSI member organizations, but if there is expertise not represented by ICSI members, 1 or 2 members may be recruited from medical groups or hospitals outside of ICSI.

The work group meets for seven to eight three-hour meetings to develop the guideline. A literature search and review is performed and the work group members, under the coordination of the ICSI staff facilitator, develop the algorithm and write the annotations and footnotes and literature citations.

Once the final draft copy of the guideline is developed, the guideline goes to the ICSI members for critical review.

## **RATING SCHEME FOR THE STRENGTH OF THE RECOMMENDATIONS**

Not applicable

## **COST ANALYSIS**

A formal cost analysis was not performed and published cost analyses were not reviewed.

## **METHOD OF GUIDELINE VALIDATION**

Internal Peer Review

## **DESCRIPTION OF METHOD OF GUIDELINE VALIDATION**

### **Critical Review Process**

Every newly developed guideline or a guideline with significant change is sent to the Institute for Clinical Systems Improvement (ICSI) members for Critical Review. The purpose of critical review is to provide an opportunity for the clinicians in the member groups to review the science behind the recommendations and focus on the content of the guideline. Critical review also provides an opportunity for clinicians in each group to come to consensus on feedback they wish to give the work group and to consider changes necessary across systems in their organization to implement the guideline.

All member organizations are expected to respond to critical review guidelines. Critical review of guidelines is a criterion for continued membership within the ICSI.

After the critical review period, the guideline work group reconvenes to review the comments and make changes, as appropriate. The work group prepares a written response to all comments.

### **Approval**

Each guideline, order set, and protocol is approved by the appropriate steering committee. There is one steering committee each for Respiratory, Cardiovascular,

Women's Health, and Preventive Services. The Committee for Evidence-based Practice approves guidelines, order sets, and protocols not associated with a particular category. The steering committees review and approve each guideline based on the following:

- Member comments have been addressed reasonably.
- There is consensus among all ICSI member organizations on the content of the document.
- Within the knowledge of the reviewer, the scientific recommendations within the document are current.
- Either a critical review has been carried out, or to the extent of the knowledge of the reviewer, the changes proposed are sufficiently familiar and sufficiently agreed upon by the users that a new round of critical review is not needed.

Once the guideline, order set, or protocol has been approved, it is posted on the ICSI Web site and released to members for use. Guidelines, order sets, and protocols are reviewed regularly and revised, if warranted.

### **Revision Process of Existing Guidelines**

ICSI scientific documents are revised every 12 to 36 months as indicated by changes in clinical practice and literature. Every 6 months, ICSI checks with the work group to determine if there have been changes in the literature significant enough to cause the document to be revised earlier than scheduled.

Prior to the work group convening to revise the document, ICSI members are asked to review the document and submit comments. During revision, a literature search of clinical trials, meta-analysis, and systematic reviews is performed and reviewed by the work group. The work group will meet for 1-2 three-hour meetings to review the literature, respond to member organization comments, and revise the document as appropriate.

If there are changes or additions to the document that would be unfamiliar or unacceptable to member organizations, it is sent to members to review prior to going to the appropriate steering committee for approval.

### **Review and Comment Process**

ICSI members are asked to review and submit comments for every guideline, order set, and protocol prior to the work group convening to revise the document.

The purpose of the Review and Comment process is to provide an opportunity for the clinicians in the member groups to review the science behind the recommendations and focus on the content of the order set and protocol. Review and Comment also provides an opportunity for clinicians in each group to come to consensus on feedback they wish to give the work group and to consider changes needed across systems in their organization to implement the guideline.

All member organizations are encouraged to provide feedback on order sets and protocol; however, responding to Review and Comment is not a criterion for continued membership within ICSI.

After the Review and Comment period, the work group reconvenes to review the comments and make changes as appropriate. The work group prepares a written response to all comments.

## RECOMMENDATIONS

### MAJOR RECOMMENDATIONS

**Note from the National Guideline Clearinghouse (NGC) and the Institute for Clinical Systems Improvement (ICSI):** For a description of what has changed since the previous version of this guidance, refer to [Summary of Changes Report--October 2008](#).

The recommendations for the initial management of abnormal cervical cytology and human papilloma virus (HPV) testing are presented in the form of five algorithms with a total of 37 components, accompanied by detailed annotations. Algorithms are provided for: [Initial Abnormal Cytology Result](#); [Benign Endometrial Cells \(BEC\)](#); [Atypical Squamous Cells of Undetermined Significance \(ASCUS\)](#); [Atypical Glandular Cells \(AGC\)](#); and [Abnormal Cervical Cytology in Adolescents \(Less than 21 years\)](#). Clinical highlights and selected annotations (numbered to correspond with the appropriate algorithm) follow.

Class of evidence (A-D, M, R, X) ratings are defined at the end of the "Major Recommendations" field.

### Clinical Highlights

- Atypical squamous cells of undetermined significance (ASCUS) as an initial cytology result in women necessitates human papilloma virus (HPV) testing. If HPV testing is unavailable, a repeat Pap smear in six months or immediate colposcopy is recommended. (*ASCUS Algorithm; Annotations # 7, 9; Aim #1*)
- Atypical glandular cells (AGC) as an initial cytology result require a colposcopy and endocervical curettage (ECC) and possible endometrial biopsy. AGC cytology results can, in some cases, be indicative of extracervical malignancy. Follow-up is highly recommended. (*AGC Algorithm; Annotation #18; Aim #1*)
- Low-grade squamous intraepithelial lesion (LSIL) as an initial cytology result in an adult generally warrants a colposcopy. Special considerations may be made for adolescent and postmenopausal women. (*LSIL Annotations #22, 23 and Abnormal Cervical Cytology in Adolescents Algorithm Annotation; Aim #1*)
- High-grade squamous intraepithelial lesion (HSIL) as an initial cytology result requires colposcopy in adolescents or colposcopy with endocervical curettage (ECC) or loop electrosurgical excision (LEEP) in adults. (*Annotations #24, 25; Aim #2*)
- In adolescents, for ASCUS and LSIL cytologic screening results, the HPV regression rate is so high that conservative management without colposcopy is recommended. (*Abnormal Cervical Cytology in Adolescent Algorithm, Annotations #30-34; Aim #1*)

### Introduction

The guideline group recognizes the difficulties faced by clinicians who must respond to abnormal cervical cancer screening test results. The group also recognizes this is an area of changing technology. Mindful of these concerns, the work group strives to present a framework based on objective evidence that will provide guidance to the clinician and patient in the management of abnormal cervical cancer screening test results.

## **Health Education**

Receiving the diagnosis of an abnormal cervical cytology is a traumatic occurrence for many women. The work group was made aware of this fact repeatedly and felt that education attempts need to be improved if patient anxiety is to be successfully reduced. It was felt that written general information provided at the time of the initial cervical cancer screening test could serve to educate patients about the role of cervical cytology, as well as to provide basic information about some of the potential results, and to emphasize the fact that most such findings may require nothing further than repeating the cytology or undergoing relatively simple evaluations such as colposcopy. It was felt to be imperative that physicians or health care personnel who provide the initial diagnosis of an abnormal result to a patient have sufficient training to allay most fears and answer basic questions. Finally, it was felt that mailing written material specific to the diagnosis and recommended procedures and follow-up would help prepare the patient for the next phase of evaluation. With a commitment to such education and continued sensitivity to the anxiety produced by the finding of an abnormal cervical cytology result, physicians and other health care workers can provide effective and compassionate evaluation and treatment as needed.

## **Benign Endometrial Cells Algorithm Annotations**

### **2-6. Benign Endometrial Cells (BEC) Present**

#### **Key Points:**

- The Bethesda System 2001 reports the presence of normal, cytologically benign-appearing exfoliated endometrial glandular cells only in women age 40 or greater.
- Benign-appearing endometrial cells are noted in up to 12% of cervical cancer screenings performed over one year, more commonly in premenopausal than in postmenopausal women.

The presence of benign endometrial glandular cells on cervical screening tests may reflect physiologic shedding or shedding in response to a pathological process. In women over age 40, the presence of benign-appearing endometrial cells on cervical cytology has been found to be less than 2% [B]. Benign-appearing endometrial cells are more likely to be identified on cervical cytology in the first 10 to 12 days of the menstrual cycle (prevalence 21% to 24%) than in the remainder of the cycle (prevalence 2%) [B], [C]. The presence of benign endometrial cells on cervical cytology is reported so that a clinician can determine the significance of the finding in an individual woman.

Eighty-four percent (84%) of pre- and postmenopausal women who underwent endometrial sampling due to findings of benign endometrial cells on cervical

pathology had no pathology, benign pathology or nondiagnostic pathology. Sixteen percent (16%) of these women were found to have significant pathology (simple or complex hyperplasia with or without atypia or carcinoma) at the time of their endometrial sampling [R].

If a woman has symptoms of endometrial cancer (abnormal uterine bleeding/spotting) or she is at increased risk of endometrial cancer (i.e., postmenopausal; family or personal history of ovarian, breast, colon or endometrial cancer; tamoxifen use; chronic anovulation; obesity [D]; or prior endometrial hyperplasia), a sampling of the endometrium with endometrial biopsy or dilation and curettage (D & C) is suggested to rule out endometrial cancer. If the above symptoms or risk factors are not present, routine gynecological care should be continued, as women have not been proven to be at increased risk of endometrial cancer based on the presence of benign endometrial cells on cytology alone [B], [C], [D].

### **Atypical Squamous Cells of Undetermined Significance (ASCUS) Algorithm Annotations**

#### **7. Atypical Squamous Cells of Undetermined Significance (ASCUS) Present**

##### **Key Points:**

- Atypical squamous cells of undetermined significance (ASCUS) is used by pathologists to denote cellular changes that are more marked than those attributable to reactive changes, but that are quantitatively or qualitatively short of a definitive diagnosis of squamous intraepithelial lesion (SIL).

The new Bethesda System has identified criteria for ASCUS on cervical cytology screening. Atypical squamous cells of undetermined significance (ASCUS) is used by pathologists to denote cellular changes that are more marked than those attributable to reactive changes, but that are quantitatively or qualitatively short of a definitive diagnosis of squamous intraepithelial lesion (SIL) [C], [D], [R].

Despite the evidence that supports a conservative approach, some clinicians favor immediate colposcopy for all ASCUS smears. The presence of these high-risk factors may influence the decision toward a more aggressive approach: teenage sexual activity, multiple sexual partners, intercourse with a male who has HPV, history of sexually transmitted disease or genital warts, tobacco use or history of tobacco use, intrauterine exposure to diethylstilbestrol (DES), poor compliance for follow-up, lack of normal immune response, no history of regular Pap smears, and age less than 30.

##### **Advantages of immediate colposcopy for all ASCUS Pap smear results include:**

- Reduced risk of missing a significant lesion
- Reduced risk of being lost to follow-up

- Faster reassurance to patient of normalcy or avoidance of multiple follow-up Pap smears, resulting poor compliance, and potentially overburdened clinics
- Avoidance of delay in diagnosis of cancer or high-grade cervical intraepithelial neoplasia (CIN)

Options for evaluation include triage to colposcopy by HPV deoxyribonucleic acid (DNA) testing, immediate colposcopy, or repeat cytology tests at 6 and 12 months [R].

## 9. Repeat Cytology at 6 and 12 Months or Do Colposcopy

### Key Points:

- Two consecutive negative cytology results at 6 and 12 months approach the sensitivity of a single HPV test for the detection of CIN-2/3 or greater.
- Immediate colposcopy may be an option for some women who have an initial cytology result of ASCUS.

One option for the low-risk reliable patient with an ASCUS result would be to have a follow-up cytology test at 6 and 12 months. Two consecutive negative follow-up tests will approach the sensitivity of a single HPV test for the detection of CIN-2/3+. Routine testing can be resumed after normal results at 12 months. If either is ASCUS or higher, colposcopy is recommended [R].

## 11. ASCUS with High-Risk HPV DNA Positive?

### Key Points:

- It is now scientifically well established that human papillomavirus (and more specifically, certain DNA subtypes like #16 and #18) has an important role in the progress of cervical dysplasia and development of squamous cervical cancer in almost all cases.
- Some experts advocate follow-up HPV DNA testing for ASCUS Pap smears. It is the consensus of the work group that this is an excellent option.

The work group is advocating the use of HPV testing to help triage patients with ASCUS. It can be cost-effective when done in a setting that includes liquid-based cytology collection methods, since the residual fluid can be saved for HPV analysis rather than calling the patient back for sampling. Since HPV testing is another viable option for evaluation of the ASCUS cytology result, colposcopy could be deferred and performed only for those women who have tested positive for high-risk HPV types [D], [R].

Clinicians ordering HPV tests should be aware of the strengths and limitations of the assay. The report that clinicians will receive from the high risk assay will often state that the patient tested positive or negative for "one or more of the following high-risk types" followed by a list of the HPV types. The careful wording is intended to convey to clinicians that the assay does not test for all

HPV types known to associate with cervical cancer. A positive test for high-risk HPV types should indicate a need to educate the patient about HPV infection. A colposcopic examination should be scheduled. A negative HPV test result tells the clinician that the patient does not have a detectable burden of the high-risk virus types included in the test. The patient may, however, have a high-risk type at a lower titer than that which is reliably tested for or the patient may have an infection with a high-risk HPV type that is not part of the HPV assay.

## **12. Repeat Cytology at 12 Months**

Women who test negative for high-risk HPV can be reassured that their risk of having CIN-2/3+ is less than 2%. They can be scheduled for repeat cytology in 12 months.

## **13. Colposcopy**

Women who test positive for high-risk HPV have a 15% to 27% chance of having CIN-2/3 or worse. They should be scheduled for colposcopy. The exception to this recommendation is the adolescent, for whom the risk of invasive cancer approaches zero and the likelihood of HPV clearance is very high [C].

## **14, 15. Atypical Squamous Cells: Cannot Exclude High-Grade Squamous Intraepithelial Lesion (ASC-H) Present**

The Bethesda System 2001 recognizes a new category of atypical squamous cells -- high grade dysplasia (ASC-H) cannot be ruled out. In the 1988 system, emphasis was placed on identifying all squamous intraepithelial lesion (SIL) Paps, including LSIL and HSIL. Currently, the emphasis of the Bethesda System 2001 is to identify HSIL and cytology associated with histologically proven high-grade disease.

ASC-H is thought to include 5% to 10% of all ASC cases and includes mixtures of true HSIL and mimics. The positive predictive value of ASC-H in detecting CIN-2 and CIN-3 lies somewhere between 48% and 56% [D], [R].

Colposcopic examination is the established appropriate evaluation of women with ASC-H Pap smear reports, regardless of the patient's HPV status. ECC should be performed if no lesion can be visualized. Initial evaluation of the ASC-H Pap smear should not routinely include the use of loop electrosurgical excision (LEEP).

## **Atypical Glandular Cells (AGC) Algorithm Annotations**

## **16, 17. Atypical Glandular Cells (AGC) Present**

AGC is a rare finding; it is present in less than 0.5% of cervical-cancer screening specimens. The causes of AGC include cervical and uterine adenocarcinoma, inflammation, hyperplasia, dysplasia, and (rarely) metastatic cancer. Therefore aggressive further evaluation is important [C].

Atypical glandular cells (which can be either uterine or cervical in origin) have enlarged nuclei, decreased cytoplasmic volume, and a variety of other unusual characteristics. Cells are classified as AGC (atypical glandular cells) with one of the following subheadings: NOS (not otherwise specified), FN (favor neoplasia) and favor either endocervical or endometrial origin.

#### **18. Perform Colposcopy/Endocervical Curettage/Endometrial Biopsy/HPV DNA Testing**

Atypical glandular cells may indicate precancerous change or frank malignancy. Colposcopic evaluation including endocervical curettage should be used to evaluate for CIN and adenocarcinoma of the cervix. HPV DNA testing should be done to stratify the risk of cervical dysplasia and neoplasia. Endometrial tissue sampling should be used to assess for endometrial cancer and hyperplasia. A pathologist should correlate the histology of the endometrial tissue with the cells on the original cytology screening specimen so as to explain the original abnormality. If the sampling does not explain the original abnormality, the provider should refer the patient to a gynecologist or a gynecologic oncologist. Findings from these initial steps will dictate further evaluation and treatment.

#### **22. Low-Grade Squamous Intraepithelial Lesion (LSIL) Present**

The LSIL category includes changes consistent with human papillomavirus (HPV), mild dysplasia or CIN-1 (grade 1 cervical intraepithelial neoplasia). Eighty percent (80%) will be high-risk HPV positive and 15% to 30% have moderate or severe dysplasia at initial colposcopy. The ALTS group could not identify a useful triage strategy for this category that could spare colposcopic evaluation. Therefore colposcopy is recommended for initial evaluation of LSIL [B], [R].

**There is consensus and expert opinion that follow-up without immediate colposcopy may be appropriate in the postmenopausal patient.** HPV prevalence is low, allowing for triage with HPV testing. If negative, patients can return to routine surveillance [R].

#### **23. Colposcopy**

The most common management option is to perform a colposcopy. One must be cautious about over-aggressive biopsy and treatment. Specifically, routine LEEP of the transformation zone as a method for evaluating a LSIL Pap smear is not recommended.

Rate of regression has been quoted as high as 62% to 80% on follow-up. (Some investigators believe this reported regression rate is falsely high because prior biopsy, in effect, "treated" the original lesion. Under this assumption, regression rates of unbiopsied low grade lesions may be as low as 25%) [C], [R].

#### **24. High-Grade Squamous Intraepithelial Lesion (HSIL) Present**

The Bethesda System 2001 combines moderate dysplasia with severe dysplasia and carcinoma-in-situ (CIS) into a single category of high-grade intraepithelial lesion (HSIL). Up to 95% of patients with high-grade cervical cytology results have been found to have high-grade lesions [C].

Of all the categories in current nomenclature for cervical cytology results, perhaps the least ambiguity and the least controversy in management is with HSIL. Histologic evaluation of directed cervical biopsies from women with HSIL will commonly show moderate or severe dysplasia or even carcinoma in situ. Thus the standard of practice for management is clearly to perform colposcopy and directed biopsy [C].

Further management of the patient will then be guided by the biopsy results [R].

## **25. Colposcopy with Endocervical Curettage (ECC) or Loop Electrosurgical Excision (LEEP)**

Colposcopic examination with ECC-directed biopsies or LEEP is the appropriate management for women with HSIL cytology results. If follow-up for the patient is unreliable or in a "see and treat" circumstance, LEEP may be performed immediately. When a LEEP is performed immediately it is not necessary to automatically do an ECC. But if endocervical disease is suspected as a result of the colposcopy and LEEP is not done, an ECC should still be performed [M], [R].

## **28. HPV DNA Testing Positive with Normal Cytology**

In 2003, the Food and Drug Administration approved HPV DNA testing in conjunction with cervical cytology screening for women aged 30 years and older [R]. Due to the high prevalence and spontaneous clearance of HPV DNA in adolescents and women in their 20s, HPV DNA should not be used for routine screening before age 30 [R].

The use of HPV DNA testing as an adjunct to cervical cytology for women aged 30 years and older increases the sensitivity of cervical cancer screening. Review of recent screening studies reported pooled sensitivity and specificity of HPV DNA testing for CIN-2/3+ for women 35 years and older was 95% and 93%, respectively [C]. Sensitivity using a combination of HPV DNA testing and cervical cytology was higher than either test alone; negative predictive values were 99% to 100% [R].

Based on this kind of evidence, the American Cancer Society and subsequently the American College of Obstetricians and Gynecologists both concluded this combination of HPV DNA testing and cervical cytology was a reasonable screening strategy for women aged 30 years and older [B], [R]. Furthermore, testing should not be done more often than every three years if both results are negative, based on a study showing less than 2% of patients with negative HPV DNA and cervical cytology screening developed CIN-3+ in 10 years of follow-up [B]. As there is no evidence of improved outcomes with this combination of screening tests, screening with cervical cytology alone remains an acceptable screening option.

Many women screened with a combination of HPV DNA and cervical cytology will test positive for HPV DNA and simultaneously have a negative cervical cytology. The risk for undetected CIN-2/3+ for patients with such a combination of screening results is quite low, with published study results varying from 2.4% to 5.1% [A]. Based on this low risk for CIN-2/3+, repeat HPV DNA testing combined with cervical cytology in 12 months appears to be reasonable for patients in this group. If the HPV DNA test remains positive on the repeat screening, the patient should undergo colposcopic evaluation despite a second negative cervical cytologic result [R].

### **Abnormal Cervical Cytology in Adolescents (Less than 21 Years)** **Algorithm Annotations**

#### **30-37. Abnormal Cytology Results in Adolescents Present**

##### **Key Point:**

- In adolescents, the HPV regression rate is so high that conservative management without colposcopy is recommended.

##### **Management of ASCUS Cervical Cancer Screening Test Results in Adolescents**

A report of ASCUS on a cervical cytological screening test often indicates a woman is harboring an HPV infection. In the adolescent population, the prevalence of HPV in that subset with an ASCUS report will be much higher than in an older population. As noted, the risk of invasive cancer in adolescents approaches zero, and the likelihood of HPV clearance is very high.

The preferred method of triage for adolescent patients with ASCUS is monitoring with cytology at 12 months intervals. If the repeat cytology test results are abnormal for 24 months, colposcopy should be performed. These alternatives avoid the expense of colposcopy and biopsy, and they allow for the high likelihood of clearance of CIN-1 and HPV in this population [B], [R].

Immediate colposcopy is an acceptable alternative for the management of the adolescent who tests positive for ASCUS and LSIL if follow-up is problematic.

##### **Management of LSIL Cervical Cancer Screening Test Results in Adolescents**

The ALTS trial showed that patients with cytological report of LSIL and ASCUS behave in a similar manner regarding clearance of HPV and the risk of developing CIN-2/3+. Due to the similarities in the natural history of these cervical cancer screening findings, management for adolescents is the same as for ASCUS [R].

##### **Management of All Cervical Cancer Screening Test Results with High Probability of CIN-2/3+ in Adolescents**

Screening test results of ASC-H, HSIL and AGC all indicate a higher probability for a CIN-2/3+ lesion and should be managed by immediate colposcopy and

endocervical assessment as for older women. The management algorithm is identical to the main algorithm for these cervical cancer screening test results [R]. However, immediate loop electrosurgical excision (LEEP) is not recommended in adolescents since surgical excision may be detrimental to future fertility and cervical competency.

Surgical treatment should be delayed until persistent disease is proven.

In pregnancy, the only diagnosis that may alter clinical management is invasive cancer. The presence of cancer may change treatment goals for the route and timing of delivery. Cervical cancer screening test results that are not likely to be associated with cancer may undergo colposcopic evaluation either during pregnancy or 8 to 12 weeks postpartum. Pregnant women whose screening test results indicate a high risk for CIN-2/3+ should undergo colposcopy without endocervical sampling, reserving biopsy for visible cervical lesions consistent with CIN-3, AIS or cancer [R].

### **Definitions:**

#### **Classes of Research Reports:**

##### A. Primary Reports of New Data Collection:

###### Class A:

- Randomized, controlled trial

###### Class B:

- Cohort study

###### Class C:

- Non-randomized trial with concurrent or historical controls
- Case-control study
- Study of sensitivity and specificity of a diagnostic test
- Population-based descriptive study

###### Class D:

- Cross-sectional study
- Case series
- Case report

##### B. Reports that Synthesize or Reflect upon Collections of Primary Reports:

###### Class M:

- Meta-analysis
- Systematic review

- Decision analysis
- Cost-effectiveness analysis

Class R:

- Consensus statement
- Consensus report
- Narrative review

Class X:

- Medical opinion

### **CLINICAL ALGORITHM(S)**

Detailed and annotated clinical algorithms are provided for:

- [Initial Abnormal Cytology Result](#)
- [Benign Endometrial Cells \(BEC\)](#)
- [Atypical Squamous Cells of Undetermined Significance \(ASCUS\)](#)
- [Atypical Glandular Cells \(AGC\)](#)
- [Abnormal Cervical Cytology in Adolescents \(Less than 21 years\)](#)

## **EVIDENCE SUPPORTING THE RECOMMENDATIONS**

### **TYPE OF EVIDENCE SUPPORTING THE RECOMMENDATIONS**

The type of supporting evidence is classified for selected recommendations (see "Major Recommendations").

## **BENEFITS/HARMS OF IMPLEMENTING THE GUIDELINE RECOMMENDATIONS**

### **POTENTIAL BENEFITS**

Improved clinical follow-up of women who undergo cervical cytologic analysis and receive an abnormal result

### **POTENTIAL HARMS**

Not stated

## **QUALIFYING STATEMENTS**

### **QUALIFYING STATEMENTS**

- These clinical guidelines are designed to assist clinicians by providing an analytical framework for the evaluation and treatment of patients, and are not intended either to replace a clinician's judgment or to establish a protocol for

- all patients with a particular condition. A guideline will rarely establish the only approach to a problem.
- This health care guideline should not be construed as medical advice or medical opinion related to any specific facts or circumstances. Patients are urged to consult a health care professional regarding their own situation and any specific medical questions they may have.

## IMPLEMENTATION OF THE GUIDELINE

### DESCRIPTION OF IMPLEMENTATION STRATEGY

Once a guideline is approved for general implementation, a medical group can choose to concentrate on the implementation of that guideline. When four or more groups choose the same guideline to implement and they wish to collaborate with others, they may form an action group.

In the action group, each medical group sets specific goals they plan to achieve in improving patient care based on the particular guideline(s). Each medical group shares its experiences and supporting measurement results within the action group. This sharing facilitates a collaborative learning environment. Action group learnings are also documented and shared with interested medical groups within the collaborative.

Currently, action groups may focus on one guideline or a set of guidelines such as hypertension, lipid treatment, and tobacco cessation.

Detailed measurement strategies are presented in the original guideline document to help close the gap between clinical practice and the guideline recommendations. Summaries of the measures are provided in the National Quality Measures Clearinghouse (NQMC).

### Key Implementation Recommendations

The following system changes were identified by the guideline work group as key strategies for health care systems to incorporate in support of the implementation of this guideline.

1. Disseminate recommendations for appropriate follow-up for each of the Bethesda classifications for abnormal cervical cytology results.
2. Implement a program or process to ensure complete follow-up of all abnormal results obtained by cervical cytology.

### IMPLEMENTATION TOOLS

Clinical Algorithm  
Pocket Guide/Reference Cards  
Quality Measures

For information about [availability](#), see the "Availability of Companion Documents" and "Patient Resources" fields below.

## RELATED NQMC MEASURES

- [Initial management of abnormal cervical cytology \(Pap smear\) and human papillomavirus \(HPV\) testing: percentage of adult women diagnosed with initial abnormal cervical cytology of atypical squamous cells of undetermined significance \(ASCUS\) with high-risk HPV type who have follow-up colposcopy within six months of abnormality identified.](#)

## INSTITUTE OF MEDICINE (IOM) NATIONAL HEALTHCARE QUALITY REPORT CATEGORIES

### IOM CARE NEED

Getting Better  
Staying Healthy

### IOM DOMAIN

Effectiveness  
Patient-centeredness

## IDENTIFYING INFORMATION AND AVAILABILITY

### BIBLIOGRAPHIC SOURCE(S)

Institute for Clinical Systems Improvement (ICSI). Initial management of abnormal cervical cytology (Pap smear) and HPV testing. Bloomington (MN): Institute for Clinical Systems Improvement (ICSI); 2008 Oct. 32 p. [63 references]

### ADAPTATION

Not applicable: The guideline was not adapted from another source.

### DATE RELEASED

1999 May (revised 2008 Oct)

### GUIDELINE DEVELOPER(S)

Institute for Clinical Systems Improvement - Private Nonprofit Organization

### GUIDELINE DEVELOPER COMMENT

Organizations participating in the Institute for Clinical Systems Improvement (ICSI): Affiliated Community Medical Centers, Allina Medical Clinic, Altru Health System, Aspen Medical Group, Avera Health, CentraCare, Columbia Park Medical Group, Community-University Health Care Center, Dakota Clinic, ENT Specialty Care, Fairview Health Services, Family HealthServices Minnesota, Family Practice

Medical Center, Gateway Family Health Clinic, Gillette Children's Specialty Healthcare, Grand Itasca Clinic and Hospital, HealthEast Care System, HealthPartners Central Minnesota Clinics, HealthPartners Medical Group and Clinics, Hutchinson Area Health Care, Hutchinson Medical Center, Lakeview Clinic, Mayo Clinic, Mercy Hospital and Health Care Center, MeritCare, Mille Lacs Health System, Minnesota Gastroenterology, Montevideo Clinic, North Clinic, North Memorial Care System, North Suburban Family Physicians, Northwest Family Physicians, Olmsted Medical Center, Park Nicollet Health Services, Pilot City Health Center, Quello Clinic, Ridgeview Medical Center, River Falls Medical Clinic, Saint Mary's/Duluth Clinic Health System, St. Paul Heart Clinic, Sioux Valley Hospitals and Health System, Southside Community Health Services, Stillwater Medical Group, SuperiorHealth Medical Group, University of Minnesota Physicians, Winona Clinic, Ltd., Winona Health

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## **GUIDELINE COMMITTEE**

Ob/Gyn Steering Committee

## **COMPOSITION OF GROUP THAT AUTHORED THE GUIDELINE**

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## **GUIDELINE STATUS**

This is the current release of the guideline.

This guideline updates a previous version: Institute for Clinical Systems Improvement (ICSI). Initial management of abnormal cervical cytology (Pap smear) and HPV testing. Bloomington (MN): Institute for Clinical Systems Improvement (ICSI); 2006 Oct. 32 p. [73 references]

## **GUIDELINE AVAILABILITY**

Electronic copies: Available from the [Institute for Clinical Systems Improvement \(ICSI\) Web site](http://www.icsi.org).

Print copies: Available from ICSI, 8009 34th Avenue South, Suite 1200, Bloomington, MN 55425; telephone, (952) 814-7060; fax, (952) 858-9675; Web site: [www.icsi.org](http://www.icsi.org); e-mail: [icsi.info@icsi.org](mailto:icsi.info@icsi.org).

## **AVAILABILITY OF COMPANION DOCUMENTS**

The following are available:

- Initial management of abnormal cervical cytology (Pap smear) and HPV testing. Executive summary. Bloomington (MN): Institute for Clinical Systems Improvement, 2008 Oct. 1 p. Electronic copies: Available in Portable Document Format (PDF) from the [Institute for Clinical Systems Improvement \(ICSI\) Web site](http://www.icsi.org).
- ICSI pocket guidelines. May 2007 edition. Bloomington (MN): Institute for Clinical Systems Improvement, 2007.

Print copies: Available from ICSI, 8009 34th Avenue South, Suite 1200, Bloomington, MN 55425; telephone, (952) 814-7060; fax, (952) 858-9675; Web site: [www.icsi.org](http://www.icsi.org); e-mail: [icsi.info@icsi.org](mailto:icsi.info@icsi.org).

## **PATIENT RESOURCES**

None available

## **NGC STATUS**

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