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Cervical Cancer Screening

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Abstract

Recent changes in cervical cancer screening and management guidelines reflect our evolving knowledge about cervical carcinogenesis. In the pursuit of precision, however, decision-making has become complicated. We provide an overview of cervical cancer screening with a focus on what clinicians can do to maximize screening benefits while minimizing screening harms. The approach relies on categorizing women at each step in the screening process by their estimated risk of high-grade precancerous lesions and cervical cancer. Current screening guidelines are designed to find a reasonable balance between benefits and harms by recommending less screening in most women. Current management guidelines are designed to assure consistent decisions regarding referral to colposcopy. After initial colposcopy, we outline three major management options based on risk assessment. For treatment, we recommend ablational procedures when appropriate because they are similarly effective, less costly, and potentially safer than excisional procedures. We advise caution in adopting new screening strategies until they demonstrate cost-effective patient-centered improvements compared with current strategies. Clinicians can maximize their effect on cervical cancer prevention by being attentive to guidelines, assuring that women have access to appropriate human papillomavirus vaccination and providing low-cost, high-quality screening and treatment.

Recent changes in cervical cancer screening and management guidelines reflect our evolving knowledge about cervical carcinogenesis. In the pursuit of precision, however, clinical decision-making has become complicated. The purpose of this article is to provide a clinically useful overview of all aspects of cervical cancer screening with a focus on what clinicians can do to maximize screening benefits while minimizing harms. The approach relies on categorizing women at each step in the screening process by their probable risk of high-grade precancerous lesions and cervical cancer. Our goal is to not reiterate the comprehensive information available in the recent American College of Obstetricians and Gynecologists (the College) Practice Bulletins,[1,2] but to suggest a simplifying framework for guiding clinicians in making consistent clinical decisions.

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PATHOPHYSIOLOGY

Consistent high-quality evidence supports the crucial role of oncogenic, or high-risk, types of human papillomavirus (HPV) in the development of most cervical cancers.[3] According to the Centers for Disease Control and Prevention, nearly all sexually active women will be exposed to HPV over their lifetimes,[4] yet the estimated lifetime risk of cervical cancer in the absence of screening is only 3.3%.[5] Screening is designed mainly to detect cervical precancerous lesions known as cervical intraepithelial neoplasia (CIN) and early cancers. Destruction or excision of CIN lesions leads to cancer prevention; diagnosis of early-stage cancers decreases morbidity by making women eligible for less morbid treatments. The average time course from the highest-grade precancerous lesions (CIN 3) progressing to invasion is estimated at 10 years,[6] allowing many opportunities for lesions to be detected and treated.

SCREENING

The U.S. Preventive Services Task Force,[7] the College,[1] and the American Cancer Society[8] (in collaboration with the American Society for Colposcopy and Cervical Pathology [ASCCP] and the American Society for Clinical Pathology) recently issued updated guidelines for cervical cancer screening (Table 1). All groups now agree about the populations to whom the guidelines apply, the ages to begin and end screening, the optimal screening intervals, and the tests to be used.

All guidelines acknowledge that some women are at high enough risk of cervical cancer that the screening approach should be more intensive. This includes women with a history of precancerous cervical lesions or cervical cancer, those who are immunocompromised (including being infected with human immunodeficiency virus), and those with a history of in utero diethylstilbestrol exposure. The management of women after treatment of CIN 2, CIN 2/3, or CIN 3 is discussed subsequently; follow-up after cervical cancer treatment is under the purview of gynecologic oncologists and is not addressed here.

On the other end of the spectrum, screening is not recommended at all in women younger than age 21 years, regardless of sexual history, and those with no prior CIN 2 or worse who have had surgical removal of the cervix (total hysterectomy). All guidelines agree that women should end screening at age 65 years if they have had three consecutive normal results on cytology or two consecutive negative results on cytology plus HPV testing within the prior 10 years with the most recent test being within the previous 5 years. Ending screening is important, because disease incidence is very low among well-screened women, but the harms of false-positive testing and unnecessary invasive procedures persist. American Cancer Society–ASCCP–American Society for Clinical Pathology guidelines specifically recommend that screening not restart in these women for any reason, including acquiring new sexual partners.

Guidelines recommend screening every 3 years and not more frequently. In fact, the College and American Cancer Society–ASCCP–American Society for Clinical Pathology guidelines specifically state that annual screen-ing should be discouraged among average-risk women

of any age. Screening with cytology alone every 3 years lowers lifetime cervical cancer risk from approximately 3.3% to 0.5%.[5] Although more frequent screening leads to further estimated reductions in cancer risk, it also leads to substantially more screening harms. Decision analyses predict increasing levels of cancer protection as screening intervals shorten but with concurrent cumulative increased risks of false-positive testing and colposcopies.[9]

For women aged 30 years and older, the addition of high-risk HPV testing to cytology (also known as cotesting) is an option to further define a group of women at such low risk that screening can be performed every 5 years if both test results are normal. The U.S. Preventive Services Task Force recommends this strategy be applied only to women who would prefer screening less often than every 3 years; the other two groups believe that cotesting should be preferred over cytology alone. The American Cancer Society– ASCCP–American Society for Clinical Pathology guidelines acknowledge that the evidence supporting the “preferred” designation of cotesting over cytology is weak. All current guidelines discourage cotesting in women younger than age 30 years.

MANAGEMENT OF INITIAL ABNORMAL SCREENING TEST RESULTS

The prevalence of abnormal screening test results varies by age, tests used, and setting.[10] In a large health maintenance organization in the United States, approximately 9% of women older than age 30 years had either an abnormal cytology test result or a positive high-risk HPV test result.[11] The College and the ASCCP have detailed consensus- and evidence-based guidance for the management of women with various test result abnormalities.[2,12] We offer a few simplifying generalizations for common results (Table 2).

Based on their relative risk of underlying high-grade precancerous lesions or cervical cancer, we categorize women with abnormal screening test results into three categories (Table 2): low risk, moderate risk, and high risk. One of three clinical actions is generally recommended for each risk category by the College and the ASCCP: testing in 3 years (low risk), testing in 1 year (moderate risk), or colposcopy (high risk). Among women with abnormal results, approximately 20% will be deemed at low risk and have routine screening in 3 years. Approximately half will be in the moderate-risk category and have repeat testing in 1 year. The remaining 30% will be in the high-risk category and proceed directly to colposcopy.[3]

MANAGEMENT AFTER INITIAL COLPOSCOPY

Again using a risk-based framework, we categorize women based on findings after initial colposcopy into three relative risk categories: low risk, moderate risk, and high risk (Table 3). For each risk category, only one of three clinical actions is generally recommended by the College and ASCCP guidelines: testing in 1 year (low risk), testing in 6 months (moderate risk), or treatment (high risk).

The low-risk group comprises those who had colposcopy but who did not have CIN 2 or worse on biopsy. According to College and ASCCP guidelines, this includes women aged 25 years and older with high-grade squamous intraepithelial lesions (HSIL) or atypical

squamous cells, cannot exclude high-grade squamous intraepithelial lesions cytology result but with adequate colposcopy (Table 3). For these women, options include cytology plus high-risk HPV testing in 1 year or treatment. Moderate-risk women are those aged 21–24 years with severe cytologic findings (atypical squamous cells, cannot exclude high-grade squamous intraepithelial lesions or HSIL) and adequate colposcopy but no CIN 2 or worse identified. In this group, close surveillance with cytology and colposcopy in 6 months is recommended to monitor for the development of an identifiable CIN 2 or worse lesion. We question whether women should be managed differently based on age. In fact, women aged 25 years and older are at higher risk of CIN 3 and cancer than women aged 21–24 years.[13] Thus, in our practices we recommend colposcopy and cytology in 6 months for all women in this category, a decision that also serves to simply clinical algorithms by eliminating a category of exception.

Women aged 21–24 years with biopsy-proven CIN 2 or CIN 2/3 can also be considered only at moderate risk as a result of high rates of lesion regression. According to College and ASCCP guidelines, they should be offered repeat cytology and colposcopy in 6 months rather than treatment (Table 4, footnote); this surveillance strategy can also be applied to all women capable of future childbearing. Treatment is warranted in women with CIN 3.

TREATMENT OF PRECANCEROUS LESIONS

In the era before colposcopy, CIN was treated with conization and hysterectomy. After the introduction of colposcopy in the 1970s, more conservative treatments such as cryotherapy and laser ablation were adopted. In the 1990s, an office-based excisional procedure known as loop electrosurgical excision procedure (LEEP) became available and was widely adopted, and ablative therapies were largely abandoned. This change was driven in part by occasional findings on LEEP specimens of clinically occult invasive cancers, resulting in a preference for treatment modalities that provided a histologic specimen.[14]

Excisional techniques, however, have been associated with an increased risk of preterm delivery before 37[15] and 34[16] weeks of gestation. The risks associated with cone biopsy appear to be more pronounced and include perinatal mortality.[16] Whereas reevaluation of existing data questions the association of the most common excisional procedure (LEEP) and preterm birth,[17] a recent meta-analysis has implicated excisional treatments with a twofold to threefold risk of second-trimester miscarriage.[18]

Screening harms are difficult to prove with certainty; thus, we recommend clinicians be thoughtful when choosing treatments considering the best balance of effectiveness, safety, acceptability, and costs (Table 4). Although a single loop excision may cause relatively few harms, repeat excisions are common among women with CIN recurrence, and adverse reproductive effects may be more substantial. Ablative techniques (cryotherapy and laser) have not been associated with preterm birth[15] and have comparable efficacy to excisional techniques.[19]

Given the evidence of benefits and harms, we choose ablative therapies in our practices over excisional procedures in women meeting World Health Organization criteria.[20] These

criteria are detailed in Table 4. When the lesion is large or cannot be covered with the cryoprobe, we offer laser ablation if the other criteria are also met. Results from a longitudinal cohort study showed that failure rates of all treatment modalities increase with age and are especially high for cryotherapy in older women, exceeding 30% over a 6-year period in women aged 40 years and older treated for CIN 3.[21] In our practices, therefore, we generally do not offer cryotherapy to women aged older than 40 years.

As discussed previously, current management guidelines suggest surveillance for women of reproductive age with CIN 2 and CIN 2/3 and adequate colposcopy. In our practices, we offer surveillance, but we recommend ablation if possible. Cure rates with treatment are about 90%[19] compared with spontaneous cure rates (regression) of approximately 40%.[22–24] Many women followed without treatment will have persistent or progressive disease after multiple colposcopies and biopsies and may no longer be candidates for ablation once treatment is advised. Because ablation is safe,[25] inexpensive, and can often be performed at the results visit, we believe that on average the benefits of early treatment with ablation outweigh the harms. We use shared informed decision-making with individual women, including a discussion of benefits and harms and the reasoning behind our recommendation. Women may choose the option that is most consistent with their preferences and values.

If surveillance or ablative therapy is not appropriate, and excisional therapy is indicated, we recommend LEEP over cone biopsy, because LEEP can be performed with a local anesthetic in the clinic and has potentially lower risks of adverse obstetric outcomes than cone biopsy. Cone biopsy is reserved for those women with distorted cervical architecture where use of the scalpel allows more precise excision than the fixed loop wire, or in situations in which information about the margin status is critical such as the presence of adenocarcinoma in situ or suspicion of cancer.

FOLLOW-UP AFTER TREATMENT OF PRECANCEROUS LESIONS

After treatment, women undergoing excisional procedures can be stratified into a low-risk group and a high-risk group (Table 5). Those with negative surgical margins are at lower risk; the ASCCP recommends annual cytology plus high-risk HPV testing (cotesting) for 2 years followed by retesting in 3 years; if all test results are normal, routine screening should resume for at least 20 years, even if this extends beyond age 65 years.[12] This extended follow-up period is based on evidence of continued elevated cervical cancer risk among these women compared with women with no prior cervical abnormalities.[21] The incorporation of co-testing in the follow-up of women after treatment is a new recommendation and is discussed subsequently. Those with positive margins are at higher risk of recurrence and follow-up in 4–6 months with colposcopy, cytology, and endocervical curettage is advised.

Total hysterectomy eliminates cervical cancer risk. In fact, the self-reported prevalence of hysterectomy among women aged 65 years and older in the United States of at least 40% suggests a substantial contribution to cancer prevention conferred by hysterectomy that has been traditionally attributed to cervical cancer screening.[26] Women who have had surgical removal of the cervix for treatment of precancerous lesions are believed to be at increased

risk for vaginal cancer. Although little evidence suggests that continued cytology screening leads to improved health outcomes, the College recommends continued routine screening with cytology every 3 years for 20 years after the initial post-treatment surveillance period in women who have had a hysterectomy and prior CIN 2 or worse.[1] This recommendation is more conservative than their 2003 recommendation suggesting screening cessation after three normal annual vaginal cytology test results. We believe that no compelling evidence has emerged to justify continued routine screening among these women. In our practices, we end screening as per the College's 2003 guidelines to avoid oversurveillance and overtreatment.

AREAS OF UNCERTAINTY

How Should Women With Persistent Minimally Abnormal Screening Test Results and Normal Colposcopy Be Managed?

Women with persistent minimally abnormal screening test results (eg, persistently positive high-risk HPV test results with normal cytology) but no evidence of CIN 2 or worse pose management challenges. The 2012 ASCCP management guidelines recommend cotesting in 1 year with colposcopy if high-risk HPV persists or if cytology is abnormal. Many women with these screening results will require another colposcopy a year later based on their cotest result. In some women, these results will persist for years and they may be consigned to repeat annual colposcopies thereafter.

We suggest that these women be stratified by findings at colposcopy. Data from the ASCUS–LSIL Triage Study suggest that the colposcopic impression can identify a subset of women eligible for less intensive surveillance.[27] All participants had colposcopy at study end; those with a second colposcopic impression of normal had a consistently lower risk of CIN 3 or worse compared with women with colposcopic impressions of low- or high-grade lesions. Women with normal cytology and a positive high-risk HPV test result had an overall absolute risk of CIN 3 or worse of 7.3%, but in those with a normal second colposcopy, the risk was 2.2%. Regardless of whether the initial cytology was normal, atypical squamous cells of undetermined significance, or low-grade squamous intraepithelial lesions, women with a normal second colposcopy had an overall risk of CIN 3 or worse of 2.7%. These risks were comparable with the overall risk of CIN 3 or worse in the group that had negative high-risk HPV test results (2.0%). Thus, a normal second colposcopy was as effective as high-risk HPV testing in identifying a low-risk group of women.

When the ASCCP management algorithms require a second colposcopy, due to persistent atypical squamous cells of undetermined significance or low-grade squamous intraepithelial lesions, we advise liberal use of biopsy and careful examination of the vagina and vulva. If the second colposcopy is normal, and biopsies (including endocervical curettage) show no CIN, we suggest a 3-year interval for retesting, a strategy clinically responsive to concerns about oversurveillance of low-risk women.

How Should Women With Persistent CIN 1 Be Managed?

In the course of surveillance, some women will have persistent biopsy-proven CIN 1. The ASCCP guidelines state that treatment is acceptable after 2 years of persistence. Because the lesions are typically the result of HPV infections, younger women have high rates of resolution and continued surveillance is reasonable. After 2 years of persistence, we offer ablation (cryotherapy or laser) to women who are candidates by World Health Organization criteria.[20] To avoid potential reproductive harms, we do not recommend excisional procedures for persistent CIN 1 in women of childbearing potential.

The management of postmenopausal women with persistent CIN 1 is more problematic, because HPV infections may be persistent. We offer excisional treatments to rule out (and potentially treat) clinically important lesions that may have gone undetected. We consider an excision of the transformation zone showing no evidence of CIN 2 or worse, a sentinel event after which we lessen the intensity of follow-up.

How Should Women Be Followed After Treatment of CIN 2, CIN 2/3, or CIN 3?

Follow-up after treatment of these women used to be based on an initial posttreatment surveillance of cytology and colposcopy at 6 months followed by annual cytology for at least 20 years with colposcopy for any abnormal result. More recently, the ASCCP recommended annual cotesting in these women, with a return to routine screening after two negative annual cotest results followed by a negative cotest result at 3 years.

These recommendations are based on limited data from a large health maintenance organization evaluating outcomes from 3,273 women.[28] The cumulative risk of a CIN 2 or worse recurrence over 5 years in this cohort was highest in women with one negative cytology (4.2%) or one negative high-risk HPV (3.7%) result, intermediate in women with two negative cytology (2.7%) or high-risk HPV test results (2.7%), and lowest in women with one or two (1.7–2.4%) negative cotest results. Although these differences were not statistically significant, the panel of experts felt that these results were compelling enough to incorporate cotesting for surveillance after treatment into the 2012 ASCCP management guidelines.[12] The authors of the publication expressed caution about their findings given the small number of outcomes.[28]

A comparative effectiveness analysis funded by the National Cancer Institute addressed this precise issue using a Markov state-transition model.[29] The model was based on clinical outcomes from more than 37,000 women from British Columbia followed for up to 18 years for CIN recurrence after treatment.[21] The investigators studied 12 different surveillance strategies using cytology, high-risk HPV testing, or colposcopy as the first posttreatment test followed by various screening intervals with cytology alone up to the age of 85 years. The unique and valuable elements of this analysis were the incorporation of women’s preferences about being in various health states (utilities) and the economic implications of choosing one strategy over another.

The results demonstrated that colposcopy at 6 months followed by cytology applied as frequently as annually was cost effective. Strategies using high-risk HPV testing provided less health benefit at greater costs than strategies using cytology alone, driven in part by the

relatively high prevalence of high-risk HPV test result positivity among treated women reported in a systematic review[30] and the lower preference expressed by women for high-risk HPV testing.[31] Thus, in our practices, we follow women with cytology at 6 months, with or without colposcopy, and then with annual cytology for at least 20 years thereafter.

Which Cervical Cancer Screening Strategy Provides the Best Balance of Benefits, Harms, and Costs?

The optimal strategy for cervical cancer screening is unknown, involving a complex interaction among multiple variables such as test performance, colposcopy accuracy, screening setting, patient acceptability, and costs. Current screening strategies are believed to confer similar benefits (decreased cervical cancer morbidity and mortality) and harms (eg, unnecessary procedures),[32] but little attention has been paid to other important screening outcomes: the effect of extended surveillance, adverse treatment effects, and economic implications.

Although it is unclear which current screening strategy provides the best balance of benefits, harms, and costs, new strategies continue to enter clinical practice. In 2014, the U.S. Food and Drug Administration approved one high-risk HPV test for stand-alone screening of women aged 25 years and older. Interim guidance from a professional society shortly followed.[33] Earlier this year, the College stated that screening by HPV testing alone is not recommended but can be considered.[1] The U.S. Preventive Services Task Force and the American Cancer Society, however, have not issued guidelines regarding this strategy.

For guideline committees and clinicians to make wise decisions, a better understanding of how new strategies compare with current strategies is critical. It is a judgment call as to where one places the fulcrum to balance benefits and harms. Traditionally, this judgment has been that of a relatively small group of experts and has not incorporated evidence about women's values and preferences. We believe that available methodology such as comparative effective analyses with quality-adjusted life-years as outcomes will be useful in framing future guidelines. To bolster confidence in guidelines, we also believe that guideline committees should avoid including those with potential conflicts of interest.

Attention to the economic consequences of recommending one strategy over another (from both the societal and individual perspectives) is also imperative. In 2010, the societal costs of cervical cancer screening were estimated conservatively at $6.6 billion.[34] As an example of costs to individuals, the charge to self-pay patients for a high-risk HPV test is approximately $1,000 in our local area; type-specific testing adds another $1,000. Sophisticated analyses are needed to evaluate the economic viability of new approaches as new tests and screening strategies emerge. Price transparency is also important to allow consumers to anticipate out-of-pocket expenses associated with various clinical decisions.

How Can Clinicians Improve Cervical Cancer Screening?

Earlier this year, the American College of Physicians published a statement, supported by the College, providing best practice advice to clinicians for cervical cancer screening.[10] Their recommendations for high-value care are concordant with current guidelines and emphasize when less is more. Screening most women less than annually is a central feature

of all current strategies and will serve to decrease screening harms and improve value. Because approximately 40% of women undergoing surveillance owing to abnormal cervical screening test results have significant psychological distress,[35] clinicians can further improve screening by following management guidelines, including appropriate return of women to routine screening once surveillance is completed.

Among all of the new screening strategies and tests, one essential fact remains: most cervical cancer occurs among women who have not been screened appropriately. From a public health perspective, focused outreach to women in these groups would be critical. Cervical cancer incidence and mortality rates are higher in black and Hispanic women compared with white women among women living in rural areas compared with urban areas.[36] Clinicians can maximize their effects on cervical cancer prevention by being attentive to guidelines, assuring that women have access to appropriate HPV vaccination and providing low-cost, high-quality screening, and treatment.

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Table 1.

Current Cervical Cancer Screening Guidelines*

Screening	Age (y)
Begin screening	21
Screening method and intervals	Ages 21–65: cytology every 3 y OR
	Ages 21–29: cytology every 3 y; ages 30–65: cytology plus high-risk HPV testing every 5 y
End screening	65†
Screening after hysterectomy with removal of the cervix	Not recommended

HPV, human papillomavirus.

The table includes 2012 recommendations by the U.S. Preventive Services Task Force,[7] the American College of Obstetricians and Gynecologists,[1] and the American Cancer Society–American Society for Colposcopy and Cervical Pathology–American Society for Clinical Pathology.[8]

*Recommendations apply to women with no prior diagnosis of cervical intraepithelial neoplasia grade 2 or a more severe lesion or cervical cancer, women who are not immunocompromised (eg, not infected with human immunodeficiency virus), and women with no in utero exposure to diethylstilbestrol.

†Only among women with three consecutive negative cytology results or two consecutive negative cytology plus high-risk HPV test results within 10 years before cessation of screening, with the most recent test performed within the previous 5 years.

Table 2.

Management of Initial Abnormal Screening Test Results

Abnormal Screening Test Result	Management	Risk of CIN 2 or Worse
ASC-US, high-risk HPV negative	Routine screening in 3 y	Low
ASC-US, high-risk HPV unknown	Cytology in 12 mo; colposcopy for any abnormality; if normal, routine screening	Moderate
Normal cytology, high-risk HPV positive, HPV genotyping unknown or negative; LSIL, high-risk HPV negative	Cytology plus HPV testing in 12 mo; colposcopy for any abnormality; if both normal, repeat cytology plus HPV testing in 3 y	Moderate
ASC-US, high-risk HPV positive; Normal cytology, high-risk HPV positive on 2 consecutive tests; Normal cytology, high-risk HPV positive, HPV genotyping positive; LSIL, high-risk HPV positive or unknown	Age 25 y or older: colposcopy*	High
	Ages 21–24 y: cytology in 12 mo (colposcopy for ASC-H or HSIL or worse) and at 24 mo (colposcopy for any abnormality); if all normal, routine screening	Moderate
HSIL; ASC-H	Colposcopy†	High
AGC‡; AIS	Colposcopy with endocervical curettage; endometrial biopsy if abnormal bleeding, chronic anovulation or age 35 y or older	High

CIN, cervical intraepithelial neoplasia; ASC-US, atypical squamous cells of undetermined significance; HPV, human papillomavirus; LSIL, low-grade squamous intraepithelial lesion; HSIL, high-grade squamous intraepithelial lesions; ASC-H, atypical squamous cells, cannot exclude high-grade squamous intraepithelial lesions; AGC, atypical glandular cells; AIS, adenocarcinoma in situ.

The table includes current recommendations of the American College of Obstetricians and Gynecologists[2] and the American Society for Colposcopy and Cervical Pathology.[12]

HSIL or worse indicates HSIL, AGC, AIS, or cancer.

*In pregnant women with ASC-US, colposcopy can be deferred to the postpartum period.

†Colposcopy should be performed even if high-risk HPV is negative.

‡If AGC is specified as endometrial, endometrial biopsy is indicated.

Table 3.

Management After Initial Colposcopy

Indication for Initial Colposcopy	Findings at Colposcopy: No Lesion, Normal Biopsy or CIN 1	Findings at Colposcopy: CIN 2, 2/3, 3	Risk of CIN 2 or Worse
Normal cytology, high-risk HPV positive on 2 consecutive tests; Normal cytology, high-risk HPV positive, HPV genotyping positive; ASC-US on 2 consecutive tests; ASC-US, high-risk HPV positive; LSIL	Age 25 y or older: cytology plus high-risk HPV testing in 12 mo; colposcopy for any abnormality; if both normal, cytology alone (women younger than 30 y) or cytology plus high-risk HPV testing (women 30 y or older) in 3 y; if testing at 3 y normal, routine screening	See Table 4	Low
	Ages 21–24 y: cytology alone in 12 mo (colposcopy for ASC-H or HSIL or worse) and at 24 mo (colposcopy for any abnormality); if all normal, routine screening		
AGC, not otherwise specified	Cytology plus high-risk HPV testing in 12 and 24 mo; colposcopy for any abnormality; if all normal, repeat cytology plus high-risk HPV testing in 3 y; if cytology and HPV testing at 3 y normal, routine screening		Low
HSIL; ASC-H	Age 25 y or older: cytology plus high-risk HPV testing in 12 and 24 mo if colposcopy adequate and endocervical curettage negative[*]; if both normal, routine screening; treatment also an option		Low
	Age 21–24 y: colposcopy and cytology in 6 and 12 mo, if colposcopy adequate and endocervical curettage negative; if all normal, routine screening		Moderate
	Diagnostic excisional procedure, if colposcopy inadequate[†‡]		High
AGC, favor neoplasia; AIS	Diagnostic excisional procedure		High

CIN, cervical intraepithelial neoplasia; HPV, human papillomavirus; ASC-US, atypical squamous cells of undetermined significance; LSIL, low-grade squamous intraepithelial lesion; AGC, atypical glandular cells; HSIL, high-grade squamous intraepithelial lesions; ASC-H, atypical squamous cells, cannot exclude high-grade squamous intraepithelial lesions; AIS, adenocarcinoma in situ.

The table includes current recommendations of the American College of Obstetricians and Gynecologists[2] and American Society for Colposcopy and Cervical Pathology.[12] HSIL or worse indicates HSIL, AGC, AIS, or cancer.

[*] In our practices, we consider women aged 25 years or older to be at moderate-risk and use the same surveillance strategy as for women ages 21–24 years.

[†] Review of prior cytology, histology and colposcopic findings may be warranted, especially for ASC-H, when potential risks of excision may exceed benefit.

[‡] Excisional procedures are deferred in pregnant women to the postpartum period unless cancer is suspected.

Table 4.

Treatments for Cervical Intraepithelial Neoplasia 2[*], 2/3[*], and 3

Treatment	Indications
Ablation	
Cryotherapy[†]	Use if the following criteria met[‡] Adequate colposcopy Lesion(s) completely visible Lesion(s) not covering more than 75% of the ectocervix Lesion(s) can be covered entirely with the cryoprobe
Laser	Use as for cryotherapy and for large (2 cm or greater), multifocal lesions, or both with or without vaginal involvement
Excision	
Loop excision	Use if criteria for ablation not met
Cone biopsy	Use if criteria for ablation not met and instead of loop excision if: suspicion for malignancy or cervical architecture distorted (eg, prior cervical treatments, severely atrophic cervix)

[*] In women of childbearing potential with cervical intraepithelial neoplasia (CIN) 2 and CIN 2/3 (but not CIN 3), colposcopy and cytology every 6 months for up to 24 months is an option if colposcopy is adequate. Routine screening may resume after 2 normal cytology tests and colposcopies and a normal cytology test and high-risk human papillomavirus testing a year later. In our practices, we recommend ablation for CIN 2, CIN 2/3, and CIN 3 in women younger than age 40 years when criteria are met.

[†] In our practices, we generally do not offer cryotherapy to women aged 40 years and older.

[‡] Data from current World Health Organization 2011 guidelines.[20]

Table 5.

Follow-up After Treatment of Cervical Intraepithelial Neoplasia 2, 2/3, and 3

Treatment	Follow-up	Risk of CIN 2 or Worse
Hysterectomy	Cytology alone every 3 y for 20 y after the initial CIN treatment and posttreatment surveillance *	NA
Cryotherapy; Laser ablation; Loop excision or cone biopsy with negative margins	Cytology plus high-risk HPV testing in 12 and 24 mo; colposcopy for any abnormality; if all normal, cytology plus high-risk HPV testing in 3 y; if cytology and HPV testing at 3 y normal, routine screening †	Medium
Loop excision or cone biopsy with positive margins	Colposcopy, cytology and endocervical curettage (nonpregnant women) in 6 mo, then cytology plus high-risk HPV testing in 12 and 24 mo; colposcopy for any abnormality; if all normal, repeat cytology plus high-risk HPV testing in 3 y; if cytology and HPV testing at 3 y normal, routine screening †	High

CIN, cervical intraepithelial neoplasia; NA, not applicable; HPV, human papillomavirus.

The table includes current recommendations of the American College of Obstetricians and Gynecologists[2] and American Society for Colposcopy and Cervical Pathology.[12]

* In our practices, we end screening after 3 normal annual vaginal cytology tests (2003 American College of Obstetricians and Gynecologists recommendation).

† In our practices, we perform cytology with or without colposcopy at 6 months followed by cytology at 12 months and then annual cytology for at least 20 years.

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