

Cervical Cancer Screening for the Primary Care Physician--Average Risk Individuals
 Clinical Practice Guideline
 MedStar Health

“These guidelines are provided to assist physicians and other clinicians in making decisions regarding the care of their patients. They are not a substitute for individual judgment brought to each clinical situation by the patient’s primary care provider-in collaboration with the patient. As with all clinical reference resources, they reflect the best understanding of the science of medicine at the time of publication, but should be used with the clear understanding that continued research may result in new knowledge and recommendations”.

General Principles: Since its introduction in 1943, Papanicolaou (Pap) smear is widely credited with reducing mortality from cervical cancer, and remains the single best method for the early detection of cervical intraepithelial neoplasia. Recently, increasing understanding of the role of high risk strains of the Human Papilloma Virus in the development of invasive cervical cancer, and the ability to test for these strains, has begun to affect the screening guidelines for cervical cancer. In particular, the ability to screen specifically for HPV 16/18 has changed the guidelines drastically. It must be remembered though, that despite these improvements, the majority of invasive cervical cancers in the US are in women who have never been screened or have not been screened in the last five years, and these women are often in underserved patient populations. Technological advances in screening techniques will only offer a significant improvement in overall cancer incidence if they reach all women in the US.

These clinical practice guidelines for Pap Smear Screening assist primary care clinicians by providing an evidence-based analytical framework for the evaluation and treatment of patients. They are not intended to replace a clinician’s judgment or to establish a protocol for all patients with a particular condition. **In particular, women with a history of CIN2, CIN3, Adenocarcinoma in situ, or cervical cancer, women exposed in-utero to diethylstilbestrol, and women who are immunocompromised are not addressed in these recommendations. Furthermore, this guideline does not address the follow up testing intervals and triage of results of testing after colposcopy.**

ACOG stresses that the revised cervical screening guidelines do not mean the end of the annual gynecological visit, as the visit is an opportunity to discuss other health problems and preventive measures. The American College of Gynecology supports annual pelvic exams for women over the age of 21, while the USPSTF states that there is insufficient evidence to recommend screening pelvic exams in asymptomatic women. The ultimate decision in the case of an

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asymptomatic woman is left to the patient and physician. Asymptomatic individuals that are younger than 21 or have undergone a total hysterectomy and bilateral oophorectomy in the absence of other indications, may undergo an external genital exam only.

1. Recommendations

Cervical Cancer Screening for Average-Risk Women

- The attached published guidelines are generally consistent: American Cancer Society (ACS), American Society for Colposcopy and Cervical Pathology (ASCCP), American Society for Clinical Pathology (ASCP), U.S. Preventive Services Task Force (USPSTF) and the American Congress of Obstetricians and Gynecologists (ACOG) and the American College of Physicians (ACP).
- **Method:** Screening should be done using either of the following cytological techniques as they have been found to have similar sensitivity and specificity for CIN2 or higher lesions
 1. **Conventional Pap test:** using a broom-type (brush) device or plastic spatula and endocervical brush combination, smearing the cytological sample directly onto a microscope slide,
 2. **Liquid based cytology :** The sample is collected as in the conventional Pap but then the brush suspends the sample cells in a fixative solution, disperses them, and then selectively collects cells on a filter.

In both cases, when two devices are used to collect the specimen, the ectocervical device should be used first.
- **Screening Initiation and Periodicity:**
 - All average-risk women average-risk should begin cervical cancer screening at age 21, regardless of history of sexual activity or other risk factors. Cervical cytology screening prior to age 21 should be avoided. However, if women less than 21 years old are inadvertently screened, the guidelines for follow up and management of abnormalities for women aged 21-24 should be employed.
 - Cytology more often than every 3 years and the use of cytology/high risk HPV co-testing more often than every 5 years should be avoided
 - Testing for non-high risk strains of HPV has no utility in cervical cancer screening and should not be employed
 - 21—29 years of age: Cervical cytology screening is recommended every 3 years. HPV co-testing is not recommended in this age group.
 - 30-65 years of age: The *preferred* method is Cytology with high risk HPV co-testing every 5 years; Cytology alone every 3 years is acceptable.

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- >65 years of age: Cervical cytology screening may stop for those women with adequate screening history (Either 3 consecutive negative pap smear results, or two consecutive negative co-tests within the last ten years, with the last occurring within at least 5 years and no history of CIN2 in the last 20 years,). Screening should not recommence for any reason, including having a new sexual partner. Following spontaneous regression or adequate treatment of CIN2, CIN3, or adenocarcinoma in situ, screening should continue *for at least 20 years*.
- Post-total hysterectomy (removal of uterus and cervix): Cervical cytology screening may stop for those women **without** history of CIN2 or higher grade lesion, even if there is no history of adequate screening. Again, screening should not resume for any reason. For those women **with a history of CIN, AIS or cancer**, Pap smear screening via cervical cytology only should continue regardless of whether the cervix is present or absent.
- Women immunized against HPV 16/18: Continue to screen according to the age-specific recommendations for the general population.

Guidelines for Ordering Pap Smears and Concomitant HPV Testing

	Age <21	Age 21-29	Age 30-64	Age >65
Pap and reflex high-risk HPV when ASCUS		+		
Pap with high risk HPV co-testing			+	+ until adequate screening has been completed or in cases of cancer or CIN history
Frequency	Avoid Screening	Every 3 years	<ul style="list-style-type: none"> • Co-testing every 5 years (preferred) • Cytology alone every 3 years (acceptable) 	<ul style="list-style-type: none"> • May Discontinue if prior adequate screening and no history of CIN2 or higher in the last 20 years) • Medicare every 2 years (or yearly if high risk).

Comments: Add CT/NG as necessary to above testing recommendations

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Results Classification System: Bethesda System

The Bethesda System was the creation of a standardized framework for laboratory reports that included a descriptive diagnosis and an evaluation of specimen adequacy.

Specimen Adequacy	
<ul style="list-style-type: none"> • Satisfactory • Unsatisfactory 	
General Categorization	Interpretation/Result
<p>A. Negative for intraepithelial lesion or malignancy</p> <p>Includes:</p> <ul style="list-style-type: none"> • "Within normal limits" • "benign cellular changes" 	<p>Organisms may be present including:</p> <p><i>Trichomonas vaginalis</i></p> <p>Fungal organisms morphologically consistent with <i>candida</i> species</p> <p>Shift in flora suggestive of bacterial vaginosis</p> <p>Bacteria morphologically consistent with <i>Actinomyces</i> species</p> <p>Cellular changes consistent with herpes simplex virus</p> <p>Other non-neoplastic findings (<i>optional to report; list not comprehensive</i>)</p> <p>Reactive cellular changes associated with Inflammation (includes typical repair) Radiation</p>
<p>B. Epithelial cell abnormality</p>	<p>Squamous cell</p> <p>Atypical Squamous Cells of Undetermined Significance (ASCUS)</p> <p>Low-grade squamous intraepithelial lesion (LSIL)</p> <p>Cannot exclude HSIL (ASC-H)</p> <p>High-grade squamous intraepithelial lesion (HSIL)</p> <p>Squamous cell carcinoma</p>

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C. Glandular cells present	Endometrial cells (may be benign or recur further evaluation if post-menopausal) Atypical glandular cells (AGC) may be atypical endometrial or endocervical cells Atypical glandular cells, favor neoplastic Adenocarcinoma in situ (AIS) Endocervical adenocarcinoma in situ Adenocarcinoma
D. Others	Cases in which there are no morphological abnormalities in the cells per se; however, the findings may indicate some increased risk: for example, benign-appearing "Endometrial cells in a woman 40 years of age" Other neoplasms identified, like small cell carcinoma

- **Follow up of Unsatisfactory Pap Smears:**
 - In cases where HPV is unknown or in a patient \geq 30 years old where HPV is negative, the cytology should be repeated in 2-4 months and the cytology results interpreted appropriately.
 - In those women 30 years or older where HPV is positive, cytology can be repeated in 2-4 months and the results interpreted in light of the positive HPV test, or the patient may be referred directly to colposcopy
 - In all cases, if the cytology remains unsatisfactory on the repeat exam, the patient should be referred for colposcopy.

- **Follow up of Cytology Negative but Endocervical or Transformation Zone Lacking Pap Smears:**
 - Ages 21-29, cytology should be repeated at the routine interval (3 years)
 - Ages 30-65, it is preferred that HPV testing be performed.
 - If the HPV is negative, the woman should undergo routine screening (the preferred co-testing in 5 years or the acceptable option of cytology alone in 3 years).
 - If the HPV testing is positive, a co-test should be done in 12 months, or 16/18 reflex testing can be performed and, if positive, indicates the need for colposcopy.
 - If HPV testing cannot be performed on the initial sample, cytology should be repeated in 3 years.

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- **Follow up of abnormal Pap Smears:**
 - **21 or older- ASC-H (atypical squamous cells cannot exclude high grade lesion), HGSIL, and Atypical Glandular Cells (including atypical endometrial cells) should be referred to gynecology for appropriate evaluation, regardless of age or preceding results**
 - **All pregnant women should be referred to obstetrics-gynecology for any abnormalities**
 - Women age 21-24 with ASCUS, the recommended course of action is repeat cytology at one year (see below for further details); however, if HR HPV is performed and is negative: continue routine screening (cytology in 3 years)
 - Women 25-64, ASCUS, HR HPV negative - co-testing is recommended in 3 years
 - Women 65 or older, ASCUS, HR HPV negative- should be managed as general population except when considering exit from screening, in that case, she should be retested in one year, and co-testing is preferred but cytology alone is acceptable
 - Women ages 21-24 with ASCUS without any HPV result (preferred), ASCUS, HR HPV + or LGSIL of any kind should repeat cytology in 12 months; if ASCUS or LGSIL again or negative, cytology should again be repeated in 12 more months but if it is ASC-H, AGC, HGSIL at any time, she should have colposcopy; if at 24 months still ASCUS or higher (including AGC), she should be referred to colposcopy, if it has regressed to negative at 24 months, she should initiate routine screening (cytology in 3 years)
 - Women 25 and above with ASCUS cytology for whom no HPV testing was performed reflexively and cannot be added on- repeat cytology in one year and if the repeat cytology is ASCUS or worse, they should be referred for colposcopy
 - Women age 25 or older with ASCUS, HR HPV positive, LGSIL w/o known HPV result, or LGSIL, HR HPV positive should be referred for colposcopy
 - Women ages 25 or older with LGSIL, HR HPV negative have two options- referral to colposcopy or the preferred method of repeat co-testing at one year; if this is not Negative, HR HPV negative, the patient is referred to colposcopy; if it is normal, she is co-tested again in 3 years
 - In post-menopausal women, LGSIL w/o HPV results can either have HPV added on and triaged appropriately, be referred to colposcopy or undergo repeat cytology at 6 AND 12 months; if the HPV test is negative she can have have cytology at 12 months; if either the HPV is positive, or either of the 6 or 12 mo cytology tests is positive, she should be referred to colposcopy; if two consecutive repeat cytology tests are negative, she can resume routine screening
 - Women ages 30-65 who co-test with cytology negative but HPV positive results can be followed with either 1) co-testing in 12 months (acceptable); if either the HPV or

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cytology is positive at the follow up exam, the women should undergo colposcopy; if the results are cytology negative, HPV negative, she should repeat testing in 3 years; or 2) immediate (reflex) HPV 16 or 16/18 co-testing; if this is positive, the woman should undergo colposcopy; if this is negative, the woman should repeat co-testing in 12 months and either HPV or cytology positivity would result in colposcopy

These recommendations are presented in algorithmic form in Massad, L , et al. “2012 Updated Consensus Guidelines for the Management of Abnormal Cervical Cancer Screening Tests and Cancer Precursors” 2013, American Society for Colposcopy and Cervical Pathology, Journal of Lower Genital Tract Disease, Volume 17, Number 5, 2013, S1-S27 and in table form below:

Follow Up of Abnormal Pap Smear Results- 2012 Guidelines ASCCP

Result	Age	Follow up Step 1	Follow up Step 2
Unsatisfactory Cytology, HPV unknown	All	Repeat cytology 2-4 months	Abnormal → fu per guidelines Negative → routine screening per age guidelines Still unsatisfactory → colposcopy
Unsatisfactory Cytology, HPV Negative	≥ 30	Repeat cytology 2-4 months	Abnormal → fu per guidelines Negative → routine screening per age guidelines Still unsatisfactory → colposcopy
Unsatisfactory Cytology, HPV Positive	≥ 30	Either A) cytology 2-4 months Or B) referral to colposcopy	Abnormal → fu per guidelines Negative → routine screening per age guidelines (since HPV+ this is co-testing one year, or if HPV 16/18 + → colposcopy) Still unsatisfactory → colposcopy
Cytology Negative but Endocervical Component or Transformation Zone Absent	21-29 ≥ 30 HPV unknown ≥ 30 HPV negative ≥ 30 HPV positive	Routine screening (cytology 3 yr) Add on HPV testing (preferred) and triage as below or repeat cytology 3 years (acceptable) Routine screening (co-testing 5 yrs preferred, cytology 3 yrs acceptable) Co-testing in one year or 16/18 Genotype (colposcopy if positive)	
ASC-H (atypical cells cannot exclude high grade lesion)	All	Colposcopy	
HGSIL	All	Colposcopy	

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Atypical Glandular Cells (including endometrial)	All	Referral to gynecology; endometrial biopsy/colposcopy	
ASCUS, HPV Negative	21-24 25-older 65 and older	Routine screening (cytology 3 yrs) Co-testing 3 years Co-testing 1 year in attempting to exit screening	
ASCUS, unknown HPV	21-24 25 or above	Cytology one year (preferred) or add on HPV and triage as appropriate (acceptable) Add on HPV and triage as appropriate, (preferred) or cytology one year (acceptable)	If at 12 mo, ASC-H, AGC, HSIL → colpo; if ASCUS, LSIL, neg → cytology another 12 mo, if cytology neg (at 24 mo) return to routine screening, if ASCUS or higher → colposcopy If Negative, resume routine screening, if ASCUS or higher → colpo
ASCUS, HPV Positive	21-24 25 and older	Cytology 12 months Colposcopy	If ASC-H, AGC, HSIL → colpo; if ASCUS, LSIL, negative → cytology another 12 mo, if cytology neg (at 24 mo) return to routine screening, if ASCUS or higher → colposcopy
LSIL	21-24 25- menopause Menopause- older	Cytology 12 months HPV unknown/ positive → colpo HPV neg → preferred to repeat co-testing one year, acceptable to refer to colpo immediately HPV known- triage as above HPV unknown	If ASC-H, AGC, HSIL → colpo; if ASCUS, LSIL, negative → cytology another 12 mo, if cytology neg (at 24 mo) return to routine screening, if ASCUS or higher → colposcopy If repeat co-testing is negative w/neg HPV, co-test in 3 years; if ASCUS or greater or positive HPV → colposcopy Either cytology at 6 & 12 months, if either is ASCUS or above → colpo; if both are negative, return to routine screening OR Referral to colposcopy immediately

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Cytology negative, HPV Positive	>=30	Either a) Repeat co-testing 1 yr Or b) Genotyping for HPV 16/18	Cytology neg/HPV neg → co-testing 3 yrs; Ascus or higher or HPV pos → colposcopy Positive → colposcopy Negative → co-testing one year and follow guideline above
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Further Emerging Technologies

Primary Screening with HPV testing (without cytology) is emerging as a possible cervical neoplasia/cancer screening technique. As of the publication of this guideline, there was only one FDA approved test for this purpose (cobas HPV test from Roche). In the journals Gynecologic Oncology, the Journal of Lower Genital Tract Disease and Obstetrics and Gynecology in January 2015, an interim guidance report of the use of this test was published. Interested clinicians may access the articles directly, but as the USPSTF has not yet recommended primary HPV screening for cervical cancer screening, MedStar Medical Group has decided to await their input before including details in our Cervical Cancer Screening Guidelines.

Patient Education/Counseling:

Suggested literature:

<https://www.acog.org/Patients/FAQs/Cervical-Cancer-Screening-Infographic>

Patient Education Fact Sheet: New Guidelines for Cervical Cancer Screening September 2013.

<https://www.acog.org/-/media/For-Patients/pfs004.pdf?dmc=1&ts=20170618T1355238917>

Pamphlets (American College of Obstetricians and Gynecologists Online Bookstore):

Cervical Cancer Screening 2016. AP085 50/pk

Abnormal Cervical Cancer Screening Results 2015. AP187 50/pk.

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2. U.S. Preventive Services Task Force (USPSTF): March 2012 Screening for Cervical Cancer: www.uspreventiveservicestaskforce.org
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4. American Congress of Obstetricians and Gynecologists (ACOG): Committee Opinion Number 463: Cervical Cancer in Adolescents: Screening, Evaluation and Management, August 2010
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10. U.S. Preventive Services Task Force (USPSTF): March 2017 Gynecological Conditions: Periodic Screening with the Pelvic Exam: www.uspreventiveservicestaskforce.org.

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