

The Cervical Screening Manual

A Guide for Health Departments and Providers

Collaboration Partners:

Chronic Disease and Injury Section
Breast and Cervical Cancer Control Program
Women's and Children's Health Section

**North Carolina Department of Health and Human Services
Division of Public Health**



State of North Carolina

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MEMORANDUM

To: Local Health Directors
Attention: Nursing Directors/Supervisors

From: Susan Kansagra, M.D., MBA, Section Chief, Chronic Disease
and Injury Section, Division of Public Health, NC Department
of Health and Human Services 

Date: December 30, 2020

Subject: Revised Edition (December 2020)
Cervical Screening Manual: A Guide for Health Departments and Providers

Enclosed is the revised edition of the Cervical Screening Manual: A Guide for Health Departments and Providers, December 2020. Please replace the previous manual, dated December 2018 with this edition.

Numerous references have been consulted to assure that current standards and guidance on care of patients with abnormal cervical cytology are used. These references include the:

- 2019 ASCCP Risk-Based Management Consensus Guidelines for Abnormal Cervical Cancer Screening Tests and Cancer Precursors
- American Cancer Society (ACS), 2020
- U.S. Preventive Services Task Force (USPSTF), 2018
- American College of Obstetricians and Gynecologists (ACOG), 2018
- *The Bethesda System for Reporting Cervical Cytology, Third Edition*, Nayar, & Wilbur, 2015
- National Breast and Cervical Cancer Early Detection Program (NBCCEDP) Program Manual, December 2017

Revisions were made by the Division of Public Health through a collaborative effort of the Chronic Disease and Injury Section, and the Women and Children's Health Section. The Division of Public Health supports these guidelines as a model for the care of patients at the local level. We hope this guide will enable you to develop written policies to better identify and control cervical cancer among women in North Carolina.

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ACKNOWLEDGEMENTS

Cervical Screening Manual: A Guide for Health Departments and Providers

This guide was reviewed and revised through the collaborative efforts of representatives of the following Division of Public Health Sections:

Chronic Disease & Injury Section

Breast and Cervical Cancer Control Program

Women's & Children's Health Section

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Cervical Screening Manual

A Guide for Health Departments and Providers

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Divider – Overview

Overview

Cervical cancer was once a leading cause of cancer death for women in the U.S. However, since the Pap test was introduced in 1948, the incidence and mortality of cervical cancer has decreased significantly. In 2017 the incidence of cervical cancer for the United States was 7.5 per 100,000 women; of those 2.2 per 100,000 women died of their disease. While cervical cancer incidence and mortality continue to decrease, both are considerably higher among Hispanic and non-Hispanic Black women. In 2020, an estimated 13,800 new cases are expected to be diagnosed, and an estimated 4,290 women will die from cervical cancer (National Cancer Institute SEER Stat Fact Sheets, Cervix Uteri Cancer). In North Carolina, an estimated 430 cervical cancer cases will be diagnosed in 2020, resulting in 120 deaths (American Cancer Society Cancer Statistics Center, 2020).

Detection and treatment of pre-cancerous cervical lesions identified by cervical screening (cervical cytology and/or HPV testing) can prevent cervical cancer from developing. Even when cancer has already developed, cervical screening may detect it while still in an early stage. With prompt diagnostic follow-up and appropriate treatment, survival of early-stage cervical cancer is almost 100 percent.

The 2020 edition of the *Cervical Screening Manual* provides guidelines designed to support the goal of identifying pre-cancerous cervical lesions and early cervical cancer and providing appropriate treatment that saves lives. Numerous references have been consulted to assure that current standards and guidance on care of patients with abnormal cervical screenings are used. These references can be found in Appendix G.

The primary sources for the *Cervical Screening Manual* are:

The American Society for Colposcopy and Cervical Pathology (ASCCP) and Risk-Based Management Consensus Guidelines Committee (2020).

The 2019 ASCCP Risk-Based Management Consensus Guidelines Committee, (2020). *2019 ASCCP Risk-Based Management Consensus Guidelines for Abnormal Cervical Cancer Screening Tests and Cancer Precursors*. Journal of Lower Genital Tract Disease vol 24, number 2, April 2020. (Perkins, Rebecca B., Guido, Richard S, Castle, Phillip E., Chelmow, David, Einstein, Mark H., Garcia, Francisco, Huh, Warner K., Kim, Jane J., Moscicki, Anna-Barbara, Nayar, Ritu, Saraiya, Mona, Sawaya, George F.)

Highlights of 2019 ASCCP Risk-Based Management Guidelines Implications for Family Planning Service Providers by the National Family Planning and Reproductive Health Association.

The United States Preventive Services Task Force: Affiliations of The US Preventive Services Task Force (USPSTF) members: University of Iowa, Iowa City (Curry); Fairfax Family Practice Residency, Fairfax, Virginia (Krist); Virginia Commonwealth University, Richmond (Krist); Veterans Affairs Palo Alto Health Care System, Palo Alto, California (Owens); Stanford University, Stanford, California (Owens); Harvard Medical School,

Boston, Massachusetts (Barry); Oregon Health & Science University, Portland (Caughey); Columbia University, New York, New York (Davidson); University of Pennsylvania, Philadelphia (Doubeni); Virginia Tech Carilion School of Medicine, Roanoke (Epling); Nationwide Children's Hospital, Columbus, Ohio (Kemper); Temple University, Philadelphia, Pennsylvania (Kubik); University of Alabama at Birmingham (Landefeld); University of California, Los Angeles (Mangione); Brown University, Providence, Rhode Island (Phipps); Boston University, Boston, Massachusetts (Silverstein); Northwestern University, Evanston, Illinois (Simon); University of Hawaii, Honolulu (Tseng); Pacific Health Research and Education Institute, Honolulu, Hawaii (Tseng); Tufts University, Medford, Massachusetts (Wong).

The 2018 American Medical Association. *Screening for Cervical Cancer: US Preventive Services Task Force Recommendation Statement JAMA. 2018; 320 (7) 674- 686. doi:10.1001/jama.2018.10897.*

Use of primary high-risk human papillomavirus testing for cervical cancer screening: Interim clinical guidance, Warner K. Huh, Kevin A. Ault, David Chelmow, Diane D. Davey, Robert A. Goulart, Francisco A.R. Garcia, Walter K. Kinney, L. Stewart Massad, Edward J. Mayeaux, Debbie Saslow, Mark Schiffman, Nicolas Wentzensen, Herschel W. Lawson, Mark H. Einstein in *Gynecologic Oncology* 2015, 136, 2015: 178–182.

The Bethesda System for Reporting Cervical Cytology, Third Edition, Ritu Nayar, David C. Wilbur Editors, 2015.

American Cancer Society, American Society for Colposcopy and Cervical Pathology, and American Society for Clinical Pathology Screening Guidelines for the Prevention and Early Detection of Cervical Cancer, Debbie Saslow, PhD; Diane Solomon, MD; Herschel W. Lawson, MD; Maureen Killackey, MD; Shalini L. Kulasingam, PhD; Joanna Cain, MD; Francisco A. R. Garcia, MD, MPH; Ann T. Moriarty, MD; Alan G. Waxman, MD, MPH; David C. Wilbur, MD; Nicolas Wentzensen, MD, PhD, MD; Levi S. Downs, Jr., MD; Mark Spitzer, MD; Anna-Barbara Moscicki, MD; Eduardo L. Franco, DrPH; Mark H. Stoler, MD; Mark Schiffman, MD; Philip E. Castle, PhD, MPH; Evan R. Myers, MD, MPH; the ACS-ASCCP-ASCP Cervical Cancer Guideline Committee, published in *CA: Cancer J. Clin.* 2012;62: 147-172.

The guidelines are supported by the North Carolina Department of Health and Human Services, Division of Public Health, as a model for the care of patients at the local level. The guidelines are not program specific. If the local health care provider agency policy differs from these guidelines, the local health care provider agency will have written policies and protocols that are consistent with the clinical practice of its clinical providers and its referral resources.

It is important to recognize that these guidelines should never be used as a substitute for clinical judgment. Clinical judgment should always be used when applying a guideline to an individual patient.

Divider – 1. Patient Management and Follow-up of Cervical Cytology Results

1. Patient Management and Follow-up of Pap Test Results

A. Introduction

LOCAL POLICIES

Local policies and procedures should be developed for patient management. The North Carolina Department of Health and Human Services, Division of Public Health's Cancer Prevention and Control Branch and the Women's Health Branch recommends this Guide to develop local policies.

MULTIPLE PUBLIC PROGRAMS

The recommendations in this Guide are for all women regardless of the specific clinic where they are enrolled. When a patient receives care at more than one location, clinic staff should coordinate efforts to prevent duplication of unnecessary cervical cytology tests.

FINANCIAL ASSISTANCE

Breast and Cervical Cancer Medicaid (BCCM) may be a source of financial assistance for treatment and other medical needs during treatment for patients diagnosed through the North Carolina Breast and Cervical Cancer Control Program (NC BCCCP), or diagnosed outside of NC BCCCP, who otherwise meet NC BCCCP eligibility criteria. See Appendix E for information on BCCM.

CERVICAL CYTOLOGY TESTS ARE NOT A SUBSTITUTE FOR MEDICAL JUDGMENT

Cervical cytology tests are screening tests meant to detect a variety of squamous epithelial lesions and neoplasias, including dysplasia, carcinoma-in-situ (CIS), and other types of neoplasia. Please note that a single negative cytology result (and occasionally multiple negative cytology results) **does not** rule out gynecologic neoplasia. Cervical cytology is a screening test. False negative tests may occur due to sampling problems, screening difficulties inherent in tests, or due to the subjective nature of cytodiagnosis.

It is important to recognize that these guidelines should never substitute for clinical judgment. Clinical judgment should always be used when applying a guideline to an individual patient because it is impossible to develop guidelines that apply to all situations.

CYTOLOGY RESULTS REQUIRING FOLLOW-UP

Any of the following abnormal findings should be reported to the physician consultant for the health care provider agency or managed according to local policies and procedures:

- Atypical Squamous Cells: Undetermined Significance (ASC-US) – if HPV positive, age 65 or older if appropriate or postmenopausal.
- Atypical Squamous Cells: Cannot Exclude High-grade SIL (ASC-H).

- Low-grade Squamous Intraepithelial Lesion (LSIL). This category encompasses HPV infection and mild dysplasia.
- High-grade Squamous Intraepithelial Lesion (HSIL). This category encompasses moderate and severe dysplasia, as well as Carcinoma-in-situ (CIS).
- Squamous cell carcinoma.
- Atypical glandular cells (AGC), including adenocarcinoma *in situ* (AIS) and adenocarcinoma.
- Other malignant neoplasms.

B. Reporting of Cervical Cytology Results

THE BETHESDA SYSTEM 2014

The Bethesda System 2014 (Nayar, Ritu, Wilbur, David C., 2015) updates the standard terminology for reporting cervical cytology findings. It has been the standard of reporting in North Carolina since October 1, 2014.

The major features of the system are the following:

SPECIMEN TYPE:

Indicate conventional smear (Pap smear) vs. liquid-based preparation vs other.

SPECIMEN ADEQUACY

- Satisfactory for evaluation (*describes the presence or absence of endocervical/transformation zone component and any other quality indicators, e.g., partially obscuring blood, inflammation, etc.*).
- Unsatisfactory for evaluation... (*specify reason*)
 - Specimen rejected/not processed (*specify reason*).
 - Specimen processed and examined, but unsatisfactory for evaluation of epithelial abnormality because of (*specify reason*).

GENERAL CATEGORIZATION (*optional*)

- Negative for Intraepithelial Lesion or Malignancy.
- Other: See Interpretation/ Result (e.g. endometrial cells in a woman \geq 45 years of age).
- Epithelial Cell Abnormality: See Interpretation/Result (specify 'squamous' or 'glandular' as appropriate).

INTERPRETATION/RESULT

NEGATIVE FOR INTRAEPITHELIAL LESION OR MALIGNANCY

(When there is no cellular evidence of neoplasia, state this in the General Categorization above and/or in the Interpretation/Result section on the report—whether there are organisms or other non-neoplastic findings).

NON-NEOPLASTIC FINDINGS *(optional to report; list not inclusive)*

- Non-neoplastic cellular variations
 - Squamous metaplasia.
 - Keratotic changes.
 - Tubal metaplasia.
 - Atrophy.
 - Pregnancy-associated changes.
- Reactive cellular changes associated with:
 - Inflammation (includes typical repair).
 - Lymphocytic (follicular) cervicitis.
 - Radiation.
 - Intrauterine contraceptive device (IUD).
- Glandular cells status post hysterectomy.

ORGANISMS

- *Trichomonas Vaginalis*.
- Fungal organism morphologically consistent with *Candida* Spp.
- Shift in flora suggestive of bacterial vaginosis.
- Bacteria morphologically consistent with *Actinomyces* spp.
- Cellular changes consistent with herpes simplex virus.
- Cellular changes consistent with cytomegalovirus.

OTHER

- Endometrial cells *(in a woman \geq 45 years of age)*
(Specify if negative for squamous intraepithelial lesion)

EPITHELIAL CELL ABNORMALITIES

SQUAMOUS CELL

- Atypical squamous cells
 - ASC-US (atypical squamous cells of undetermined significance).
 - ASC-H (atypical squamous cells, cannot exclude high-grade lesion).

- Low-grade squamous intraepithelial lesion (LSIL).
 - (encompassing HPV/ mild dysplasia/ CIN 1).
- High-grade squamous intraepithelial lesion (HSIL)
 - (encompassing moderate and severe dysplasia, CIS; CIN 2 and CIN 3).
 - with features suspicious for invasion (if invasion is suspected).
- Squamous cell carcinoma.

GLANDULAR CELL

- Atypical
 - Endocervical cells (Not otherwise specified or specify).
 - Endometrial cells (Not otherwise specified or specify).
 - Glandular cells (Not otherwise specified or specify).
- Atypical
 - Endocervical cells, favor neoplastic.
 - Glandular cells, favor neoplastic.
- Endocervical adenocarcinoma in situ.
- Adenocarcinoma
 - Endocervical.
 - Endometrial.
 - Extrauterine.
 - Not otherwise specified (NOS).

OTHER MALIGNANT NEOPLASMS: (specify)

ADJUNCTIVE TESTING

Provide a brief description of the test method(s) and report the result so that it is easily understood by the clinician.

COMPUTER-ASSISTED INTERPRETATION OF CERVICAL CYTOLOGY

If case examined by an automated device, specify device and result.

EDUCATIONAL NOTES AND COMMENTS APPENDED TO CYTOLOGY REPORTS (optional)

Suggestions should be concise and consistent with clinical follow-up guidelines published by professional organizations (references to relevant publications may be included) (Nayar et.al, 2015).

2. Who Needs to Have a Cervical Cytology Test and When to Screen

A. Expert Recommendations:

Guidelines for cervical cancer screening have been issued by the American Cancer Society (ACS), the U.S. Preventive Services Task Force (USPSTF), and the American College of Obstetricians and Gynecologists (ACOG). The 2019 ASCCP Risk-based Management Consensus Guidelines for Abnormal Cervical Cancer Screening Tests and Cancer Precursors were published in April 2020 (M. Policar and P. Cason, 2020; Perkins, Guido, Castle, Chelmow, Enstein, Garcia, Huh, Kim, Moscicki, Nayar, Saraiya, Sawaya, Wentzensen, Schiffman, 2020). These guidelines are the 4th edition of the management Guidelines, updating the 2001, 2006 and 2012 versions. The new guidelines were developed based on a greater amount of longitudinal data derived from a larger database than was available with the previous guidelines. These guidelines bring significant changes which are based on estimated risk for combinations of current and past screening results. Access to the recommendations have also shifted for ease of access to providers. The North Carolina Breast and Cervical Cancer Control Program (NC BCCCP) has revised The NC BCCCP Cervical Screening Policy (2020) to reflect the use of these guidelines. See pages 70- 75.

B. When to Begin Screening:

Current Recommendations for Cervical Screening for Average Risk Women

Organization	Cervical Cancer Screening Recommendation for Average- Risk women
National Breast and Cervical Cancer Early Detection Program, Center for Disease Control (NBCCEDP)	Average risk: Cervical cytology (Pap test) every 3 years for women beginning age 21 to 29; Primary HPV or co-testing every 5 years for women ages 30 to 64 is preferred; or cervical cytology every 3 years.
North Carolina Breast and Cervical Control Program (NC BCCCP)	<p>Average risk: Cervical cytology (Pap test) every 3 years for women beginning age 21 to 29; Primary HPV or co-testing every 5 years for women ages 30 to 64 is preferred; or cervical cytology every 3 years is acceptable.</p> <p>Women who are high risk and have a history of cervical cancer or pre-cancer should be screened more frequently per ASCCP Risk Based Management Consensus Guidelines.</p> <p>Women over age 65 who are not high risk and who have had adequate screening should not be screened.</p>
American Cancer Society (ACS)	Begin screening at age 25 with Primary HPV testing or co-testing with hrHPV and cervical cytology every 5 years; cervical cytology every 3 years is acceptable if HPV-based testing is unavailable.

US Preventive Services Task Force (USPSTF)	Average risk: Cervical cytology (Pap test) every 3 years for women beginning age 21 to 29; Primary HPV or co-testing every 5 years for women ages 30 to 64; or cervical cytology every 3 years is acceptable.
American Society of Colposcopy and Cervical Pathology (ASCCP)	ASCCP currently has not recommended a beginning age for women to begin cervical cancer screening. Risk-based management consensus guidelines are recommended on an individual basis.
American College of Obstetricians and Gynecology (ACOG)	<p>Women ages 21 to 29 are recommended to have cervical cytology (Pap tests) alone every 3 years. HPV-based tests are not recommended.</p> <p>Women ages 30 to 65 are recommended to have co-testing every 5 years. Joint decision making between patient and provider is encouraged if a Pap test alone every 3 years is preferred by the patient.</p> <p>After age 65, patients may stop receiving cervical cancer screenings if patients have never had abnormal cervical cells detected or cervical cancer diagnosed, and documentation of three negative Pap tests in a row. Screening can also be stopped if patients have had two negative Pap and HPV tests in a row in the past 10 years, with at least one test in the past 5 years. ACOG adopted the ASCCP risk-based management guidelines in October 2020.</p>

References:

1. National Breast and Cervical Cancer Early Detection Program, Center for Disease Control (NBCCEDP), 2020.
2. North Carolina Breast and Cervical Control Program (NC BCCCP), 2020-2021.
3. American Cancer Society (ACS), 2020.
4. US Preventive Services Task Force (USPSTF), 2020.
5. American Society of Colposcopy and Cervical Pathology (ASCCP), 2020.
6. American College of Obstetricians and Gynecology (ACOG), 2020.

According to the American Cancer Society (ACS), the recommended age to begin screening is 25 years rather than 21 years of age (Fontham, T., Wolf, A., Church, T., Etzioni, R., Flowers, C., Herzig, A. Guerra, C., Oeffinger, K., Shih, Y., Walter, L., Kim, J., Andrew K., Desantis, C., Fedewa S., Manassaram-Baptiste, D., Saslow, D., Wender, R., Smith, R., 2020; M. Policar and P. Cason, 2020; Perkins, et.al., 2020). The USPSTF, NBCCEDP and the ASCCP, ACOG recommend beginning cervical screening at age 21 for average risk women; HPV-based screening is recommended beginning at age 30 by USPSTF, NBECCEP and NC BCCCP. The preferred screening strategy per the ACS is primary HPV testing every 5 years, with co-testing and cytology alone is

acceptable where access to US FDA-approved primary HPV testing is not available (ACA, 2020; M. Policar and P. Cason, 2020; Perkins, et.al, 2020). At this time, the current cervical cancer screening guidelines of the US Preventative Services Task Force, ASCCP, and the American College of Obstetricians and Gynecologists (ACOG) have not been modified or updated to match the 2020 guideline update of the American Cancer Society.

C. Recommended Screening Intervals:

All the nationally recognized guidelines base their screening recommendations on age and clinical history. Annual screenings by any method are not recommended at any age unless as a follow up to an abnormal cytology result per current guidelines (2020). The screening guidelines for average risk women were developed to address cervical cancer screening in the general population. These guidelines do not address special, high-risk populations who may need more intensive or alternative screening. These *special* populations include women 1) with a history of cervical cancer, 2) who were exposed *in utero* to diethylstilbestrol (DES), and 3) who are immune-compromised (e.g., HIV positive) (M. Policar and P. Cason, 2020; Perkins, et.al., 2020; USPSTF, 2018; CDC, 2018; ACOG, 2018; Saslow, Soloman, Lawson, Killackey, Kulasingam, Cain, Garcia, Moriarty, Waxman, Wilbur, Wentzensen, Downs, Spitzer, Moscicki, Franco, Stoler, Schiffman, Castle, Myers, 2012; NC BCCCP, 2019).

- **High Risk HPV Testing:** The American Cancer Society currently recommends hrHPV testing alone or hrHPV testing in combination with cytology (co-testing) every 5 years for women ages 25 and over. Cervical cytology is recommended if primary HPV or co-testing is not available (ACS, 2020; Perkins, et.al., 2020; M. Policar and P. Cason, 2020).
- **Hysterectomy:** ASCCP as well as USPSTF recommends against screening for cervical cancer in women who have had a hysterectomy with removal of the cervix and do not have a history of a high-grade precancerous lesion (i.e. cervical intraepithelial neoplasia [CIN] grade 2 or 3) or cervical cancer (Perkins, et.al., 2020; M. Policar and P. Cason, 2020; USPSTF, 2018). Women who have had history of cervical neoplasia or in situ disease may have a cervical cytology screening every year or hrHPV-based testing (co-testing or primary HPV testing) every three years for twenty years after treatment even if it extends past age 65. For women who have a history of invasive cervical cancer, screenings should continue indefinitely as long as the woman is in good health (CDC, 2018; NC BCCCP, 2020).
- **Women Older than 65:** Screening for cervical cancer in women older than 65 years who have had adequate prior screening and are not otherwise at high risk for cervical cancer is not recommended. (Perkins, et.al, 2020; USPSTF, 2018; ACOG, 2018; CDC, 2018). Adequate negative prior screening results are defined as three consecutive negative cytology results or two consecutive negative co-test results within the previous 10 years, with the most recent test performed within the past 5 years (Perkins, et.al., 2020; M. Policar and P. Cason, 2020; ACS, 2020, USPSTF Curry et al., 2018; CDC, 2018; NC BCCCP, 2020).

D. Recommended Primary HPV Screening:

Primary hrHPV screening is an important scientific and clinical advance in cervical cancer screening since it offers better reassurance of low cancer risk compared to cytology-only screening conducted at the same interval. Primary hrHPV screening can be considered as an alternative to current cytology-based cervical cancer screening approaches including cytology alone and co-testing. The use of HPV 16/18 genotyping and reflex cytology for women positive for the 12 other hrHPV genotypes achieves a reasonable balance of disease detection with the number of screening tests and colposcopies required to achieve that detection. Primary hrHPV testing has the potential to further reduce morbidity and mortality of cervical cancer in the US. However, to achieve the maximum benefit of screening, we need to continue to identify women who are either unscreened or under-screened (Huh, WK, Auit, KA, Chelmow, D, Davey, DD, Goulart, RA, Garcia, FAR, Kinney, WK, Massad, S, Mayeaux, EJ, Saslow, D, Sciffman, M, Wentzensen, N, Lawson, HW, Einstein, MH, 2015).

E. Patient Notification and Education:

Notify and counsel the patient regarding the benefits and risks of the hrHPV screening as well as the seriousness of the test report and the need for immediate medical care. Document your actions. Additional evaluation may be necessary. The 2019 Risk-based Management Consensus Guidelines (Perkins, et.al, 2020) can be found at: [ASCCP Risk-based Consensus Guidelines](#). Moreover, it should be noted:

- No cancer screening test has the ability to detect all cases of prevalent or incipient cervical cancer.
- Higher detection of CIN3+ at the baseline screening and reduced detection of CIN3+ at subsequent screenings are considered as benefits.
- Increased number of colposcopies is considered a potential for harms of screening (Huh, et al., 2015).

F. Clinical Management:

Current research indicates primary hrHPV screening detected approximately 50% more CIN3+ compared to cytology, it also resulted in approximately double the number of colposcopies compared to cytology. Because of equivalent or superior effectiveness, primary hrHPV screening can be considered as an alternative to current US cytology-based cervical cancer screening methods (Huh, et al., 2015).

- At least three attempts must be made to locate and inform the patient of **abnormal screening results**. The last attempt must be by certified letter. Written documentation of all attempts must be included in the medical record. For all abnormal test results, the following information shall be documented in the patient's medical record: Patient contact information (number and date of attempts made to

follow-up); follow-up appointment information (date, follow-up provider, and follow-up location); date the referral was made; and results of all referrals, including the report from the follow-up provider (National Breast and Cervical Cancer Early Detection Program [NBCCEDP], 2017).

- Patient navigation is required for all abnormal cervical screening results. See page 59.
- Treatment and follow-up are individualized as directed by the Qualified Health Care Providers, who should follow the current ASCCP guidelines for risk-based management (NC BCCCP, 2020). Refer to [ASCAP Risk-based Consensus Guidelines](#).

G. Family Planning (TITLE X) Patients

The Title X Family Planning Program is a federal grant program created in 1970 to provide comprehensive and confidential family planning services and preventive health services. Services for those enrolled in the Family Planning Program include contraception counseling and provision, clinical breast exams and cervical cancer screenings, testing and treatment for sexually transmitted infections, and pregnancy diagnosis and counseling.

Title X is administered by the U.S. Department of Health and Human Services, Office of Population Affairs (OPA) and the Office of Assistant Secretary. The program prioritizes serving people and families with low incomes. In NC, the Title X Grantee is the State of NC Family Planning Program. Subrecipients are the agencies that provide the Title X services, such as Local Health Departments.

Title X Family Planning Clinics provide cervical cancer screening to clients following USPSTF/ACOG/ACS/ASCCP/ASCP guidelines. Quality Family Planning (QFP) Services, recommendations of CDC and the U.S. Office of Population Affairs provides clinical recommendations for how to provide family planning services in a manner that is consistent with the best available scientific evidence and medical practice.

H. Sexually Transmitted Disease/ Sexually Transmitted Infection Clinic Patients

Please refer to the NC Department of Health and Human Services, Communicable Disease Branch Sexually Transmitted Diseases Public Health Program Manual (2015) for specific details on STD Examination and wet mount instructions at the link below:

<http://epi.publichealth.nc.gov/cd/lhds/manuals/std/toc.html>

The NC Communicable Disease Branch follows the guidance put forth by the CDC, Centers for Disease Control and Prevention Sexually Transmitted Disease Treatment Guidelines, 2015 (MMWR Recommendations and Report 2015;64 No. RR-3; 1-137). These guidelines can be found on the CDC's STD Homepage at

<https://www.cdc.gov/std/tg2015/default.htm>

I. N.C. Breast and Cervical Cancer Control Program (NC BCCCP)

Patients:

See Appendix B for specifics of the policy.

WHEN TO DISCONTINUE SCREENING:

Screening may be discontinued in women older than 65 if they have had adequate recent screening (CDC, 2018; NC BCCCP, 2020; USPSTF, 2018) with normal cervical cytology tests and are not otherwise at high-risk for cervical cancer. Adequate negative prior screening results are defined as three consecutive negative cytology results or two consecutive negative co-test results within the previous 10 years, with the most recent test performed within the past 5 years (NC BCCCP, 2020; Perkins, et.al., 2020; ACS, 2018, USPSTF Curry et al., 2018; CDC, 2018).

ACS/ASCCP/ASCP/USPSTF/ ACOG: Women over 65 years of age with evidence of adequate negative prior screening and no history of CIN2+ within the last 20 years should not be screened for cervical cancer with any modality. Once screening is discontinued it should not resume for any reason, even if a woman reports having a new sexual partner (Perkins, et.al., 2020; USPSTF, 2020; CDC, 2020; ACOG, 2020; Saslow et al., 2012).

SCREENING AFTER HYSTERECTOMY:

ACS/ASCCP/ASCP: Cervical cancer screening is not indicated for women who have had a total hysterectomy (with removal of the cervix) for benign gynecologic disease at any age and they should not be screened for vaginal cancer using any modality. Recommendations per ASCCP is for continued surveillance with HPV testing or co-testing completed for at least 25 years after treatment and initial post-treatment management of histologic HSIL, CIN2, CIN 3, or AIS. See ASCCP Guidelines [ASCCP Risk-based Consensus Guidelines](#) (Perkins, et.al, 2020; NC BCCCP, 2020; USPSTF, 2020; CDC, 2020; Saslow et al., 2012).

ACOG: In women who have had a hysterectomy with removal of the cervix (total hysterectomy) and have never had CIN2 or higher, routine cytology and HPV testing should be discontinued and not restarted for any reason. Women should continue to be screened if they have had a history of CIN2 or higher in the past twenty years. Screening for the 20 years after the initial post treatment surveillance period is recommended (ACOG, 2020).

USPSTF: Cervical cancer screening is not recommended in women who have had a hysterectomy with removal of the cervix and do not have a history of a high-grade precancerous lesion or cervical cancer. Women should continue to be screened if they have had a history of CIN2 or higher in the past twenty years. Screening for the 20 years after the initial post treatment surveillance period is recommended (USPSTF, 2020; CDC, 2020; NC BCCCP, 2020).

NC BCCCP: Screening should be discontinued in women who have had a hysterectomy for benign reasons. Women should continue to be screened if they have had a history of CIN2 or higher. Risk-based screening for the patient is recommended

utilizing the 2019 Risk-based Consensus Guidelines. Refer to [ASCCP Risk-based Consensus Guidelines](#) (NC BCCCP, 2020; Perkins, et.al, 2020; M. Policar and P. Cason, 2020).

See Appendix B for specifics of the NC BCCCP Cervical Screening Policy.

3. Adequacy/Quality of Pap Test Specimen

The Bethesda System for reporting of cervical cytology tests requires the cytotechnologist to report on whether the specimen is adequate for meaningful evaluation (Nayar et al., 2015).

A. Cervical Cytology Collection Technique

An adequate cytology test specimen samples cells from the squamocolumnar junction (transformation zone or t-zone) of the cervix. When a test is correctly obtained from a pre-menopausal non-pregnant woman with a cervix, the specimen will usually contain both endocervical cells and cells from the ectocervix.

Possible causes of cytology tests lacking endocervical cells include:

- The transformation zone was not well sampled.
- The patient is pregnant.
- The transformation zone has receded into the canal in a woman who is post-menopausal.
- The transformation zone will be absent if the woman has had a hysterectomy and the cervix was removed. Endocervical cells may also be absent in Pap tests from women who have had cervical conization or LEEP procedures.
- The sampling device was not rinsed properly into the vial.

BETHESDA 2014 REPORTING

Specimen type is indicated: Indicate conventional smear (Pap smear) versus liquid-based preparation versus other.

Cervical cytology reports that use the Bethesda System of reporting will describe specimen adequacy in one of two categories:

1. *Satisfactory for evaluation.* (Describe presence or absence of endocervical/transformation zone component and any other quality indicators, e.g., partially obscuring blood, inflammation, etc.)
 - a. Presence or absence of endocervical t-zone cells
 - b. Slightly more than 5,000 cells on the slide
 - c. Cells partially obscured by elements such as blood cells or inflammatory exudate
 - d. Other limitations described in the report.
2. *Unsatisfactory for evaluation.* This category is divided into two sub-categories:

- a. *Specimen rejected/ not processed (specify reason)*. The cytologist did not attempt to evaluate these specimens. Possible reasons are:
 - (1) Unlabeled specimens
 - (2) Names on the specimen and on the form do not match
- b. Specimen processed and examined, but unsatisfactory for evaluation of epithelial abnormality (specify reason). The cytologist attempted to evaluate the specimen but was not able to arrive at an interpretation/result. Possible reasons are:
 - (1) Insufficient cells (less than 5,000 cells on the slide)
 - (2) Cells obscured by too much blood or inflammatory exudate (Nayar et al., 2015)

B. Management Protocols:

1. Clinical Management of Women with Unsatisfactory Cytology

Unsatisfactory cytology tests in premenopausal women who have a cervix should be repeated in two to four months, allowing sufficient time for the cervix to repair itself from the previous specimen collection.

Refer to [ASCCP Risk-based Consensus Guidelines](#) for management of current or previous abnormal cervical cytology screening results. The ASCCP Risk-based Consensus Guidelines are based on guiding principles with management guidelines that apply to patients with current or previous abnormal screening test results.

2. Negative for Intraepithelial Lesion of Malignancy (NILM)

PATIENT NOTIFICATION

Notify the patient of normal cervical cytology results according to local policy.

PATIENT EDUCATION

Instruct your patient regarding the importance of returning for a primary hrHPV test or co-test or cervical cytology at appropriate intervals, or if she notices symptoms of any gynecologic problems.

Appropriate intervals for routine screening are determined by each individual woman's risk status. Refer to [ASCCP Risk-based Consensus Guidelines](#).

3. Management for Risk of CIN Disease per 2019 ASCCP Risk-based Consensus Management Guidelines

The 2019 ASCCP Risk-based management consensus guidelines for abnormal cervical cancer screening test and cancer precursors [ASCCP Risk-based Consensus Guidelines](#) was published in the Journal of Lower Genital Tract

Diseases in April 2020. This new data indicates that a patient's risk of developing cervical precancer or cancer can be estimated using the following:

- Current screening test results.
- Previous screening tests and biopsy results.
- Personal factors - age and immunosuppression/ immunity system health.

The 2019 ASCCP risk-based consensus guideline recommendations were based on risk estimates calculated with data from a large, prospective, longitudinal cohort of greater than 1.5 million patients (Perkins et.al. 2020).

ASCCP has released a free web application that providers can use to determine follow-up management of abnormal cervical cancer screening results. The free web application can be accessed at <https://app.asccp.org/>.

Routine screening applies to asymptomatic individuals who do not require surveillance for a prior abnormal screening result. The 2012 ASCCP guidelines were based on the principle of equal management for equal risk, relying on complicated algorithms and the incorporation of the patient's screening history. The 2019 guidelines align further management recommendations with the current understanding of HPV natural history and cervical carcinogenesis. This method allows for more frequent surveillance, colposcopy and treatment that is recommended for patients who are at progressively higher risk. Additionally, this allows for those patients at a lower risk to be deferred for colposcopy and undergo follow-up at longer surveillance intervals and when at a sufficiently low risk, these patients can return to routine screening. With the 2019 guidelines, there are defined risk thresholds to guide management which are designed to continue along with a framework for the incorporation of new data and technologies (Perkins, et.al, 2020, p.103).

The 2019 ASCCP Risk-based management Guidelines are the 4th Consensus Guidelines with the 2001, 2006 and 2012 Guidelines issued in previous years. The key difference between the 2019 document and the previous guidelines is the change from primarily test results-based algorithms to primarily risk-based guidelines. These 2019 Consensus Guidelines update and replace all previous guidelines (Perkins, et.al, 2020, p.109). Refer to [ASCCP Risk Tables](#).

4. Essential Changes of 2019 ASCCP Risk-Based Management Guidelines From Prior Management Guidelines [ASCCP Risk-based Consensus Guidelines](#):

- 1) Recommendations are based on risk, not results.
 - Recommendations of colposcopy, treatment, or surveillance will be based on a patient's risk of CIN 3+ determined by a combination of current results and past history (including unknown history). The same current test results may yield different management recommendations depending on the history of recent past test results.

2) Colposcopy can be deferred for certain patients.

3) Guidance for expedited treatment is expanded (*i.e.*, treatment without colposcopic biopsy).

- Expedited treatment was an option for patients with HSIL cytology in the 2012 guidelines; this guidance is now better defined.
- For non-pregnant patients 25 years or older, expedited treatment is defined as treatment without preceding colposcopic biopsy.
- Shared decision-making should be used when considering expedited treatment, especially for patients with concerns about the potential impact of treatment on pregnancy outcomes.

4) Excisional treatment is preferred to ablative treatment for histologic HSIL (CIN 2 or CIN 3) in the United States.

5) Observation is preferred to treatment for CIN 1.

6) Histopathology reports based on Lower Anogenital Squamous Terminology (LAST)/World Health Organization (WHO) recommendations for reporting histologic HSIL should include CIN 2 or CIN 3 qualifiers, *i.e.*, HSIL (CIN 2) and HSIL (CIN 3).

7) All positive primary HPV screening tests, regardless of genotype, should have additional reflex triage testing performed from the same laboratory specimen (*e.g.*, reflex cytology).

- Additional testing from the same laboratory specimen is recommended because the findings may inform colposcopy practice. For example, HPV-16 positive HSIL cytology results qualify for expedited treatment.
- HPV 16 or 18 infections have the highest risk for CIN 3 and occult cancer, so additional evaluation (*e.g.*, colposcopy with biopsy) is necessary even when cytology results are negative.
- If HPV 16 or 18 testing is positive, and additional laboratory testing of the same sample is not feasible, the patient should proceed directly to colposcopy.

8) Continued surveillance with HPV testing or co-testing at 3-year intervals for at least 25 years is recommended after treatment and initial post-treatment management of histologic HSIL, CIN 2, CIN 3, or AIS. Continued surveillance at 3-year intervals beyond 25 years is acceptable for as long as the patient's life expectancy and ability to be screened are not significantly compromised by serious health issues.

- The 2012 guidelines recommended return to 5-year screening intervals and did not specify when screening should cease. New evidence indicates that

risk remains elevated for at least 25 years, with no evidence that treated patients ever return to risk levels compatible with 5-year intervals.

9) Surveillance with cytology alone is acceptable only if testing with HPV or co-testing is not feasible. Cytology is less sensitive than HPV testing for detection of precancer and is therefore recommended more often.

10) Human papilloma virus assays that are Food and Drug Administration (FDA)-approved for screening should be used for management according to their regulatory approval in the United States. (*Note: all HPV testing in this document refers to testing for high-risk HPV types only*) (Perkins, et al., 2020).

5. Guiding Principles of 2019 ASCCP Risk-based Management Consensus Guidelines

Guidelines are based on several guiding principles. The first 4 guiding principles are new for 2019, whereas the others are from the 2012 guidelines. As the 2012 guidelines are familiar to providers, management recommendations were changed only when new evidence favored an altered management strategy. Note that management guidelines apply only to patients with current or previous abnormal screening test results (Perkins, et.al, 2020, p.105). Screening guidelines for individuals in the general population that are not being followed for a screening abnormality, are addressed elsewhere in this manual. See pages 8 - 10.

New 2019 Principles

1. HPV-based testing is the basis for risk estimation. The term HPV-based testing refers to use of either primary HPV testing alone or HPV testing in conjunction with cervical cytology (co-testing).

Characteristics of HPV infections, including HPV type and the duration of infection, determine a patient's risk of CIN 3+. Although cytology has high specificity (apart from ASC-US) and can be helpful when estimating immediate risk, its lower sensitivity and lower negative predictive value compared with HPV testing reduces its utility for long-term risk prediction. The results of HPV tests alone or in conjunction with cytology are used to guide recommendations that allow lengthening of follow-up intervals and deferral of colposcopy for low-risk results. Risk estimates underlying the 2019 management guidelines are based on HPV DNA testing (Perkins, et.al, 2020, p.105).

2. Personalized risk-based management is possible with knowledge of current results and past history. A patient's risk of having or developing CIN 3+ is estimated based on current and previous results, as well as history of previous precancer treatment. Management recommendations use thresholds of risk (Perkins, et.al, 2020, p.105).

Recommendations of *a) routine screening, b) 1-year or 3-year surveillance, c) colposcopy, or d) treatment* correspond to a risk stratum, a range of risk for CIN 3+. The lower threshold of each risk stratum, called Clinical Action Threshold, defines the level at which the management recommendation changes. The Clinical Action Thresholds for each risk stratum were determined through the consensus process. Risks were

estimated for all combination of current results and past history (including unknown history). Management can be determined via look-up tables and use of the tables can be facilitated using decision aids [ASCCP Risk Tables](#). (Perkins, et.al, 2020, p.105).

3. Guidelines must allow updates to incorporate new test methods as they are validated, and to adjust for decreasing CIN3+ risks as more patients who received HPV vaccination reach screening age. The 2019 guidelines build a framework that allows incorporation of new technologies and modified strategies without requiring full consensus conferences, so that revisions may rapidly incorporate new findings and be quickly disseminated to optimize patient care (Perkins, et.al, 2020, p.105).

4. Colposcopy practice must follow guidance detailed in the ASCCP Colposcopy Standards. Colposcopy with targeted biopsy remains the primary method of detecting precancers requiring treatment. Because patients are managed less aggressively after a colposcopic examination where CIN grade 2 or higher (CIN 2+) is not found, maximizing detection of CIN 2+ at each colposcopy visit is paramount. Evidence-based practice recommends that biopsies be taken of all discrete acetowhite areas, usually 2 to 4 biopsies at each colposcopic examination. For those at lowest risk, defined as less than HSIL cytology, no evidence of HPV 16/18 infection, and a completely normal colposcopic impression (*i.e.*, no acetowhitening, metaplasia, or other visible abnormality, and a fully visualized squamocolumnar junction), untargeted (random) biopsies are not recommended and patients with a completely normal colposcopic impression can be observed without biopsy. To ensure that CIN 2+ is not missed, the ASCCP Colposcopy Standards emphasize the need for biopsies even when the colposcopic impression is normal but any degree of acetowhitening, metaplasia, or other abnormality is present (Perkins, et.al, 2020, p.105).

2012 Principles Carried Forward

5. The primary goal of screening and management is cancer prevention through detection and treatment of cervical precancer. This remains the primary goal of the 2019 management guideline. Numerous population-level studies indicate that incidence and mortality from cervical cancer decrease as detection and treatment of high-grade histologic cervical abnormalities (generally defined as CIN 2+) increases. Timely detection and treatment of the highest grade of precancers (CIN 3/AIS) have been the benchmark used for previous guidelines. A secondary goal (because of the rarity of this finding in the United States) is early diagnosis of cervical cancer to reduce related morbidity and mortality. A patient's risk of having or developing CIN 3+ is estimated based on current and previous results, as well as history of previous precancer treatment. Management recommendations are guided by risk thresholds. Recommendations of *routine screening, 1- or 3-year surveillance, colposcopy, or treatment* each correspond to a risk stratum. These risk strata (ranges of risk for CIN 3+) are defined by Clinical Action Thresholds (Perkins, et.al, 2020, p.106).

6. Guidelines apply to all individuals with a cervix. Guidelines apply to women, transgender men with a cervix, including individuals who have undergone supracervical hysterectomy. Risk estimates were validated in individuals of diverse racial, ethnic, and socioeconomic backgrounds and shown to be comparable. Although not the primary

focus of the 2019 guidelines, management recommendations are also provided for patients who have undergone hysterectomy with removal of the cervix and who have a previous diagnosis of histologic HSIL, CIN 2, CIN 2/3, CIN 3, and/or AIS, irrespective of whether the hysterectomy was performed for precancer treatment or another indication (Perkins, et.al, 2020, p.106).

7. *Equal management for equal risk.* History and current test results are used to calculate a patient's current and future risk of CIN 3+. Similar risks are managed similarly, regardless of the combination of results/history used to estimate the risk (Perkins, et.al, 2020, p.106).

8. *Balancing benefits and harms.* Providing the best care means balancing cancer prevention with over-testing and over-treatment. Preventing all cervical cancers is unfortunately not an achievable goal. Interventions to prevent cervical cancer can cause harm. The 2019 guidelines are designed to maximize cervical cancer prevention and minimize harms from over-testing and over-treating by managing patients according to their current and future risks of CIN 3+. High-risk patients require closer follow-up to maximize detection of CIN 3+, whereas low-risk patients require fewer tests and procedures (Perkins, et.al, 2020, p.106).

9. *Guidelines apply to asymptomatic patients that require management of abnormal cervical screening test results.* Patients with symptoms such as abnormal uterine or vaginal bleeding or a visibly abnormal-appearing cervix require appropriate diagnostic testing as this may be a sign of cancer. This evaluation may include cervical cytology, colposcopy, diagnostic imaging, and cervical, endocervical, or endometrial biopsy. Guidelines cannot cover all clinical situations and clinical judgment is advised, especially in those circumstances which are not covered by the 2019 guidelines (Perkins, et.al, 2020, p.106).

10. *Guidelines are intended for use in the United States.* Appropriate management may differ in countries with limited follow-up capabilities, less availability of colposcopy, limited pathology infrastructure, or different views of the trade-offs between cancer risk, cost, and over-testing/overtreatment (Perkins, et.al, 2020, p.106).

6. Paradigm Shift: From Results-Based to Risk-Based Guidelines

Primary Clinical Action Thresholds are described regarding which management recommendation in which they are based and the clinical situations in which these Clinical Action Thresholds are applied. For most abnormal screening results and subsequent management visits, the recommendations are based on risks estimated and validated by prospective data from large cohorts. Clinicians can use the 2019 guidelines to manage their patients via the tables or by using an app designed to facilitate navigation of the tables available at [ASCCP Risk Tables](#).

7. Management Recommendations Based on Clinical Action Thresholds and Correspond to Risk Strata

Primary Clinical Action Thresholds have been developed for management recommendations. For a given current result and history combination, the immediate CIN 3+ risk is examined.

If the risk is 4% or greater, immediate management via colposcopy or treatment is indicated.

If the immediate risk is less than 4%, the 5-year CIN 3+ risk is examined to determine whether patients should return in 1, 3, or 5 years.

The 5-year return Clinical Action Threshold approximates the risk for a patient after a negative screening test using HPV testing or co-testing in the general population and retesting in 5 years is recommended by national screening guidelines. Patients with risks at or below this threshold are recommended routine screening at 5-year intervals with HPV-based testing.

The 3-year return Clinical Action Threshold approximates the risk for a patient after a negative cervical cytology screen in the general population and retesting in 3 years is recommended by national screening guidelines. Patients with risks at or below this threshold but above the 5-year threshold are recommended HPV-based testing in 3 years.

One-year return testing is recommended for patients with risk above the 3-year threshold but below the Clinical Action Threshold for colposcopy (Perkins, et.al, 2020, p.108- 109). Specific information regarding HPV positive results and cytology results and recommendations for specific colposcopy and expedited treatment is found via website or app at [ASCCP Risk-based Consensus Guidelines](#) and [ASCCP Risk Tables](#).

8. Clinical Action Thresholds Leading to Recommendation of Surveillance

Guideline: Surveillance is defined as follow-up testing at a shorter interval than is currently recommended for routine screening with either HPV primary testing or co-testing (5 years). Surveillance is recommended for patients whose risk of CIN 3+ based on current test results and screening history is higher than the risk for the general screening population, but lower than the risk at which colposcopy is recommended (Perkins, et.al, 2020, p.108- 109).

Rationale: Using the principle of equal management for equal risk, this Clinical Action Threshold corresponds to the 5-year CIN 3+ risk after negative HPV-based screening (HPV testing or co-testing) in the general population for whom national guidelines recommend a 5-year return. Note that cytology alone is never recommended at 5-year intervals (Perkins, et.al, 2020, p.108- 109).

9. Clinical Action Threshold Leading to Recommendation of Colposcopy

Guideline: When patients have an estimated immediate risk of diagnosis of CIN 3+ of 4.0% or greater based on history and current results, referral to colposcopy is recommended.

Rationale: The following principles were used to develop the Clinical Action Threshold for referral to colposcopy: (a) colposcopy visits recommended by the threshold should

yield information useful for clinical decision-making. The threshold was based on the risk of diagnosing CIN 3+ upon immediate referral to colposcopy. (b) In the absence of a compelling rationale, the colposcopy threshold should be similar to 2012 referral recommendations that are generally accepted as an appropriate balance of benefits and harms (Perkins, et.al, 2020, p.110).

10. Clinical Action Thresholds Leading to Recommendations of Treatment

The primary goal of treatment is cancer prevention through destruction or excision of precancerous lesions (CIN 3, AIS) preventing the development of invasive cancer. Treatment is generally recommended as soon as possible after the identification of a precancerous lesion. Historically, the treatment threshold has been histologic CIN 2. Consistent with previous guidelines, the threshold for treatment remains histologic HSIL/AIS or CIN 2+ except in special circumstances. In considering expedited treatment versus colposcopy with biopsy, clinicians should have a thorough discussion with patients regarding the risks and benefits. Treatment without preceding histologic confirmation can be conducted in one visit among those at high immediate risk of CIN 3+. Reasons for choosing expedited treatment vary and may include personal preference, limited healthcare access, financial concerns, and cancer-related anxiety. The age cutoff is 25 years or older for the recommendation of expedited treatment in considering benefits and harms due to very low cancer rates and high rates of cope regression of precancers among women in this age group (Perkins, et.al, 2020, p.111).

11. Clinical Situations Leading to Management Recommendations

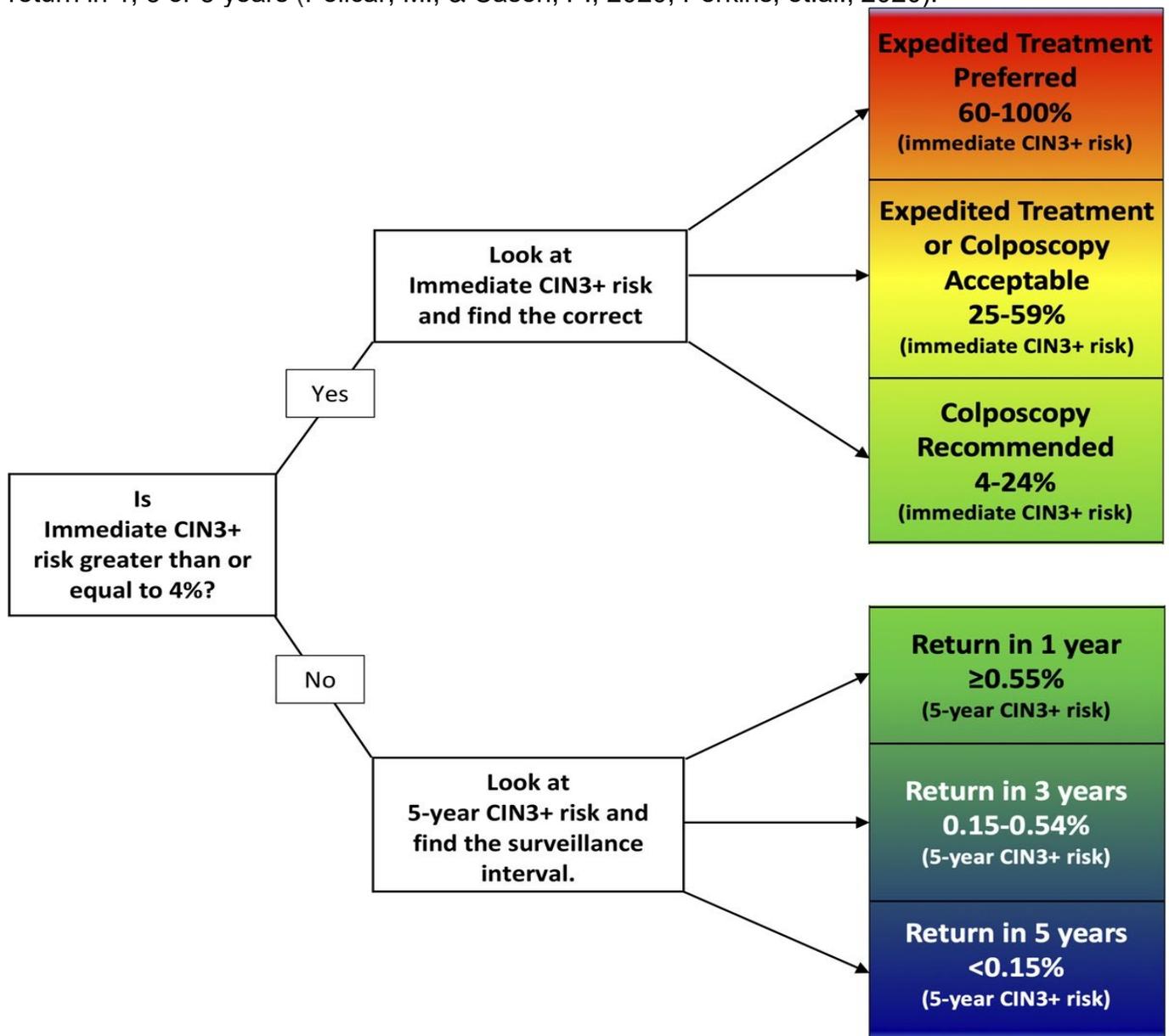
Patients with abnormal cervical cancer screening results enter management via 5 common clinical situations:

1. Initial management of an abnormal screening test result
2. Return visit for surveillance of a previous abnormal result that did not lead to colposcopy referral (e.g., HPV-negative ASC-US), with consideration of whether to continue surveillance or refer to colposcopy
3. Evaluation of the colposcopic biopsy results with consideration of whether to treat or begin post colposcopy surveillance managing test results
4. Return visit for surveillance after a colposcopic biopsy showing less than CIN 2
5. Follow-up after treatment of CIN2 or CIN3

Recommendations are based on risks of immediate and future CIN 3+ diagnoses considering current and past results. Regardless of the pathway by which patients enter management, equivalent risks are managed similarly. For each of the 5 clinical situations, risk tables and recommendations based on the Clinical Action Thresholds are detailed in [ASCCP Risk-based Consensus Guidelines](#) [ASCCP Risk Tables](#).

C. ASCCP Risk-Based Management Consensus Guideline Thresholds

The figure below demonstrates how patient risk is evaluated. Scenarios are categorized in one of six clinical action thresholds, which contain a management recommendation for either surveillance, colposcopy, colposcopy or treatment, or expedited treatment. The immediate CIN 3+ risk threshold for colposcopy is at 4%. If immediate risk is less than 4%, the 5-year CIN 3+ risk is examined to determine whether patients should return in 1, 3 or 5 years (Policar, M., & Cason, P., 2020; Perkins, et.al., 2020).



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Management Option	Clinical Action Threshold
Expedited treatment preferred *	60% or greater †
Expedited treatment or colposcopy * acceptable	25% to < 60% †
Colposcopy recommended	4% to < 25% †
Repeat test in 1 year	0.55% to < 4% ‡
Repeat test in 3 years	0.15% to < 0.55% ‡
Return to routine screening at 5-year intervals	<0.15% ‡
*For non-pregnant patients 25 years or older † Refers to immediate CIN 3 + risk ‡ Refers to 5-year CIN 3 + risk	

Permission for use obtained from ASCCP @ American Society for Colposcopy and Cervical Pathology 2020. No copies of the figure may be made without the prior consent of ASCCP (Perkins, et.al, 2020, p.115).

D. Updates Related to Pathology Reporting and Laboratory Tests

Although most of the 2019 guidelines describe clinical management of patients by providers, the consensus process also addressed laboratory considerations that directly relate to results reporting and use of ancillary tests.

Statement on the Use of a 2-Tier Terminology (Histologic LSIL/HSIL) for Reporting Histopathology of Squamous Lesions of the Lower Anogenital Tract:

Guideline: The p16 is a tissue marker of HPV oncogene overexpression and transformation and can support histologic assessment. A positive p16 immunostain supports the diagnosis of histologic HSIL if the morphological assessment of hematoxylin and eosin (H&E) slides is consistent with CIN 2 or CIN 3. There is a risk of overcalling cervical histology results when p16 is used incorrectly.

Rationale: This CIN qualification can have clinical importance (e.g., to identify cases of CIN 2 in patients for whom conservative management is an acceptable option).

Current guidelines are based on CIN 3 end points, which is the most reliable correlate of a cervical precancer. There are insufficient data to evaluate risk estimates with histologic HSIL end points (Perkins, et.al, 2020, p.112).

Updated Management of Primary HPV Screening

Guideline: When primary HPV screening is used, performance of an additional reflex triage test (e.g., reflex cytology) for all positive HPV tests regardless of genotype is preferred (this includes tests positive for genotypes HPV 16/18). However, if primary HPV screening test genotyping results are HPV 16 or HPV 18 positive and reflex triage testing from the same laboratory specimen is not feasible, referral for colposcopy before obtaining additional testing is acceptable. If genotyping for HPV 16 or HPV 18 is positive, and triage testing is not performed before the colposcopy, collection of an additional triage test (e.g., cytology) at the colposcopy visit is recommended (Perkins, et.al, 2020, p.112).

Rationale: Because HPV16- positive and HPV 18- positive test results have the highest risk of CIN 3 and occult cancers, additional diagnostic procedures are recommended for all positive test results (e.g., colposcopy with biopsy for NILM and low-grade cytology and expedited treatment for HSIL cytology that is positive for HPV type 16- positive). The immediate risk of CIN3+ in patients with HPV 16- positive and HSIL cytology exceeds the treatment threshold of 60%; therefore, these patients should be given the option for expedited treatment without preceding confirmatory biopsy. Expedited treatment is only possible if cytology is performed. Therefore, reflex cytology is recommended for all HPV-positive primary screening results, regardless of HPV genotype. If reflex testing from the same laboratory specimen as the HPV test is not feasible, patients should proceed directly to colposcopy. In this situation, collection of an additional triage test (e.g., cytology) is recommended at the time of colposcopy to provide further information for risk-based management (e.g., if HPV 16- positive HSIL cytology is identified, treatment may be considered even if CIN 2+ is not identified on biopsy). Combining a test with high specificity (e.g., cytology when it is interpreted as HSIL) with a test with high sensitivity (i.e., HPV test) allows more precise, risk-based management of these patients (Perkins, et.al, 2020, p.112).

E. Statement on HPV Tests Used in Management

Guideline: HPV assays should be used for management according to regulatory approval for screening, unless there are sufficient data to support use of the assay differently (Perkins, et.al, 2020, p.112).

Rationale: Several HPV assays have been approved in the United States for clinical use in screening and triage. These assays do not have specific indications for management but are widely used for post-colposcopy and posttreatment surveillance. HPV assays approved for screening should be used according to their regulatory approval. Approved assays include target- and signal-amplification assays of HPV DNA, as well as HPV mRNA. Most assays are approved for adjunct testing with cytology (co-

testing), whereas a subset of HPV DNA assays have also been approved for primary HPV testing alone (Perkins, et.al, 2020, p.112).

4. Evaluation of Cytology Interpreted as AGC or AIS

Guideline: For nonpregnant patients of all ages with all subcategories of AGC and AIS, except when atypical endometrial cells are specified, colposcopy is recommended regardless of HPV test result; endocervical sampling is recommended at initial colposcopy except in pregnancy (for management in pregnancy, see page 28) (Perkins, et.al, 2020, p.113). Triage by reflex HPV testing is not recommended, and triage by repeat cytology is unacceptable. Endometrial sampling is recommended in conjunction with colposcopy and endocervical sampling in nonpregnant patients 35 years or older with all categories of AGC and AIS. Endometrial sampling is also recommended for nonpregnant patients younger than 35 years at increased risk of endometrial neoplasia based on clinical indications (e.g., abnormal uterine bleeding, conditions suggesting chronic anovulation, or obesity). For patients with atypical endometrial cells specified, initial evaluation limited to endometrial and endocervical sampling is preferred, with colposcopy acceptable at the time of initial evaluation. If colposcopy was deferred and no endometrial pathology is identified, additional evaluation with colposcopy is then recommended (Perkins, et.al, 2020, p.113).

For patients with cytology showing AGC not otherwise specified or atypical endocervical cells not otherwise specified in whom histologic HSIL (CIN 2+) or AIS/cancer is not identified, co-testing at 1 and 2 years is recommended. If both co-tests are negative, repeat co-testing at 3 years is recommended. If any test is abnormal, then colposcopy is recommended. If CIN 2 or CIN 3 but no glandular lesion is identified histologically for patients with cytology atypical glandular, endocervical, or endometrial cells not otherwise specified, management should be according to the 2019 guidelines for the lesion diagnosed. **Refer to:** [ASCCP Risk-based Consensus Guidelines](#) [ASCCP Risk Tables](#) (Perkins, et.al, 2020, p.113).

Rationale: Atypical glandular cells on cytology is considered a poorly reproducible diagnostic category. Positive HPV test results, especially when positive for HPV type 18, can be indicative of higher risk of CIN 2+ lesions. Colposcopy is recommended for all patients regardless of HPV result for atypical glandular cells on cytology. Atypical glandular cells can be associated with polyps and metaplasia as well as adenocarcinomas of the cervix. Cancers of the endometrium, fallopian tube, ovary, and other sites may also be found, especially in older women who test HPV negative. Using the Bethesda terminology, AGC, favor neoplasia, or adenocarcinoma cytology is frequently indicative of invasive or preinvasive disease. Although endometrial cancer is rare in premenopausal patients without risk factors, the prevalence of premenopausal endometrial cancer is increasing, underscoring the importance of endometrial sampling when indicated (Perkins, et.al, 2020, p.113).

5. Unsatisfactory Cytology

For patients with an unsatisfactory cytology result and no, unknown, or a negative HPV test result, repeat age-based screening (cytology, co-test, or primary HPV test) in 2 to 4 months is recommended. Triage using HPV testing is not recommended. Before repeat cytology, treatment to resolve atrophy or obscuring inflammation when a specific infection is present is acceptable. For patients 25 years and older who are co-tested and have unsatisfactory cytology and a positive HPV test without genotyping, repeat cytology in 2 to 4 months or colposcopy is acceptable. If a positive HPV test with partial genotyping is positive for HPV 16 or HPV 18, direct referral for colposcopy is recommended. A negative HPV result from a co-test with inadequate cellularity on cytology should not be interpreted as negative primary HPV test and should be repeated. **Refer to:** [ASCCP Risk-based Consensus Guidelines](#) [ASCCP Risk Tables](#) (Perkins, et.al, 2020, p.114).

6. Absent Transformation Zone on Screening Cytology

For patients aged 21 to 29 years with negative screening cytology and absent endocervical cells/transformation zone component (*i.e.*, endocervical cells or squamous metaplastic cells), routine screening is recommended. When cervical cytology alone is performed for screening, HPV testing as a triage test after negative cytology and absent endocervical cells/transformation zone component in this age group is unacceptable. For patients 30 years or older with NILM cytology and absent endocervical cells/transformation zone component and no or unknown HPV test result, HPV testing is preferred. Repeat cytology in 3 years is acceptable if HPV testing is not performed. If HPV testing is performed, manage using Clinical Action Thresholds according to 2019 consensus guidelines **Refer to:** [ASCCP Risk-based Consensus Guidelines](#) [ASCCP Risk Tables](#) (Perkins, et.al, 2020, p.115).

7. Benign Endometrial Cells in Premenopausal Patients or Benign Glandular Cells in Post-hysterectomy Patients

Guideline: For asymptomatic premenopausal patients with benign endometrial cells, endometrial stromal cells, or histiocytes, no further evaluation is recommended. For postmenopausal patients with benign endometrial cells, endometrial assessment is recommended. For post-hysterectomy patients with a cytology report of benign glandular cells, no further evaluation is recommended. **Refer to:** [ASCCP Risk-based Consensus Guidelines](#) [ASCCP Risk Tables](#) (Perkins, et.al, 2020, p.115).

Rationale: In the Bethesda system for reporting cervical cytology, cytologically benign-appearing endometrial cells are reported in women 45 years or older under the “other” general category, and follow-up left to the clinical provider. Benign glandular cells in women after hysterectomy are reported in the negative (NILM) Bethesda category. Literature review for the 2012 guidelines indicated increased risk of endometrial pathology in postmenopausal patients with endometrial cells on cytology but did not

indicate increased endometrial cancer risk for premenopausal patients with benign endometrial cells in the absence of abnormal uterine bleeding (Perkins, et.al, 2020, p.115).

8. Colposcopy Practice Standards and Exceptions to Colposcopy Clinical Action Threshold

ASCCP Colposcopy Standards

The ASCCP Risk-Based Management Consensus Guidelines reaffirm that colposcopy should be practiced according to the ASCCP Colposcopy Standards. For those at lowest risk, defined as less than HSIL cytology, no evidence of HPV 16/18 infection, and a completely normal colposcopic impression (*i.e.*, no acetowhitening, metaplasia, or other visible abnormality, and a fully visualized squamocolumnar junction), random biopsies are not recommended and patients with a completely normal colposcopic impression can be observed without biopsy. For those not meeting the lowest risk criteria, multiple targeted biopsies, at least 2 and up to 4, are recommended targeting all acetowhite areas to improve detection of prevalent precancers. The ASCCP Colposcopy Standards emphasize the need for biopsies even when the colposcopic impression is normal but any degree of acetowhitening, metaplasia, or other abnormality is present to ensure that CIN 2+ is not missed. As more patients are permitted to defer colposcopy under the ASCCP Risk-Based Management Consensus guidelines, obtaining adequate biopsies to effectively rule out CIN 2+ at each colposcopy examination is of greatest importance (Perkins, et.al, 2020, p.116).

The recommendations against untargeted biopsies are based on the risk of occult CIN 2+ of 1% to 7% and CIN 3+ of less than 1% among patients with less than HSIL cytology, HPV 16/18 negative, and normal colposcopic impression. According to the recommendations pertaining to the use of ECC from the 2012 guidelines, ECC is preferred for non-pregnant patients when colposcopy is inadequate, in those not at lowest risk in whom no lesion is identified, and is acceptable when a lesion is seen **Refer to: [ASCCP Risk-based Consensus Guidelines ASCCP Risk Tables](#)** (Perkins, et.al, 2020, p.116).

Exceptions to Colposcopy Threshold

Guideline: For patients with ASC-H cytology, colposcopy is recommended regardless of HPV result (Perkins, et.al, 2020, p.116).

Rationale: In the KPNC data, HPV-negative ASC-H and HPV-positive ASC-H had very different CIN 3+ rates, but similar cancer rates. The HPV-positive ASC-H had an immediate CIN 3+ risk of 26% and a cancer risk of 0.92%, whereas HPV-negative ASC-H had an immediate CIN 3+ risk of 3.4%, but an immediate cancer risk of 0.69%. Because the immediate cancer risk for ASC-H is disproportionately high compared with the CIN 3+ risk, the working group carried forward the 2012 recommendations and recommended colposcopy for all patients with ASC-H, regardless of HPV test results

Refer to: [ASCCP Risk-based Consensus Guidelines ASCCP Risk Tables](#) (Perkins, et.al, 2020, p.116).

Guideline: For patients with HPV 18–positive NILM, colposcopy is recommended. (Note colposcopy is also recommended for HPV 16–positive NILM, repeated here for clarity.)

Rationale: HPV 18–positive NILM had a 3.0% prevalent CIN 3+ risk, less than the Clinical Action Threshold for colposcopy. However, HPV 18–positive NILM had a disproportionately high cancer risk compared with other results: 0.2% immediately and 0.56% at 5 years. This suggests that HPV 18-related CIN 3 or AIS may be difficult to diagnose and/or more apt to rapidly progress from precancer to cancer. The elevated cancer prevalence with HPV 18 positivity has been previously noted, and HPV 18 is one of the most common HPV types found in invasive cervical cancers. Given the elevated cancer risk, referral to colposcopy is recommended.

Guideline: Colposcopy should be performed after 2 consecutive unsatisfactory screening tests.

Rationale: No new evidence was found, so the 2012 guideline was carried forward.

9. Treatment Considerations for Patients 25 Years or Older

Individuals who exceed treatment thresholds may undergo expedited treatment, defined as excisional treatment without preceding histologic confirmation. However, most patients will require both screening test and colposcopic biopsy results to determine the next step in management. Treatment guidelines are dichotomized by younger than 25 years or 25 years or older because of high spontaneous regression rates of HPV infection and CIN 2 and low incidence of cancer in those younger than 25 years. The consensus guidelines recognize that patients of various ages are concerned with the potential impact of treatment on future pregnancy outcomes. Shared decision-making is especially important when individuals consider treatment of histologic HSIL (CIN 2) and abnormalities with a relatively low likelihood of underlying CIN 3+, such as histologic LSIL (CIN 1) preceded by HSIL or ASC-H cytology, or persistent histologic LSIL (CIN 1).

Refer to: [ASCCP Risk-based Consensus Guidelines ASCCP Risk Tables](#) (Perkins, et.al, 2020, p.117).

10. Management of Histologic HSIL, not Further Specified or Qualified

Histologic reporting of cervical biopsies has moved to the LAST/WHO criteria, but its uptake by pathologists has not been universal. The consensus recommendation of the LAST guidelines is to qualify histologic HSIL using the CIN classification (CIN 2 or CIN 3). Because of measurable regression rates for CIN 2, the present guidelines subdivide treatment options based on the CIN qualifiers of CIN 2 and CIN 3. Pathology reports

incorporating the LAST criteria may not specify a CIN diagnosis **Refer to:** [ASCCP Risk-based Consensus Guidelines](#) [ASCCP Risk Tables](#) (Perkins, et.al, 2020, p.117).

Guideline: Treatment is preferred if histologic HSIL cannot be specified (e.g., reported as histologic HSIL or histologic HSIL [CIN 2,3]).

Rationale: CIN 3 is considered a direct cervical cancer precursor. If CIN 3 cannot be excluded, managing the patient as if CIN 3 is present is preferred. This conservative approach was considered safest for patients. Alternatively, the clinician could call the pathologist to further qualify the CIN equivalent and issue an additional report, then manage using the revised diagnosis (Perkins, et.al, 2020, p.117).

11. Management of Histologic HSIL (CIN 2 or CIN 3)

Guideline: In all nonpregnant patients with a diagnosis of histologic HSIL (CIN 3), treatment is recommended, and observation is unacceptable. In nonpregnant patients with histologic HSIL (CIN 2), treatment is recommended, unless the patient's concerns about the effect of treatment on future pregnancy outweigh concerns about cancer. Observation is unacceptable when the squamocolumnar junction or the upper limit of the lesion is not fully visualized or when the results of an endocervical sampling, if performed, is CIN 2+ or ungraded (Perkins, et.al, 2020, p.117).

Rationale: CIN 3 is considered an immediate cancer precursor and treatment is always recommended and observation is never acceptable, except during pregnancy. Observation is acceptable for CIN 2 in patients concerned about the potential effects of treatment on future pregnancy outcomes. [ASCCP Risk-based Consensus Guidelines](#) [ASCCP Risk Tables](#) (Perkins, et.al, 2020, p.117).

Guideline: When treatment of histologic HSIL is planned, excisional treatment is preferred, and treatment with ablation is acceptable. Outside of the setting of a clinical research trial, nonsurgical therapies, including topical agents, therapeutic vaccines, and other biologics, are unacceptable for the treatment of histologic HSIL (CIN 2 or CIN 3). Hysterectomy is unacceptable as primary therapy solely for the treatment of histologic HSIL (CIN 2, CIN 3, or unqualified). When considering ablative therapy, particularly cryotherapy, ablation is unacceptable in the following circumstances, as defined by the WHO: (a) the lesion extends into the canal and (b) when the lesion covers more than 75% of the surface area of the ectocervix or extends beyond the cryotip being used. Additional situations for which cryotherapy is not recommended include the following: (a) the squamocolumnar junction or the upper limit of any lesion is not fully visualized; (b) endocervical canal sample is diagnosed as CIN 2+ or CIN that cannot be graded; (c) after previous treatment for CIN 2+; (d) in the setting of inadequate biopsies of the cervix to confirm histologic diagnosis; and (e) if cancer is suspected (Perkins, et.al, 2020, p.117- 118).

Rationale: The WHO recommends LEEP over cryotherapy in settings where LEEP is available. In the United States, excisional treatment is used more commonly than

ablation treatment for the treatment of histologic HSIL. Excisional therapy consists of loop electrosurgical excision procedure (LEEP or LLETZ), cold knife conization, and laser cone biopsy. Ablation treatment includes cryotherapy, laser ablation, and thermoablation [ASCCP Risk-based Consensus Guidelines](#) [ASCCP Risk Tables](#) (Perkins, et.al, 2020, p.118).

12. Management of CIN 2 in Those Who Are Concerned About the Potential Effect of Treatment on Future Pregnancy Outcomes

Guideline: For patients with a diagnosis of histologic HSIL (CIN 2) whose concerns about the effects of treatment on a future pregnancy outweigh their concerns about cancer, either observation or treatment is acceptable provided the squamocolumnar junction is visible and CIN 2+ or ungraded CIN is not identified on endocervical sampling. If the histologic HSIL cannot be specified as CIN 2, treatment is preferred, but observation is acceptable. For patients 25 years or older, observation includes colposcopy and HPV-based testing at 6-month intervals for up to 2 years. If during surveillance, all evaluations demonstrate less than CIN 2 and less than ASC-H on 2 successive occasions, 6 months apart, subsequent surveillance should occur at 1 year after the second evaluation and use HPV-based testing. If negative on 3 consecutive annual surveillance tests, proceed to long-term surveillance. If CIN 2 remains present for a 2-year period, treatment is recommended (Perkins, et.al, 2020, p.118).

Rationale: Unlike CIN 3, which is considered a direct cancer precursor, CIN 2 has a significant regression rate. Most regression has been documented to have occurred within the first 12 months, whereas rates of progression continued to increase over time. Regression rates were higher (60%) in women younger than 30 years according to the current literature (Perkins, et.al, 2020, p.118). The primary rationale for deferring treatment of CIN 2 is the potential risk of adverse obstetric outcomes after excisional or ablative therapy. Refer to: [ASCCP Risk-based Consensus Guidelines](#) [ASCCP Risk Tables](#) (Perkins, et.al, 2020, p.118).

13. Management of LSIL (CIN 1) or Less Preceded by ASC-H or HSIL Cytology

Guideline: When CIN 2+ is not identified histologically after an ASC-H or HSIL cytology result, it is acceptable to review the cytologic, histologic, and colposcopic findings. If the review yields a revised interpretation, management should follow guidelines for the revised diagnosis. When CIN 2+ is not identified, HSIL cytology is managed more aggressively than ASC-H cytology. For cytology showing HSIL, but biopsy showing histologic LSIL (CIN 1) or less, either an immediate diagnostic excisional procedure or observation with HPV-based testing and colposcopy at 1 year is acceptable, provided in the latter case that the initial colposcopic examination fully visualized the squamocolumnar junction and the upper limit of any lesion, and that the endocervical

sampling, if collected, was less than CIN 2. For ASC-H, if the colposcopic examination can fully visualize the squamocolumnar junction and the upper limit of any lesion and that the endocervical sampling, if collected, is negative, observation at 1 year with HPV-based testing is recommended; a diagnostic excisional procedure is not recommended. For both HSIL and ASC-H cytology, if observation is elected, and all tests are negative at the 1-year visit, repeat HPV-based testing is recommended in 1 year (at 2 years from the original cytology). If all tests are negative at both the 1- and 2-year follow-up visits, return for retesting with HPV-based testing in 3 years is recommended, then proceed with long-term surveillance. If any test is abnormal during the observation period, repeat colposcopy is recommended, and management based on resulting biopsies is recommended. A diagnostic excisional procedure is recommended for patients with HSIL cytology results at either the 1- or 2-year visit, or ASC-H results that persist at the 2-year visit (Perkins, et.al, 2020, p.118- 119).

Rationale: Patients with a diagnosis of histologic LSIL (CIN 1) after HSIL and ASC-H cytology have 1-year CIN 3+ risks of 3.9% and 1.4%, respectively. Because HSIL cytology is associated with a higher risk than ASC-H cytology, colposcopy is recommended in addition to HPV-based testing at the 1-year follow-up if excision is not elected. Failure to detect CIN 2+ at colposcopy in patients with HSIL cytology does not mean that a CIN 2+ lesion has been excluded, although occult carcinoma is unlikely. As a result, patients with HSIL cytology who do not have immediate diagnostic excision require close follow-up. Few studies of HSIL cytology managed without treatment have been reported, and follow-up in those is limited; management relies on expert opinion. At all colposcopic examination when no lesion is identified on the cervix, the vagina and vulva must be examined for vaginal or vulvar intraepithelial neoplasia. Refer to [ASCCP Risk-based Consensus Guidelines ASCCP Risk Tables](#) (Perkins, et.al, 2020, p.118-119).

14. Histologic LSIL (CIN 1) Diagnosed Repeatedly for at Least 2 Years

Guidelines: For patients 25 years or older with histologic LSIL (CIN 1) who are diagnosed at consecutive visits for at least 2 years, observation is preferred but treatment is acceptable. If treatment is selected and the entire squamocolumnar junction and all lesions were fully visualized during colposcopic examination, either excision or ablation treatments are acceptable (Perkins, et.al, 2020, p.119- 120).

Rationale: Histologic LSIL (CIN 1) is the histologic manifestation of HPV infection. CIN 1 may be associated with high-risk or low-risk HPV infections and may be due to persistent infection with 1 type or sequential infections with different types. Regression rates are high, especially in younger patients, and subsequent diagnosis of CIN 2+ is uncommon regardless of whether CIN 1 is found on endocervical sampling or a biopsy of the transformation zone. Treatment is an acceptable option based on patient preference, after shared decision-making. Because the immediate estimated CIN3+ risk is less than the 25% treatment threshold, this is considered a special situation. Refer to

15. Management of AIS

Guidelines: A diagnostic excisional procedure is recommended for all patients with a diagnosis of AIS on cervical biopsy to rule out invasive adenocarcinoma, even when definitive hysterectomy is planned (Perkins, et.al, 2020, p.120). Excisional procedures should remove an intact specimen to facilitate accurate interpretation of margin status. An excisional specimen length of at least 10 mm is preferred, and this can be increased to 18 to 20 mm for patients who are not concerned about the effect of treatment on future pregnancy. These dimensions are preferred regardless of whether hysterectomy is planned (Perkins, et.al, 2020, p.120).

After the initial diagnostic procedure, hysterectomy is the preferred management for all patients who have a histologic diagnosis of AIS. Fertility-sparing management for appropriately selected patients is acceptable. For patients with confirmed AIS with negative margins on the excisional specimen, simple hysterectomy is preferred. For patients with confirmed AIS with positive margins on the excisional specimen, re-excision to achieve negative margins is preferred, even if hysterectomy is planned. For patients with AIS and persistent positive margins for whom additional excisional procedures are not feasible, either a simple or modified radical hysterectomy is acceptable. After hysterectomy, surveillance per the ASCCP surveillance guidelines for treated CIN 2+ is recommended. Refer to [ASCCP Risk-based Consensus Guidelines ASCCP Risk Tables](#) (Perkins, et.al, 2020, p.120).

For patients of reproductive age who desire future pregnancy, fertility-sparing management with an excisional procedure is acceptable provided that negative margins have been achieved on the excisional specimen, and the patient is followed with surveillance recommendations. If negative margins cannot be achieved after maximal excisional attempts, fertility-sparing management is not recommended. For patients who undergo fertility-sparing management, surveillance with co-testing and endocervical sampling is recommended every 6 months for at least 3 years, then annually for at least 2 years, or until hysterectomy is performed. For patients who have consistently negative co-testing and endocervical sampling results for 5 years, extending the surveillance interval to every 3 years starting in the sixth year of surveillance is acceptable. For patients who have had positive HPV test results or abnormal cytology/histologic results during surveillance, hysterectomy at the completion of childbearing is preferred (Perkins, et.al, 2020, p.121).

Rationale: Hysterectomy is recommended for AIS for several reasons. Adenocarcinoma in situ is frequently located within the endocervical canal and colposcopic changes may be minimal and determination of the necessary length of a cervical excisional specimen may be difficult. Adenocarcinoma in situ also has a higher risk of being multifocal and negative margins on an excisional procedure specimen do not ensure complete excision of disease. In the setting of histologic AIS on biopsy, invasive cancer cannot be excluded without a diagnostic excisional procedure. Although

increased detection and treatment of squamous cell cancer precursors (e.g., CIN 3) is associated with a decrease in the incidence of invasive squamous cell carcinoma, the same has not been demonstrated for AIS. Because of the challenges in diagnosing and monitoring AIS, hysterectomy remains the standard treatment for AIS for patients who do not desire future pregnancy. For patients desiring future pregnancy, observation after an excisional procedure remains an option, but this carries a risk of recurrent AIS and a small risk of invasive cancer even with negative margins. Both margin status and endocervical sampling performed at the time of excisional procedure predict residual disease and risk of invasive cancer on hysterectomy specimen. After treatment, HPV test results are the strongest predictor for recurrent AIS. Refer to **ASCCP Risk-based Consensus Guidelines** (Perkins, et.al, 2020, p.121).

16. Surveillance after Abnormalities

Guidance for Specific Tests and Testing Intervals When Managing Abnormal Results

Guideline: After abnormal cervical cancer screening test results for patients 25 years or older, colposcopic biopsy results, or treatment of histologic HSIL, surveillance with either HPV testing alone, or co-testing is preferred. Surveillance with cervical cytology alone is acceptable only if testing with HPV or co-testing is not feasible. Cytology is recommended at 6-month intervals when 1-year intervals are recommended for HPV or co-testing, and annually when 3-year intervals are recommended for HPV or co-testing. Cytology should be used for patients younger than 25 years, with transition to HPV-based testing at 25 years or older (Perkins, et.al, 2020, p.121).

Rationale: Individuals treated for histologic HSIL or with a recent abnormal screening test result have an elevated risk of cervical precancer warranting close follow-up. HPV testing and co-testing are more sensitive than cytology alone in detecting CIN 2+ in both the post-colposcopy and posttreatment settings. There is marginal difference between co-testing and HPV testing alone in detection of recurrent or persistent CIN 2+ and either test may be used for surveillance. Because cytology is less sensitive than HPV or co-testing, cervical cytology must be performed more frequently to achieve similar sensitivity for the detection of CIN 3+. Refer to **ASCCP Risk-based Consensus Guidelines** (Perkins, et.al, 2020, p.121).

17. Short-Term Follow-up after Treatment for Histologic HSIL

Guideline: After treatment, HPV-based testing at 6 months is preferred regardless of the margin status of the excisional specimen. If HPV-based tests are positive, colposcopy and appropriate biopsies should be performed. Follow-up at 6 months with colposcopy and ECC is acceptable (Perkins, et.al, 2020, p.121).

When margins are positive for CIN 2+ or ECC performed at the time of the excisional procedure shows CIN 2+ in patients 25 years or older who are not concerned about the potential effect of treatment on future pregnancy outcomes, repeat excision or observation is acceptable. For observation, HPV-based testing in 6 months is preferred; it is also acceptable to perform a colposcopy and ECC at 6 months. For patients

younger than 25 years or those who are concerned about the potential effect of treatment on future pregnancy outcomes, observation is recommended. If recurrent histologic HSIL (CIN 2+) develops after excisional treatment, and repeat excision is not feasible or not desired, hysterectomy is recommended (Perkins, et.al, 2020, p.121).

Rationale: The preferential use of HPV-based testing (e.g. co-testing or HPV primary testing) is supported by evidence and current literature to be that posttreatment HPV testing is the most accurate predictor of treatment outcomes. Repeat excisional treatment without repeat testing is considered acceptable for certain patients after patient counseling and considerations of age, likelihood of subsequent resolution of histologic HSIL/HPV infection, concern for the effect of treatment on future pregnancy, and the ability to adhere to appropriate surveillance recommendations **ASCCP Risk-based Consensus Guidelines** (Perkins, et.al, 2020, p.121- 122).

18. Guidance for Long-Term Follow-up after Treatment for High-Grade Histology or Cytology

Guidelines: In patients treated for histologic or cytologic HSIL, after the initial HPV-based test at 6 months, annual HPV or co-testing is preferred until 3 consecutive negative tests have been obtained (Perkins, et.al, 2020, p.122). After the initial intensive surveillance period, continued surveillance at 3-year intervals is recommended for at least 25 years after treatment of high-grade histology (histologic HSIL, CIN 2, CIN 3, or AIS) or high-grade cytology (HSIL or persistent ASC-H) even if this is beyond the age of 65 years. When patients with a history of treated high-grade histology or cytology reach the age of 65 years, if they have completed the initial 25-year surveillance period, continued surveillance at 3-year intervals is acceptable and may continue as long as the patient is in reasonably good health. Discontinuation of screening is recommended if a patient has a limited life expectancy. Management according to the highest-grade abnormality found on histology or cytology is recommended (Perkins, et.al, 2020, p.121-122).

Rationale: According to KPNC data for risks, the 5-year CIN 3+ risks after treatment of CIN 3 for 1, 2, and 3 negative co-tests/primary HPV tests were recommended for annual surveillance by co-testing or HPV testing is recommended until 3 negative annual HPV-based tests have been obtained. After a third negative HPV-based test, KPNC data suggest that the 5-year CIN 3+ risk remains above the 0.15% threshold for return to routine, 5-year HPV-based cervical screening. Long-term population studies support this finding, and they demonstrate a persistent two-fold increase in cervical cancer risk after treatment of histologic HSIL. Risk persists for at least 25 years and seems to be increased for patients older than 50 years. Because of these findings, continued 3-year surveillance is recommended for a minimum of 25 years. As cervical cancer risk seems to remain above general population levels, continued screening for as long the patient remains in good health is acceptable **ASCCP Risk-based Consensus Guidelines** (Perkins, et.al, 2020, p.122).

19. Guidance for Long-Term Follow-up after Low-Grade Cytology (HPV-Positive NILM, ASC-US, or LSIL) or Histologic LSIL (CIN 1) Abnormalities without Evidence of Histologic or Cytologic High-Grade Abnormalities

Guidelines: Among patients initially diagnosed with low-grade cytology or histologic abnormalities or HPV infections, continued surveillance according to risk estimation using available data is recommended (Perkins, et.al, 2020, p.122).

Rationale: The 5-year CIN 3+ risks for abnormal screening test results without evidence of cytologic or histologic HSIL followed by negative HPV-based testing were 0.51% after the first negative test and 0.23% after the second negative test. Patients reach criteria for a 3-year return after the second negative HPV-based test. The ability to perform accurate risk estimation for 3 or more rounds of negative testing after abnormalities is limited by very small numbers of CIN 3+ diagnoses in patients with persistently negative follow-up testing after low-grade cytologic or histologic abnormalities. The 5-year CIN3+ risks for various clinical scenarios can be found in ASCCP Risk Tables. Refer to [ASCCP Risk-based Consensus Guidelines](#); [ASCCP Tables](#).

20. Special Populations

Guidelines described previously apply to the average risk individual with an intact cervix and are based primarily on screening and management data from patients aged 25 to 65 years. However, several populations require special management considerations. Management of patients who are younger than 25 years, pregnant, immunosuppressed, post-hysterectomy, and older than 65 years are detailed in the following paragraphs (Perkins, et.al, 2020, p.123- 125).

A. Management of Patients Younger Than 25 Years, Initial Management after an Abnormal Screening Test Result

Guideline: In patients younger than 25 years with low-grade cytology screening results of LSIL, ASC-US HPV-positive, or ASC-US without HPV testing, repeat cytology alone at 1 and 2 years after the initial abnormal result is recommended. Colposcopy is recommended if high-grade cytology is found at any point (HSIL, ASC-H, AGC, AIS) or if low-grade cytology persists at the 2-year follow-up visit. If reflex HPV testing for ASC-US is performed and the results are negative, repeat cytology in 3 years is recommended. After 2 consecutive negative cytology results, return to routine age-based screening is recommended. If colposcopy is performed and the results are less than CIN 2 (histologic LSIL [CIN 1] or less), repeat cytology in 1 year, and manage as above (repeat cytology for ASC-US/LSIL, colposcopy for ASC-H or higher). Clinicians should switch to using risk estimates when patients reach the age of 25 years (Perkins, et.al, 2020, p.123).

Rationale: The HPV vaccinations became available in the United States in 2006, and patients at the target age for vaccination have now entered the younger than 25-year age group. Population-level risks of CIN 3+ for a given screening result are expected to decrease through a combination of individual and herd immunity. Observation is indicated for low-grade cytology results (ASC-US, LSIL), which are likely to represent non-16/18 HPV infections with a high probability for regression and a low risk for rapid progression to cancer. Accurate risk estimation for this age group is very difficult because vaccination is rapidly changing population-level CIN 3+ risk. The conservative 2012 management guidelines recommend against colposcopy/biopsy for lesser cytology abnormalities. This limits the ability to accurately measure CIN 3+ rates in this age group. In the absence of new compelling data to change management in this age group, the 2012 algorithms are carried forward at this time **ASCCP Risk-based Consensus Guidelines** (Perkins, et.al, 2020, p.123).

B. Management of Cytology ASC-H and HSIL in Patients Younger Than 25 Years

Guideline: Colposcopy is recommended for patients younger than 25 years with ASC-H or HSIL cytology. Immediate treatment without histologic confirmation is not recommended (Perkins, et.al, 2020, p.123).

Rationale: Although overall CIN 3+ prevalence is lower, cytology results of ASC-H are associated with higher risks of CIN 3+ than ASC-US, even in patients younger than 25. For this reason, colposcopy is warranted to evaluate the cervix for CIN 3+. Immediate treatment without histologic confirmation is not warranted in this population because of the high rate of resolution of CIN 2+ and the potential harms of treatment **ASCCP Risk-based Consensus Guidelines** (Perkins, et.al, 2020, p.123).

C. Management of Histology of Less than CIN 2 Preceded by Cytology ASC-H and HSIL in Patients Younger Than 25 Years

Guideline: Observation is recommended and diagnostic excisional procedures are not recommended for patients younger than 25 years with a preceding cytology of ASC-H or HSIL and a colposcopy with biopsy of CIN 1 or less as long as the squamocolumnar junction and the upper limit of all lesions are fully visualized, the endocervical sampling is less than CIN 2, and review of histology/cytology does not change the diagnosis. Observation with colposcopy and cytology in 1 and 2 years is recommended for those with HSIL cytology. Cytology at 1 and 2 years is recommended for those with ASC-H cytology, with colposcopy recommended for ASC-US or above on repeat testing. If CIN 2+ is diagnosed, this is managed per guidelines (Perkins, et.al, 2020, p.124). If a high-grade cytologic abnormality (HSIL, ASC-H) without histologic HSIL persists for 2 years, a diagnostic excisional procedure is recommended (unless the patient is pregnant). A diagnostic excisional procedure is recommended in patients when the squamocolumnar junction or the upper limit of all lesions are not fully visualized (Perkins, et.al, 2020, p.124).

Rationale: CIN 1 or less preceded by cytologic ASC-H or HSIL is a rare diagnosis. Refer to: **ASCCP Risk-based Consensus Guidelines** (Perkins, et.al, 2020, p.124).

D. Management of Histologic HSIL (CIN 2 or CIN 3) for Patients Younger Than 25 Years

Guideline: In patients younger than 25 years with histologic HSIL (CIN 3), treatment is recommended, and observation is unacceptable. In patients younger than 25 years with histologic HSIL (CIN 2), observation is preferred, and treatment is acceptable. In patients younger than 25 years with histologic HSIL unspecified as CIN 2 or CIN 3, observation or treatment is acceptable. Observation includes colposcopy and cytology at 6-month intervals. If during surveillance of histologic HSIL, all cytology results are less than ASC-H and histology results are less than CIN 2 at 6 and 12 months, subsequent surveillance should be at 1 year after the second evaluation. If CIN 2 or unspecified histologic HSIL persists for a 2-year period, treatment is recommended. Excisional treatment is recommended when the squamocolumnar junction or the lesion(s) are not fully visualized. Refer to (Perkins, et.al, 2020, p.124).

Rationale: Cervical cancer is uncommon in patients younger than 25 years despite the high prevalence of HPV infections and high-grade histologic lesions. Younger patients have higher rates of regression for histologic HSIL (particularly CIN 2) and lower risks of progression to invasive cancer. Less intensive management strategies that do not include HPV testing are appropriate for this population. CIN 3, which is considered a direct cervical cancer precursor should be treated at any age **ASCCP Risk-based Consensus Guidelines** (Perkins, et.al, 2020, p.124).

E. Managing Patients during Pregnancy

Guideline: During pregnancy, management of abnormal screening results using the same Clinical Action Thresholds for surveillance and colposcopy established for nonpregnant patients is recommended (Perkins, et.al, 2020, p.124). Endocervical curettage, endometrial biopsy, and treatment without biopsy are unacceptable during pregnancy. A diagnostic excisional procedure or repeat biopsy is recommended only if cancer is suspected based on cytology, colposcopy, or histology. If histologic HSIL (CIN 2 or CIN 3) is diagnosed at the first colposcopy examination during pregnancy, surveillance colposcopy and testing (diagnostic cytology/HPV depending on age) is preferred every 12 to 24 weeks. Deferring colposcopy to the postpartum period is also acceptable. Repeat biopsy is recommended if invasion is suspected or the appearance of the lesion worsens. Treatment of histologic HSIL (CIN 2 or CIN 3) during pregnancy is not recommended. If AIS is diagnosed during pregnancy, referral to a gynecologic oncologist is preferred, but management by a gynecologist skilled in the colposcopic diagnosis and treatment of AIS is acceptable (Perkins, et.al, 2020, p.124).

In the postpartum period, colposcopy is recommended no earlier than 4 weeks after delivery. If a lesion is detected at postpartum colposcopy, and the patient was diagnosed with histologic HSIL (CIN2 or CIN3) during pregnancy, then an excisional treatment procedure or full diagnostic evaluation (cervical cytology, HPV, and biopsy) is acceptable. In the absence of a lesion on colposcopy, a full diagnostic evaluation is recommended. Expedited treatment is not recommended in this scenario (Perkins, et.al, 2020, p.124).

Rationale: Pregnancy is considered as a special population for management and treatment options that weigh the risk to fetus and mother versus the risk of missing cancer. The rate of precancer or progression to cancer is not known to be different in pregnancy. The increased vascular state of the cervix or hyperemia and other physiologic changes of pregnancy may impact the detection of precancer and cancer. Colposcopy by an experienced provider during pregnancy is preferred (Perkins, et.al, 2020, p.124). Colposcopy-directed biopsies in pregnant patients is believed by experts to be safe (Perkins, et.al, 2020, p.124). In general, research data in pregnancy is limited. Shared decision-making that considers both the pregnant patient and the fetus is critical for management (Perkins, et.al, 2020, p.124). Individuals who are screened infrequently or are unable to complete appropriate follow-up are at increased risk for developing cervical cancer. Refer to **ASCCP Risk-based Consensus Guidelines** (Perkins, et.al, 2020, p.124).

F. Managing Patients with Immunosuppression

Immunocompromised patients include those patients with HIV, solid organ transplant, or allogeneic hematopoietic stem cell transplant, as well as those with systemic lupus erythematosus, and those with inflammatory bowel disease or rheumatologic disease who require current immunosuppressive treatments. Although the literature for some immunosuppressed populations remains limited, many of these conditions that suppress cell-mediated immunity have been associated with virally induced cancers, including cervical cancer. For this reason, the same guidelines for cervical cancer screening and abnormal result management recommendations are used for immunocompromised individuals with or without HIV. Screening should begin within 1 year of known high risk status and continue throughout a patient's lifetime: annually for 3 years, then every 3 years (cytology only) until the age of 30 years, and then either continuing with cytology alone or co-testing every 3 years after the age of 30 years (Perkins, et.al, 2020, p.124- 125).

Guideline: In immunocompromised patients of any age, colposcopy referral is recommended for all cytology results of HPV-positive ASC-US or higher. If HPV testing is not performed on ASC-US results, then repeat cytology in 6 to 12 months is recommended, with colposcopy referral for ASC-US or higher. For any result of ASC-US or higher on repeat cytology or if HPV positive, referral to colposcopy is recommended. For all cytology results of LSIL or worse (including ASC-H, AGC, AIS, and HSIL), referral to colposcopy is recommended regardless of HPV test result if done (Perkins, et.al, 2020, p.125).

Rationale: Because of higher risk of CIN 3+ with low-grade cytologic abnormalities among HIV+ individuals and immunosuppressed patients, colposcopic referral is recommended for HPV-positive ASC-US. Because of the relatively high HPV prevalence before age 30 years, HPV co-testing is not recommended for patients younger than 30 years of age with HIV **ASCCP Risk-based Consensus Guidelines** (Perkins, et.al, 2020, p.125).

G. Managing Patients after Hysterectomy

Guideline: After a diagnosis of high-grade histology or cytology, patients may undergo hysterectomy for reasons related or unrelated to their cervical abnormalities. If hysterectomy is performed for treatment, patients should have 3 consecutive annual HPV-based tests before entering long-term surveillance. Long-term surveillance after treatment for histologic HSIL (CIN 2 or CIN 3) or AIS involves HPV-based testing at 3-year intervals for 25 years, regardless of whether the patient has had a hysterectomy either for treatment or at any point during the surveillance period. Among patients who have undergone hysterectomy but either have no previous diagnosis of CIN 2+ within the previous 25 years or have completed the 25-year surveillance period, screening is generally not recommended. However, if performed, abnormal vaginal screening test results should be managed according to published recommendations (Perkins, et.al, 2020, p.125).

Rationale: The risk of high-grade vaginal intraepithelial neoplasia is elevated among patients who have had a hysterectomy for treatment of histologic HSIL. Although HPV testing is not FDA approved for vaginal samples, sensitivity of HPV-based testing in the setting of post-hysterectomy for histologic HSIL is superior to cytology alone. For patients who have undergone a hysterectomy for benign disease and received a cervical cytology and/or HPV testing results are ASC-US, HPV-positive or LSIL, management will include follow-up in 12 months. Patients with high-grade cytology (HSIL, ASC-H, AGC) should be referred immediately for vaginal colposcopy **ASCCP Risk-based Consensus Guidelines** (Perkins, et.al, 2020, p.125).

H. Managing Patients Older Than 65 Years with a History of Prior Abnormalities

Guideline: If patients over age 65 years undergo HPV testing, co-testing, or cytology, management guidelines for patients aged 25 to 65 years should be followed. Long-term surveillance testing is recommended for patients with a history of abnormal screening results or treatment for precancer. Discontinuing surveillance is unacceptable if the patient is in reasonably good health (Perkins, et.al, 2020, p.125).

Rationale: Screening for patients older than 65 years should follow national guidelines. Approximately 20% of cervical cancers occur in patients older than 65 years of age. Patient comfort and the limitations of positioning and examining older patients should have shared decision-making conversation about when to discontinue screening for patients beyond the age of 65. Vaginal estrogen use for a limited 3-week interval can be considered to obtain adequate sampling **ASCCP Risk-based Consensus Guidelines** (Perkins, et.al, 2020, p.125).

21. Current and Future ASCCP Considerations

The 2019 guidelines are designed to take into consideration factors that influence the Clinical Action Thresholds. The 2019 ASCCP Risk-based Consensus Working groups considered risk factors to determine their importance for inclusion in clinical applications of these guidelines, to include the magnitude of effect on the estimated risk, as well as the feasibility of collecting accurate data in clinical practice to inform the clinician

management. Screening history greatly influences risk estimates, specifically current HPV and cytology test results, previous HPV test results, and patient history of histologic HSIL. Patient screening history may often be unknown. Cases with unknown history are considered separately as a risk factor. Additional factors considered because of the association with cervical cancer include HPV vaccination, age, hormonal contraception use, history of sexually transmitted infection, parity, cigarette smoking, obesity, and sexual behaviors including age of first intercourse and having multiple sexual partners. Even though HPV vaccination in adolescence (generally before the age of 18 years) is believed to reduce the risk of HPV 16/18 infections and the associated histologic HSIL, HPV vaccination status was omitted from this revision of the guidelines because of the following: (a) management guidelines are very conservative in the population younger than 25 years, (b) the population prevalence of on-time HPV vaccination in the 25- to 29-year-old population is currently lower than that needed for herd immunity, and changing recommendations for this population as a whole is not yet warranted, and (c) making person-specific recommendations based on age at vaccine series initiation and number of doses received is impractical in the United States in the absence of linkable, comprehensive, state-based immunization registries. Analyses were limited for heavy smoking history and younger than 30 years. Refer to **ASCCP Risk-based Consensus Guidelines** (Perkins, et.al, 2020, p.125- 126).

Future updates to guidelines as new tests become available for management are expected. Decreases in the overall population prevalence of HPV infection, especially HPV 16/18 genotypes, are expected as individuals vaccinated as adolescents reach screening age. As data on the CIN 3+ risks associated with screening test results become available for individuals aged 25 to 29 years who received timely vaccination, it is anticipated that decreases in population-level prevalence of HPV infections will affect the management recommendations for this age group in the near future. It is expected that new technologies that enter the market will be evaluated for their use in improving the diagnosis and management of CIN 3+. Expectations are that clinically useful products with increased specificity for detecting high-grade abnormalities or the ability during clinical follow-up to distinguish new from persistent HPV infections (Perkins, et.al, 2020, p.126).

Completed analyses related to costs, benefits, and effectiveness is expected in the future. Quality-of-life and economic effects of management is also expected. These guidelines within the United States are expected to create a new national standard of care for management of abnormal cervical cancer screening test results. The result of successful adoption of these guidelines is believed to lead to reduction of unnecessary testing and invasive procedures in low-risk patients and identification of high-risk patients who will benefit from more intensive surveillance. Maximizing cancer prevention benefits while minimizing the harms of over testing and overtreatment is the expected outcome (Perkins, et.al, 2020, p.126).

22. Other Malignant Neoplasms

Cytologic evaluation sometimes discovers metastatic lesions such as ovarian, gastrointestinal, melanoma, etc. In these cases, the lab will report the findings as “other malignant neoplasms.”

PATIENT NOTIFICATION AND EDUCATION

Notify and counsel the patient regarding the seriousness of the cytology test report and the need for immediate medical care. Document your actions. Additional evaluation is necessary.

CLINICAL MANAGEMENT

- **IMMEDIATE** referral must be made for medical follow-up to a Qualified Health Care Provider (QHCP).
- Since patients with this test finding all require colposcopy, the health care provider agency should assure that referral is for colposcopic evaluation and treatment.
- At least three attempts must be made to locate and inform the patient of **abnormal screening results**. The last attempt must be by certified letter. Written documentation of all attempts must be included in the medical record. For all abnormal Pap test results, the following information shall be documented in the patient's medical record: Patient contact information (number and date of attempts made to follow-up); follow-up appointment information (date, follow-up provider, and follow-up location); date the referral was made; and results of all referrals, including the report from the follow-up provider.
- Patient navigation is required for all other malignant neoplasms results. See page 64.
- Treatment and follow-up are individualized as directed by the QHCP.

23. Non-Neoplastic Comments on Negative Results

Cytologic findings not considered abnormal, but which nonetheless may be of concern, are noted on the cytology test report. These may include:

- Non-neoplastic cellular variations
 - Squamous metaplasia.
 - Keratotic changes.
 - Tubal metaplasia.
 - Atrophy.
 - Pregnancy-associated changes.
- Reactive cellular changes associated with:
 - Inflammation (includes typical repair).
 - Lymphocytic (follicular) cervicitis.
 - Radiation.
 - Intrauterine contraceptive device (IUD).
- Glandular cells status post hysterectomy.
- Organisms
 - Trichomonas vaginalis*

- Fungal organisms morphologically consistent with *Candida* spp.
- Shift in flora suggestive of bacterial vaginosis.
- Bacteria morphologically consistent with *Actinomyces* spp.
- Cellular changes consistent with herpes simplex virus.
- Cellular changes consistent with cytomegalovirus.
- Other
 - Endometrial cells (in women \geq 45 years of age.).

(Specify if “negative for squamous intraepithelial lesion”)

Do not repeat a cytology test for any of these findings unless the specimen was unsatisfactory for evaluation. However, it is appropriate to address the cause of the non-neoplastic findings. Endometrial evaluation is recommended in postmenopausal women (Nayar et al., 2015).

INFECTION: Refer to local health care provider agency protocols for treatment of infection or inflammation.

Nonneoplastic Cellular Variations:

1. Squamous Metaplasia - Cells which show a range of cytoplasmic differentiation from immature parabasal-like cells to those that approximate the appearance of differentiated intermediate/ superficial cells. The mean nuclear area is larger than that of the intermediate cell and similar to the parabasal cell. The process of metaplasia represents the replacement of one type of epithelium (endocervical) with another (squamous) as a protective response. Squamous metaplastic cells can exhibit a spectrum of morphology from relatively undifferentiated small round cells to highly differentiated intermediate/ superficial squamous cells. In metaplasia, stimuli such as infection, inflammation, or other type of trauma cause an alteration in the pathway of development of new cells replacing those lost by wear and tear. The newly generated cells become progressively more differentiated along the squamous pathway in response to the noxious stimulus.
2. Keratotic Cellular Changes - Normally, the cervix is nonkeratinizing, stratified squamous epithelium. Keratotic changes usually occur as a protective reactive phenomenon or in association with human papillomavirus (HPV) - induced cell changes. Both processes lead to hyper-maturation of the native squamous epithelium, more closely approximating the normal appearance of skin. Keratotic changes can be considered a second-order protective reaction for subepithelial tissues with metaplasia being the first-order reaction. “Keratosis,” “hyperkeratosis,” “parakeratosis,” and “dyskeratosis” are descriptive terms for keratotic cellular changes which have been used inconsistently in the past. These terms are not specifically listed in Bethesda terminology due to a lack of consensus definitions. They are included parenthetically for clarification only. Although some cytologists may choose to include such terms to describe a morphologic feature that may

correlate with leukoplakia on colposcopy, they should not be used as an interpretive category in cytology reports.

- a. Typical Parakeratosis - Miniature superficial squamous cells with dense orangeophilic or eosinophilic cytoplasm. Cells may be seen in isolation, in sheets, or in whorls; cell shape may be round, oval, polygonal, or spindle shaped.
- b. Hyperkeratosis - Anucleate but otherwise unremarkable mature polygonal squamous cells, often associated with mature squamous cells showing keratohyaline granules. Empty spaces or “ghost nuclei” may be noted. The Bethesda classification and interpretation of keratonic changes depends on the nuclear alterations present. Miniature squamous cells with small pyknotic nuclei and orangeophilic to eosinophilic cytoplasm (“parakeratosis”) are a nonneoplastic reactive cellular change. Single cells or cell clusters that demonstrate pleomorphism of nuclear shape and/or increased nuclear size and/or chromasia (“atypical parakeratosis”, “dyskeratosis”, or “pleomorphic parakeratosis”) are representative of an epithelial cell abnormality. Such findings should be categorized as atypical squamous cells (ASC) or as a squamous intraepithelial lesion (SIL), depending on the degree of cellular abnormality identified. Anucleate, but otherwise unremarkable mature, squamous cells (“hyperkeratosis”) constitute a nonneoplastic cellular change. When extensive hyperkeratosis is present, an underlying neoplastic or nonneoplastic process may be associated and should be considered when evaluating such cytologic preparations. Thick plaques of pleomorphic anucleate squamous cells with irregular contours may rarely be the only clue to an underlying squamous cell carcinoma. Similar to parakeratosis, hyperkeratosis alone does not constitute a specific interpretive category.
- c. Tubal Metaplasia - A metaplastic phenomenon in which the normal endocervical epithelium is replaced by an epithelium that recapitulates that of the normal fallopian tube. This metaplastic epithelium includes several cell types (ciliated cells, peg cells, and goblet cells). Tubal metaplasia is a frequent finding in the upper endocervical canal/ lower uterine segment. Tubal metaplasia is among the most common benign processes to be misinterpreted as endocervical atypia or neoplasia. This is due to the tendency toward enlarged nuclei, crowded nuclei, and nuclear stratification. However, terminal bars and cilia establish a benign interpretation.
- d. Atrophy - Normal aging phenomenon associated with a lack of hormonal stimulation that leads to thinned epithelium consisting of only immature basal/ parabasal cells. Atrophic changes are due to decreased hormonal support of epithelial tissues. The degree of atrophic change is highly variable, reflecting the differing levels of hormonal support that may be present. Cytomorphology can range from intermediate cell predominant to parabasal predominant to deeply atrophic (atrophic vaginitis) patterns in postmenopausal women. These differences may reflect alternate sources of endogenous estrogen or the presence of exogenous estrogenic substances. Reporting of atrophic changes is variable and poorly reproducible. Atypical cellular changes associated with

atrophy warrant an interpretation of atypical squamous cells (ASC). A patient is more likely to have significant disease in face of a history of previous cervical abnormality or a prior positive high-risk HPV test. Atrophy may coexist with dysplasia or neoplasia. Atrophic changes may also be seen for weeks after parturition and other situations where estrogen and progesterone levels have decreased. In postmenopausal and postpartum states, multinucleated histiocytes (or giant cells) are found in cervical samples associated with chronic inflammatory processes.

- e. Pregnancy-Related Cellular Changes - During pregnancy, a variety of epithelial and non-epithelial cell changes can be identified in cervical cytology specimens. These changes can be misinterpreted as representing neoplastic abnormalities.
- f. Hormonal Changes - The altered hormonal stimulation in pregnancy leads to incomplete maturation of the squamous epithelium resulting in an intermediate cell-dominant pattern. In association with this pattern, a particular appearance of the intermediate squamous cell showing prominent glycogen with a flattened “boat-like” appearance is common. This appearance is referred to as “navicular” cells. When progesterone secretion is prolonged (as in pregnancy), the navicular cells have greatly thickened borders and form dense clusters.
 - i. Decidua - Present in pregnancy and during the postpartum period. These cells are derived from hormonally stimulated endocervical or endometrial stroma.
 - ii. Cytotrophoblast - Derived from the placenta in late pregnancy and in the postpartum period. Rarely, they can be present for months after delivery. Cytotrophoblast are rarely identified as such. They may resemble small squamous metaplastic or endometrial cells, as well as high-grade squamous intraepithelial lesion cells. When recognized, the background often has either findings of exudate or other elements of pregnancy which give a clue to the identity.
 - iii. Syncytiotrophoblast - Derived from fusion of cytotrophoblastic cells. They may be identified in cervical cytology specimens in late pregnancy and postpartum periods. They rarely are present for months after delivery.
 - iv. Arias-Stella Reaction - A benign process which involves glandular epithelial cells (either endocervical or endometrial) and is found in association with pregnancy or occasionally in nonpregnant hormonally stimulated individuals (Nayar et al., 2015)

Note: The changes seen in pregnancy can be misinterpreted as being of preneoplastic or neoplastic origin, primarily because they may show concerning nuclear features. It is important to be aware of the patient’s pregnancy or postpartum status to avoid overinterpretation of these findings (Nayar et al., 2015).

Other Non-Neoplastic Findings on Cervical Cytology Test Reports and Definitions

1. **Reactive/ Reparative Cellular Changes** – Reactive cellular changes which are associated with inflammation, physical or chemical trauma, radiation, IUD irritation, or other nonspecific causes (Nayar et al., 2015).
2. **Reactive Cellular Changes Associated with Inflammation (Includes Typical Repair)** - Reparative changes may involve mature squamous, squamous metaplastic, or columnar epithelium. Cognizance of criteria for reactive/ reparative changes is important for stratifying the boundaries between Negative for Intraepithelial Lesion or Malignancy (NILM) and epithelial abnormalities. Reactive and reparative processes can show wide variation in nuclear area. In some instances, the nuclear size may fall into the range noted in SIL or cancer. When a combination of anisonucleosis irregularities in chromatin distribution, nuclear contour irregularities, or variation in size and shape of nucleoli are present (features of so-called atypical repair), the differential widens to include not only reactive conditions but also squamous intraepithelial lesions and invasive cancers. When present, such changes may be better categorized as “atypical glandular cells” (AGC) or “atypical squamous cells” (ASC-US or ASC-H) (Nayar et al., 2015).
3. **Lymphocytic (Follicular) Cervicitis** - This condition is a form of chronic cervicitis that results in the formation of mature lymphoid follicles in the sub-epithelium of the cervix. These sub-epithelium lymphocytes may be sampled while obtaining a cervical specimen (Nayar et al., 2015).
4. **Reactive Cellular Changes Associated with Radiation** - The effects of ionizing radiation on cells can lead to cytologic features which may be mistaken for neoplastic or preneoplastic conditions. Acute radiation-induced changes, consisting of degenerated blood, bizarre cell forms, and cellular debris, generally resolve within 6 months following therapy. However, in some patients, chronic radiation-induced cellular changes may persist indefinitely. Certain chemotherapeutic agents may produce changes in cervical epithelial cells similar to those seen with acute and chronic radiation effects. It is important to note that bona fide squamous intraepithelial lesions in patients who have received pelvic radiation therapy will appear identical to such lesions in non-radiated patients. Care must be taken to not overinterpret specimens from radiated patients, especially in the face of perceived low-grade lesions associated with degenerated cells. Also, pelvic examinations and colposcopic procedures are more difficult in an irradiated pelvis which can complicate management (Nayar et al., 2015).
5. **Reactive Cellular Changes Associated with Intrauterine Contraceptive Device** - Reactive glandular cell clusters occasionally seen in women with intrauterine devices (IUD) may represent either endometrial or endocervical columnar cells exfoliated as a result of chronic irritation by the IUD device. Cells associated with the presence of an IUD may persist for several months after

removal of the device. The characteristic changes fall into two distinct patterns: IUD-associated cells may resemble clusters of cells derived from adenocarcinoma of the endometrium, fallopian tube, or ovary when present as three-dimensional clusters; IUD-associated cells mimic a high-grade squamous intraepithelial lesion when present as single atypical cells. If there is any doubt as to the significance of the cellular abnormalities, the cyto-pathologist should consider recommending removal of the IUD followed by repeat cervical cytology sampling (Nayar et al., 2015).

6. **Glandular Cells Status Post Hysterectomy** - Occasionally benign-appearing glandular cells can be present in cervical cytology specimens from women who have undergone prior hysterectomy. While the origin of these benign cells may be obscure, the morphology should not be of concern for neoplasia. There are a number of explanations for this phenomenon to include the existence of glandular rests adjacent to vaginal mucosa, development of adenosis after trauma, mucinous or goblet cell metaplasia in response to atrophy, or prolapse of the remaining fallopian tube after simple hysterectomy. Following supracervical hysterectomy, benign endocervical-type glandular cells should be expected. The most important task is to exclude adenocarcinoma, especially if the hysterectomy was performed for glandular neoplasia. If not atypical, post hysterectomy glandular cells have no clinical significance and reporting them is optional since they do not change the management (Nayar et al., 2015).
7. **Endometrial Cells Present in a Woman over 45** - If the patient is premenopausal, this is not clinically significant. If she is postmenopausal, refer to QHCP for further evaluation.
8. **Sexually Transmitted Diseases** - STDs cannot reliably be diagnosed by Pap tests. Any STD identified on the Pap test should be confirmed by additional testing. Consult the current version of the *North Carolina Sexually Transmitted Diseases Public Health Program Manual* and current recommendations regarding sexually transmitted diseases from the *Centers for Disease Control and Prevention, Clinical Practice and Treatment Guidelines*.

Please refer to the NC Department of Health and Human Services, Communicable Disease Branch, Sexually Transmitted Diseases Public Health Program Manual (2015) for specific details on STD Examination and wet mount instructions at the link below:

<http://epi.publichealth.nc.gov/cd/lhds/manuals/std/toc.html>

The NC Communicable Disease Branch follows the guidance put forth by the CDC, Centers for Disease Control and Prevention of Sexually Transmitted Disease Treatment Guidelines, 2015 (MMWR Recommendations and Report 2015;64 No. RR-3; 1-137). These guidelines can be found on the CDC's STD Homepage at:

<https://www.cdc.gov/std/tg2015/tg-2015-print.pdf>

Note: The wet mount specimen is taken from the vaginal vault and not the cervix, so it should not normally matter if the Pap or the wet mount is completed first, but in

the case of manipulation of the cervix which may lead to bleeding, the clinician may want to collect the wet mount specimen first to decrease the risk of contaminating the wet mount specimen with blood which may make it hard to visualize microscopically.

From Wet Mount:

Trichomonas vaginalis: On wet mount, *Trichomonas vaginalis* is seen as pear-shaped, oval, or round cyanophilic organism ranging in area from 15 to 30 μm^2 . The nucleus is pale, vesicular, and eccentrically located. Eosinophilic cytoplasmic granules are often evident and sometimes flagella are observed. Leptothrix may be seen in association with *T. vaginalis*. Associated background changes include mature squamous cells with small perinuclear halos (trich change) and 3-dimensional clusters of neutrophils or polyballs. In liquid-based preparations, organisms tend to be smaller due to fixation in the solution and rounding. Nuclei and cytoplasmic eosinophilic granules are often better visualized. Flagella may be better preserved and therefore identified more readily. Occasional kite-shaped forms may be seen especially in SurePath preparations. In conventional smears, it is common to have increased neutrophilic infiltrate and flagella are less often identifiable (Nayar et al., 2015). *Trichomonas* PCR testing is available and can be used as a confirmatory test if needed.

Bacterial Vaginosis and Bacterial Vaginitis: Bacterial vaginosis has been associated with pelvic inflammatory disease, preterm birth, postoperative gynecologic infections, and abnormal cervical cytology. Consultation with clinical services is suggested before routinely reporting findings of vaginitis/ vaginosis to tailor reports to meet clinical needs (Nayar et al., 2015). Bacterial vaginosis should be diagnosed via Amsel's criteria if using wet mount. Transitional flora can only be diagnosed via gram staining (for example, pap smear) with Nugent's criteria. Amsel's criteria is diagnosed by at least 3 of the four criteria: 1) Thin, homogenous vaginal discharge; 2) Vaginal pH >4.5; 3) Positive whiff test (positive amine odor when a solution of 10% KCl is added); 4) At least 20% clue cells. Modified Amsel's has been used which is to have 2/3 criteria.

Candida Cells: Budding yeast and/or pseudohyphae, sometimes spanning many cells and are eosinophilic to gray brown on the Papanicolaou stain. Pseudohyphae formed by cytoplasmic extension of budding yeasts, lack true septations but show complete constrictions along their length that indicate the formation of new cells. Fragmented leukocyte nuclei and groups of squamous epithelial cells speared by pseudohyphae and held together in a rouleaux are often seen. *Candida glabrata* shows small uniform, round budding yeast forms surrounded by clear halos on Papanicolaou stain. Unlike other *Candida* species, it does not form pseudohyphae in vivo or in culture (Nayar et al., 2015).

Divider – 2. Procedure for Obtaining a Cervical Cytology Test

Procedure for Obtaining a Cervical Cytology Test

A. Purpose

It is important to remember that a cervical cytology test is a screening test, and as such it is intended to be used in an asymptomatic population. Symptoms that may be due to neoplasia should be completely evaluated. A cervical cytology test in this situation is not appropriate management. In the presence of frank bleeding, the cytology test should not be obtained. If there is suspicion that the patient's bleeding may be due to a neoplastic process, the patient should be referred for prompt, complete evaluation (Huh et al., 2015). **When considering the order of collecting specimens:** The cervical cytology test is normally collected without cleaning of the cervix except in cases of copious discharge. In the case of copious discharge, a dry cotton tip can be utilized to visualize the os of the cervix. If too much cleaning is done, this could alter the sensitivity of the Pap test. Normally, the test should be performed first, before any testing is undertaken for gonorrhea or chlamydia infection. Collect gonorrhea, chlamydia, and cytology specimens according to local protocol using review of patient symptoms and clinic requirements. Liquid-based cytology systems allow testing for cytology, HPV, gonorrhea, chlamydia, and trichomonas from a single specimen.

Note 1: The wet mount specimen is taken from the vaginal vault and not the cervix, so it should not normally matter if the pap or the wet mount is completed first, but in the case of manipulation of the cervix which may lead to bleeding, the clinician may want to collect the wet mount specimen first to decrease the risk of contaminating the wet mount specimen with blood which may make it hard to visualize microscopically.

Note 2: Collecting any other test(s) sample(s) before collecting the cytology test may remove cells diagnostic for cancer and its precursor lesions and may cause false negative cervical cytology test results.

B. Preparation of the Patient

If newer generation Pap tests are utilized, the following may not be a concern. However, depending on the availability of the provider to access the newer generation Pap tests, the following may be considered: At the time the appointment is made for an examination which includes a cervical cytology test, the patient should be advised that the likelihood of getting a higher quality test is increased by putting **nothing** in the vagina for 48 hours prior to the exam. This includes:

- No intercourse
- No tampons
- No douching
- No vaginal medications or lubricants

- No vaginal contraceptive

In addition to the above recommendations, if possible, the patient should be tested as close to 2 weeks after the first day of her last menstrual period, to schedule when the patient is not menstruating. If the appointment falls at a time the patient is menstruating, this should not be a reason to reschedule an appointment, unless it is the patient's preference.

C. Equipment

A clinic room set up for a female pelvic exam should include the following:

- Good lighting (gooseneck lamp) must be available
- Specula
- Broom (preferred) or Plastic spatula
- Endocervical brush (Do not use in pregnant women.)
- Vial of preservative solution for liquid base Pap test
- Test tubes with normal saline (saline replaced every 30 days and when expired)
- Cotton applicators (large and small)
- Reference Lab Forms
- Individual zip lock bag
- Mailing container for vials or container from Reference Lab

D. Procedure for Preservative Solution Testing

1. Vial of preservative solution may be labeled **before** the test is taken. Print patient's last name and then first name on vial. Make sure name is legible. A computer-generated name label may be used (preferred). Place computer printed or hand-written label **horizontally** around the vial. The uncovered portion of the vial remains uncovered and toward the top of the vial, so the vial's expiration date remains viewable. This positioning will allow the depth of liquid in the vial to be viewed and allow a place for a bar code to be added sometime in the future.

Note: If specimen vial is not used, make sure label is removed or vial is discarded prior to the next patient.

Certain elements for Pap smears are required by federal CLIA 04 regulations such as the patient's last menstrual period and documentation of whether the patient had a previous abnormal report, treatment, or biopsy. Other elements (e.g., IUC use, hysterectomy, BCP or Depo-Provera use, etc.) are important in the evaluation of any cellular changes.

2. Offer the patient an opportunity to empty her bladder. Give patient a gown with instructions for wearing. Assist patient onto the examining table.

3. Assist patient to lithotomy position, drape and adjust light.
4. Put on gloves. Proceed at relaxed pace and explain each step of procedure to patient.
5. Insert the speculum
 - a. Place one or two fingers just inside or at introitus.
 - b. Press down gently on perineal body to relax muscles unless patient is uncomfortable with this procedure.
 - c. Tell patient that speculum is about to be inserted and ask her to relax pelvic floor muscles.
 - d. Gently insert closed speculum at a slight angle downward as you withdraw fingers.
 - e. Hold bills at oblique angle and direct speculum toward posterior wall.
 - f. With handle, rotate bills to horizontal position maintaining downward angle and pressure posteriorly.
 - g. Insert speculum fully, and direct bills accordingly.
 - h. If unable to locate cervix, pull back on speculum slightly and redirect bills anteriorly; cervix will usually become visible.
 - i. Lock bills when cervix becomes visible.

6. Obtain the Pap Test Sample

Collect samples for the liquid-based Pap test from **both ecto- and endocervix**.

a. TO COLLECT THE SAMPLE FROM THE ECTOCERVIX

- (1) Select broom and rotate 5 times maintaining contact with the ectocervical surface **or** select the contoured end of plastic spatula and rotate 360° around entire ectocervix while maintaining tight contact with ectocervical surface. Remove spatula.
- (2) If using a broom, the tip is slipped off and left in the solution. If using a plastic spatula, rinse contoured end of plastic spatula in vial of preservative solution by swirling vigorously **ten (10)** times. Leave the spatula in the vial while collecting the endocervical sample. (Step 2.)

It is **most** important that an adequate sample be taken from the squamocolumnar junction, also called the transformation zone. The location of the squamocolumnar junction can be identified by a change in color and texture between the squamous and columnar epithelia. The squamous epithelium appears as pale pink, shiny and smooth. The columnar epithelium appears reddish with a granular surface.

b. TO COLLECT THE SAMPLE FROM THE ENDOCERVIX

- (1) Insert the cytobrush device into the endocervix only until the bottom-most bristles are exposed. Slowly rotate one-fourth to one-half turn in one direction.

Remove brush. **Do not over-rotate. Additional rotation may cause bleeding and contaminate specimen.**

(2) Rinse the cytobrush in the preservative solution while pushing it against the wall of the vial. Break off the cytobrush and leave in the solution.

c. TO CLOSE THE VIAL FOR SHIPPING

Tighten the preservative vial cap so that the **torque line** on the cap **meets** the **torque line** on the vial.

d. **Make sure** that the vial is properly labeled with the patient's name, **last name and first name**. Make sure the name on the **vial matches** the name on the **form**.

7. Special Considerations for Pap Test Collection:

- a. Do not use endocervical brush in pregnant women. Cervical cytology is completed as indicated according to professional guidelines. Standard of care is to use a broom in place of a cytobrush. Otherwise, screening guidelines do not differ for women who are pregnant; however, follow up of abnormal findings may differ according to guidelines (McIntyre-Seltman, K. and Lesnock, J.L., 2008).
- b. For the patient who has had a hysterectomy, use regular tip of plastic spatula to scrape the area of the vaginal cuff. (Refer to page 7 to determine if your patient who has had a hysterectomy should have a screening cervical cytology test (Huh et al., 2015).
- c. Remove excess mucus or other discharge present before taking sample. This should be gently removed with ring forceps holding a folded gauze pad.
- d. Remove inflammatory exudate from the cervical canal before taking the sample. Remove by placing a dry 2x2 piece of gauze over the cervix and peeling it away after it absorbs the exudate or by using a dry proctoswab or scopette.
- e. The cervix should not be cleaned by washing with saline or it may result in a relatively acellular specimen.
- f. The sample should be obtained before the application of acetic acid.
- g. If you also have STD samples to collect, the order of testing is not important and should be based upon the primary purpose for the visit.

8. Packaging and Shipping of Pap Test Samples/Specimens

Refer to reference lab instructions for detailed instructions.

- a. Make sure that preservative vial is labeled with two patient identifiers including the patient's last and first names and preferably date of birth.
- b. Follow lab procedures as specified by your laboratory to make sure all information is provided to the reference laboratory.

- c. Follow packaging and shipping instructions provided by the reference laboratory.

PROCEDURE NOTES

- Have readied a vial of preservative solution labeled with two patient identifiers. Double-check for accuracy.
- Be sure Expiration Date on the preservative solution is current. The laboratory **will not test samples when the expiration date has passed.**
- Do not hold specimens in the lab for extended periods. Ship specimens to the lab frequently to avoid specimen rejection. FDA regulations require that the Pap slide must be prepared within three weeks of collection.
- Improved patient preparation or clinician technique may correct the cause of the unsatisfactory or partially obscured Pap. Refer to your lab for procedure notes.

E. Unsatisfactory Cytological Specimens

Unsatisfactory cytological specimens fall into two categories:

- Unsatisfactory: examined.
 - Unsatisfactory: rejected.
1. The most common reasons for unsatisfactory: examined samples/specimens are:
 - a. Insufficient number of cells.
 - b. Failure to properly rinse collection devices in vial of preservative solution.
 - c. Bloody specimens.
 - d. Inflammation.
 - e. Presence of organisms.
 2. The most common reasons for unsatisfactory or rejected specimens are:
 - a. Vial not labeled with at least two patient identifiers.
 - b. Illegible handwriting or stamped name.
 - c. Name on vial does not match name on form.
 - d. Specimen collected after expiration date of vial.
 - e. Two vials with same patient's name and two forms with two different names.
 - f. Slide breakage or leakage of liquid specimens.
 3. The most common errors in usage of form are:
 - a. Incomplete patient information.
 - b. Failure to indicate patient name change.
 - c. The patient history is incomplete.

- d. There is no return address of provider.
- e. Writing is illegible on form.
- f. The patient's name on the vial and the form do not match.
- g. Two vials are sent with one form.

Divider – 3. Quality Assurance Recommendations

Quality Assurance Recommendations

A. Quality Assurance Recommendations for Cervical Cancer Screening

For a cervical cancer screening to be effective, health care providers need to have systems in place to ensure that any abnormalities detected by clinical pelvic exam or Pap test are appropriately followed up. Notify patients with abnormal test results promptly. Track patients who need additional diagnostic tests or treatment to assure they get proper follow-up care (NBCCEDP, 2017).

Six key steps are necessary for managing the results of cervical cancer screening:

1. Track Pap test and any diagnostic tests until results are obtained.
2. Follow requirements for patient notification. At least three attempts must be made to locate and inform the patient of **abnormal screening results**. The last attempt must be by certified letter. Written documentation of all attempts must be included in the medical record.
3. Document that notification has occurred.
4. Refer patients with any abnormalities on clinical pelvic exam or Pap test for appropriate follow up.
5. Patient Navigation for abnormal test results (NBCCEDP, 2017).
6. Track referrals to make sure that patients have received follow-up.

Tracking systems remind staff to:

- Document all patient contacts.
- See tests and examinations ordered and compare to tests with no results.
- Review patients with incomplete interval follow-ups (monthly, quarterly, etc.).
- Develop procedures and implement evidence-based interventions to overcome patient-related barriers to follow-up, for example telephone or mailing reminders.
- If patients with abnormal results cannot be reached on the first attempt, make at least 3 attempts to locate patient before determining the patient is lost to follow-up.

Each clinic might have a different mechanism for ensuring that all these steps have occurred, but all clinics should have written guidelines, standards, and policies for management of cervical cancer screening. Written policies must be accessible to staff. This manual contains recommendations that should be considered in the development of local policies. Agencies providing Pap screening by Enhanced Role Registered Nurses (ERRNs) must have policies and procedures in place for assuring competency and documentation of competency for each ERRN performing clinical exams. Policies should be reviewed at least annually and revised as needed.

Elements Integral to a Good Follow-Up System

1. **Designation of a responsible person:** The person designated as having responsibility for follow-up of cervical cancer screening should be a nurse or provider who has knowledge of cervical cancer screening programs and familiarity with guidelines regarding follow-up of patients with abnormal Pap test results.
2. **A referral plan:** The referral plan will contain written procedures for referring patients with abnormal findings, including referral resources, the process of referring, and the preparation of eligibility forms, if applicable. All education and counseling protocols should be included, along with a list of educational materials used to assist the patient in understanding the abnormal test result or any additional diagnostic tests that may be done.
3. **A follow up-plan:** The follow up plan will contain written procedures that ensure the patient was referred to a provider, needed services were provided, and results of the referral returned to the agency.
4. **A tracking system:** Clinical management of patients is improved with a tracking system. Tickler files, computerized databases or handwritten logs are common methods of tracking patients. The system alerts staff of patients' status, especially abnormal cervical screening, and provides a simple tool for follow-up. Any tracking system must be checked at predetermined intervals to ensure follow-up is completed. The following is a suggested general process for cervical screening tracking:
 - All cervical cytology tests ordered are logged into a tracking system.
 - When results are received by the agency, the person responsible for follow-up reviews the reports.
 - Patients should be notified of all results including those with no abnormal findings. The report is signed off and stored in the medical record.
 - Results requiring follow-up are reviewed, the patient is notified, and the Patient Navigation process begins. The plan of care is determined based on this manual, local policy, and consultation with the agency medical advisor.
 - When further assistance is needed to determine the plan of care, providers/ agencies may consult NC BCCCP Nurse Consultants or Women's Health Nurse Consultants, depending on which program is appropriate.
 - Medical record documentation will include patient notification, any patient navigation services, plan of care, and all follow-up information.
 - The nurse responsible for patient follow-up enters information in the tracking system and monitors the progress of the patient until follow up is complete.

Internal quality assurance: Periodically (at least annually), chart audits should be performed to ensure all program requirements are being met. Documentation of findings and any corrective actions must be on file (NBCCEDP, 2017).

B. Patient Navigation Recommendations

Patient Navigation: For purposes of the National Breast and Cervical Cancer Early Detection Program (NBCCEDP), Patient Navigation is defined as, “Individualized assistance offered to clients to help overcome health care system barriers and facilitate timely access to quality screening and/or diagnostics as well as initiation of treatment services for women who are diagnosed with cancer” (NBCCEDP, 2017). Patients often face significant barriers to accessing and completing cancer screening and diagnostics. Patient Navigation is a strategy aimed at reducing disparities by assisting patients to overcome these barriers.

Required Patient Navigation Activities - Patient Navigation services vary based on individual patient needs. At a minimum, patient navigation services will include the following activities:

1. A written assessment of the patient’s barriers to cancer screening, diagnostic services, and initiation of cancer treatment.
2. Client education and support.
3. Resolution of client barriers (i.e. transportation, translation services).
4. Client tracking and follow-up to monitor progress in completing screening, diagnostic testing, and initiating cancer treatment.
5. Given the centrality of the patient-navigator relationship, patient navigation must include a minimum of two, but preferably more contacts with the patient.
6. Collection of data to evaluate the primary outcomes of patient navigation: patient adherence to cancer screening, diagnostic testing, and treatment initiation. Patients lost to follow-up should also be tracked.

Priority Populations for Patient Navigation

Navigation is an individual intervention, intensive in nature, and potentially costly. Priority should be given to patients who would not complete the screening or diagnostic process without it. Women who receive navigation should either be enrolled in NBCCEDP programs or have low incomes. Documentation of Patient Navigation must be completed.

Patient Navigation-Only

The North Carolina Division of Health Benefits (DHB) allowed a broader definition of NC BCCCP providers effective October 1, 2020. Women who have been diagnosed with breast or cervical cancer (or a breast or cervical precancerous lesion) outside of NC BCCCP and who meet all other BCCCP eligibility criteria may receive patient navigation-only services through NC BCCCP to apply for BCCM coverage for treatment. This allows BCCCP-eligible women who have completed their screening and diagnostic work-up through an outside provider to receive BCCCP-funded patient navigation-only services to apply for BCCM.

County Departments of Social Services (DSS) in North Carolina can make BCCM coverage retroactive for 90 days from the day a complete application is received by the DSS if patients meet all other NC BCCCP eligibility criteria. Patients will need to sign a BCCCP consent form, the HIPAA Notice of Privacy Practices and records release for records that support the patient's cancer diagnosis. A medical history statement for reason for referral including a clear statement of patient's diagnosis will be required for the patient's medical record and EMR. A Patient Navigation Needs Assessment should be completed. A BCCM application packet consisting of the DMA 5079 and DMA 5081 should be completed and submitted to the DSS in the patient's county of residence and a copy of these forms should be housed in the patient's medical record/ EMR. Data for patients who receive PN-only services should be reported to NC BCCCP via the PN-Only Data Reporting Sheet. Reimbursement for PN-only services will be reported by local health departments via the LHD Monthly Expenditure Report or by contracted providers via the Contract Expenditure Report.

(See Appendix F for NC Breast and Cervical Medicaid).

Terminating Patient Navigation

Depending on screening and diagnostic outcomes, patient navigation services are terminated when a patient (1) completes screening and has a normal result; (2) completes diagnostic testing and has a normal result; or (3) initiates cancer treatment or refuses cancer treatment. When a patient concludes her cancer treatment and has been released by her treating physician to return to a routine screening schedule, patient navigation services resume.

C. Checklist for Laboratory Contract

Methodology

What is the Pap method being provided?

- Liquid based.
- Conventional.

What types of HPV testing are provided?

- High-risk type.
- Types 16 and 18 only.
- Cobas HPV test.

Is reflex HPV testing provided if Pap result is ASC-US? Yes No

What are the dysplasia and ASC-US rates for each method used and the lab's overall rates? _____.

What is the reporting format used?

- Bethesda 2014.
- Other (specify) _____

Cost

What is the current cost per test? _____

How long is the current price guaranteed? _____

How often does the price of testing increase? _____

Are billing invoices clear and correct? Yes No

Service

What is the turnaround time? _____

Is consultation available for reporting and follow-up guidelines? Yes No

Are statistical reports provided with the number of tests submitted, breakdown of results in each reporting and specimen adequacy category, and a report of follow-up of abnormal results? Yes No

Is it easy to contact lab personnel and get answers or resolutions to problems?
 Yes No

Can the status of a specimen be checked, or can a report be downloaded from the Internet? Yes No

Quality

What is the correlation rate of biopsy to Pap report? _____

How many slides are cytotechnologists required to read per day? _____

How many cytotechnologists are employed? Are all cytotechnologists? _____

Average years of experience of cytotechnologist staff? _____

What is the frequency of staff turnover? _____

What is the average number of slides studied per day per cytotechnologist?

Are all slides screened during regular working hours? _____

Is overtime mandatory for cytotechnologists? _____

What percentage of work is screened after hours? _____

Is all work done at one site? _____

What percentage of negative slides is rescreened? _____

Are the cytotechnologists responsible for performing this rescreening in addition to the daily requirement of first screens? _____

What Proficiency Testing Program is used and what has the performance history been for the lab and individual cytotechnologists? _____

What type of competency assessment is done for cytotechnologists? _____

Ask for a copy of the Cytology Laboratory Quality Assessment Plan.

Is an automated screening device used for screening? Yes No

If yes, does a cytotechnologist still review every slide? Yes No

Ask for an organizational chart showing chain of command and certification of each level.

Is an ASCP certified cytotechnologist in charge of the cyto-preparation area?
 Yes No

How many years of experience does this person have? _____

Must these duties be performed in addition to screening slides? Yes No

If so, how many slides per day does this person average? _____

Are any off-label procedures being used in the processing of gynecologic slides?
 Yes No

How many staff pathologists review Pap slides? _____

What percentage of slides received does a pathologist review? _____

Is there any pending litigation concerning Pap reporting? Yes No

Has the lab been involved in prior litigation of any kind related to Pap screening services? _____

Ask for certificates of accreditation (CAP, CLIA, JCAH, etc.) and accreditation inspection reports.

References

Ask for customer references. _____

Using the questions listed above as a guide, are customers satisfied with:

Methodology

Cost

Service

Quality

Divider – 4. Appendices

Divider Appendix - A

A. Critical Value Notification

Critical Value Pap Reports

CLIA requires notification to a nurse of all Pap reports containing critical values. This alerts the submitter that a critical value report has been sent and that its receipt should be tracked to avoid a lost critical value report. The lab must have confirmation that the critical value report was received by the submitter when the notice is left on voicemail. The nurse must call or email the lab to verify receipt of the message and to get the patient's name and the cytodiagnosis.

The lab should be notified if the report is not received within a few days.

The lab issues Critical Value notification for the following Pap reports:

- High-grade intraepithelial lesions (HSIL).
- Cancer.
- Herpes in pregnancy.
- Amended report.

Divider Appendix - B

B. NC BCCCP Cancer Screening Policies

BCCCP Eligibility for Family Planning Patients

NORTH CAROLINA BREAST & CERVICAL CANCER CONTROL PROGRAM (NC BCCCP)

12/1/2020 Effective Immediately

Introduction:

The North Carolina Breast and Cervical Cancer Control Program is legally required to be the payer of last resort for women enrolled in the program. (Public Law 101-354, 42 U.S.C. § 300n [d]). As a result, NC BCCCP is unable to provide screening services that may be provided by the Family Planning (Title X) program.

Impact on local agencies:

Because Family Planning provides a clinical breast exam and Pap test for eligible women, NC BCCCP funds should not be used to pay for these services if the woman is eligible for or enrolled in family planning.

However, Family Planning may not be able to cover all expenses related to a screening cycle. In those cases, NC BCCCP funds may be able to help.

Local BCCCP agencies should develop a policy and standing orders regarding situations in which they will accept a Family Planning patient for diagnostic work up to balance service to women in need with the goal of protecting BCCCP funds for the BCCCP priority population. Policies must be approved by the agencies' BCCCP Nurse Navigators.

Situations in which NC BCCCP may be used to help:

Breast circumstances

- Women ages 50 to 64 may have a screening mammogram and/or diagnostic workup provided through NC BCCCP, using Federal BCCCP funds. These women will count toward Federal service targets. The local agency is eligible to be reimbursed \$325 of Federal funds for these patients.
- Women ages 40 to 49 may have a screening mammogram and/or diagnostic workup provided through NC BCCCP, using State BCCCP funds. These women will count toward State service targets. The local agency is eligible to be reimbursed \$325 of State funds for these patients.
- Women ages 30 to 39 are not eligible for screening through NC BCCCP; however, if women in this age range present with an abnormal clinical breast examination, they

may qualify for a mammogram and/or diagnostic workup through NC BCCCP. These women will count toward NC BCCCP service targets. The local agency is eligible to be reimbursed \$325 for these patients.

- If women ages 21 to 29 present with an abnormal clinical breast examination, they *may* qualify for a BCCCP-funded ultrasound and/or diagnostic workup. These women will count toward NC BCCCP service targets. The local agency is eligible to be reimbursed \$325 for these patients.

Cervical circumstances

- Women ages 21 to 64 who have a Family Planning Pap result of ASC-H, HSIL or worse may have a diagnostic workup provided through NC BCCCP. These women will count toward Federal service targets. The local agency is eligible to be reimbursed \$325 of Federal funds for these patients. Serving these patients through BCCCP may enable them to qualify for Breast and Cervical Cancer Medicaid to pay for treatment if they meet other eligibility requirements and have a diagnosis of CIN 2 or worse.
- Women ages 25 to 64 who have a Family Planning Pap result of persistent ASC-US or LSIL may have a diagnostic workup provided through NC BCCCP. These women will count toward NC BCCCP service targets. The local agency is eligible to be reimbursed \$325 of BCCCP funds for these patients. Serving these patients through BCCCP may enable them to qualify for Breast and Cervical Cancer Medicaid to pay for treatment if they meet other eligibility requirements and have a diagnosis of CIN 2 or worse; however, the likelihood of CIN disease in these patients is relatively low and follow-up for women under the priority age of 40-64 may be more appropriately done with funding other than BCCCP.
- Women ages 21 to 24 who have a Family Planning Pap result of ASC-US or LSIL that progresses to ASC-H, HSIL, or AGC may have a diagnostic workup provided through NC BCCCP. These women will count toward BCCCP service targets. The local agency is eligible to be reimbursed \$325 of BCCCP funds for these patients. Serving these patients through BCCCP may enable them to qualify for Breast and Cervical Cancer Medicaid to pay for treatment if they meet other eligibility requirements and have a diagnosis of CIN 2 or worse. Immediate colposcopy is not appropriate for this youngest population with an ASC-US or LSIL result and no prior history of abnormal Pap results.

Date written: April 8, 2015

Approved by: _____



NC BCCCP Medical Advisor



Date revised: December 1, 2020

NC BCCCP Program Director

NORTH CAROLINA BREAST & CERVICAL CANCER CONTROL PROGRAM

(NC BCCCP)

CERVICAL CANCER SCREENING POLICY

Effective July 16, 2020

INTRODUCTION:

Cervical cancer incidence and mortality is low, but it remains a problem in the U.S.

From 2012 to 2016, the incidence rate was 7.6 per 100,000. The mortality rate was 2.3 per 100,000 from years 2013 through 2017 (CDC State Cancer Profiles). ACS projects an estimated 13,800 new cases in the U.S. for 2020 (ACS Cancer Facts & Figures 2020). The North Carolina Central Cancer Registry estimates 406 cases and 129 deaths in NC for 2020 (North Carolina State Center for Health Statistics Cancer Projections 2020). Incidence and mortality for African American women remains higher than for white women. Early detection leads to nearly 100% survival with timely and adequate treatment.

In August 2018, new joint screening guidelines were released by three major organizations:

- United States Preventive Services Task Force (USPSTF).
- American Cancer Society (ACS).
- American College of Obstetricians and Gynecologist (ACOG).

The National Breast and Cervical Cancer Early Detection Program (NBCCEDP) adopted the new guidelines on August 24, 2018.

The 2019 revised ASCCP risk-based management consensus guidelines were published in early 2020. These new guidelines allow for more frequent surveillance, colposcopy and treatment that is recommended for patients who are at progressively higher risk. The guidelines also allow for those patients at a lower risk to be deferred for colposcopy and undergo follow-up at longer surveillance intervals and when at a sufficiently low risk, can return to routine screening. The 2019 risk-based guidelines replace all previous guidelines. The risk threshold tables can be accessed at <http://www.asccp.org>. To facilitate use of the tables, the information will be accessible via smartphone app available for purchase through the website.

This policy for the North Carolina Breast and Cervical Cancer Control Program (NC BCCCP) repeats NBCCEDP guidance.

ELIGIBLE WOMEN:

NC BCCCP reimburses for cervical cancer screening and diagnostic services provided to women ages 21 to 64, who are at or below 250% of the current federal poverty level and have no other source of health care reimbursement such as medical insurance.

- Women ages 21 to 64 may be screened using state or federal NC BCCCP dollars. The priority population includes women who have never been screened (defined by CDC as not screened in 10 years or more). Recruitment efforts should be concentrated on the priority population.
- Women covered by Medicare-Part B and/or Medicaid are not eligible to enroll in NC BCCCP. Women covered by Title X (Family Planning) are not eligible to have cervical cytology reimbursed using NC BCCCP funds.
- Eligible women may enroll in NC BCCCP for diagnostic work-up of abnormal screening results obtained by providers outside of NC BCCCP.

NC BCCCP CERVICAL SCREENING SERVICES PRIORITIES:

Increasing Screening for NC BCCCP-Eligible Women Who Have Never Been Screened:

At least 20% of all NC BCCCP cervical screening tests must be for women who have not been screened for at least 10 years.

Cervical Cancer Screening for Average-Risk Women Ages 21 to 64:

For average-risk women ages 21 to 29 years, NC BCCCP will cover cervical cytology alone every three years.

For average-risk women ages 30 to 64 years, NC BCCCP funds will cover **one** of these:

- Cervical cytology alone every 3 years.
- High Risk Human papillomavirus (hrHPV) test alone every 5 years.
- Co-testing with the combination of cervical cytology and hrHPV testing every 5 years.

Women should discuss with their clinician which strategy is right for them.

Screening for women younger than 21 years is not covered.

Cervical Cancer Screening for High-Risk Women Ages 21 to 64:

Women who are at high risk for cervical cancer need to be screened more often.

NBCCEDP defines high risk as those who have or had:

- HIV infection.
- Organ transplantation.
- Another condition that causes them to be immunocompromised.
- In-utero exposure to diethylstilbestrol or DES.
- A history of cervical cancer or pre-cancer.

For high-risk women ages 21 to 29, NC BCCCP will cover cervical cytology alone every year and hrHPV testing per 2019 ASCCP Guidelines (ASCCP Consensus Risk-based Management Guidelines April 2020).

For high-risk women ages 30 to 64, NC BCCCP funds will cover **one** of these:

- Cervical cytology alone every year.
- Co-testing with the combination of cervical cytology and HPV testing every 3 years.

NC BCCCP does not cover cervical cancer screening for women under age 21.

Cervical Cancer Screening for Women Over 64 Years of Age:

Cervical cancer screening is not recommended for women once they reach age 65 if they have had adequate screening and are not at high risk. NC BCCCP eligibility continues only through age 64 for most women.

At age 65 most women are eligible for Medicare, which covers extended screening for certain high-risk women. If an eligible woman over 64 is not enrolled in Medicare, she should be encouraged to enroll. Women enrolled in Medicare Part B are not eligible for NC BCCCP clinical services.

Women who are not eligible for Medicare Part B or who cannot afford the premium may receive NC BCCCP services if they are income eligible.

Cervical Cancer Screening Following Hysterectomy or Other Treatment for Cervical Neoplasia or Cancer:

NC BCCCP does not cover cervical cancer screening after total hysterectomy unless it was performed for treatment of cervical cancer or pre-cancer.

NC BCCCP may serve a woman who remains eligible after cervical cancer treatment is completed and she has returned to routine screening.

A woman with a *history of cervical neoplasia or in situ disease* may have one of these for 20 years after treatment, even if it extends past age 65:

- Cervical cytology alone every year.
- Co-testing with the combination of cervical cytology and hrHPV testing every 3 years.

A woman with a *history of invasive cervical cancer* may have one of these indefinitely as long as she is in good health:

- Cervical cytology alone every year.
- Co-testing with the combination of cervical cytology and hrHPV testing every 3 years.

A woman with a total hysterectomy for *unknown reasons* may be screened until there is a 10-year history of negative screening results.

If it is *unknown if a patient's cervix was removed*, NC BCCCP can cover a one-time exam to determine if the patient's cervix is present. NC BCCCP does not cover additional pelvic exams in the absence of cervical cytology.

Women who have had a *supracervical hysterectomy* remain eligible for NC BCCCP cervical cancer screening.

MANAGING WOMEN WITH ABNORMAL CERVICAL CANCER SCREENING RESULTS

The standard of care for management of women with abnormal cervical cancer screening results is found in:

The Cervical Screening Manual: A Guide for Health Departments and Providers (2020)

Covered diagnostic services for follow-up of an abnormal cervical cancer screening test include:

- Colposcopy.
- Colposcopy-directed biopsy.
- Endocervical curettage.
- Certain pre-approved procedures in unusual cases.

Diagnostic excisional procedures **must be pre-approved** by a NC BCCCP nurse consultant. These include:

- Loop Electrode Excision Procedure (LEEP).
- Cold-knife excisions.
- Endometrial biopsies.
- Pathology associated with diagnostic procedures.

REIMBURSEMENT OF HPV DNA TESTING:

High-risk HPV DNA testing is allowed for co-testing, primary HPV testing, and triage of ASC-US cervical cytology results. Providers should specify the high-risk HPV DNA panel. Reimbursement for a low-risk HPV DNA panel is not permitted.

REIMBURSEMENT OF OTHER SERVICES:

NC BCCCP **may not pay for any treatment services.**

NC BCCCP funds may not pay for diagnostic services not included on the NC BCCCP services fee schedule *unless pre-approved*.

NC BCCCP may only pay for repeat cervical screening with colposcopy *if it has been more than four months* since the initial screening.

Date revised July 16, 2020

Approved by: _____



NC BCCCP Medical Advisor



NC BCCCP Program Director

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Divider Appendix - C

Procedure for Referral, Evaluation and Treatment

1. Procedure for Referring Patients

Referral/Eligibility Requirements

Definition

Qualified Health Care Providers (QHCPs) provide outpatient services for the evaluation of an abnormal Pap test via colposcopy, and for the treatment of local cervical lesions via cryosurgery, laser conization, electrocautery or LEEP, or cold knife conization (CKC). They may also provide outpatient services for evaluation and treatment of non-cervical gynecologic dysplasia (vaginal and vulvar lesions) identified by physical examination, cytology, or biopsy (NC BCCCP, 2018-19).

A. Procedure

1. Health care provider (i.e., local health care provider agency) referral to a QHCP
 - a. Referral is made to the QHCP for those patients with a Pap test result that is:
 - (1) Second consecutive Pap test reported as Atypical Squamous Cells of Undetermined Significance (ASC-US); or
 - (2) Single Pap test reported as Atypical Squamous Cells of Undetermined Significance (ASC-US) and a positive test for high-risk HPV DNA; or
 - (3) Single Pap test reported as Atypical Squamous Cells: Cannot Exclude High-grade Squamous Intraepithelial Lesion (ASC-H); or
 - (4) Single Pap test reported as Atypical Glandular Cells (AGC); or
 - (5) Single Pap test reported as Low-grade Squamous Intraepithelial Lesion (LSIL); or
 - (6) Single Pap test reported as High-grade Squamous Intraepithelial Lesion (HSIL) or Carcinoma.
 - b. Referral is made to the QHCP for those patients with lesions of the vagina or vulva identified during physical exam that are suspicious for dysplasia or malignancy. (NOTE: if you notice any lesions that appear chancroid or suggestive of syphilis, please refer the patient immediately to STD services.)
 - c. Each patient has the right to choose to be referred to a QHCP who can provide a colposcopic examination.

- d. Each patient served by a QHCP is expected to pay for services through medical insurance, Medicaid, or self-pay. Limited diagnostic services for eligible patients may be paid by North Carolina's Breast and Cervical Cancer Control Program (NCBCCCP, 2018- 19).
 - e. Referrals are made by the health care provider via telephone to the QHCP near the patient's residence or of the patient's choice.
2. Track and document the outcome of your referral.
 3. Document the results in the patient's medical record and complete the Patient Navigation documentation per format (NBCCEDP, 2017).

B. Patient Education

The patient should be given instructions along with counseling when the appointment is made for the QHCP. The following points should be stressed prior to appointment:

1. Do not douche, use intravaginal medications or tampons, lubricants, have intercourse, or use vaginal contraceptives for at least 48-72 hours prior to appointment.
2. When scheduling the appointment, suggest that the patient select a day not likely to be during her menstrual period.
3. Determine if patient has transportation needs and/or other barriers and assist in facilitating transportation or removing other barriers if necessary. Complete Patient Navigation assessment and care plan if applicable. See page 64 for Patient Navigation policy (NBCCEDP, 2017).

Divider Appendix - D

Glossary of Terms

CIN 2+: this term includes CIN 2, CIN 3, AIS, and cancer.

CIN 3+: this term includes CIN 3, AIS, and cancer.

Clinical Action Threshold: this term refers to risk levels that prompt different clinical management strategies. For example, an immediate CIN 3+ risk of 4% is the Clinical Action Threshold for colposcopy; risks below this threshold undergo surveillance, whereas risks above this threshold, but below the expedited treatment threshold, undergo colposcopy.

Colposcopy Standards: this term refers to the ASCCP Colposcopy Standards that provide evidence-based recommendations for the practice of colposcopy.

Co-testing: this term refers to screening or surveillance performed with both cytology and HPV testing.

Expedited treatment: this term means treatment without confirmatory colposcopic biopsy (*e.g.*, see and treat).

Excisional treatment: this term includes procedures that remove the transformation zone and produce a specimen for histologic analysis, such as loop electrosurgical excision procedure (LEEP), laser cone biopsy, large loop excision of the transformation zone (LLETZ), and cold knife conization.

HPV: this term refers to human papillomavirus. Within this text, HPV refers specifically to high-risk HPV as defined by IARC, including the 12 types that are considered class 1 carcinogens, plus type 68 which is considered a class 2A carcinogen (*i.e.*, HPV types 16, 18, 31, 33, 35, 39, 45, 51, 52, 56, 58, 59, and 68).

HPV-based testing: this term is used in this document to describe the use of either co-testing or primary HPV screening for surveillance after abnormalities. It does not apply to reflex HPV testing for triage of ASC-US cytology in this document. *The HPV testing and positive HPV results discussed throughout this document refer to high-risk HPV types only.*

Lower Anogenital Squamous Terminology (LAST): this term refers to 2-tiered pathology criteria for evaluating histologic specimens obtained via colposcopic biopsy.

NILM: Negative for intraepithelial lesion or malignancy.

ASC-US: Atypical Squamous Cells: Undetermined Significance.

ASC-H: Atypical Squamous Cells: Cannot exclude High-grade Squamous Intraepithelial Lesion.

LSIL: Low-grade squamous intraepithelial lesion; mild dysplasia.

HSIL: High-grade squamous intraepithelial lesion; Moderate to severe dysplasia to carcinoma in-situ.

CIS: Carcinoma in situ; early stage of cancer; Stage 0.

SCC: Squamous Cell Carcinoma; strongly suspicious of malignancy.

AGC: Atypical glandular cells; includes adenocarcinoma in situ and adenocarcinoma.

Primary HPV testing: testing with HPV testing alone as a screening or surveillance test.

Reflex testing: this means that laboratories should perform a specific additional triage test in the setting of a positive screening test to inform the next steps in management. For example, an ASC-US cytology should trigger a reflex HPV test. New for these guidelines, a positive primary HPV screening test should trigger both a reflex genotyping test (to determine the presence/absence of HPV 16/18 if that information is not included in the initial primary test result) and also a reflex cytology test to determine whether the patient would be a candidate for expedited management.

Surveillance: this term refers to repeat testing (HPV primary screening, co-testing, or cytology alone) that occurs at shorter intervals than those recommended for routine screening. For example, HPV primary testing or co-testing at intervals of less than 5 years, or cytology alone at intervals of less than 3 years.

Divider Appendix - E

NC Breast and Cervical Cancer Medicaid

If a patient is diagnosed with a breast or cervical cancer or precancerous lesion while enrolled in NC BCCCP, the patient may apply for Breast and Cervical Cancer Medicaid (BCCM) for cancer treatment. Patients diagnosed outside of NC BCCCP who meet all of the NC BCCCP eligibility criteria may be referred to a NC BCCCP provider to receive patient navigation services to assist with the BCCM application.

Patient Navigation-Only

The North Carolina Division of Health Benefits (DHB) allowed a broader definition of NC BCCCP providers effective October 1, 2020. Women who have been diagnosed with breast or cervical cancer (or a breast or cervical precancerous lesion) outside of NC BCCCP and who meet all of the NC BCCCP eligibility criteria may receive patient navigation-only services through NC BCCCP to apply for BCCM coverage for treatment. This allows women who have completed their screening and diagnostic work-up through an outside provider to receive BCCCP-funded patient navigation-only services to apply for BCCM.

County Departments of Social Services (DSS) in North Carolina can make BCCM coverage retroactive for 90 days from the day a complete application is received by the DSS. Patients will need to sign a BCCCP consent form, the HIPAA Notice of Privacy Practices and records release for records that support the patient's cancer diagnosis. A medical history statement for reason for referral including a clear statement of patient's diagnosis will be required for the patient's medical record and EMR. A Patient Navigation Needs Assessment should be completed. A BCCM application packet consisting of the DMA 5079 and DMA 5081 should be completed and submitted to the DSS in the patient's county of residence and a copy of these forms should be housed in the patient's medical record/ EMR. Data for patients who receive PN-only services should be reported to NC BCCCP via the PN-Only Data Reporting Sheet. Reimbursement for PN-only services will be reported by local health departments via the LHD Monthly Expenditure Report or by contracted providers via the Contract Expenditure Report.

North Carolina Breast and Cervical Cancer Control Program (NC BCCCP)

Breast and Cervical Cancer Medicaid (BCCM)

Do you have patients who would benefit from BCCM to pay for their breast and/or cervical cancer treatment?

Women must FIRST be eligible for NC BCCCP:

Eligibility criteria include:

- ◆ Women with income at or below 250% of the Federal Poverty Level, who are uninsured or underinsured, and who are not covered by Medicare Part B or another federally-funded program*
- ◆ Patients must be referred to the local NC BCCCP to apply for BCCM

NC BCCCP services include:

- ◆ Screening for breast and/or cervical cancer and/or
- ◆ Diagnostic work-up for abnormal findings and/or
- ◆ Assistance with application for BCCM



Physicians Be Aware: It is preferable that a patient be referred and enrolled in BCCCP prior to being diagnosed with breast or cervical cancer.

*Women with Be Smart Family Planning Medicaid may be eligible for some limited services through NC BCCCP.

For more information, contact NC BCCCP
at (919) 707-5300 or visit
<https://bcccp.ncdhhs.gov/BCCM.htm>


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Divider Appendix - F

Frequently Asked Questions

1. How do I advise patients who are due for screening but are leery of unnecessary exposure to COVID-19? How much leeway do we have?

Answer: Routine screening can be postponed until the restrictions for the public health emergency have been loosened in your community and the client is comfortable being seen in-person. Depending on the client's age and prior history, a 6-month to 12-month postponement is reasonable. ASCCP has developed specific guidelines for females who were screened before or during the public health emergency and who have *abnormal* test results.

In response to the current COVID-19 pandemic, and in settings where all non-essential medical office visits and elective procedures have been suspended, ASCCP recommends the following guidelines:

- Individuals with low-grade cervical cancer screening tests may have a postponement of diagnostic evaluations up to 6 to 12 months.
- Individuals with high-grade cervical cancer screening tests should have documented attempts to contact the patient and to schedule diagnostic evaluation within 3 months.
- Individuals with high-grade cervical disease without suspected invasive diseases should have documented attempts to contact and procedures scheduled within 3 months.
- Individuals with suspected invasive disease should have contact attempted within 2 weeks and evaluation within 2 weeks of that contact (4 weeks from the initial report or referral) (M. Policar and P. Cason, 2020). See **Recommendations**.

2. Is it recommended for HPV to screen more in high-risk HIV patients? Any difference in screening for HIV positive patients? If there is a difference, where can we find guidance for the HIV positive patient?

Answer: The Panel on Opportunistic Infections in HIV-Infected Adults and Adolescents (2018) recommends that females who are infected with HIV should have age-based cervical cancer screening.

- HIV-positive individuals should begin screening with cytology alone within one year of onset of sexual activity or, if currently sexually active, within the first year after HIV diagnosis, but no later than 21 years of age. Repeating cytology in 6 to 12 months (without HPV testing) is recommended for HIV-infected females younger than 21 years with ASCUS test results.

- If the patient is younger than 30 years of age and the initial cytology screening result is normal, the next cytology screening should be in 12 months. After 3 consecutive normal annual screenings, follow-up should be every 3 years.
- Patients who are 30 years of age and older can be screened with cytology alone or co-testing. Once those screened with cytology alone have had 3 consecutive annual normal test results, or a single negative co-test result, screen every three years (M. Policar and P. Cason, 2020). See [Guidelines](#).

3. How do these new guidelines transfer over to HIV patients with needed follow up?

Answer: See Section K Special Populations of the 2019 ASCCP Risk-based Management Consensus Guidelines [ASCCP Risk-based Consensus Guidelines](#) (Perkins, et.al, 2020, p.124- 125) for important management recommendations for patients with immunosuppression, including those who are HIV positive. This patient information can be entered into the app and tool at the ASCCP website.

- In immunocompromised patients of any age, colposcopy referral is recommended for all cytology results of HPV-positive ASCUS or higher.
- If HPV testing is not performed on ASCUS results, then repeat cytology in 6 to 12 months is recommended, with colposcopy referral for ASCUS or higher.
- For any result of ASCUS or higher on repeat cytology or if HPV positive, referral to colposcopy is recommended.
- For all cytology results of LSIL or worse (including ASC-H, AGC, AIS and HSIL), referral to colposcopy is recommended regardless of HPV test results if done.

4. Do we need to screen pregnant women? Can't we wait until they are postpartum?

Answer: The screening intervals contained in the USPSTF recommendations apply equally to pregnant and non-pregnant females. For example, if a 32-year-old client seen for an initial prenatal visit had a negative screening 2 years ago by cytology-alone, hrHPV-alone, or co-test, she should not have cervical cancer screening at this visit. Re-screening after her delivery should occur only when 3 years have passed since her last cytology test or 5 years from her last hrHPV-alone or co-test.

There are no reasons to routinely screen pregnant females for cervical cancer, either prenatally or post-partum, simply because they are pregnant (M. Policar and P. Cason, 2020).

5. Are there any changes in collection technique?

Answer: There are no changes in technique but it is recommended reviewing the techniques because many clinicians were not trained initially in such a manner to maximize the likelihood of submitting adequate cellular material to allow for both cytology and HPV testing as needed (M. Policar and P. Cason, 2020).

6. What does the future hold for rectal cytology with the routine (cervical) cytology test?

Answer: There are no guidelines for this rectal cytology yet. In order to have a screening program (any screening - but this applies to anal CA), we need to know the following:

- The best way to screen and have clinicians training in screening.
- Have data showing that screening impacts disease.
- Know what to do with screening results.
- Have the manpower/capacity to manage abnormal results (clinicians trained in high resolution anoscopy (HRA)).
- Have sufficient data suggesting that use of HRA and treatments impacts disease.

We have none of these things in place currently. Hopefully in the future we can.

7. How do you advise a patient who is asking about her boyfriend who may be positive regarding his plan of treatment?

Answer: There is currently no recommended testing or treatment for male partners of patients testing positive for HPV (M. Policar and P. Cason, 2020).

8. When will the screening guidelines be updated to reflect the preference for HPV as primary screening?

Answer: Either co-testing or primary HPV screening are both HPV-based screening. On July 20, 2020, the American Cancer Society (ACS) published a new screening guideline entitled *Cervical cancer screening for individuals at average risk: 2020 guideline update from the American Cancer Society* (ACS 2020). See [ACS Updated Cervical Guidelines](#).

These new screening recommendations differ in 4 important ways compared with the 2012 ACS recommendations:

- The preferred screening strategy is primary HPV testing every 5 years, with co-testing and cytology alone acceptable where access to US FDA-approved primary HPV testing is not yet available.
- The recommended age to start screening is 25 years rather than 21 years old.
- Primary HPV testing, as well as co-testing or cytology alone when primary testing is not available, is recommended starting at age 25 rather than age 30; and
- The guideline is transitional, i.e., options for screening with co-testing or cytology alone are provided but should be phased out once full access to primary HPV testing for cervical cancer screening is available (ACS 2020).

At this time, the current cancer screening guidelines of the United States Preventative Services Task Force, ASCCP, and the American College of Obstetricians and Gynecologists (ACOG) have not been modified or updated to match the 2020 guideline update of the American Cancer Society (M. Policar and P. Cason, 2020).

Divider Appendix - G

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