CME

Cervical cancer screening guidelines: An update

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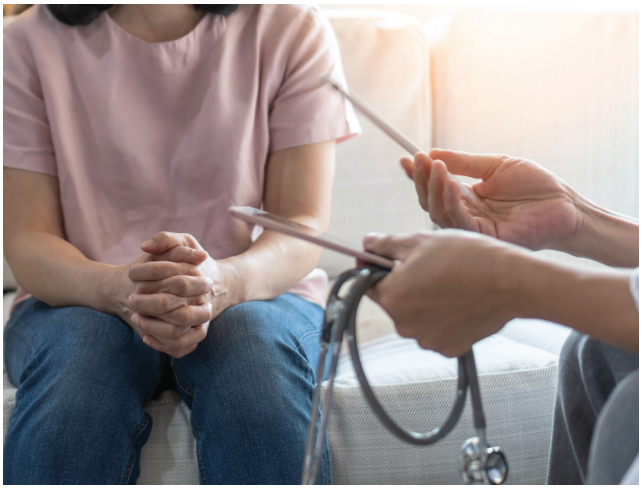
ABSTRACT

Cervical cancer screening practices in the United States have been inefficient, with variable screening rates. Some women are screened too frequently, overmanaged, lost to follow-up, or are at risk and should be screened but are not. Timely screening, identification, and management of abnormal cervical cells is vital in order to prevent progression to cervical cancer. Educating, counseling, screening, and offering the human papillomavirus vaccine continue to be the primary methods of cervical cancer prevention practices. Guidelines and primary screening methods have been updated because of supporting evidence, and clinicians must stay up-to-date in order to provide effective patient care.

Keywords: cervical cancer, guidelines, prevention, screening, American Cancer Society, HPV

Learning objectives

- Recognize the common risk factors for cervical cancer.
- Describe screening recommendations for cervical cancer.
- Outline key factors that aid in cervical cancer prevention.



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Cervical cancer is no longer the leading cause of death for women in the United States, as it was 40 years ago.[1] The number of deaths and cervical cancer cases have decreased significantly since then, largely due to women and healthcare providers being proactive about regular screening.[1] The primary goal of screening has been to identify precancerous cells before they transform into invasive cancer.[2] About 90% of cervical cancers occur in low- to middle-income countries, which lack resources, education, programs, and screening modalities.[3] In recent US statistics, Black and Hispanic women have the highest cervical cancer incidence, with Black women having the highest mortality.[4]

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All women are at risk for cervical cancer, especially those over age 30 years.[5] Factors that increase the risk of cervical cancer include:

- Sexually transmitted infections (STIs) such as human papillomavirus (HPV), chlamydia trachomatis, HIV, and herpes simplex virus.
- Multiple sexual partners
- Sexually active at age 15 years or younger
- Not using condoms
- Increased parity
- Using oral contraceptives
- Cigarette smoking
- Obesity
- Poor nutrition and diet
- Immunosuppression.[5]

HPV is the most important risk for cervical cancer, with more than 150 strains of the virus known to date. Most cases of cervical cancer are linked to high-risk HPV strains, primarily strains 16 and 18, which are all sexually transmitted.[6] High-risk HPV strains not only cause cervical cancer, but pose a risk for cancers such as anal, vulvar, vaginal, penile, oropharyngeal, head, and neck.[6]

Cervical cancer is highly preventable because screening tests and vaccines are available; if cancer is detected early, it is highly treatable with long survival prognosis and good quality of life.[7] However, annual cervical cancer screening is no longer recommended for patients at average risk.[8,9]

Key points

- Guidelines for cervical cancer screening have changed as researchers gain a better understanding of the disease progression.
- Clinicians must understand the new guidelines for cervical cancer screening.
- Encouraging patients to obtain the HPV vaccination and educating them about its importance is a vital part of cervical cancer prevention.

By being aware of screening guidelines, specifically who and when to screen, clinicians can help keep the rates of cervical cancer low.

WHY THE GUIDELINES HAVE CHANGED

Guidelines for cervical cancer screening have changed as researchers gain a better understanding of the disease progression, as well as the strong evidence linking HPV and cervical cancer.[8] Previously, guidelines from the American Cancer Society either suggested screening for cervical cancer at the onset of sexual intercourse, annually, and/or at least by age 18 or 20 years.[8] Cervical cancer is uncommon in women younger than age 21 years; even with exposure to HPV, progression to cervical cancer can take decades, and these young patients have a high chance of clearing the virus.[8,9] Testing patients younger than age 21 years, or screening patients more frequently than recommended, means that transient HPV infections will show up on screening tests, resulting in further unnecessary testing as well as financial and emotional burdens.[10] Unnecessary testing and procedures have more harms than benefits, such as adverse pregnancy outcomes for those undergoing unnecessary excisional procedures before pregnancy.[9]

The American Cancer Society (ACS) recently updated its guidelines to focus on using HPV testing alone for cervical cancer screening.[11] Although HPV testing has been available for many years, studies were limited, and using it solely without the Pap smear is now an emerging screening protocol.[11-13] The ACS evaluated data across various age groups in relation to the prevalence and incidence of HPV infection, as well as invasive disease and cervical cancer. From this, the ACS made a strong recommendation to begin cervical cancer screening at age 25 years because of the low cervical cancer incidence and mortality among younger patients, the high incidence of transient infections, and benefits outweighing the harms.[8,11]

Screening recommendations by ACS, the US Preventive Services Task Force (USPSTF), American College of Obstetricians and Gynecologists (ACOG), American Academy of Family Practice (AAFP), and American Society of Colposcopy and Clinical Pathology (ASCCP) are summarized in **Table 1**. These organizations generally agree on the recommended patient age to start screening (21 years), screening frequency, and age to discontinue screening, regardless of the patient's age at initiation of sexual activity.

TABLE 1. Cervical cancer screening recommendations[8,11-15]

Primary HPV testing refers to HPV testing alone, an FDA-approved test for cervical cancer screening, and specifically high-risk strains.

USPSTF
- Ages 21 to 65 years, Pap test only every 3 years
- Ages 30 to 65 years, add primary HPV testing every 5 years

OR

- Ages 30 to 65 years, Pap plus HPV (co-testing) every 5 years

ACS
- Ages 25 to 65 years, primary HPV testing every 5 years

OR

- Ages 25 to 65 years, Pap test only every 3 years

OR

- Ages 25 to 65 years, Pap plus HPV (co-testing) every 5 years

AAFP
- Ages 21 to 65 years, Pap test only every 3 years
- Ages 30 to 65 years, primary HPV testing only every 5 years

OR

- Ages 30 to 65 years, Pap plus HPV (co-testing) every 5 years

ACOG
- Ages 21 to 65 years, Pap test only every 3 years
- Ages 30 to 65 years, Pap plus HPV (co-testing) every 5 years

ASCCP
- Ages 21 to 65 years, Pap test only every 3 years
- Ages 30 to 65 years, Pap plus HPV (co-testing) every 5 years

The five cancer screening organizations agree to discontinue screening after age 65 years in patients who have had adequate previous screening, specifically 10 years of negative results, and are not otherwise at high risk for cervical cancer.[8,11-17] Patients who have had a hysterectomy including cervix removal, in addition to no history of a high-grade cervical precancerous lesion or cervical cancer, do not need to be screened.[16,17]

These guidelines and recommendations are for patients considered average-risk, with normal cytology and HPV results. Patients who are considered high-risk, including those who have had previous abnormal cytology and/or HPV results, and/or are immunosuppressed, will have more frequent recommended testing and follow-up.

CURRENT SCREENING METHODS

Screening for cervical cancer should begin with a thorough history that primarily focuses on the patient's social and sexual history. Ask when the patient last had a cervical cancer screening and what the results were; cervical cancer

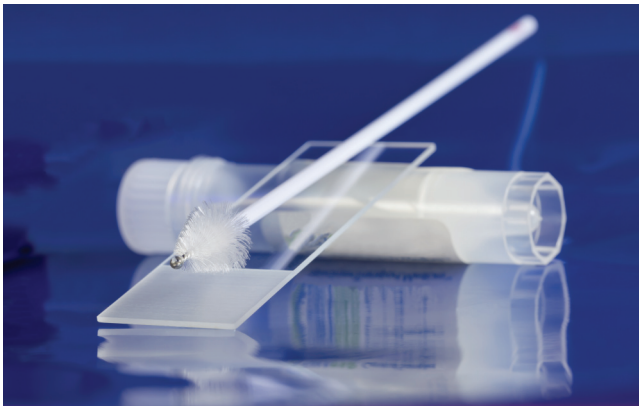

FIGURE 1. HPV testing equipment

can be asymptomatic in the early stages. Symptoms such as abnormal vaginal bleeding (intermenstrual and/or postcoital) and abnormal vaginal discharge may suggest late stages; pelvic invasion may present with lower limb swelling, flank pain, or sciatica.[3]

Current cervical cancer screening methods include cytology (Papanicolaou or Pap) testing, primary HPV testing (HPV alone), co-testing (Pap and HPV), and/or reflex testing (cytology or HPV). Depending on the various organization recommendations, a cytology test alone typically is recommended every 3 years for patients ages 21 to 65 years.[13,18] If a cytology test result is abnormal, reflex HPV testing with a focus on high-risk strains may be performed to indicate whether the abnormal cytology results were caused by an HPV strain.[13,18] The sole use of HPV testing has been gaining popularity, primarily in women age 25 years and older, due to its high sensitivity for detecting precancers and predicting future risk; this test is even considered superior to cytology alone.[11,13,18]

If the HPV results are positive, reflex cytology testing may be performed to evaluate the severity of abnormality at the cellular level.[17] As women age, the risk of cervical cancer increases, with the average age at diagnosis being 50 years, and the most frequent time of diagnosis between ages 35 and 44 years.[17] Performing HPV testing, whether alone or as a co-test, primarily for the age groups that are at most risk, will identify persistent high-risk HPV infections earlier.[18] Traditionally, co-testing with cytology and HPV have been used every 5 years for all women ages 30 to 65 years.[18]

ABNORMAL SCREENING CYTOLOGY RESULTS

Atypical glandular cells (AGC) This result raises the concern for the presence of precancer or cancer. Glandular cells usually are found in a layer that covers the inner canal of the cervix, as well as inside the uterus.

Atypical squamous cells, cannot exclude HSIL (ASC-H) This result indicates that changes have been found in the cervical cells, raising the concern for the presence of a high-grade squamous intraepithelial lesion (HSIL).

HSIL This result is more likely to be associated with precancer and cancer, and suggests more serious cervical cellular changes than the low-grade squamous intraepithelial lesion (LSIL).

LSIL This result indicates cervical cells that show mildly abnormal changes. These changes typically are caused by an HPV infection that may resolve on its own in a healthy patient.

Atypical squamous cells of undetermined significance (ASC-US) This result indicates changes in cervical cells that are almost always a sign of an HPV infection. These changes, with an HPV-negative result, can be due to inflammation or a vaginal infection. ASC-US is the most common abnormal Pap test result and typically resolves on its own within 2 years in a healthy patient.[19]

ADDITIONAL TESTING AND TREATMENT

Because cervical cancer screening can be performed by clinicians in many specialties, clinicians must be able to explain to their patients what the next steps or options entail, especially for patients with abnormal results. Typically, patients with abnormal Pap smear results are referred to women's health for further treatment and discussion.

Follow-up and screening intervals vary depending on the results, patient age, and risk factors. The ASCCP website and guidelines application provide appropriate guidance through algorithms based on the results and patient age.[20] Patients with abnormal cervical cancer screening results may be advised to repeat testing as early as 1 year, or to undergo a confirmatory procedure called a colposcopy.[21] A colposcopy can be performed in an outpatient office setting without anesthesia while the patient is awake and alert. Using a colposcope, the clinician can get a closer look at the cervix and obtain biopsy tissue samples to identify abnormal cells on the cervix.[21]

Based on the results of the biopsy, the patient's previous history, as well as the patient's desire to conceive, some patients may be advised to have treatments such as cold knife conization, cryotherapy, laser therapy, and/or loop electrosurgical excision procedure, all of which remove or destroy abnormal tissue.[22]

PREVENTION

Counseling and educating patients about cervical cancer screening is important to help patients adhere to screening recommendations. Even if patients have never had an abnormal result, talk to them about factors such as abstinence, condom use, HPV vaccination, maintaining a healthy immune system (no smoking, drinking, or illicit drug use), and the importance of following up for routine screenings.[13] Although sexually active women frequently become exposed and infected with HPV, having a strong immune system can assist in clearing the HPV infection, particularly for women under age 30 years.[8,13]

Advise patients about the Gardasil-9 vaccine, the only HPV vaccine distributed in the United States, which protects against nine of the most concerning cancer-causing strains of HPV.[23] These strains are associated with cervical, anal, penile, vaginal, vulvar, oropharyngeal, head, and neck cancers.[13,23,24] Gardasil-9 is approved for males and females ages 9 through 45 years, and is most effective in patients ages 9 to 26 years.[24] Although benefits for patients ages 27 to 45 years are reduced, increasing the number of vaccinated patients can generate herd immunity.[22,24]

CONCLUSION

Clinicians working in various specialties must be aware of current guidelines and recommendations for cervical cancer screening in order to keep patients educated and informed. Although many organizations publish cervical cancer screening recommendations, most agree on the patient age to begin and discontinue screening, as well as methods and intervals for screening.

Although keeping patients on schedule can be challenging, take steps to ensure that patients are well informed through a reminder system using phone calls, letters, emails, or text messages.[25] Inquiring about patients' screening history, as well as vaccination history can be life-changing. If a patient's cervical cancer screening is not up-to-date, or there are gaps, discuss the importance of screening, screen, and refer as necessary, even if the patient reports sexual abstinence. Encourage patients to obtain the HPV vaccination and educate them about its importance. By identifying patients with risk factors, as well as raising awareness, clinicians can help reduce the rate of cervical cancer.[26] **JAAPA**

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