BONUS DIGITAL CONTENT

U.S. Preventive Services Task Force

Screening for Cervical Cancer: Recommendation Statement

Summary of Recommendations and Evidence

The USPSTF recommends screening for cervical cancer every 3 years with cervical cytology alone in women aged 21 to 29 years. For women aged 30 to 65 years, the USPSTF recommends screening every 3 years with cervical cytology alone, every 5 years with high-risk human papillomavirus (hrHPV) testing alone, or every 5 years with hrHPV testing in combination with cytology (cotesting) *(Table 1)*. **A recommendation.**

See the Clinical Considerations section for the relative benefits and harms of alternative screening strategies for women 21 years or older.

The USPSTF recommends against 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. **D recommendation.**

See the Clinical Considerations section for discussion of adequate prior screening and risk factors that support screening after age 65 years.

The USPSTF recommends against screening for cervical cancer in women younger than 21 years. **D recommendation.**

The 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 grade 2 or 3) or cervical cancer. **D recommendation.**

The first 3 recommendations apply to individuals who have a cervix, regardless of their sexual history or HPV vaccination status. These recommendations do not apply to individuals who have been diagnosed with a high-grade precancerous cervical lesion or cervical cancer. These recommendations also do not apply to individuals with in utero exposure to diethylstilbestrol or those who have a compromised immune system (e.g., women living with human immunodeficiency virus [HIV]).

See related Putting Prevention into Practice on page 253.

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This summary is one in a series excerpted from the Recommendation Statements released by the USPSTF. These statements address preventive health services for use in primary care clinical settings, including screening tests, counseling, and preventive medications.

The complete version of this statement, including supporting scientific evidence, evidence tables, grading system, members of the USPSTF at the time this recommendation was finalized, and references, is available on the USPSTF website at https://www.uspreventiveservicestaskforce.org/.

This series is coordinated by Kenny Lin, MD, MPH, Deputy Editor.

A collection of USPSTF recommendation statements published in *AFP* is available at https://www.aafp.org/afp/uspstf.

Rationale

IMPORTANCE

The number of deaths from cervical cancer in the United States have decreased substantially since the implementation of widespread cervical cancer screening and continue to decline, from 2.8 per 100,000 women in 2000 to 2.3 deaths per 100,000 women in 2015.[1] Most cases of cervical cancer occur among women who have not been adequately screened.[2] Strategies that aim to ensure that all women are appropriately screened and receive adequate follow-up are most likely to succeed in further reducing cervical cancer incidence and mortality in the United States.

DETECTION

The USPSTF found convincing evidence that screening with cervical cytology alone, primary testing for high-risk HPV types (hrHPV testing) alone, or in combination at the same time (cotesting) can detect high-grade precancerous cervical lesions and cervical cancer.

USPSTF ASSESSMENT

The USPSTF concludes with high certainty that the benefits of screening every 3 years with cytology alone in women aged 21 to 29 years substantially outweigh the harms. The USPSTF concludes with high certainty that the benefits of screening every 3 years with cytology alone, every 5 years

TABLE 1

Screening for Cervical Cancer: Clinical Summary of the USPSTF Recommendations

Population	Women aged 21 to 29 years	Women aged 30 to 65 years	Women younger than 21 years, women older than 65 years with adequate prior screening, and women who have had a hysterectomy
Recommendations	Screen for cervical cancer every 3 years with cytology alone. Grade: A	Screen for cervical cancer every 3 years with cytology alone, every 5 years with hrHPV testing alone, or every 5 years with cotesting. Grade: A	Do not screen for cervical cancer. Grade: D
Risk assessment	All women aged 21 to 65 years are at risk for cervical cancer because of potential exposure to hrHPV types through sexual intercourse and should be screened. Certain risk factors further increase risk for cervical cancer, including HIV infection, a compromised immune system, in utero exposure to diethylstilbestrol, and previous treatment of a high-grade precancerous lesion or cervical cancer. Women with these risk factors should receive individualized follow-up.		
Screening tests	Screening with cervical cytology alone, primary testing for hrHPV alone, or both at the same time (cotesting) can detect high-grade precancerous cervical lesions and cervical cancer. Clinicians should focus on ensuring that women receive adequate screening, appropriate evaluation of abnormal results, and indicated treatment, regardless of which screening strategy is used.		
Treatment and interventions	High-grade cervical lesions may be treated with excisional and ablative therapies. Early-stage cervical cancer may be treated with surgery (hysterectomy) or chemotherapy.		

Note: These recommendations apply to individuals who have a cervix, regardless of their sexual history or HPV vaccination status. These recommendations do not apply to individuals who have been diagnosed with a high-grade precancerous cervical lesion or cervical cancer, those with in utero exposure to diethylstilbestrol, or those who have a compromised immune system (e.g., individuals living with HIV).

Note: For a summary of the evidence systematically reviewed in making this recommendation, the full recommendation statement, and supporting documents, go to https://www.uspreventiveservicestaskforce.org/.

HIV = human immunodeficiency virus; hrHPV = high-risk HPV; USPSTF = U.S. Preventive Services Task Force.

with hrHPV testing alone, or in combination in women aged 30 to 65 years outweigh the harms.

The USPSTF concludes with moderate certainty that the benefits of screening in women older than 65 years who have had adequate prior screening and are not otherwise at high risk for cervical cancer do not outweigh the potential harms.

The USPSTF concludes with moderate certainty that the harms of screening in women younger than 21 years outweigh the benefits.

The USPSTF concludes with high certainty that the harms of screening in women who have had a hysterectomy with removal of the cervix for indications other than a high-grade precancerous lesion or cervical cancer outweigh the benefits.

Clinical Considerations

PATIENT POPULATION UNDER CONSIDERATION

This recommendation statement applies to all asymptomatic individuals with a cervix, regardless of their sexual history. This recommendation statement does not apply to women who have been diagnosed with a high-grade precancerous cervical lesion or cervical cancer, women with in utero exposure to diethylstilbestrol, or women who have a compromised immune system (e.g., women living with HIV).

ASSESSMENT OF RISK

High-risk HPV infection is associated with nearly all cases of cervical cancer, and women are exposed to hrHPV through sexual intercourse. Although a large proportion of HPV infections resolve spontaneously, the high likelihood of exposure to hrHPV means that women are at risk for precancerous lesions and cervical cancer.

Certain risk factors increase risk for cervical cancer, including HIV infection, a compromised immune system, in utero exposure to diethylstilbestrol, and previous treatment of a high-grade precancerous lesion or cervical cancer. Women with these risk factors are not included in this recommendation and should receive individualized follow-up. 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 are not at risk for cervical cancer and should not be screened. As part of the clinical evaluation, clinicians should confirm through review of surgical records or direct examination that the cervix was removed.

SCREENING TESTS

Current evidence indicates that there are no clinically important differences between liquid-based cytology and conventional cytology. A variety of platforms are used to detect hrHPV; most use either signal or nucleic acid amplification methods. Published trials of hrHPV testing used in situ hybridization, polymerase chain reaction, and hybrid capture technology to test for HPV strains associated with cervical cancer. hrHPV testing has been used for primary screening, cotesting with cytology, and follow-up testing of positive cytology results (reflex hrHPV).[2]

Screening with cytology alone, hrHPV testing alone, and both in combination offer a reasonable balance between benefits and harms for women aged 30 to 65 years; women in this age group should discuss with their health care professional which testing strategy is best for them. Evidence from randomized clinical trials (RCTs) and decision modeling studies suggest that screening with cytology alone is slightly less sensitive for detecting CIN 2 and CIN 3 than screening with hrHPV testing alone. Although screening with hrHPV testing alone or in combination with cytology detects more cases of CIN 2 and CIN 3, this method results in more diagnostic colposcopies for each case detected.[2-5]

There are a number of different protocols for triage of abnormal results from screening with cytology, hrHPV testing, or cotesting. Clinical trial evidence and modeling suggest that different triage protocols have generally similar detection rates for CIN 2 and CIN 3; however, proceeding directly to diagnostic colposcopy without additional triage leads to a much greater number of colposcopies compared with using other triage protocols. Maintaining comparable benefits and harms of screening with cytology alone or hrHPV testing alone requires that patients, clinicians, and health care organizations adhere to currently recommended protocols for repeat testing, diagnostic colposcopy, and treatment.[6,7]

TIMING OF SCREENING

Women Younger Than 21 Years. Cervical cancer is rare before age 21 years.[8] Exposure of cervical cells to hrHPV during vaginal intercourse may lead to cervical carcinogenesis, but the process has multiple steps, involves regression, and is generally not rapid. Because of the slow progression of disease and the high likelihood of regression in this age group, evidence suggests that screening earlier than age 21 years, regardless of sexual history, would lead to more harm than benefit. Treatment of CIN 2 or CIN 3 among women younger than 21 years may increase risk for adverse pregnancy outcomes.[2,8]

Women Older Than 65 Years. Joint guidelines from the American Cancer Society, American Society for Colposcopy and Cervical Pathology, and American Society for Clinical Pathology (ACS/ASCCP/ASCP) define adequate prior screening as 3 consecutive negative cytology results or 2 consecutive negative cotesting results within 10 years before stopping screening, with the most recent test occurring within 5 years.[6] The guidelines further state that routine screening should continue for at least 20 years after spontaneous regression or appropriate management of a precancerous lesion, even if this extends screening past age 65 years. Once screening has stopped, it should not resume in women older than 65 years, even if they report having a new sexual partner.

Women Older Than 65 Years Who Have Not Been Adequately Screened. Screening may be clinically indicated in older women with an inadequate or unknown screening history. Recent data suggest that one-fourth of women aged 45 to 64 years have not been screened for cervical cancer in the preceding 3 years.[9] In particular, women with limited access to care, women from racial/ethnic minority groups, and women from countries where screening is not available may be less likely to meet criteria for adequate prior screening. Certain considerations may also support screening in women older than 65 years who are otherwise at high risk (i.e., women with a history of high-grade precancerous lesions or cervical cancer, in utero exposure to diethylstilbestrol, or a compromised immune system).[2]

SCREENING INTERVAL

Screening more frequently than every 3 years with cytology alone confers little additional benefit, with a large increase in harms, including additional procedures and assessment and treatment of transient lesions. Treatment of lesions that would otherwise resolve on their own is

harmful because it can lead to procedures with unwanted adverse effects, including the potential for cervical incompetence and preterm labor during pregnancy. Evidence from RCTs, observational studies, and modeling studies suggest that a 5-year screening interval for primary hrHPV testing alone or cotesting offers the best balance of benefits and harms. Screening more frequently than every 5 years with primary hrHPV testing alone or cotesting does not substantially improve benefit but significantly increases the number of screening tests and colposcopies.

TREATMENT

Screening aims to identify high-grade precancerous cervical lesions to prevent progression to cervical cancer. High-grade cervical lesions may be treated with excisional and ablative therapies. Early-stage cervical cancer may be treated with surgery (hysterectomy) or chemotherapy. Treatment of precancerous lesions is less invasive than treatment of cancer.[2]

RACE/ETHNICITY, GEOGRAPHY, AND CERVICAL CANCER

The incidence of and mortality from cervical cancer remain relatively high among certain populations. The overall mortality rate from cervical cancer among African American women is 10.1 deaths per 100,000 women,[10] which is more than twice the rate among white women (when adjusted for hysterectomy rate), although the gap has narrowed over time. Mortality is higher among older African American women. Several studies have found that African American women are screened for cervical cancer at rates similar to those for white women and that inadequate follow-up after screening and differences in treatment may be important contributing factors. The higher mortality rate in African American women may also be attributable, in part, to the higher than average rate of adenocarcinoma, which carries a worse prognosis than the most common type of cervical cancer (squamous cell carcinoma).[10-12]

American Indian/Alaska Native women also have higher rates of cervical cancer mortality (3.2 deaths per 100,000 women) than the U.S. average.[10] Factors driving this higher rate may include lower screening rates (16.5% of American Indian/Alaska Native women in the 2012 Behavioral Risk Factor Surveillance System reported not receiving a Papanicolaou [Pap] test in the past 5 years)[13] and inadequate follow-up.[2] Hispanic women have a significantly higher incidence rate of cervical cancer and slightly higher mortality rate (2.6 deaths per 100,000 women [unadjusted for hysterectomy rate]), with especially high rates occurring along the Texas-Mexico border. Although white women overall have the lowest mortality rate from cervical cancer, white women living in geographically isolated and medically underserved areas (particularly Appalachia) have much higher mortality rates than the U.S. average. Asian women also have lower screening rates, especially those who have recently immigrated to the United States and may have language or cultural barriers to screening.[10]

In addition to race/ethnicity and geography, insurance coverage plays an important role in access to cervical cancer screening; 23.1% of women without health insurance and 25.5% of women with no regular health care clinician reported not receiving a Pap test in the past 5 years, compared with 11.4% of the general population. Insurance status may interact with other demographic factors, such as race/ethnicity and age, to increase disparities.[13] In addition, there are no screening data for women with disabilities and those who identify as lesbian or transgender.[14-16]

Progress in reducing cervical cancer incidence and mortality has been uneven. The most important factors contributing to higher incidence and mortality rates include financial, geographic, and language or cultural barriers to screening; barriers to follow-up; unequal treatment; and difference in cancer types, all of which vary across subpopulations.

ADDITIONAL APPROACHES TO PREVENTION

The Centers for Disease Control and Prevention's Advisory Council on Immunization Practices recommends routine HPV vaccination. A 2-dose schedule is recommended for girls and boys who initiate the vaccination series at ages 9 to 14 years. Three doses are recommended for girls and boys who initiate the vaccination series at ages 15 to 26 years and for those who have a compromised immune system.[17] The overall effect of HPV vaccination on high-grade precancerous cervical lesions and cervical cancer is not yet known. Current trials have not yet provided data on long-term efficacy; therefore, the possibility that vaccination might reduce the need for screening with cytology or hrHPV testing is not established. Given these uncertainties, women who have been

vaccinated should continue to be screened as recommended until further evidence accrues.

USEFUL RESOURCES

The 2012 ACS/ASCCP/ASCP guidelines[6] and 2015 interim guidance from the ASCCP and the Society of Gynecologic Oncology[7] provide algorithms for follow-up of abnormal screening results.

The Centers for Disease Control and Prevention, the National Institutes of Health, and the HIV Medicine Association of the Infectious Diseases Society of America have issued recommendations on screening for and management of cervical cancer in patients living with HIV.[18]

The National Cancer Institute provides strategies for reducing cervical cancer mortality in its report "Excess Cervical Cancer Mortality: A Marker for Low Access to Health Care in Poor Communities."[19]

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The "Other Considerations," "Discussion," "Update of Previous USPSTF Recommendation," and "Recommendations of Others" sections of this recommendation statement are available at https://www.uspreventiveservicestaskforce.org/Page/Document/UpdateSummaryFinal/cervical-cancer-screening2.

The USPSTF recommendations are independent of the U.S. government. They do not represent the views of the Agency for Healthcare Research and Quality, the U.S. Department of Health and Human Services, or the U.S. Public Health Service.

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