REVIEW ARTICLE

CERVICAL CANCER SCREENING: REVIEW OF CURRENT RECOMMENDATIONS

John M. Allen, MS, DO, PGY3[1]; Delaney T. Drew, MPH, MD, PGY1[1]; Maurell L. James, DO, PGY1[1]; Bijal R. Patel, DO, PGY1[1]; Fenny Zen, MS, MD[1]

[1]University Hospitals Community Consortium Geauga Regional Medical Center Family Medicine Residency, Chardon, OH

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ABSTRACT

The annual rate of cervical cancer death has been in slow decline in part due to the broad implementation of screening technology. This annual death rate is also affected by risk factor exposure and discovery of new treatments. While the current rate, 2.2 deaths in 100,000 women, is the lowest recorded, cervical cancer still claimed the lives of over 5000 women last year. Early detection through screening remains central to the fight against cervical cancer. Current cervical cancer screening guidelines are provided and updated by professional organizations including the U.S. Preventive Services Task Force (USPSTF), American College of Obstetricians and Gynecologists (ACOG), Society of Gynecologic Oncology (SGO), American Society for Colposcopy and Cervical Pathology (ASCCP), and American Cancer Society (ACS). As the primary interface between the public and the healthcare system, and as purveyors of preventative medicine, it is the charge of the family physician to be current and well-versed in cervical cancer screening guidelines.

INTRODUCTION

Since being introduced in the late 1940s, the Papanicolaou (Pap) smear has remained the cornerstone of cervical cancer screening[1-3] and has helped to reduce rates of cervical cancer.[4] That being said, testing and prevention methods have become more sophisticated over time leading to a variety of changes in guidelines for when and how the test should be administered. One recent change in human papilloma virus (HPV)-related cancer prevention that can be readily accessed in primary care is the Gardasil 9 vaccine, introduced in 2014.[5] Wide availability of safe and effective HPV vaccines, as well as improving HPV DNA testing, have the potential to change screening guidelines in the near future,[6-8] with guidelines already changing in some countries[8]; however, as of this publication, the 2018 guidelines remain in place in the United States.[9] In any case, early detection and treatment remain central to reducing HPV-related cancers, particularly cervical cancer, as its indolent course can be devastating by the time of symptom onset.[10] This paper will provide a detailed review of current guidelines regarding cervical cancer screening from a variety of expert organizations including U.S. Preventive Services Task Force (USPSTF), American College of Obstetricians and Gynecologists (ACOG), Society of Gynecologic Oncology (SGO), American Society for Colposcopy and Cervical Pathology (ASCCP), and American Cancer Society (ACS) with the goal of providing concise clinically relevant information for the practicing family physician. For brevity, a variety of acronyms are used throughout this paper, and are detailed in Table 1.

METHODS

Literature Search and Data Sources

Guidelines as published by expert organizations through their respective official channels were automatically included in our analysis. Current USPSTF guidelines were obtained from the USPSTF website (https://www.uspreventiveservicestaskforce.org/uspstf/recommendation/cervical-cancer-screening),including the active research regarding potential guideline changes 6,7,9,11 on April 24, 2024. As of that date, the USPSTF guidelines from 2018 remain the most current version. More recently published 2020 guidelines from ACS were also reviewed,[12] as well as an updated guideline statement published by ACOG and reaffirmed in 2023.[13] Database searches were conducted on April 24, 2024. Cochrane Library (https://www.cochranelibrary.com/search?cookiesEnabled), PubMed (https://pubmed.ncbi.nlm.nih.gov/), and AHRQ Effective Healthcare Program (https://effectivehealthcare.ahrq.gov/) database searches for keywords "cervical cancer screening," Pap smear," and "Pap test" were undertaken. Inclusion criteria were for papers that primarily discussed cervical cancer screening, and for those focused on clinical practice guidelines. Papers mentioning cervical cancer screening, but with a primary focus on other subjects were excluded. Due to the vast breadth of results in the PubMed

CORRESPONDENCE:
John M. Allen, MS, DO, PGY3 | john.allen@uhhospitals.org
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database, results were principally restricted to 2020 to present, and filtered to only include clinical practice guidelines. The search strategy is summarized in a Prisma-style flow diagram[14] in Figure 1. Four relevant reviews were identified from Cochrane library.[15-18] Of the 4 papers identified, one was identified by Cochrane to be out of date and subsequently excluded.[15] After filtering and exclusion, 3 records from PubMed were ultimately reviewed for analysis, although other papers are cited where necessary to provide context; one of these was found to be focused on information for laboratories receiving cytologic samples rather than on clinicians and was subsequently exluded.[19] Search of the AHRQ Effective Healthcare Program database ultimately yielded no additional results for analysis after excluding those that did not meet criteria.

ANALYSIS

Guidelines for cervical cancer screening from USPSTF and major relevant clinical societies (ACOG, SGO, ASCCP, ACS) were used in this review and can be seen in Table 2 below. The 2018 USPSTF guidelines are endorsed and adopted by ACOG, SGO, and ASCCP. These shared guidelines were compared to the 2020 ACS guidelines to determine agreement between these expert organizations. Also included were National Institutes of Health (NIH) guidelines screening for patients with HIV, for which an equivalent comparison was not included in the ACS guideline statement. Finally, we reviewed recommendations from ACOG and ASCCP regarding the approach to abnormal cervical cancer screening results, which are summarized for rapid reference for use by clinicians.

FIGURE 1.

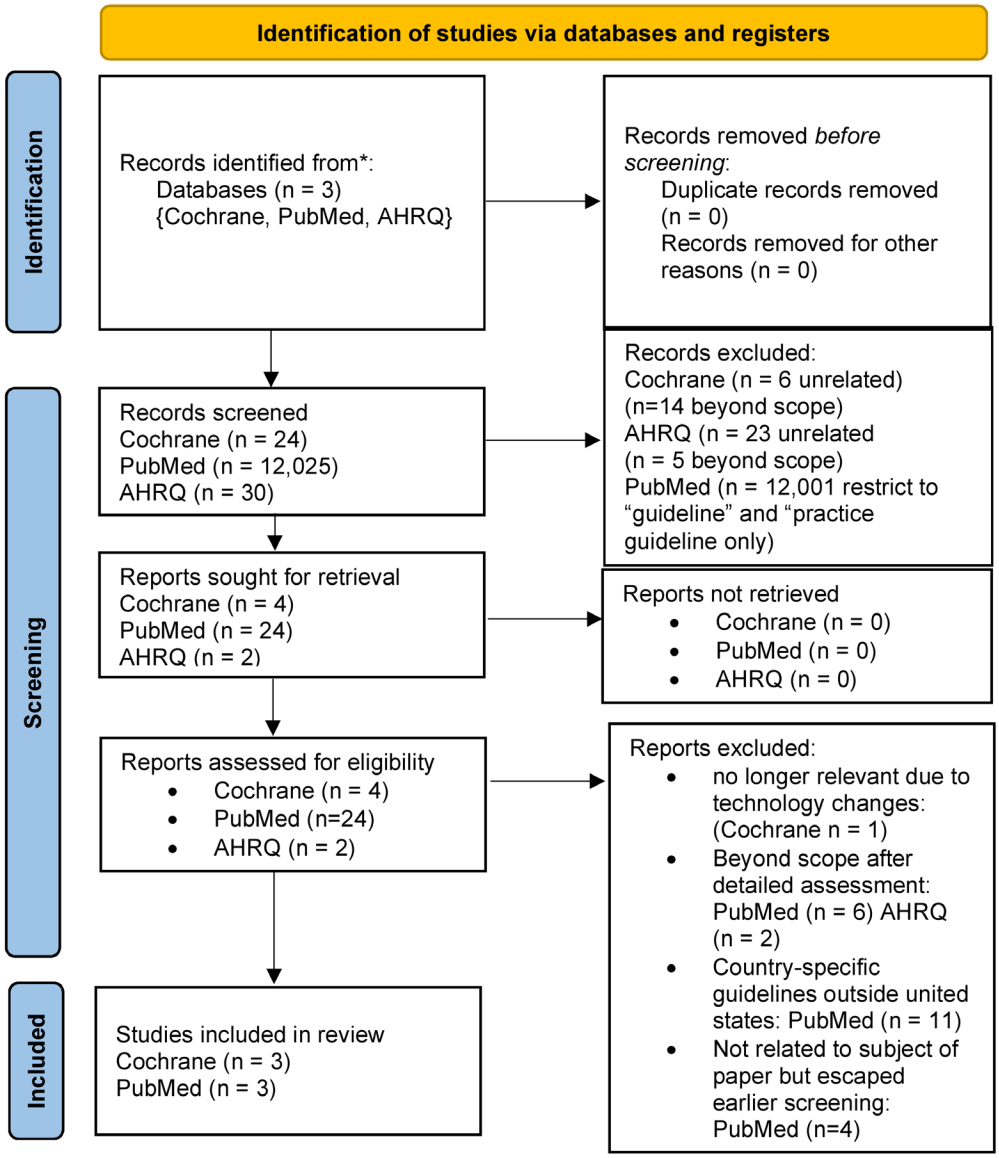


TABLE 1:
Acronyms used in this text

Abbreviation	Full Text
USPSTF	United States Preventive Services Task Force
ACS	American Cancer Society
ACOG	American College of Obstetricians and Gynecologists
ASCCP	American Society for Colposcopy and Cervical Pathology
SGO	Society for Gynecologic Oncology
AHRQ	Agency for Healthcare Research and Quality
CDC	Centers for Disease Control and Prevention
HPV	Human papilloma virus
HIV	Human immunodeficiency virus
HAART	Highly active antiretroviral therapy
NILM	Negative for intraepithelial lesion or malignancy
ASCUS	Abnormal squamous cells of unknown significance
LSIL	Low-grade squamous intraepithelial lesion
HSIL	High-grade squamous intraepithelial lesion
ASC-H	Atypical squamous cells, cannot rule out high-grade lesion
AGC	Atypical glandular cells
AIS	Adenocarcinoma in situ
CIN 1	Cervical intraepithelial neoplasia, grade 1
CIN 2	Cervical intraepithelial neoplasia, grade 3
CIN 3	Cervical intraepithelial neoplasia, grade 3
CIN 3+	Cervical intraepithelial neoplasia, grade 3 or adenocarcinoma in situ

RESULTS

Cervical Cancer Screening

USPSTF[9] guidelines for screening average-risk patients, endorsed by ACOG, SGO, and ASCCP13 for cervical cancer screening, as of this time remain concordant, while ACS guidelines have shifted to reflect newer technology, as shown in Table 2. Briefly, USPSTF continues to recommend initiation of screening by Pap test alone every 3 years from ages 21 to 30 years, followed by either continued Pap test every 3 years, or Pap with HPV co-test or HPV test alone every 5 years until age 65 years. After age 65 years, Pap tests may be discontinued if there are 3 negative cytology results or 2 negative co-testing results within 10 years and the most recent test occurred within 5 years.

TABLE 2:
Current guidelines for cervical cancer screening in the general population from USPSTF and ACS

Population	USPSTF 2018 (endorsed by ACOG, ASCCP, and SGO)	ACS 2020
<21 years	• Screening not recommended	Screening not recommended
21-24 years	• Cytology alone every 3 years	Screening not recommended
25-29 years	• Cytology alone every 3 years	• HPV testing every 5 years • Co-testing (HPV testing with cytology) every 5 years • Cytology alone every 3 years
30-65 years	• Cytology alone every 3 years • HPV testing every 5 years • Co-testing (HPV testing with cytology) every 5 years	• HPV testing every 5 years • Co-testing (HPV testing with cytology) every 5 years • Cytology alone every 3 years
>65 years	Screening not recommended if adequate prior screening and low risk for cervical cancer	Screening not recommended if adequate prior screening and low risk for cervical cancer
History of hysterectomy with removal of the cervix	Screening not recommended unless history of a high-grade precancerous lesion (ie, cervical intraepithelial neoplasia [CIN] grade 2 or 3) or cervical cancer	
Any age with limited life expectancy		Screening not recommended

ACS, by contrast, recommends screening to start at age 25 years, and to use primary HPV testing without a Pap test every 5 years until age 65 years. ACS recommendations also state that Pap test every 3 years or co-test every 5 years is a reasonable alternative in areas where primary HPV testing is unavailable.[12]

Of note, USPSTF is currently in the process of reviewing and updating cervical cancer screening guidelines. This is bolstered by maturation of HPV testing technology, which allows for better sensitivity and specificity as compared to Pap testing, particularly when Pap testing is done without an HPV co-test.[8] The United States is large and heterogeneous in population and area as compared to countries that have moved toward exclusive primary HPV testing, which has complicated the large-scale conversion to new testing modalities.

Patients with HIV

Infection with HIV can increase risk of HPV infection and cancers resulting from HPV infection,20 In fact, rates of cervical cancer in individuals with HIV are approximately 4 times higher than the general population, despite the availability of effective highly active antiretroviral therapy (HAART).[21] Based on the higher risk for this population, cervical cancer screening guidelines vary as compared to those at average risk.

Typically, those 21 to 29 years at time of HIV diagnosis should have a Pap test (without HPV co-test) at time of initial diagnosis with HIV. Even if the initial Pap test is normal, it should be repeated annually for 3 years. If the results of 3 consecutive cervical cytology studies are normal, patients may then transition to Pap test every 3 years until age 30 years. HPV testing is not typically done in addition to Pap testing in this population due to the extremely high prevalence of infection leading to false positives.[22]

Patients aged 30 years or above at initial HIV diagnosis should have a Pap smear with HPV co-test at time of diagnosis. If both tests are negative, continue Pap with HPV co-testing every 3 years for life—an important difference from the general population.[22]

Perhaps unsurprisingly, abnormal test results for this population require closer follow-up than those among the general population. Particularly, the threshold for colposcopy is much lower. Generally speaking, atypical squamous cells of undetermined significance (ASCUS) with negative HPV testing requires a repeat Pap test in 1 year. ASCUS with positive HPV testing requires colposcopy. Any more significant results (eg, low-grade squamous intraepithelial lesion [LSIL], high-grade squamous intraepithelial lesion [HSIL]) warrant colposcopy regardless of HPV co-test result, as do high-risk HPV genotypes even with normal cytology.[22] See Table 3 for more details, including comparison to guidelines for the general population.

HPV vaccination is still recommended for prevention in this population, with one key difference: the recommended age for primary immunization remains the same as for individuals without HIV, however, among those with HIV infection, HPV vaccination always requires a 3-dose series, regardless of the age at which it is given.[22]

Approach to Abnormal Screening Results

The appropriate response to abnormal cervical cancer screening results depends largely on the result in question and, more importantly, the likelihood of progression to a clinically significant lesion. The most recent recommendations from the ASCCP, developed in 2019, shifted from a focus on cytology results to a comprehensive and complex risk assessment that tailors management to each patient based on history, risk factors, previous screening results, HPV testing, and cervical cytology. These changes aimed at reducing the burden of unnecessary colposcopies in low-risk patients. Current ACOG guidelines note a full endorsement of those published by ASCCP. They state a preference for HPV testing as a core component of screening, whether primary HPV testing or cytology (Pap) with HPV co-test.[23]

TABLE 3:
Current guidelines for cervical cancer screening in patients with HIV vs the general population

	Patients With HIV (increased risk)	General Population (average risk) {USPSTF guidelines}
21-29 years	• Cytology at time of diagnosis and yearly for 3 years even if normal	• Cytology alone every 3 years
30+ years	• Co-testing at diagnosis	• Cytology alone every 3 years OR • HPV testing every 5 years OR • Co-testing (HPV testing with cytology) every 5 years
>65 YEARS	• cotesting at diagnosis • if negative cytology and HPV, then repeat every 3 years for life OR • If cotesting not available, then cytology at diagnosis and yearly for 3 years even if normal • If 3 consecutive normal results, then cytology every 3 years for life *option to discontinue in patients with limited life expectancy	

Broadly speaking, abnormal tests can require follow-up with surveillance, colposcopy, or treatment. How to proceed is determined by the likelihood of progression to cervical intraepithelial neoplasia grade 3 or above (CIN 3+). This includes CIN grade 3, adenocarcinoma in situ, and cancer. CIN 3 is defined as a precancerous lesion of greater than two-thirds the thickness of the cervical epithelium.[24] Treatment for these high-grade cervical lesions includes excisional and ablative options, while cervical cancer treatments escalate to chemotherapy and/or surgery (hysterectomy).

Currently, guidelines recommend follow-up for any comprehensive risk assessment result of 4% or more for development of CIN 3+. Risk assessment results can be categorized as high, low, or intermediate risk for progression, with intermediate- and high-risk results meeting criteria for further evaluation.

Low-risk results would include first-time negative for intraepithelial lesion or malignancy (NILM) with positive HPV test, ASCUS with negative HPV test, and first-time LSIL with negative HPV test. Intermediate-risk results would include ASCUS with positive HPV test, LSIL with positive HPV test, and second-time NILM with positive HPV test. High-risk results include HSIL, atypical

TABLE 2:

List of possible Pap smear test results and further management.

Pap test results	Definition	Next Steps
NILM	Negative for intraepithelial lesion or malignancy, ie normal	See figure 2.
ASC-US	Atypical squamous cells of uncertain significance	See figure 3.
LSIL or CIN1	Low-grade squamous intraepithelial lesion Cervical intraepithelial neoplasia grade 1	See figure 4.
HSIL or CIN2, 3	High-grade squamous intraepithelial lesion Cervical intraepithelial neoplasia grade 2, 3	See figure 5.
ASC-H	Atypical squamous cells, cannot rule out a high-grade lesion	See figure 5.
AGC	Atypical glandular cells	Colposcopy

FIGURE 2.

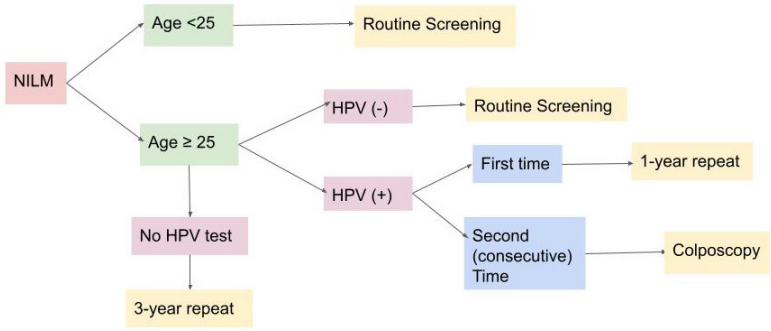
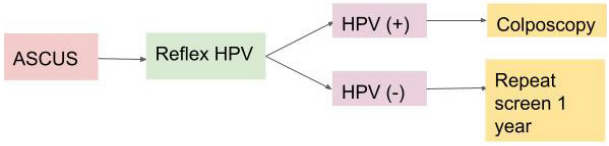


FIGURE 3.



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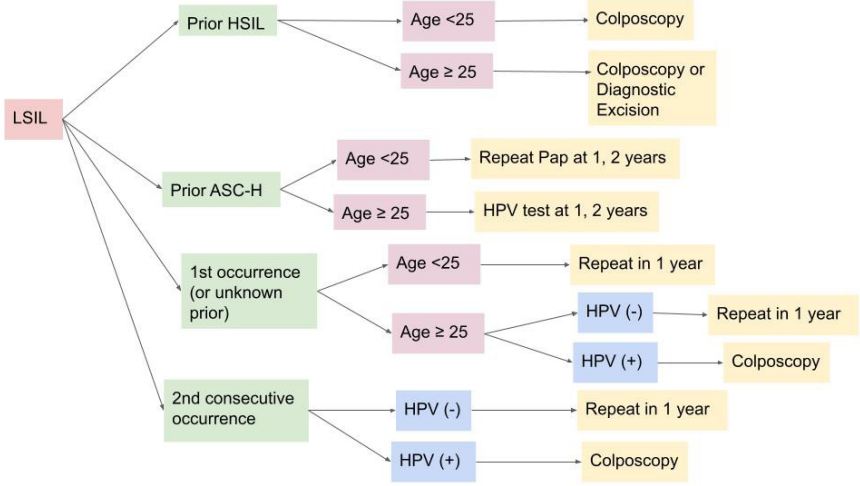

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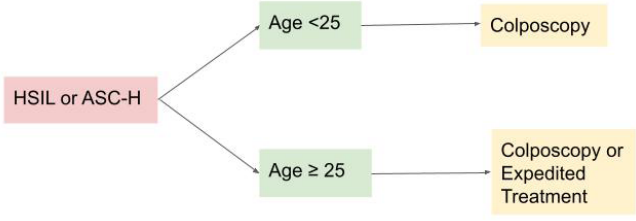

squamous cells, cannot rule out high-grade lesion (ASC-H), and AGC [atypical squamous cells where HSIL cannot be excluded and atypical glandular cells]. Results are summarized in Table 4, and the basic approach to their management appears in Figures 2 to 5 with references in Table 4. Adenocarcinoma in situ (AIS) management is not included in the figures; this should always receive expedited treatment. Similarly, AGC is not shown in the figures; this result should lead to colposcopy and endometrial sampling if the patient is not pregnant.[22]

There are more possible situations and risk strata than were able to be summarized here, and readers may refer to Perkins, et al. for additional details if needed for their clinical context.[23] Figures are intended to provide guidance for common clinical situations and do not represent an exhaustive list of possible results and outcomes. Additionally, guidelines only apply to asymptomatic individuals; those with symptoms should be managed as appropriate for disease state.

Improving Adherence to Follow-up After Abnormal Results

Rates of inadequate follow-up after abnormal pap results range from 4% to 75%,25 highlighting a significant opportunity for improvement in management. Individual factors associated with poor follow-up include younger age, lower socioeconomic status, lack of health insurance, and lower education, while protective factors include regular visits with a primary care provider and direct communication of abnormal test results. Thus in order to improve follow-up, consider direct notification of abnormal laboratory results, appointment reminders via telephone or text messages, and improving patient self-efficacy through education initiatives and even HPV self-sampling.[25,26]

CONCLUSIONS

Despite the wide availability of an effective vaccine, HPV infection and HPV-related cervical cancers remain disturbingly common. Increased vaccination rates have potential to dramatically change this reality within many of our lifetimes. However, at this time, cervical cancer screening to allow early identification and treatment remains a necessity. As of April 2024, Pap testing with or without HPV co-testing is still the standard of care per USPSTF guidelines. It is the authors' opinion that USPSTF guidelines will most likely be updated to offer an option for either continued screening, per existing 2018 guidelines, or for younger patients, initiating screening per the newer ACS guidelines. This is likely due in part to disparities in availability of screening tools in the heterogeneous communities of the United States. Regardless, it will remain vitally important for family physicians to continue to assist their patients in obtaining appropriate screening and follow-up based on those results.

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