# Cervical Cancer Screening

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**KEYWORDS**

• Cervical cancer screening • Cervical cancer prevention
• Human papillomavirus vaccination • Human papillomavirus testing
• Cervical cytology • High-value care • Preterm birth

**KEY POINTS**

- Cervical cancer screening in the United States has accompanied profound decreases in cancer incidence and mortality over the last half century.
- Current screening guidelines issued by major groups are largely consistent and strive to find a reasonable balance between benefits and harms by recommending less screening in most women.
- Two strategies are endorsed by major US-based guideline groups: (1) triennial cytology for women aged 21 to 65 years, and (2) triennial cytology for women aged 21 to 29 years followed by cytology plus testing for high-risk human papillomavirus types every 5 years for women aged 30 years and older.
- Maintaining gains in cervical cancer prevention requires a continued vigilant approach that includes access to low-cost, high-quality screening for all women and appropriate human papilloma virus vaccination.
- As new screening strategies emerge and are adopted, comparative effectiveness analyses will be needed to outline the patient-centered and economic implications of choosing one rather than another.

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## INTRODUCTION

Cervical cancer is an uncommon disease in the United States, with an estimated 13,000 incident cases and 4100 deaths occurring in 2016.[1] Rates have steadily declined over the last few decades coincident with widespread, population-based screening. Disparities in incidence and mortality are still noted, with black and Hispanic women continuing to have higher rates of cervical cancer than white women.

High-quality evidence implicates high-risk human papillomavirus (HPV) types as the causative agents in cervical cancer. HPV infections are common; the US Centers for Disease Control and Prevention (CDC) estimates that nearly all sexually active women are exposed to HPV over their lifetimes.[2] Although most infections resolve without consequence, persistent infections can lead to precancerous cervical lesions and, in a minority of women, invasive cancer.

The most common precancerous lesions are of squamous cell origin, called cervical intraepithelial neoplasia (CIN), and are graded by the proportion of abnormal epithelium.

- CIN grade 1 indicates an active HPV infection and these lesions are considered low grade with a high spontaneous regression rate; these lesions are generally not treated.
- CIN grade 2 is often considered a high-grade lesion but has a spontaneous regression rate of up to 40%.
- CIN grade 3 lesions have the highest likelihood of progression to invasion and are universally treated.

The estimated time for CIN grade 3 progression to cancer is on average 10 years, allowing many opportunities for these lesions to be found and treated. Preinvasive lesions of glandular cell origin (adenocarcinoma in situ) are less common but are of such concern that hysterectomy is recommended when diagnosed. Of note, cytology-based screening has led to declines in the incidence and mortality of squamous cell cancer but not in cancers of glandular origin.

High-grade CIN lesions (CIN2 and CIN3) are treated with either ablation (eg, laser, cryotherapy) or excision (eg, loop excision, cone biopsy).[3] Both treatments have high efficacy (short-term cure rates of 85%–95%) but have different side effects. The association between excisional procedures and preterm birth has led to a more cautious use of these techniques. Prior systematic reviews have found no associations between cryotherapy and laser ablation and preterm birth.[4] More recent reviews have noted increases in the risk of preterm birth as excision depths increase as well as small increases with unspecified ablative treatments.[5] As with much evidence about harm, the observational nature of current studies limits causal inference; the relationship between cervical treatments and preterm birth may be confounded by a third factor affecting risk of both. Acknowledging these potential harms, treatment guidelines by the American Congress of Obstetricians and Gynecologists (ACOG) suggest a judicious approach when treatment is warranted; for example, the guidelines encourage surveillance of CIN2 rather than treatment, especially in young women.[6]

Three highly effective HPV vaccines have been developed to target up to 9 HPV subtypes, covering either the most common oncogenic types (bivalent vaccine against 16/18), or a combination of these plus the condyloma-causing HPV types 6 and 11 (quadrivalent vaccine, now replaced by a nonavalent vaccine). Targeted to adolescents of both sexes, the vaccines have been shown to decrease the incidence of both HPV and CIN, with rates of up to 100% efficacy against the vaccine-specific HPV types and related disease in women who have not been previously exposed.[7,8] HPV