

## EVIDENCE-STATEMENT: CERVICAL CANCER (Screening)

Why This Chapter is Important for Employers: An Overview

- Cervical cancer was once the most common cause of cancer death among women in the United States. Screening, earlier detection, and more effective treatment methods reduced the death rate from cervical cancer 74% between 1955 and 1992.<sup>1</sup>
- Nevertheless, cervical cancer remains a concern. In 2005, it was estimated that 10,370 women would be diagnosed with cervical cancer and 3,710 women would die as a result of the disease.<sup>1</sup>
- The direct medical care costs associated with cervical cancer were estimated to equal \$1.7 billion in year 1996 dollars.<sup>2</sup>
- Screening can prevent cervical cancer by allowing clinicians to identify and remove precancerous lesions before they develop into cancer. Screening can also identify cancer early in the course of the disease when treatment is more effective and the chance of recovery is high.<sup>3</sup>
- The cost of screening is typically less than the cost of treating cancer and, when screening identifies a lesion in its early stages, the cost of treatment is often much less expensive than if the lesion was identified at a later stage.

### Clinical Preventive Service Recommendations for Screening

U.S. Preventive Services Task Force Recommendation

The U.S. Preventive Services Task Force (USPSTF) strongly recommends cervical cancer screening for all women who have been sexually active and have a cervix.<sup>3</sup>

Evidence Rating: A (Strongly Recommended/ Good Evidence)

The USPSTF found good evidence that the benefits of screening for cervical cancer substantially outweigh the risks associated with screening.<sup>3</sup>

Information Sources

The recommendations and supporting information contained in this document came from several sources, including the:

- Advisory Committee on Immunization Practices (ACIP)
- Alliance for Cervical Cancer Prevention; Program for the Appropriate use of Technology in Health (PATH)
- American Cancer Society (ACS)
- National Cancer Institute (NCI)
- Peer-reviewed research

The background and supporting information contained in this document is a compilation of research findings. All information presented in this document should be attributed to its referenced source and should not be considered a reflection of other organizations cited in the text.

### Condition/Disease Specific Information

Epidemiology of Condition/Disease

Cervical cancer was once the most common cause of cancer death among women in the United States, but the death rate from cervical cancer dropped 74%

between 1955 and 1992, due to screening, earlier detection and treatment, and more effective treatment methods.<sup>1</sup> Despite this progress, cervical cancer remains a major cause of premature morbidity and mortality among women in the United States.

In 2005, it was estimated that 10,370 women would be diagnosed with cervical cancer and 3,710 women would die as a result of the disease.<sup>1</sup> Cervical cancer is most common among women in their 40s to 60s, although some women develop cancer in their 30s.<sup>4</sup>

Cervical cancer screening has been conducted using the conventional Pap test screening method since 1940; the Pap test has proven to be one of the most successful methods of cancer prevention and early detection available.<sup>5</sup> More than 50% of women who develop cervical cancer have never been screened for cervical cancer and 60% of women who develop cervical cancer have not been screened in the previous 5 years.<sup>5-6</sup> The dose-response relationship between the number of times a woman is screened during her lifetime and her likelihood of developing cervical cancer is illustrated in the following table:

Frequency of Screening	Reduction in Cancer Rate
At least every three years *Screening interval recommended by the USPSTF	75%-88%
Five times per lifetime	61%-75%
Three times per lifetime	35%-55%
Twice per lifetime	29%-42%
Once per lifetime	17%-32%

**Source:** Alliance for Cervical Cancer Prevention. Cervical cancer prevention fact sheet. Seattle, WA: Program for the Appropriate use of Technology in Health (PATH); 2003.

**Condition/Disease  
Risk Factors**

The major risk factor for cervical cancer is infection with the human papillomavirus (HPV), a common sexually transmitted infection (STI). Clinical research shows that 95% to 100% of all squamous cell cervical cancers and 75% to 95% of all cervical intraepithelial neoplasia (CIN) lesions (a precursor to cervical cancer) can be linked to infection with HPV.<sup>7</sup>

HPV is the most common sexually transmitted disease in the United States; over 50% of adults contract an HPV infection during their lifetime.<sup>8</sup> In most women infected with HPV, the virus remains asymptomatic and does not progress to precancerous lesions (CIN or dysplasia) or cervical cancer.<sup>9-10</sup> However, approximately 5% to 10% of women with persistent HPV infection develop cervical cancer during their lifetimes if they do not have a Pap test to detect precancerous lesions and do not receive appropriate follow-up care.<sup>10</sup>

In 2006, the Food and Drug Administration (FDA) licensed a vaccine to reduce the risk of cervical cancer. The Advisory Committee on Immunization Practices (ACIP) has issued provisional recommendations for use of this vaccine.<sup>11</sup> The

vaccine is not a substitute for recommended screening services: screening is still the primary method of cervical cancer prevention.<sup>11</sup> Additional information on the HPV vaccine is provided in the *Immunization Evidence-Statement*.

Although cervical cancer precursor lesions only develop after HPV infection, other factors—such as age, being a smoker, starting sexual intercourse at an early age, having a large number of sexual partners, using oral contraceptives, and having seven or more live births—increase a woman’s risk of cervical cancer.<sup>9</sup> Some research suggests that diet; a woman’s immune status and genetic predisposition; and co-infection with chlamydia, HIV/AIDS, or other sexually transmitted infections (STIs) may also influence risk of developing cervical cancer.<sup>9, 12</sup>

**Value of Prevention**

**Economic Burden of Condition/Disease**

The direct medical care costs associated with cervical cancer were estimated to equal \$1.7 billion in year 1996 dollars based on SEER (Surveillance, Epidemiology, and End Results) and Medicare-linked data.<sup>2</sup>

**Workplace Burden of Condition/Disease**

The cost of cervical cancer (\$1.7 billion) would be significantly higher if work loss and premature deaths were included in the analysis. For example, 25.9 years of life are lost, on average, by each woman who dies of cervical cancer. These lost years of life—which often occur during the prime working years—translate into lost earnings for women and their families, worker-replacement costs for businesses, and are a significant cost to society.<sup>13</sup>

**Economic Benefit of Preventive Intervention**

As with most preventive services, screening for and treating cervical cancer in its early stages is much less expensive than intervening at later stages in the disease process. For example, the cost of treating a single case of localized (early-stage) cervical cancer averages \$20,255, while the cost of treating a single case of distant (late-stage) disease averages \$36,912 (both figures in year 2000 dollars).<sup>14</sup> In addition to reduced medical care costs, the years of life gained from early detection and treatment are valuable to families, businesses, and the community at large.<sup>13</sup>

**Estimated Cost of Preventive Intervention**

The cost of a conventional Pap smear test will vary depending on location, type of provider, and the patient’s age. In 2004, the private-sector cost of screening for cervical cancer among women under age 65 averaged \$31 including specimen collection, laboratory processing, and interpretation; approximately 95% of all paid claims fell within the range of \$9 to \$64.<sup>15</sup> For Medicare eligible women, cervical cancer screening cost an average of \$28 and approximately 95% of all paid claims fell within the range of \$0 to \$62.<sup>15</sup>

Costs of vaccination are in addition to the costs for recommended screening services.

**Estimated Cost of Treatment**

The costs associated with an abnormal Pap test as a result of HPV infection, including the cost of physician visits, laboratory tests, colposcopies, and treatment of cervical neoplasia if present, were estimated to be \$1,281 per patient in year 2000 dollars.<sup>14</sup>

The cost of treating established cervical cancer varies. Localized (early-stage) cervical cancer costs an average of \$20,255 to treat and distant (late-stage) disease costs an average \$36,912 to treat (both figures in year 2000 dollars).<sup>14</sup>

Cost-Effectiveness and/or Cost-Benefit Analysis of Preventive Intervention

The relative costs and benefits of screening will vary depending on the age of patients screened and the screening interval. A recent study (that included patient-time costs) estimated that the cost-effectiveness ratio of a conventional Pap test repeated every three years up to the age of 75 was \$11,830 per quality-adjusted life year (QALY) saved (in year 2000 dollars).<sup>7</sup> In comparison to other preventive interventions and to commonly accepted cost-effectiveness benchmarks, cervical cancer screening is highly cost-effective.<sup>16</sup>

**Preventive Intervention Information**

Preventive Intervention: Purpose of Screening

The purpose of screening for cervical cancer is twofold. First, screening reduces the risk of cervical cancer by identifying women with precancerous conditions that can be treated before the conditions progress to cancer. The primary precursor lesions of cervical cancer, CIN III and carcinoma *in situ*, progress slowly, often over more than 8 to 9 years. Pap test screening detects these lesions before they develop into invasive cancers and, with appropriate and timely treatment, a full recovery is likely. Second, screening can identify women with cervical cancer before symptoms appear. Early detection, which allows for early treatment, improves outcomes.<sup>3</sup>

Benefits and Risks of Intervention

The benefits of cervical cancer screening are substantial. Screening reduces cervical cancer incidence and mortality. When Pap test screening programs are introduced into populations for the first time, the risk of developing cervical cancer is typically reduced by 60% to 90% within 3 years.<sup>12</sup> Mathematical models suggest that population-wide screening with the Pap test every 3 years reduces the rate of invasive cervical cancer by 91%; screening with the Pap test every 5 years reduces the rate by 84%.<sup>6, 12</sup> In North America and Europe, the introduction of screening programs was associated with reductions in cervical cancer mortality of between 20% and 60%.<sup>12</sup>

The harms of screening for cervical cancer are small compared to the benefits. False-positive screening results may lead to unnecessary treatment of low-grade lesions, unnecessary evaluations and biopsies, and psychological stress.<sup>12</sup>

Screening is of little or no value among women who have undergone a hysterectomy for benign disease. The USPSTF suggests that clinicians obtain a full and accurate surgical history to confirm indication for hysterectomy and that a total hysterectomy has been performed before deciding against screening.<sup>12</sup>

Initiation, Cessation, and Interval of Screening

The USPSTF recommends that screening begin within 3 years of the onset of sexual activity or the age of 21, whichever occurs first, and continue until the age of 65 for adult women of normal risk. Some professional organizations recommend more frequent Pap tests, but the USPSTF found no direct evidence that annual screening achieves better outcomes than screening every 3 years. Further, although screening women who are not sexually active has little value,

many professional organizations recommend that clinicians screen all women over the age of 21 for cervical cancer because women may not always accurately report their history of sexual activity.<sup>12</sup>

Because the risk of cervical cancer decreases after the age of 65 in women who have a history of normal Pap test results, the risks associated with screening, including false-positive results and inconvenience, outweigh the benefits of screening for older women.<sup>3</sup> Screening is recommended in older women who have not been previously screened, when information about previous screening is unavailable, or when screening is unlikely to have occurred in the past (e.g., among women from countries without screening programs).<sup>3</sup> Evidence is limited to define “adequate recent screening.” The American Cancer Society (ACS) guidelines recommend that older women who have had three or more documented, consecutive, technically satisfactory normal/negative cervical cytology tests, and who have had no abnormal/positive cytology tests within the last 10 years, can safely stop screening.<sup>1</sup>

**Note:** In addition to screening, coverage should be provided for immunization with the HPV vaccine in accordance with recommendations by the Advisory Committee on Immunization Practices (ACIP). For more information on the HPV vaccine, please refer to the *Immunization Evidence-Statement*.

Intervention Process	The approved screening method for cervical cancer is the conventional Pap test. Newer screening methods, such as liquid-based, thin-layer preparations (e.g., ThinPrep®), computer-assisted screening (e.g., AutoCyte®), and human papillomavirus (HPV) tests, such as Hybrid Capture II®, are available. Purchasers may choose to cover these screening tests in addition to the conventional Pap test. <sup>5</sup>
Treatment Information	Health coverage should include provisions for diagnostic and treatment services.

**Strength of Evidence for the Clinical Preventive Service (Screening)**  
 The level of evidence supporting the recommendations contained in this chapter is described below.

***Evidence-Based Research:***

U.S. Preventive Service Task Force (USPSTF)

Strength of Evidence: A (Strongly Recommended/Good Evidence)

- The USPSTF found good evidence to recommend cervical cancer screening for all women who have been sexually active and have a cervix.<sup>3</sup>

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