Natural History of Cervical Cancer: Even Infrequent Screening of Older Women Saves Lives

According to the most recent data, an estimated 466,000 new cases of cervical cancer occur among women worldwide each year, the vast majority of them in developing countries. Of the 231,000 women who die of cervical cancer annually, some 80 percent are from developing countries, where cervical cancer is the most common cause of cancer deaths among women.\(^\text{1}\) Cervical cancer screening is a cost-effective way to save lives. A 1993 World Bank study found that screening women every five years with standard follow-up for identified cases costs about $100 per disability-adjusted life year (DALY) gained, compared with about $2,600 per DALY for treatment of invasive cancer and palliative care.\(^\text{2}\) In order to ensure that cervical cancer prevention interventions save women’s lives, programs must be based upon a clear understanding of the most recent research on the natural history of cervical cancer.

**HPV is the primary cause of cervical cancer**

- Human papillomavirus (HPV), a common sexually transmitted infection, is the primary underlying cause of cervical cancer.\(^\text{3}\)
- Preventing HPV transmission is very difficult. Barrier contraceptive methods are only partially effective because the virus can exist throughout most of the anogenital area (including areas not covered by male condoms) and can remain infectious for years.\(^\text{4}\)
- HPV cannot be treated, but infection becomes undetectable in the majority of cases. In some women, however, HPV infection persists and leads to precancerous lesions, called dysplasia. Immunocompromised women may be at particularly high risk of persistent infection.\(^\text{5}\)
- Detectable HPV infection is most common in younger women. Although prevalence varies among regions, it generally reaches a peak of about 20 percent among women aged 20 to 24, with a subsequent decline to approximately 3 percent among women over age 30.\(^\text{6}\)

Cervical cancer generally takes many years to develop; older women are at greatest risk and in need of screening

- Many women with HPV infection likely will develop mild dysplasia, most of which regresses or does not progress, particularly among women under age 35.

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**Figure 1. Natural History of Cervical Cancer and Program Implications**

<table>
<thead>
<tr>
<th>HPV Infection</th>
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<tbody>
<tr>
<td><strong>Characteristics:</strong> HPV infection is extremely common among women of reproductive age.</td>
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<tr>
<td>HPV infection can remain stable, lead to dysplasia, or become undetectable.</td>
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<td><strong>Management:</strong> While genital warts resulting from HPV infection may be treated, there is no treatment that eradicates HPV. Primary prevention through use of condoms offers some protection.</td>
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<tr>
<th>Low-grade Cervical Dysplasia</th>
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<tr>
<td><strong>Characteristics:</strong> Low-grade dysplasia usually is temporary and disappears over time. Some cases, however, progress to high-grade dysplasia.</td>
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<td>It is not unusual for HPV to cause low-grade dysplasia within months or years of infection.</td>
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<td><strong>Management:</strong> Low-grade dysplasia generally should be monitored rather than treated since most lesions regress or do not progress.</td>
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<thead>
<tr>
<th>High-grade Cervical Dysplasia</th>
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<tbody>
<tr>
<td><strong>Characteristics:</strong> High-grade dysplasia, the precursor to cervical cancer, is significantly less common than low-grade dysplasia.</td>
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<tr>
<td>High-grade dysplasia can progress from low-grade dysplasia or, in some cases, directly from HPV infection.</td>
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<tr>
<td><strong>Management:</strong> High-grade dysplasia should be treated, as a significant proportion progresses to cancer.</td>
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<th>Invasive Cancer</th>
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<td><strong>Characteristics:</strong> Women with high-grade dysplasia are at risk of developing invasive cancer; this generally occurs slowly, over a period of several years.</td>
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<tr>
<td><strong>Management:</strong> Treatment of invasive cancer is hospital-based, expensive, and often not effective.</td>
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</table>
• Progression to detectable, precancerous lesions can take as long as 10 years. One study estimates that the risk of progression from moderate to severe precancerous lesions is 32 percent within 10 years.7

• Women aged 35 or older with identified moderate or severe precancerous lesions are at high risk for developing cancer.

• Cervical cancer most often develops in women after age 40 and is most frequent among women in their fifties and sixties.3,9

• Tobacco use, young age at first birth, use of hormonal contraceptives, and the hormonal and physical implications of high parity appear to independently increase a woman’s risk of cervical cancer.9

• Clinical impressions of increasing cervical cancer rates among younger women may reflect a population’s age structure or screening patterns rather than a shift in age-specific rates.10 Some country data suggest, however, that age-specific rates for dysplasia and cervical cancer have shifted downward by about five years, possibly due to increasing sexually transmitted infection and HIV/AIDS rates.11

Even infrequent screening can be effective

• Infrequent screening and associated follow-up of women in their 30s or older is an acceptable, cost-effective approach to preventing cervical cancer, assuming that the screening approach is effective and coverage is high.

• Women with at least one previous negative cervical smear have low rates of invasive cancer for five years, with rates remaining low for ten or more years.12

• Screening women every ten years can reduce the cumulative cervical cancer rate by 64 percent. Even screening women just once in their lives, ideally at ages 40 to 45, can significantly reduce cervical cancer mortality (see Table 1).9

Table 1: Potential Reduction in Cumulative Cervical Cancer Rates With Different Frequencies of Screening

<table>
<thead>
<tr>
<th>Frequency of Screening*</th>
<th>Percent Reduction in Cumulative Rate†</th>
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<tbody>
<tr>
<td>1 year</td>
<td>93</td>
</tr>
<tr>
<td>2 years</td>
<td>93</td>
</tr>
<tr>
<td>3 years</td>
<td>91</td>
</tr>
<tr>
<td>5 years</td>
<td>84</td>
</tr>
<tr>
<td>10 years</td>
<td>64</td>
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</tbody>
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Adapted from: IARC, 1986.12

*Screening all women aged 35 to 64 who have had at least one previous negative smear.

†Reductions assume 100% screening sensitivity, screening coverage over 80%, and effective treatment of every woman in whom high-grade dysplasia is detected.

“In countries where resources are limited, the aim should be to screen every woman in the target group once in her lifetime at about the age of 40 years. When resources are available the frequency of screening should be increased to once every 10 years, and then once every 5 years for women aged 35-55 years. If resources are high and a large proportion of the target group are being screened, screening should be extended, first to older women (up to age 60) and then to younger women (down to age of 25). If additional resources are available and a high proportion of the target group are being screened every 5 years, the frequency of screening should then be increased to once every 3 years for women aged 25-60 years.”

—World Health Organization, 19929

References