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What is the most appropriate age to start screening women for cervical cancer?

A literature review suggests there are good reasons for initiating routine population-based screening at age 25.

ABSTRACT: The age to begin routine population-based screening for cervical cancer is controversial, with jurisdictions internationally recommending an age between 21 and 30, and many recommending that screening begin when a woman becomes sexually active, regardless of age. A review of the literature suggests four reasons for starting routine screening at age 25. First, invasive cervical cancers in women younger than age 25 are rare. Second, current screening methods are less effective in younger women. Third, the majority of oncogenic HPV infections and precancerous lesions resolve spontaneously in healthy younger women. Fourth, there are likely harms associated with screening and treating younger women.

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Jurisdictions do not agree on when to begin routine population-based screening for cervical cancer. Recent guidelines in the United States[1] and Ontario[2] recommend that screening start at age 21, while screening in some European countries begins at age 25 (e.g., England) or even as late as age 30 (e.g., the Netherlands). Many jurisdictions recommend that screening begin when a woman becomes sexually active, regardless of age.

The Canadian Task Force on Preventive Health Care (CTFPHC) recently noted that they "found no benefit to outweigh the potential harms" of screening in women younger than age 25.[3] In their joint response to the CTFPHC guidelines, the Society of Obstetricians and Gynaecologists of Canada, the Society of Gynecologic Oncology of Canada, and the Society of Canadian Colposcopists concluded that "until better data exists to support the safety of delaying the initiation of screening, we are of the opinion that screening be initiated at the age of 21."[4]

A review of the literature suggests four reasons for initiating screening at age 25: (1) the low incidence rates for cervical cancer in younger women, (2) the relative ineffectiveness of screening in younger women, (3) the spontaneous resolution of HPV infections and precancerous lesions common in younger women, and (4) the likely harms associated with screening.

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Low incidence of cervical cancer

A British Columbian analysis of 24 years of data collected from 1986 to 2009 indicates an incidence rate for cervical cancer of 0.50 cases per 100 000 women at age 20, increasing to 9.86 cases for women at age 29 (see **Figure 1**). This results in an incidence rate of 1.35 per 100 000 for women age 20 to 24 and 7.24 per 100 000 for women age 25 to 29. An incidence rate of 1.35 per 100 000 equates to less than two cases per year in women age 20 to 24.

In Canada between 2005 and 2007, a total of 39 women age 20 to 24 (an average of 13 per year) were diagnosed with invasive cervical cancer, for an incidence rate of 1.20 per 100 000.[5] Such a low incidence rate may not satisfy a key criterion for screening, which requires that a screening program facilitate prevention of an important public health problem at a population level.[6]

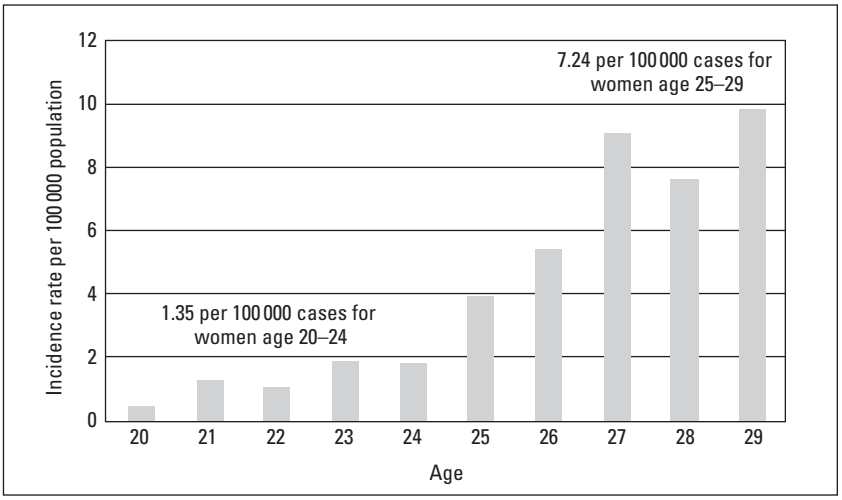

Figure 1. Cervical cancer incidence rates in British Columbia for young women age 20–29, 1986–2009.

Ineffectiveness of screening

The cervical cancer screening program in BC has existed for many years and predates the collection of data that began in 1986. While one argument holds that the low rate of cervical cancers in younger BC women indicates the effectiveness of the screening program for this age group, evidence from multiple sources suggests otherwise.

Gustafsson and colleagues assessed 17 international registries of invasive cervical cancers before and after the implementation of cytological screening.[7] Only populations with a minimum 15-year follow-up period were included to allow sufficient time for possible screening effects to occur and to assess the consistency of the observed effects. A 25% or greater overall reduction in the age-standardized incidence of cervical cancers was observed in 11 of the 17 populations following the initiation of screening. When assessing age-specific reductions in these 11 populations, the greatest reductions were observed in women age 40 to 55, with no significant reduction observed in women age 25 to 35.

In the UK, a 2009 population-based case-control study by Sasieni and colleagues used histology laboratory records from 1990 to 2008 to identify 4012 cases of invasive cervical cancer. The study included 351 women diagnosed between age 25 and 29.[8] The purpose of the study was to examine the rate of cancer in four 5-year cohorts according to the screening history of each cohort in the preceding 5 years (see **Table**). For younger age cohorts, the data demonstrate no significant difference in cancer rates among women diagnosed with cervical cancer at age 25 to 29, who were screened at either age 20 to 21 (OR 1.51; 95% CI, 0.95-2.38) or age 22 to 24 (OR 1.11; 95% CI, 0.83-1.50) when compared with women who were not screened at any time between age 20 and 24 (OR 1.00). In contrast, for older age cohorts of women diagnosed with cervical cancer (35 to 39, 45 to 49, and 55 to 59), there was a significant reduction in cancer rates among those screened in the preceding 5 years when compared with women who were not screened.

In England, a recent increase in the incidence rates of cervical cancer in women age 20 to 29 coincides with a change in screening policy implemented in 2004, when the age to start screening changed from 20 to 25 years. This has raised concerns that the increase may be partially attributable to the change in policy.[9] Between 1992 and 2006 in England, a 2.16% annual increase was observed in women age 20 to 29,[10] increasing to 10.3% between 2000 and 2009.[9] An annual increase of 3.5% was observed in women age 30 to 39 between 2000 and 2009, while rates for all other age groups between 40 and 70 either stabilized or declined.[9]

In addition to an increase in cervical cancer in younger women, there was also a significant increase in sexually transmitted diseases such as chlamydia, herpes simplex, and genital warts.[9,10] Furthermore, increasing rates of both cervical cancers in

Table. Protective effect of past screening for cervical cancers[8]

Age (years) at cancer diagnosis	Cases		Controls		Odds ratio (95% CI)
	n	%	n	%	
25–29					
Screened 22–24	202	58%	399	57%	1.11 (0.83-1.50)
Screened 20–21, but not 22–24	46	13%	70	10%	1.51 (0.95-2.38)
Not screened 20–24	103	29%	226	33%	1.00
Total	351	100%	695	100%	—
35–39					
Screened 32–34	346	53%	842	66%	0.55 (0.44-0.69)
Screened 30–31, but not 32–34	88	14%	144	11%	0.79 (0.57-1.10)
Not screened 30–34	214	33%	288	23%	1.00
Total	648	100%	1274	100%	—
45–49					
Screened 42–44	214	45%	583	63%	0.37 (0.29-0.48)
Screened 40–41, but not 42–44	55	12%	133	14%	0.40 (0.27-0.58)
Not screened 40–44	203	43%	207	22%	1.00
Total	472	100%	923	100%	—
55–59					
Screened 52–54	111	33%	389	58%	0.26 (0.19-0.36)
Screened 50–51, but not 52–54	32	9%	103	15%	0.27 (0.17-0.43)
Not screened 50–54	198	58%	183	27%	1.00
Total	341	100%	675	100%	—

younger women and sexually transmitted disease were observed in Wales, where screening continued to begin at age 20.[9] The observed recent increase in cervical cancers in younger women in England is therefore more likely attributable to changes in sexual behavior in these women than to a change in screening policy.

In Finland, data are available on the incidence of cervical cancers from 1953 to 2002 (see **Figure 2**).[11] In 1964, a pilot cervical cancer screening project was introduced in three municipalities, with 80% of women aged 30 to 50 being screened by 1969.[12] Of note is the fact that women younger than 30 were not invited to be screened until at least 1992, when some municipalities began to screen women age 25 to 30. Looking at trends in cervical cancer incidence for women age 20 to 39 in Finland by 5-year age group, incidence rates for women age 20 to 24 have averaged 0.51 cases per 100 000 compared with 1.35 cases per 100 000 in BC, despite similar HPV infection rates in both jurisdictions, and the fact that women younger than 25 in Finland are not screened.[13] The observed increases in all cohorts from age 20 to 39 since the early 1990s coincides with similar increases in the UK. These increases are likely due to changes in sexual behavior observed in Finnish women, a decrease in the age of onset of sexual activity, and an increase in the lifetime number of sexual partners.[12,14]

Spontaneous resolution of HPV infections and precancerous lesions

It is now known that cervical cancers are caused by persistent infection with oncogenic strains of HPV. Most HPV infections, however, are cleared by the body's immune system, particularly in adolescents and younger women. Rodriguez and colleagues found that HPV infection persists at 30 months follow-up in only 9% of women younger than 30, compared with 21% of women 30 and older.[15] Castle and colleagues have concluded that 14.2% of oncogenic HPV infections persist at 5.6 years follow-up, but that these persistent infections gradually become more prominent with age: 7.5% in women younger than 25, 12.4% in women 25 to 34, 13.7% in women 35 to 44, 15.7% in women 45 to 54, 26.6% in women 55 to 64, and 33.3% in women 65 and older.[16]

The rate of regression to normal tissue following cervical dysplasia is also higher in women younger than 25. With a low-grade squamous intraepithelial lesion (LSIL), the probabil-

ity of regression in young women is approximately 60% at 1 year and 90% at 3 years, with a median time to normal status of under 6 months.[17,18] Even higher grade dysplasia detected by histology (CIN2 and 3) tends to regress at a rate of 60% to 70% in younger women over a period of 1 to 3 years.[19,20] An older study using BC data suggested that 84% of cervical lesions will regress in women younger than 34, but only 40% in women older than 34.[21]

Likely harms associated with screening

A considerable amount of research has focused on the possibility of increased risk of preterm birth following treatment for precancerous cervical lesions.[22,23] The 2011 review by Bruinsma and Quinn concluded that excisional treatment was associated with a significantly increased risk of preterm birth (RR 2.19; 95% CI, 1.93-2.49). While noting that the presence of a lesion, even without treatment, may also increase the risk of preterm birth, the authors suggest a common risk factor could be responsible.[23] This increased risk is most often observed for late preterm births of 32 to 36 weeks gestation, which are associated with suboptimal long-term outcomes.[24-26]

Treating precursor lesions that might otherwise resolve spontaneously can also have an impact on a young woman's quality of life. As well as being uncomfortable, invasive tests and procedures typically require taking time away from work or studies and often lead to anxiety.[27,28]

Conclusions

Internationally, jurisdictions recommend starting to screen for cervical cancer between age 21 and 30, with many recommending that screening begin when a woman becomes sexually active, regardless of age. Literature about the optimal age to start routine population-based screening for cervical cancer points toward a later screening age than is used currently in most jurisdictions.

Cervical cancers in women younger than 25 are rare, possibly related to the fact that the majority of oncogenic HPV infections as well as precursor lesions tend to resolve spontaneously in younger women. In addition, current screening methods do not appear to lead to a reduction in cervical cancers in this cohort of women as they age. At the same time, treatment of precursor lesions may be associated with an increased risk of preterm births.

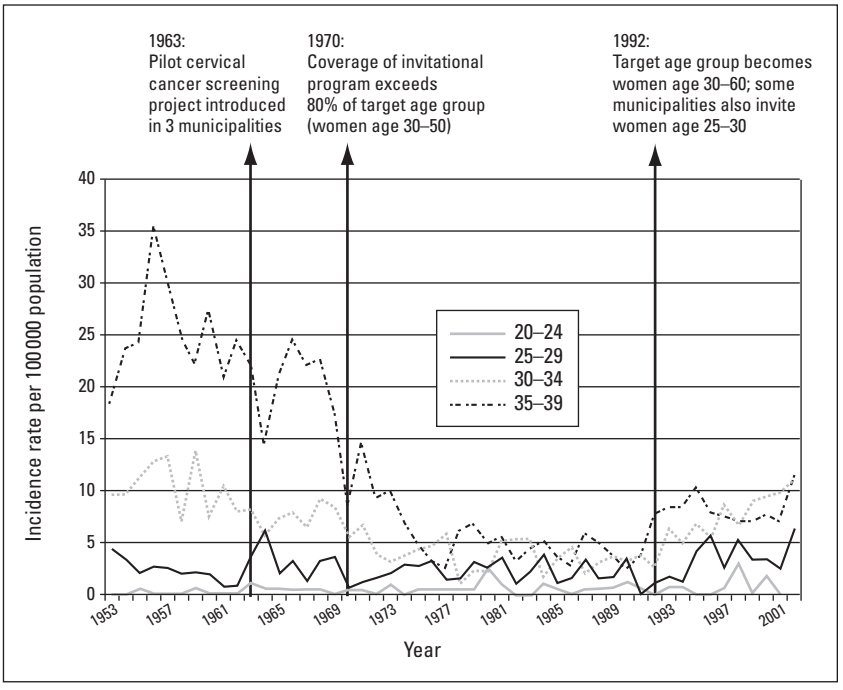

Figure 2. Comparison of cervical cancer incidence in Finland for women age 20–39 by 5-year age groups, 1953–2002.

Competing interests

None declared.

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