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Screening 3 years after negative test, rather than annually, would result in three additional cases of cervical cancer per 100,000 women screened ☆

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KEYWORDS
Cervical cancer;
Mass screening;
Women;
Markov model;
Screening frequency

Summary

Question How many additional cervical cancers would occur if annual screening reduced to screening 3 years after the last negative test?

Study design Outcomes analysis with Markov model using screening programme data.

Main results Among 32,230 women with $\geqslant 3$ consecutive negative tests, none had cancer; 16 had grade 2 or three cervical intraepithelial neoplasia. Among 938,576 women with no prior tests, 511 women had cancer. Cases were more common in women in whom fewer negative tests were performed. The model predicted that screening 3 years after the last negative test, rather than annually, would lead to five extra cases of cervical cancer in a cohort of 100,000 women aged under 30 years. Three extra cases among women aged 30–44 years, one extra case among women aged 45–59, and no additional cases among women aged 60–64, were predicted.

Authors' conclusions An average of three additional cases of cervical cancer per 100,000 is predicted if women between 30 and 64 years are screened 3 years after their last negative test, rather than annually for 3 years.

Commentary

The sensitivity of the conventional Pap test is less than 65%. Although the risk of cancer associated with screening intervals of more than 12 months for women who had negative results on previous tests has yet to be determined, many clinicians continue to perform annual screening because of the perception that there is a high excess risk of cervical cancer.

Using a Markov model that estimates the rate at which dysplasia will progress to cancer, Sawaya et al. have estimated the risk of cancer within 3 years after one or more negative Pap tests in a population of 938 576 women younger than 65 years of age. Compared with annual screening for 3 years, screening performed 3 years after the last

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negative test in women aged 30–64 years who have had three or more negative consecutive Pap tests, is associated with an excess risk of cervical cancer of approximately 3/100 000. However, it is possible to argue that this excess risk could be as high as 30%, based on an estimated current cervical cancer incidence of 10/100 000 in developed countries.

Several limitations of this study must be acknowledged. There is no information on other risk factors, the data overestimate the prevalence of neoplasia and there is no verification of cytologic and histologic outcomes. The assumptions used in the model affect the calculated risk. If liquid based cytology, which shows a greater sensitivity had been used, the risk of cancer would be lower.

Implications

This study shows that a short interval between conventional Pap tests does not completely prevent the occurrence of invasive cervical cancer in regularly screened women. Recently, research has found that combining more sensitive tests, such as the HPV DNA test (detects oncogenic human papillomavirus), in women aged 30 years or over, increases sensitivity,[1] even when screening is performed every 3 years. Cuzick et al.[2] reported on HPV testing for primary screening. The combined test increases sensitivity of detection of high-grade diseases to more than 95%. Primary screening studies involving more than 50 000 women worldwide have demonstrated HPV testing to be more sensitive than cytology alone and that the combination provides a negative predictive value of more than 99%. Recently the EUROGIN expert consensus conference[3] stated that the most cost-effective method is to use the most sensitive possible test at the longest possible interval. The cost-effectiveness of this combined approach is currently under evaluation.

Study parameters

Question	How many additional cervical cancers would occur if annual screening reduced to screening 3 years after the last negative test?
Study design	Outcomes analysis with Markov model using screening programme data.
Setting	National Breast and Cervical Cancer Early Detection Program for low-income, underinsured women, across USA; January 1991–March 2000.
To	Anonymised data (including demographics, screening results, diagnostic procedures, histologic outcomes) from 938,576 women undergoing Papanicolaou cervical screening, aged under 65 years were used to generate a Markov model. Main exclusion criteria: unsatisfactory screening tests, pending results, unclassified results, missing information.
Analysis	Women's data were grouped according to the number of cervical screening tests. Consecutive tests were carried out between 9 and 36 months of each other (one test $n = 938{,}576$, one negative test followed by a second test $n = 136{,}588$, two negatives followed by a third test $n = 49{,}316$, at least three negative tests $n = 32{,}230$). The model predicted rates of newly diagnosed cancers according to a given prevalence of dysplasia in hypothetical cohorts of 100,000 women screened 3 years after their last negative test rather than annually. Results were stratified by age and number of previous negative tests.
Main outcomes	Predicted incidence of dysplasia, cervical cancer.
Notes	Sensitivity analyses were performed on model assumptions regarding rates of progression of cancer, and with a doubled dysplasia prevalence rate (this led to excess cases of two, one and one in women aged 30–44, 45–59 and 60–64, respectively).

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