Original Articles

Effect of screening on the incidence of cervical cancer in Alberta

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The rates of registration of cases of in-situ and invasive cancer of the cervix in Alberta have fallen for women aged 35 and over since the introduction of screening in the early 1960s, as predicted by theory and described in Finland. However, for women aged 15 to 34 years of age the predicted pattern was followed only initially: the registration rate for in-situ and probably also invasive cancer increased after 1973. This could be due to an actual increase in the incidence of in-situ cancer of the cervix among younger women, as might be expected from the epidemiologic aspects of the disease, but it might also be due to increased recruitment of younger women to the screening program.

Comme il était théoriquement prévu et tel qu'on l'a décrit en Finlande, depuis l'introduction du dépistage au début des années 60, le taux des cas de cancer in situ ou invasif du col utérin enregistrés en Alberta a diminué chez les femmes de 35 ans et plus. Toutefois, pour les femmes de 15 à 34 ans la tendance prévue n'a été observée qu'au début: après 1973 le taux des cancers in situ enregistrés, et probablement aussi celui des cancers invasifs, a augmenté. Cette constatation pourrait être attribuable à une augmentation réelle de l'incidence du cancer in situ du col utérin chez les femmes jeunes, comme on pourrait s'y attendre, compte tenu des aspects épidémiologiques de la maladie, mais elle pourrait être aussi due à une augmentation du nombre de jeunes femmes adhérant au programme de dépistage.

Although the effectiveness of cytologic screening has never been tested experimentally, there is now a general consensus that screening programs have reduced the mortality of cervical cancer in Canada.[1] The effect of screening on the incidence of invasive cancer can be observed only in regions where a population-based cancer registry has existed over the period when screening was introduced. Finland, for example, has a national cancer registry, and Hakama[2] has described the trends in the registration of in-situ and invasive cancer of the cervix following the introduction of a mass screening program in the 1960s.

A similar situation exists in Alberta, where a cancer registry has been in operation since 1953 and intensive screening for cervical cancer also began in the early 1960s. In this paper we review the trends in registration of cases of in-situ and invasive cancer of the cervix. For older women the trends are similar to those seen in the Finnish statistics, and we show that these are in keeping with predictions from a simple compartment model. For younger women, however, the trends are different, and we examine the possible causes of this finding. In particular, we examine the trends in the stage of the cancer at the time of presentation and in the rate of survival following diagnosis. We also present some information relating to the intensity of screening in older and younger women.

Methods

Statistics on the registration of cases of in-situ and invasive cancer of the cervix and on survival following the diagnosis of invasive cancer were abstracted from the records of the Alberta Cancer Registry for the years 1953 through 1978. All statistics on malignant neoplasms of the cervix in persons aged 15 years and over were included. Most such tumours are squamous cell carcinomas. Rates per 100 000 women-years were calculated with the use of official mid-year population estimates as published annually by Statistics Canada in "Estimates of Population by Sex and Age for Canada and the Provinces" (catalogue no. 91-202).

In the years 1964 through 1978 all patients registered in northern Alberta had their cancer uniformly staged, usually under general anesthesia, by a radiotherapist and a gynecologist at the time of presentation. The TNM (tumour–nodes–metastases) system of classification[3] was used for staging.

Statistics on the numbers of claims for payment for cytologic examination (fee code E-311) by age of the patient for the 9 fiscal years 1970–71 through 1978–79 were obtained from the Alberta Department of Hospitals and Medicare. Rates were calculated with

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the use of the population estimates for the dominant calendar year. Only a proportion of all the cervical cytologic examinations performed in the province were included in these statistics, and a small fraction (probably less than 10%) of the claims were for cytologic tests other than Papanicolaou smears. The rates were therefore imperfect indicators of the extent of cervical screening by age, but no better information was available.

Results

Registration

Fig. 1 shows the trends in registration of cases of in-situ and invasive cancer of the cervix in Alberta women aged 15 years and over during the period 1953–78. The predicted trends, derived from a simple compartment model based on screening theory (see Appendix), are shown for comparison. Following the introduction of screening for cervical cancer the rate of registration of cases of in-situ cancer rose sharply in the mid-1960s. Then, as predicted, this rate declined together with the rate for invasive cancer. The registration rate for invasive cancer levelled out, as would be predicted if the screening practice remained constant, but beginning in 1973 the registration rate for in-situ cancer rose sharply. However, this recent increase was restricted to women below 35 years of age, as Figs. 2A and 2B show. The registration rates for the older women (Fig. 2B) followed the predicted pattern, but for the younger women (Fig. 2A) the registration rate for in-situ cancer initially rose, then flattened but did not decline, and finally, after 1973, rose again. The registration rates for invasive cancer in the younger women were erratic owing to small numbers (Tables I and II), but there was some indication of a decline following the onset of screening, or at least a flattening out of a previous slight upward trend, with a resumption of that trend since 1973.

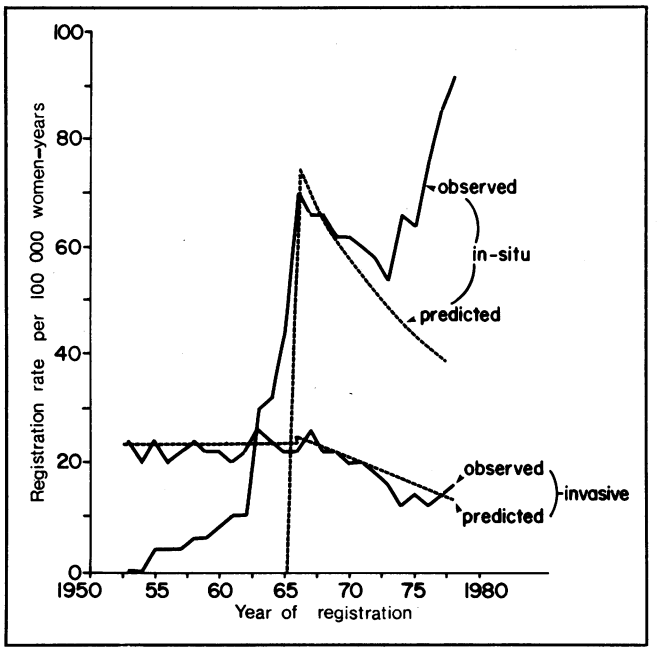

FIG. 1—Incidence of cervical cancer among women aged 15 years and over in Alberta in 1953 through 1978: predicted rates, based on theoretical model, and observed registration rates.

Survival

Fig. 3 shows the 5-year survival rates for patients in Alberta with invasive cancer of the cervix diagnosed

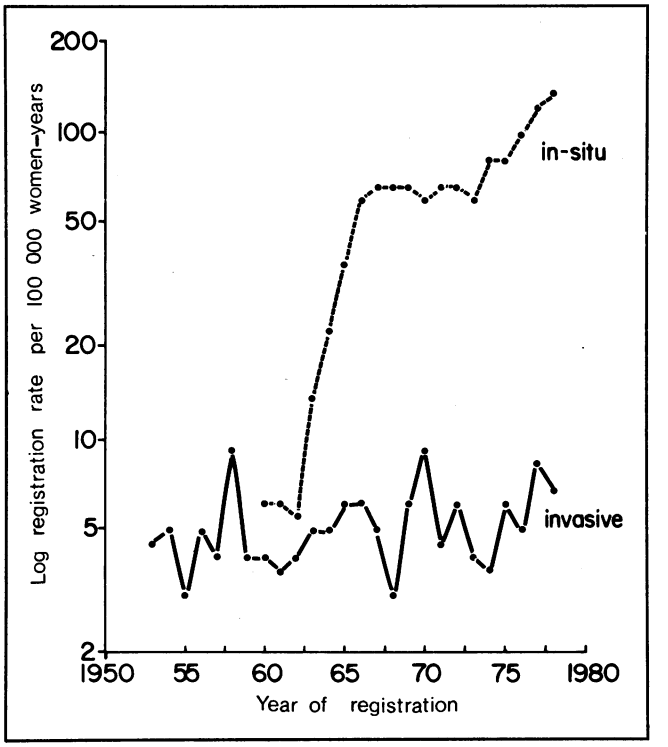

FIG. 2A—Incidence of cervical cancer in Alberta in 1953–78 in women aged 15 to 34 years.

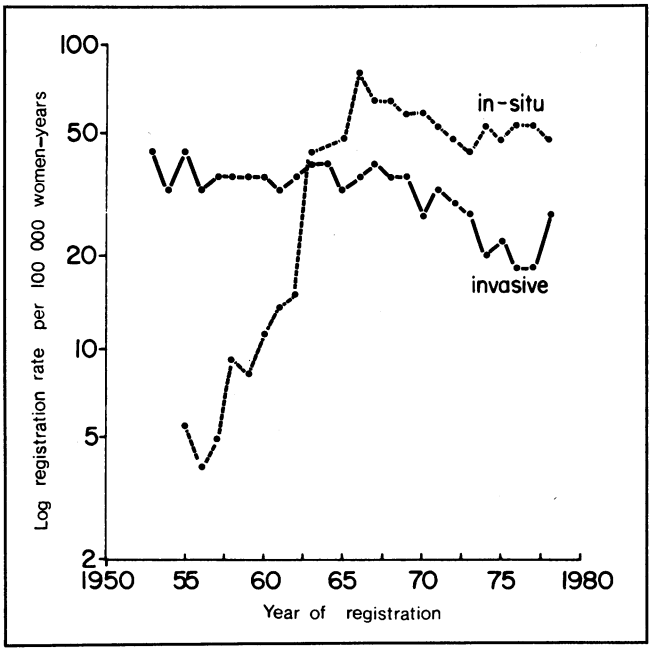

FIG. 2B—Incidence of cervical cancer in Alberta in 1953–78 in women aged 35 years and over.

in four consecutive 5-year periods beginning with 1953–57. Among women aged 15 to 34 years at the time of diagnosis the rate increased progressively over the 20 years, with an accelerated increase in the last two 5-year periods. Among women aged 35 years and over the rate increased in the first three periods but declined in the last period.

Table I—Numbers of cases and incidence per 100 000 women-years of in-situ cancer of the cervix in Alberta in 1953 through 1978

Year of diagnosis	Patient age (yr); no. of cases (and incidence)					
	15–34		35+		15+	
1953	0	(0)	3	(1.8)	3	(0.9)
1954	1	(0.6)	1	(0.6)	2	(0.6)
1955	3	(1.8)	10	(5.4)	13	(3.7)
1956	3	(1.8)	8	(4.2)	11	(3.1)
1957	4	(2.4)	10	(5.1)	14	(3.8)
1958	4	(2.3)	19	(9.2)	23	(6.1)
1959	5	(2.8)	18	(8.5)	23	(5.9)
1960	11	(6.1)	25	(11.3)	36	(9.0)
1961	11	(5.9)	30	(13.1)	41	(9.9)
1962	11	(5.8)	36	(15.3)	47	(11.0)
1963	26	(13.2)	110	(45.2)	136	(31.0)
1964	44	(22.0)	104	(41.7)	148	(33.0)
1965	75	(36.8)	129	(50.6)	204	(44.5)
1966	122	(58.5)	205	(79.0)	327	(69.9)
1967	138	(64.0)	175	(66.0)	313	(65.1)
1968	148	(65.6)	184	(67.8)	332	(66.8)
1969	151	(63.8)	165	(59.5)	316	(61.5)
1970	155	(62.7)	177	(62.3)	332	(62.5)
1971	167	(64.6)	159	(54.8)	326	(59.4)
1972	171	(63.8)	152	(51.3)	323	(57.2)
1973	174	(62.0)	142	(46.9)	316	(54.1)
1974	229	(78.1)	173	(55.8)	402	(66.6)
1975	255	(81.9)	156	(47.3)	411	(65.1)
1976	313	(94.9)	186	(56.3)	499	(75.6)
1977	405	(116.8)	183	(53.4)	588	(85.3)
1978	481	(131.9)	176	(49.8)	657	(91.8)

Table II—Numbers of cases and incidence per 100 000 women-years of invasive cancer of the cervix in Alberta in 1953 through 1978

Year of diagnosis	Patient age (yr); no. of cases (and incidence)					
	15–34		35+		15+	
1953	7	(4.5)	74	(43.2)	81	(24.9)
1954	8	(5.0)	60	(33.6)	68	(20.1)
1955	5	(3.1)	80	(43.3)	85	(24.5)
1956	8	(4.8)	62	(32.5)	70	(19.7)
1957	7	(4.1)	73	(37.0)	80	(21.9)
1958	16	(9.3)	75	(36.7)	91	(24.1)
1959	7	(4.0)	76	(35.7)	83	(21.3)
1960	7	(3.9)	84	(30.1)	92	(22.9)
1961	7	(3.8)	75	(32.1)	82	(19.8)
1962	8	(4.2)	85	(37.0)	93	(21.8)
1963	10	(5.1)	100	(41.1)	110	(25.0)
1964	10	(5.0)	96	(30.5)	106	(23.6)
1965	12	(5.9)	88	(34.5)	100	(21.8)
1966	12	(5.8)	92	(35.5)	104	(22.2)
1967	11	(5.1)	110	(41.5)	121	(25.2)
1968	7	(3.1)	102	(37.6)	109	(21.9)
1969	14	(5.9)	98	(35.4)	112	(21.8)
1970	22	(8.9)	79	(27.0)	101	(19.0)
1971	12	(4.6)	95	(32.8)	107	(19.5)
1972	16	(6.0)	86	(29.0)	102	(18.1)
1973	11	(3.9)	79	(26.1)	90	(15.4)
1974	11	(3.7)	61	(19.7)	72	(11.9)
1975	19	(6.1)	70	(21.9)	89	(14.1)
1976	16	(4.9)	63	(19.1)	79	(12.0)
1977	27	(7.8)	65	(19.0)	92	(13.3)
1978	24	(6.6)	93	(26.5)	117	(16.3)

Stage at time of presentation for northern Alberta patients

Fig. 4 shows the distribution of invasive cancer of the cervix by stage at the time of diagnosis for women whose cancer was diagnosed in three consecutive 5-year periods beginning with 1964–68. Among the women aged 15 to 34 years at the time of diagnosis the proportion presenting with stage I, especially Ia, disease increased over the three periods, the increase being greater between the first two periods than between the last two. In contrast, among the older women the overall proportion presenting with stage I or II disease remained practically unchanged, although there was a consistent increase in the proportion with stage Ia disease. There was a slight increase over the 15 years in the proportion of older women presenting with stage III or IV disease.

Medicare claims

Fig. 5 shows the numbers of claims for payment for cytologic examination per 1000 women in Alberta over the 9 fiscal years 1970–71 through 1978–79. For the women aged 35 years and over the rate increased for the first 6 years, then flattened out. For the younger women the initial increase was more pronounced, and the rate continued to rise throughout the decade, though less steeply than before.

Discussion

Assuming a stationary, homogeneous population with fixed rates of disease progression, the predicted pattern of incidence rates for in-situ and invasive cancer of the cervix after the abrupt introduction of a screening program is as shown in Fig. 1. Following the onset of screening the incidence of in-situ cancer should rise sharply to a peak and then fall exponentially. The incidence of invasive cancer, constant prior to screening, should rise almost imperceptibly as presymptomatic cases are detected by screening, then

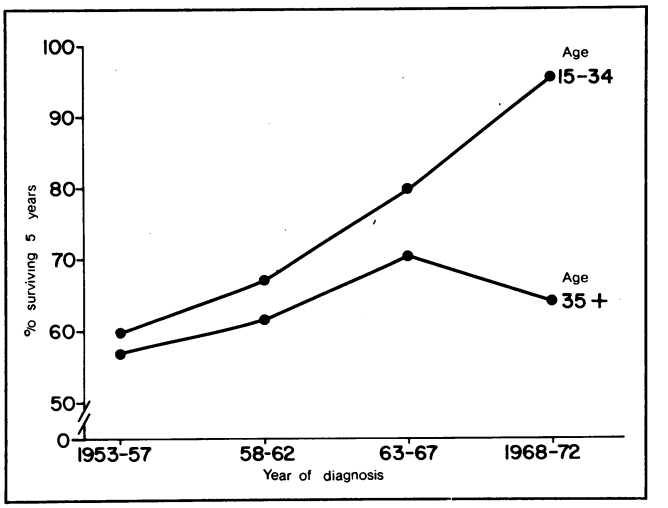

FIG. 3—Five-year survival rates for women in Alberta with invasive cervical cancer according to patient's age at time of diagnosis.

should fall exponentially as the stock of in-situ cases is depleted by screening. The registration rates in Finland[2] and for older Alberta women have followed this pattern fairly closely. For younger Alberta women, however, the registration rate for in-situ cancer fell and then rose again; although the numbers were small there was some indication that the registration rate for invasive cancer changed similarly.

There are three possible explanations for this finding. First, the true incidence of the disease may be increasing in younger women. If so, the model would predict the observed pattern, with an increasing rate as the mounting incidence forces through the downward trend. An increasing incidence of in-situ cancer, and eventually of invasive cancer, in younger women would be in keeping with what is known about the epidemiologic aspects of the disease. Case–control studies have shown that the most important risk factors for cervical cancer are an early onset of sexual activity and the number of sexual partners.[4] Increasing rates of death from cervical cancer in women under 35 years of age have been reported from England and Wales,[5] and Anello and Lao[6] have said that "an increase in cervical cancer death rates among U.S. women below the age of 25 cannot be excluded" — a cautiously formulated conclusion since the rates were based on small numbers. Studies of mortality have demonstrated increasing rates of death from cervical cancer in certain countries in women who were young adults in years of unusual sexual promiscuity (e.g., times of war).[7] If, as is widely believed, the changes in sexual mores in North America in the past two or three decades have led to earlier and more promiscuous sexual activity, then an increase in the incidence of cervical cancer is to be expected, particularly with the increased use of nonbarrier contraceptives such as the Pill and intrauterine devices.

The second possibility is that the intensity of screening among younger women has increased. There is some support for this possibility from the Medicare claims data we have analysed, though they do not represent all the cytologic smears that were performed. Although the slope of the rate of claims between 1970–71 and 1978–79 for payment for cytologic examination of the younger women was not steep, it could explain the increased rate of registration of

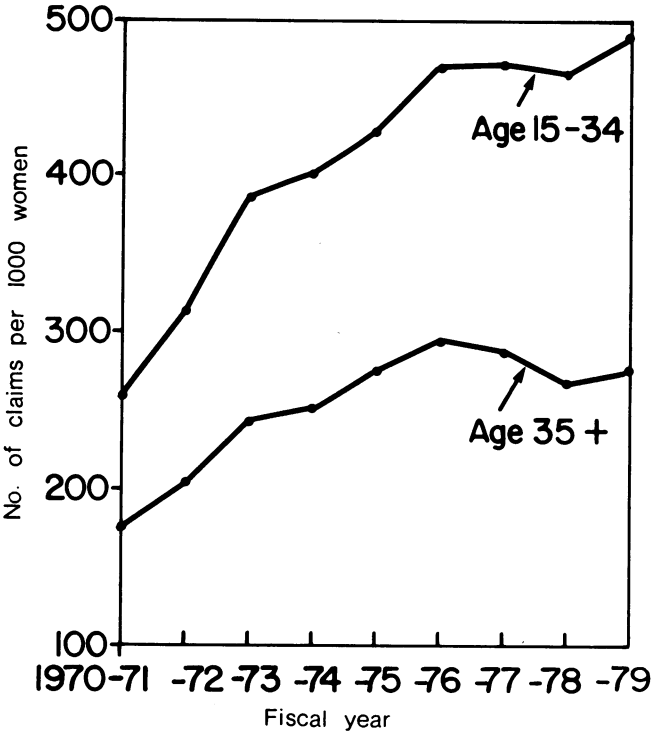

FIG. 5—Numbers of claims for payment for cytologic examination in Alberta according to patient's age.

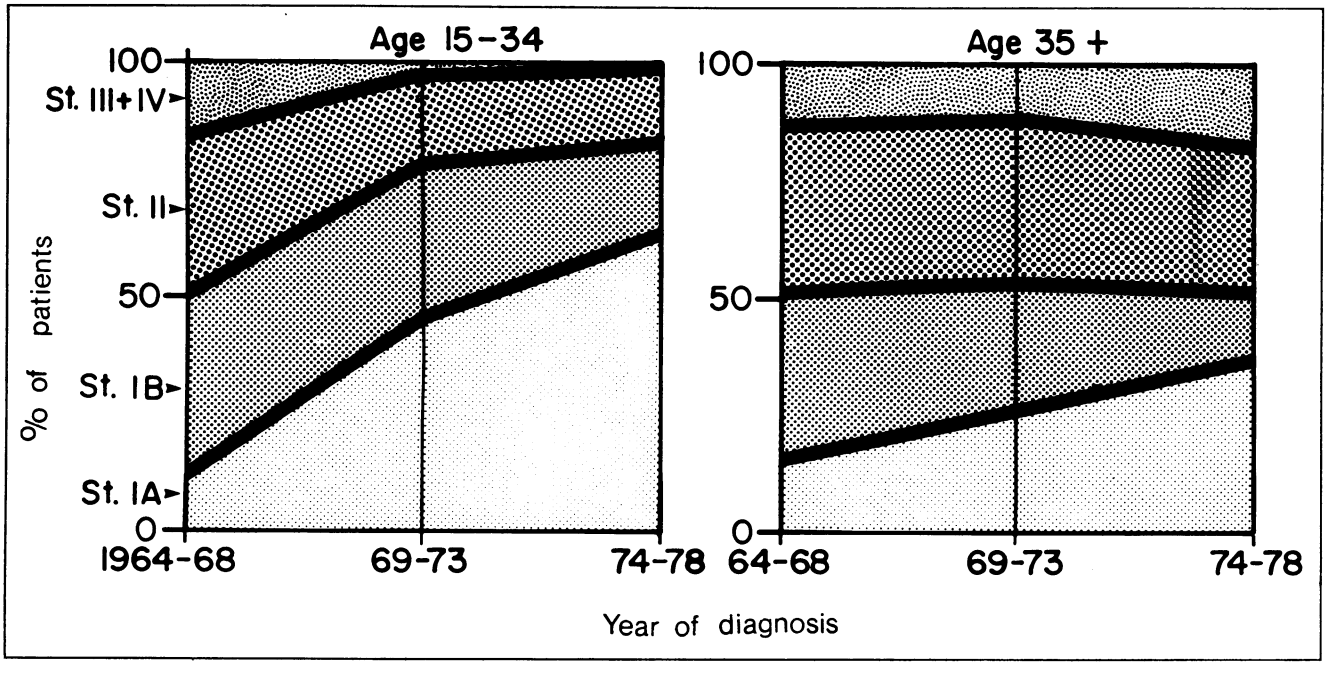

FIG. 4—Distribution of stages of invasive cervical cancer at time of diagnosis according to patient's age.

younger women if it represented an increase in recruitment to the screening program rather than repeated screening of the same individuals. In the absence of a central registry for the results of Papanicolaou tests the contribution from repeated screening of the same individuals to the screening rates for young and for old women is hard to estimate.

A third possible explanation for the increasing registration rate for in-situ cancer is that the completeness of registration has increased. There were, in fact, changes in the administration procedures of the Alberta Cancer Registry in the mid-1970s; in particular, an increased effort was made to obtain information from pathology reports and other records. However, it is difficult to see why this would selectively affect the records of younger women.

The progressive improvement in survival of patients with invasive cancer of the cervix who were 15 to 34 years old when the diagnosis was made is well explained by the increasing proportion presenting with stage I, particularly Ia, disease. Despite the screening program they continued to present with invasive disease, but it was detected earlier. The overall proportion of older women presenting with stage I or II disease remained practically unchanged, although there was a consistent increase in the proportion with stage Ia disease.

Late-stage cancer of the cervix has virtually disappeared among younger women, whereas the proportion of older women presenting with stage III or IV disease has not been reduced.

The sharply rising registration rates for in-situ cancer, together with the increasing proportion of stage Ia disease among the younger patients, supports an actual increase in the incidence of cervical cancer since 1973. Increased recruitment of younger women to the screening program can explain these findings only in part.

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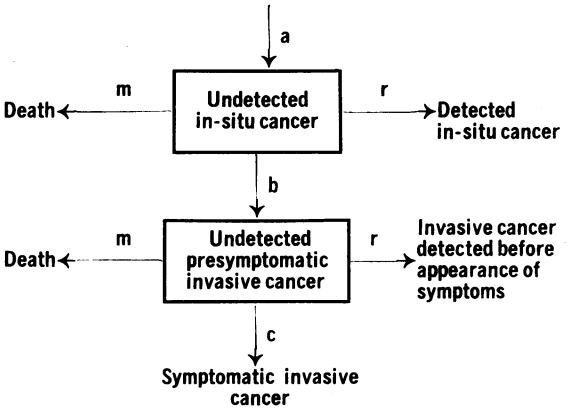
Appendix—Compartment model of screening for cervical cancer



Let x(t) be the number of cases of undetected in-situ cancer and y (t) the number of cases of undetected presymptomatic invasive cancer "t" years after the onset of screening. Then, with the transition rates identified above:

$$x(t) = \frac{a}{m+b+r} + \frac{ar}{(m+b)(m+b+r)} e^{-(m+b+r)t}$$

$$y(t) = \frac{ab}{(m+b+r)(m+c+r)} + abr\left[\frac{e^{-(m+b+r)t}}{m+b+r} - \frac{e^{-(m+c+r)t}}{m+c+r}\right]/(c-b)(m+b)$$

Prior to screening (i.e., with $r = 0$) the observed incidence of invasive cancer is $abc/(m+b)(m+c)$. After screening the observed incidence of in-situ cancer is $rx(t)$ and that of invasive cancer $(c+r)y(t)$. In Fig. 1 these functions are plotted with $a = 40$, $b = 0.025$, $c = 0.5$, $r = 0.075$ and $m = 0.015$.