Selective screening for cervical cancer

Experience of the Finnish mass screening system

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SUMMARY Names of women eligible to be screened for cervical cancer are taken from the national population registry and the women are invited by a personal letter. The data, from these mass screenings are analysed and stored at the screening registry. To reduce the costs of the system and to increase the yield of preinvasive lesions the idea of selective screening was considered. It was decided that if people were selected according to their risk factors, as recorded in the national population registry, the screening would be ineffective as many cases of invasive cancer were found in the low risk groups. High risk factors were determined from anamnestic data on symptoms and from previous cytological diagnoses. The proportion of women with symptoms of bleeding or with class II-V smears without positive histological results constituted fewer than 10% of the participants, but 20% and 40% respectively of invasive carcinomas were found in these groups during the subsequent follow-up period. Thus it is suggested that selective screening apart from that based on age has a limited application and should be restricted mainly to the interval between the organised screenings, which in Finland is five years.

Voluntary cancer organisations started mass screening for cervical cancer in Finland in the early 1960s. After some field trials a permanent programme was introduced and now all Finnish women who are at an age of high risk for cervical cancer are screened every five years. Those to be screened are chosen by municipal authorities and there are some variations in methods of selection between the different municipalities. Women eligible for screening are selected by a computer from the national population registry. Individual data are printed on a notification card, on special lists, and in a personal letter of invitation. The letter is posted and those invited attend the screening clinics. At the clinic anamnestic data are completed on the notification card when the smear is taken. The cytological diagnosis and if necessary the histological confirmation of the diagnosis is entered on the card by the laboratory.

These notification cards are sent to the national mass screening registry at the Finnish Cancer Registry, where the data are linked with the original population data and with any record of previous screenings. Details describing the organisation of such mass screenings are given elsewhere (Hakama *et al.*, 1975). This central feedback system makes it possible to identify groups of women who have a greater risk of cervical cancer. They may be identified by demographic variables from the

national population registry or by variables recorded at previous screenings. The demographic variables may be used to select high risk groups, whereas the variables from previous screenings are used only to define the interval between screenings.

Materials and methods

The data were taken from the number of screenings during the period 1963-71. The women to be screened were generally chosen from age groups 30-34, 35-39, 40-44, 45-49, and 50-54 years. The smears taken for the screening programme were analysed at the 11 cytological laboratories founded by the Cancer Society of Finland. All women participating were notified of the results. A special follow-up visit was arranged at a hospital for women with malignant or suspicious smears. The hospital then reported the results of the tests with details of treatment to the laboratory.

All the laboratories sent full details to the national mass screening registry. The attenders as well as the non-attenders were followed-up to estimate the subsequent risk of both cervical cancer and preinvasive lesions after the first screening. The follow-up was determined by the subsequent reports at a later examination within the mass screening programme and by the notifications of cancer sent to the Finnish Cancer Registry. The

women were followed-up until the end of 1972.

The lesions confirmed at surgery or biopsy were divided according to their diagnostic group—dysplasia of low degree, dysplasia of high degree, carcinoma *in situ*, microinvasive carcinoma, and frankly invasive carcinoma—in accordance with the histological examination of the lesion. As this classification is subjective (Hulme *et al.*, 1968), and as both dysplasia of high degree and carcinoma *in situ* lesions are operated on in Finland, these are grouped together in the tables. A detailed description of the diagnostic criteria and procedures has been given (Kauraniemi, 1969).

The risk of cervical cancer was evaluated in terms of incidence rates in the different population groups. Variables characterising the group were taken from the results of the first screening based on personal history or diagnostic results. The incidence rates for invasive cervical cancer after the first screening were estimated by dividing the number of new cases of invasive cancer diagnosed after the first screening by the person-years from the date of the first screening to the diagnosis of invasive cancer until the end of 1972.

The incidence rates for microinvasive and pre-invasive stages were evaluated only for the population that had been screened more than once. These incidence rates were estimated as the ratio of new cases detected at repeated screenings to the person-years from the date of the first screening until the date of diagnosis of a lesion, or until the date of the last reported screening. It was assumed, that the growth had appeared at exactly half-way between the two last screenings.

Incidence rates were given per 100 000 person-years and were adjusted for age to the European standard population (Doll *et al.*, 1970). Because there were few women examined outside the age group 30–54 years, the age adjusted rates were based on five-year age groups within this range.

Results

The total Finnish female population was 2.4 millions in 1971. The overall incidence of cervical cancer has shown a decreasing trend since the mid 1960s. The detection rates for carcinoma *in situ* lesions increased from two to about 10 per 100 000 during the study period (Fig. 1).

The organised mass screening programme started gradually. In 1963 the number of smears reported to the mass screening registry was 2000 and since 1970 the annual number of smears has been about 100 000. Out of the 407 000 attenders (390 000 by personal invitation), 78 000 had been rescreened

Fig. 1 Cancer of the cervix uteri in Finland: annual age-adjusted incidence and mortality rates of invasive carcinomas and age-adjusted detection rates of carcinoma *in situ* lesions in 1953–72.

at least once by the end of 1972. The number of non-attenders was 35 000. Table 1 shows the age distribution for the Finnish female population in 1971 and for the women screened and invited for screening during 1963–72.

INCIDENCE

The Finnish mass screening programme is based on the principle of selective screening by age. Figure 2 shows the age specific incidence curve for invasive carcinomas and age specific detection rates for carcinoma *in situ* lesions in Finnish women.

Tables 2 and 3 show the incidence rates for different lesions by marital state and by parity,

Fig. 2 Age-specific incidence rates of invasive carcinomas and detection rates of carcinoma *in situ* lesions of the cervix uteri in Finland 1966–70 (Teppo *et al.*, 1975).

Table 1 *The mean female population in Finland in 1971 and the number of women selected for screening from the Finnish mass screening registry 1963-72, by age*

Age (years)	Female population (1971)		Attendees (1963-1972)		Non-attenders (1963-72)	
	No.	%	No.	%	No.	%
<30	1 130 200	47.4	4 972	1.2	1 181	3.3
30-34	147 000	6.2	18 974	4.7	4 794	13.6
35-39	135 300	5.7	46 807	11.5	4 660	13.2
40-44	147 200	6.2	120 948	29.8	7 615	21.6
45-49	148 200	6.2	99 745	24.5	8 257	23.4
50-54	134 100	5.6	94 882	23.3	7 482	21.2
55-59	136 300	5.7	16 118	4.0	1 144	3.2
> 59	406 800	17.1	3 912	1.0	146	0.5
Total	2 385 100	100	406 358	100	35 279	100

Table 2 *Age-adjusted incidence rates (per 100 000 person-years) of cervical lesions in Finland 1963-72 after the first Papanicolaou smear, by marital state*

Marital state	Histological diagnosis			
	Dysplasia levis	Dysplasia gravis/ carcinoma in situ	Microinvasive carcinoma	Invasive carcinoma
Single	2	17	0	2
Married	6	25	3	3
Widowed	7	119	0	5
Divorced	33	55	6	6
Total	7	27	2	3

Table 3 *Age-adjusted incidence rates per 100 000 person-years of cervical lesions in Finland 1963-72 after the first Papanicolaou smear, by parity*

No. of pregnancies	Histological diagnosis			
	Dysplasia levis	Dysplasia gravis/ carcinoma in situ	Microinvasive carcinoma	Invasive carcinoma
0	4	15	1	2
1	4	20	2	2
2	6	17	3	2
3	8	28	3	3
4	2	40	0	3
5	21	40	2	3
6	42	71	1	7
7	9	21	0	3
8 or more	0	49	8	5
Total	7	27	2	3

which are risk factors in the national population registry. There was an approximate fivefold risk of a preinvasive lesion for those in the highest risk groups (previously married or multiparous women), compared with the low risk groups defined by these two variables.

Anamnestic symptoms and previous electrocoagulation indicated an increased risk of cervical cancer during the subsequent follow-up period (Table 4). Those with coital bleeding but a negative smear had a relative risk of 15 for frankly invasive carcinoma. Relative risks for other diagnostic groups were smaller and symptoms of bleeding were likely to be less associated with risk of a preinvasive lesion. Those who had had a previous electrocoagulation had a reduced risk of cervical malignant disease.

If a woman had a history of several symptoms of bleeding simultaneously, she had an increased risk of frankly invasive carcinoma, whereas other cervical lesions were generally preceded by none, one, or two different symptoms of bleeding (Table 5).

Women with cytological diagnoses of Papanicolaou class II to V combined with negative histological result at the initial screening had a higher risk of cervical cancer (Table 6). The incidence of frankly invasive carcinoma increased from two in class I to 78 in class IV. The relative changes were of the same order of magnitude in the other groups of dysplasias and malignancy. Women with a class IV smear had a particularly high risk of dysplasia gravis or carcinoma *in situ* lesion, the age-adjusted annual incidence being 4%.

Table 4 Age-adjusted incidence rates per 100 000 person-years of cervical lesions in Finland 1963-72 after the first Papanicolaou smear, by anamnestic history

Anamnestic history	Histological diagnosis			
	Dysplasia levis	Dysplasia gravis/ carcinoma in situ	Microinvasive carcinoma	Invasive carcinoma
Continuous leucorrhoea	10	41	5	3
Bloody discharge	24	44	3	4
Coital bleeding	8	0	0	46
Irregular bleeding	0	19	6	5
Postmenopausal bleeding	0	0	0	7
Electrocoagulation	3	17	0	1

Table 5 Age-adjusted incidence rates per 100 000 person-years of cervical lesions in Finland 1963-72 after the first Papanicolaou smear, by number of different symptoms of bleeding

No. of symptoms of bleeding	Histological diagnosis			
	Dysplasia levis	Dysplasia gravis/ carcinoma in situ	Microinvasive carcinoma	Invasive carcinoma
0	7	27	2	3
1	12	19	4	3
2	0	53	0	38
3	0	0	0	39
4	0	0	0	0
Total	7	27	2	3

Table 6 Age-adjusted incidence rates per 100 000 person-years of cervical lesions after the first Papanicolaou smear, by cytological diagnosis with negative histological result at first screening. Finland 1963-72

Cytological diagnosis	Histological diagnosis			
	Dysplasia levis	Dysplasia gravis/ carcinoma in situ	Microinvasive carcinoma	Invasive carcinoma
I	6	18	2	2
II	10	139	15	13
III	144	705	23	31
IV	0	3 878	48	78
V	0	503	0	0
Total	7	27	2	3

PREVALENCE OF HIGH RISK INDICATORS

By selecting women in the age group 30 or 35 to 50 or 55 years there was a reduction of 70% in the total female population (Table 1). Marital groups with a high incidence (widowed and divorced) comprised only 9% of the total number of women screened (Table 7). Multiparous women (Fig. 3), with five or more deliveries represented less than 15%.

The prevalence of reported previous electro-

coagulation was 14% and that of various symptoms of bleeding varied from 2.3% to 0.5% (Table 8); cases with two or more different symptoms of bleeding

Table 7 Distribution of women who participated in the Finnish mass screening programme 1963-72, by marital state

Marital state	No.	%
Single	39 984	9.9
Married	327 728	81.0
Widowed	21 421	5.3
Divorced	15 587	3.9
Total*	404 720	100

*Those for whom marital state is known

Fig. 3 Percentage distribution of the participants in the Finnish mass screening programme by parity in 1963-71.

Table 8 *Prevalence of anamnestic characteristics among those participating in the Finnish mass screening programme 1963-72. One participant may belong to several groups*

Anamnestic characteristic	No.	%
Continuous leucorrhoea	84 899	20.9
Bloody discharge	7 222	1.8
Coital bleeding	2 648	0.7
Irregular bleeding	9 280	2.3
Postmenopausal bleeding	2 076	0.5
Electrocoagulation	57 209	14.1
Total no. of participants	406 321	100

Table 9 *Distribution of histologically normal cases by cytological diagnosis after the first screening in Finland 1963-72*

Cytological diagnosis	No.	%
I	372 863	92.25
II	29 809	7.37
III	1 357	0.34
IV	1 28	0.03
V	23	0.01
Total	404 180*	100

*Excluding those for whom cytological diagnosis is unknown

constituted only a small proportion of the total number of smears. Cytological diagnoses II to V with normal histological result totalled 8% of all the primary smears (Table 9).

THE PROPORTION OF LESIONS WITH A HIGH RISK HISTORY

Most of the frankly invasive cases were diagnosed in women who were at an age that entitled them to be screened every five years (Fig. 2). The age specific incidence curves are known only for invasive carcinomas, as the other lesions were diagnosed by screening. Those who were widowed or divorced constituted less than 20% of the positive diagnoses (Table 10) and the multiparous women represented less than 30% (Table 11). Symptoms of bleeding were also relatively rare and more than half of the invasive cases were in women who had neither symptoms of bleeding nor continuous leucorrhoea (Table 12). Out of the 109 cases with invasive carcinoma 90 did not have any symptoms of bleeding and the women with such symptoms were even fewer in the other histological groups.

About 40% of the cases with an invasive cancer diagnosed after the first screening had a class II to class V smear at the beginning of the follow-up period (Table 13).

Discussion

Successful selective screening is based on the presumption that there is a subpopulation with a

Table 10 *The number and percentage distribution of cervical lesions diagnosed after the first Papanicolaou smear, by marital state. Finland 1963-72*

Marital state	Histological diagnosis							
	Dysplasia levis		Dysplasia gravis/ carcinoma in situ		Microinvasive carcinoma		Invasive carcinoma	
	No.	%	No.	%	No.	%	No.	%
Single	3	6.1	15	6.7	0	—	5	4.6
Married	35	71.4	170	75.9	20	90.5	86	78.9
Widowed	3	6.1	18	8.0	0	—	7	6.4
Divorced	8	16.3	19	8.5	2	9.1	10	9.2
Total*	49	100	224	100	22	100	109	100

*Including those for whom marital state is unknown

Table 11 *The number and percentage distribution of cervical lesions diagnosed after the first Papanicolaou smear, by parity. Finland 1963-72*

Parity	Histological diagnosis							
	Dysplasia levis		Dysplasia gravis/ carcinoma in situ		Microinvasive carcinoma		Invasive carcinoma	
	No.	%	No.	%	No.	%	No.	%
0	5	10.2	16	7.1	1	4.5	9	8.3
1	8	16.3	30	13.4	3	13.6	10	9.2
2	9	18.4	46	20.5	4	18.2	19	17.4
3	13	26.5	36	16.1	7	31.8	20	18.3
4	2	4.1	35	15.6	1	4.5	14	12.8
5	6	12.2	25	11.2	3	13.6	8	7.3
6	4	8.2	13	5.8	1	4.5	11	10.1
7	1	2.0	6	2.7	0	—	6	5.5
8 or more	0	—	13	5.8	2	9.1	11	10.1
Unknown	1	2.0	4	1.8	0	—	1	0.9
Total	49	100	224	100	22	100	109	100

Table 12 *The number and percentage distribution of cervical lesions diagnosed after the first Papanicolaou smear, by anamnestic history. Finland 1963-72*

Anamnestic history	Histological diagnosis							
	Dysplasia levis		Dysplasia gravis/ carcinoma in situ		Microinvasive carcinoma		Invasive carcinoma	
	No.	%	No.	%	No.	%	No.	%
Continuous leucorrhoea	17	34.7	53	23.7	6	27.3	29	26.6
Bloody discharge	2	4.1	6	2.7	1	4.5	4	3.7
Coital bleeding	1	2.0	0	—	0	—	8	7.3
Irregular bleeding	0	—	4	1.8	2	9.1	6	5.5
Postmenopausal bleeding	0	—	0	—	0	—	1	.9
Electrocoagulation	2	4.1	10	4.5	0	—	6	5.5
Total	49	100	224	100	22	100	109	100

Table 13 *The number and percentage distribution of cervical lesions after the first Papanicolaou smear, by cytological diagnosis with negative histology at the first screening. Finland 1963-72*

Cytological diagnosis	Histological diagnosis							
	Dysplasia levis		Dysplasia gravis/ carcinoma in situ		Microinvasive carcinoma		Invasive carcinoma	
	No.	%	No.	%	No.	%	No.	%
I	38	77.6	137	61.2	13	59.1	67	61.5
II	8	16.3	52	23.2	6	27.3	30	27.5
III	3	6.1	21	9.3	2	9.1	8	7.3
IV	0	—	11	4.9	1	4.5	4	3.7
V	0	—	1	0.4	0	—	0	—
*Total	49	100	224	100	22	100	109	100

*Including those for whom cytological diagnosis is unknown

high risk of the disease and that these people can be identified. Furthermore, the subpopulation should be large enough to make the costs of the programme worthwhile compared with unselective screening. Finally the screening programme should be designed to select a large proportion of the total number of cases in the total population—that is, few cases should be found in women in low risk groups who are not subjected to the selective screening. Thus the definition of a high risk group for the purposes of selective screening should consider not only a group with a high incidence of the disease, but also the size of the group and the reduction in cost.

Data which were recorded during the primary screening of the Finnish mass screening programme for cervical cancer defined a subpopulation with a high incidence of cervical cancer. This subpopulation was characterised by symptoms of bleeding or a class II to V smear which was followed by negative histological results. Relative risk for a preinvasive lesion diagnosed during the subsequent follow-up period was on average five for the former and eight for the latter subpopulation. Women with coital bleeding had up to a 15-fold risk compared with those without bleeding symptoms. The basic demographic data (previously married or multiparous women) were also used to identify

high risk groups with a greater risk of cervical cancer.

These high risk groups were small enough to yield a substantial reduction in the population to be screened. The annual number of smears has recently been about 100 000 in Finland. Selective screening of widows or divorced women would reduce the number of smears by 90%, reduction based on coital bleeding would be more than 98%, and that based on previous cytological diagnosis would be 92%.

But even if it were possible to distinguish small population groups with an increased risk of cancer, the second criterion was in general not met. The cases with positive lesions did not as a rule originate from the high risk groups, and many cases were found in the population not characterised by a high risk factor. A similar experience is true for other diseases such as breast cancer (Shapiro *et al.*, 1973) and tuberculosis (Kannisto, 1972). Cytological diagnosis at the previous screening was the most reliable high risk indicator in those studied. Papanicolaou classes II to V (with negative histological results) had a prevalence of only 8%, but 40% of the cases with invasive cancer were diagnosed in this group.

Selective screening is thus likely to depend upon data obtained from the previous screening—such as anamnestic symptoms or cytological diagnosis—

which cannot be obtained from the national registry. Hence a programme in conjunction with the present Finnish selection of predetermined cohorts from the national population registry is not applicable. Only the interval of five years between screenings may be affected in Finland. In addition to the original invitation for mass screening those with high risk indicators from the previous screening may be invited again before the normal five years. A reduction of this period for those with bleeding and class II to V cytological diagnosis would presumably identify more than half of those with invasive carcinomas.

The predictive value of the high risk indicators varied in the different histological groups; for example, bleeding was indicative of frankly invasive carcinomas and multiparous women had a high risk of dysplasias. A class II to V smear was a lower risk indicator for preinvasive lesions than for invasive carcinomas; 80% of dysplasias of low degree were diagnosed in the group of class I smear, whereas the percentage was 70 for dysplasias of high degree and carcinoma *in situ*, and 60% for invasive carcinomas.

Irrespective of the method of selection, a woman with positive anamnestic signs should be reached by health education, and in clinical practice cytological smears classes II to V with a negative histological result may need to be followed-up regularly because the strongest risk indicators are likely to be found in the anamnestic history or by cytological diagnosis. In identifying high risk groups it does not matter whether the excess risk is due to false cytological results or because of aetiological significance.

The decreasing trend in the recent incidence of cervical cancer in Finland shows close correlation with the screening programme (Fig. 1), and it was estimated that exfoliative cytology may possibly have reduced the incidence of clinical carcinoma by about 60% in Finland (Hakama and Räsänen-Virtanen, 1976). The response rate was about 80% and there is no obvious selection in the attendance by age (Table 1) or other demographic characteristics (Kauppinen *et al.*, 1970). We conclude that this system has been successful in reducing the risk of cervical cancer in Finnish women and in encouraging a high proportion of them to attend screenings. The organisation was designed for unselected screenings. It seems unlikely that a similar

result could be achieved by a selective screening programme. Selective screening will be used as a supplement only and as a method of selecting women for more thorough screening—that is, for reducing the interval between screenings for certain high risk groups.

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