Improving the effectiveness of cervical cancer screening

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SUMMARY. A review of 100 cases of invasive cervical cancer was designed to assess what changes in cervical screening services might be most effective in reducing mortality. In 68 cases there had apparently never been screening: no system of individual invitation existed for unscreened women. In 10 cases the last smear was reported as normal over five years earlier: a five-year recall system existed but was inefficient. In 13 cases suspicious cervical smear reports had not been followed up adequately. Two cases might have been diagnosed earlier, in spite of 'normal or inflammatory' smears, if the symptoms had been fully elicited. For the remaining seven cases one or more smear was reported as normal within five years of diagnosis of invasive cancer. Overall, 15 cases might have been picked up earlier if suitable opportunities for screening which did arise had been exploited. It was concluded that a substantial proportion of these 100 women might have received treatment at an earlier stage solely by the rigorous implementation of the present screening policy.

Introduction

THERE is now strong evidence, notably from Scandinavia,[1] that screening can reduce the incidence of, and mortality from, invasive cervical cancer. In England, evidence of success from screening is still equivocal, either because screening has been less systematic or because of difficulties of interpretation against a background of marked swings between cohorts in cervical cancer risks.[2,3] Well-kept person-based screening records are needed for rational decision-making about the ideal intervals between screening tests, but these do not exist in the British system. By means of a confidential enquiry into how cases of invasive cervical cancer evade early detection, this study aimed to determine what improvements to the screening service would be most likely to have an appreciable effect on cervical cancer mortality.

Method

The area on which this population study was based consists of Surrey and that part of Greater London which lies within the South West Thames Health Authority. The total population of the area is 2,287,000 and includes 735,000 women aged between 20 and 70 years. The number of cervical cytology tests performed in the region annually is sufficient to provide one test each for all women aged 20–65 years every five years if evenly distributed. Even allowing for 20 per cent of the tests being repeats on account of some degree of abnormality, the laboratory resources could cover at least 75 per cent of the eligible population.

In 1980, 106 cases of invasive cervical cancer were registered from this population at the South Thames Cancer Registry, but on closer inspection six were excluded (one was a double registration, and five were wrongly classified as invasive carcinoma of the cervix).

With consultants' permission, hospital records were examined for the remaining 100 cases. Cervical smear reports were also sought for all cases from the largest cytology laboratory in the region. Here records are stored alphabetically with all years together, and a search is relatively easy provided patients have not changed their names. In other laboratories, where records are stored by year or even quarter year, searches are more laborious and hence were restricted to cases lacking positive evidence of screening from other sources, and to cases involving patients who lived or attended hospitals within the likely catchment area of the laboratory. Search back beyond five years in these other laboratories was not made unless there was mention of obstetric or gynaecological treatment or investigations in the patient's notes.

In cases where some or all of the hospital records had been lost (nine cases) and in those where records did not mention whether or not cervical smears had ever been taken before the episode which led to diagnosis, general practitioners were approached either in writing or by telephone for further information. Some of these patients had died and their notes had to be

retrieved from the Family Practitioner Committee. Forty-seven general practitioners were approached and all except three were able to give further information from their records. General practitioners could not be traced for two patients. From these three sources — hospital, laboratory and general practitioner — the gynaecological and screening history in all but five cases could be traced with reasonable confidence. Patients themselves were not questioned.

It is possible that previous screening was underestimated, particularly in the five cases where no information was available and in cases where screening might have occurred outside the area more than five years ago. For the purpose of this analysis it was assumed that in these five cases there had been no screening.

Results

Screening history

Figure 1 shows the age distribution of women with invasive cancer of the cervix and indicates how many in each age group had been previously screened. Cervical smears taken during the period of observation which led up to the diagnosis are not included. The figure shows that 23 (74 per cent) out of 31 women under 40 years of age had had previous cervical smear tests. This was in marked contrast to the older women where there was evidence of previous screening for only nine (13 per cent) out of 69 women aged over 40 years.

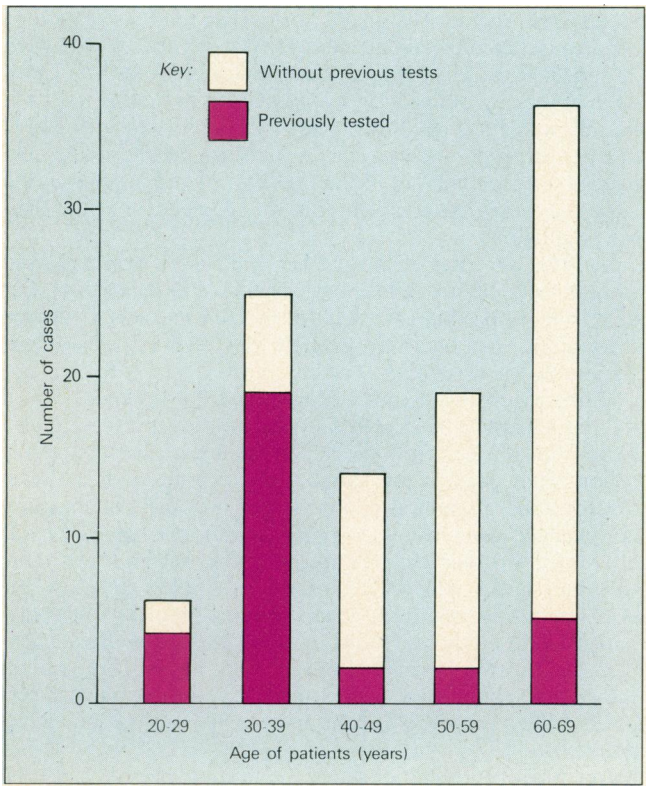

Figure 1. *Age distribution of cases with and without evidence of cervical smear tests before the episode which led to diagnosis of cancer.*

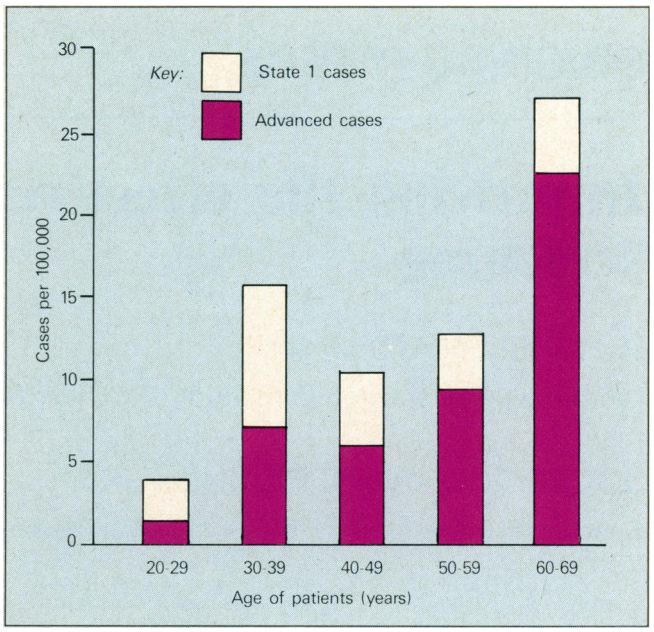

Figure 2. *Age-specific rates for invasive carcinoma of the cervix in the study population from South Thames Cancer Registry.*

Age of women and stage of cancer at diagnosis

Figure 2 shows the age-specific cancer registration rates for invasive cervical cancer in the study area; six per cent of cases involved women under the age of 30 years and a further 25 per cent of cases involved women under 40 years old. The numbers are small and the peak observed among women in their thirties is a chance finding that was not apparent in the preceding and subsequent years. Figure 2 also shows that, while the majority of cases of invasive cancer in younger women are discovered at stage 1, the proportion of early diagnoses falls with age.

Previous smears reported as normal or inflammatory

Nineteen women had had one or more previous smears reported as normal or indicating inflammation. Six women had been repeatedly screened and all of these cases of cancer were diagnosed when the carcinoma was still at stage 1. The remaining 13 women had had only one previous screening and in nine of these women the cancer was advanced by the time it was diagnosed.

Some of these normal smears were taken long before the diagnosis of cancer. Since in Britain the recommended interval between routine smear tests is five years, Table 1 excludes cases in which the last smear was taken more than five years before the episode leading up to the diagnosis of invasive cancer. Nine cases remained in which smears had been reported as normal or inflammatory within five years of diagnosis of invasive cancer. Four were advanced cases by the time the cancer was diagnosed, two being endocervical, and it is acknowledged that the Papanicolaou smear is inefficient at detecting such cases. Histories of the other two patients revealed

Table 1. *Possible explanations for negative smear results within five years of diagnosis of invasive cancer of the cervix*

	Number of cases
Endocervical carcinoma	2
False negative report on already invasive lesion, symptoms not elicited	2
Rapidly invasive lesion	3
Rapid invasion or false negative reporting equally probably on available evidence	2

that they had had symptoms of bleeding going back to about the time of the supposed 'screening' test. Had their symptoms then been fully elicited, investigation might have been more thorough since it is well recognized that invasive lesions may give false negative results. Among the five cases diagnosed when still at stage 1 there were three for which, within the episode leading to diagnosis, treatment of the cancer was delayed, because the first smears showed only mild dyskaryosis. These cases may represent rapid disease, progressing from dyskaryosis to invasion within a matter of months. The remaining two cases might have been false negatives or rapidly progressing cases.

Failure of follow-up

Thirteen women had had suspicious smears in the past, one of whom had subsequently had a single repeat normal smear which led to follow-up being discontinued. In all but two of the cases the invasive cervical cancer was diagnosed within five years of the last suspicious smear and the majority of cases (eight out of 13) were diagnosed as still at stage 1. Reasons of failure of follow-up, where known, are summarized in Table 2.

Table 2. *Failures in follow-up of abnormal cervical smear reports.*

	No. of cases
Patient moved from the area	4[a]
Patient ignored request to reattend	2
Inadequate communication between laboratory and GP	3
Inadequate hospital follow-up	3
Unknown explanation	1

[a]One of these patients had an oophorectomy four months later but no smear was taken then.

[In an additional case follow-up ceased after a single normal smear despite three previous reports of dyskaryosis.]

Missed opportunities for cervical smear testing

Since many women at high risk of cervical cancer are among those least likely to seek screening, it is important to take advantage of occasions when women who have not recently been screened seek medical advice. It may be impracticable to take cervical smears when a women presents with unrelated complaints, but where a woman seeks advice on a gynaecological problem or where a rectal examination is being performed a smear should add little to the patient's embarrassment or discomfort and should have a negligible effect on staff time for taking the smear.

There were 15 cases in this series in which opportunities for smear testing arose more than a year before diagnosis. In three cases endometrial curettage had been performed (the laboratory specifically requested smears after one of these but no action was taken) and in another a polyp had been removed but not examined histologically. Other cases included patients being treated for pelvic inflammatory disease, sterilization, an erosion observed during investigation of infertility, two cases where rectal examination for possible malignancy was performed, lichen sclerosis of the vulva, postnatal rectal bleeding, blood spotting during pregnancy, premenstrual depression with heavy periods for which progesterone pessaries were prescribed, and a case in which a patient with postmenopausal bleeding was advised by her general practitioner to go to a hospital outpatient clinic but was not followed up when she failed to attend. (In addition, in three of the cases for which full records could not be traced there was reference to sterilization or oophorectomy but not to cervical smears.)

Delay during episode culminating in diagnosis of cancer

In 11 cases there was a delay in diagnosis of more than six months from the time the patient first reported suspicious symptoms or, if asymptomatic, the patient was first found to have a suspicious lesion. It is possible that in some of these patients the lesion progressed from *in situ* to invasive cancer during this interval. In two cases smears were not taken initially because vaginal discharge was attributed to infection, but in the other cases delay occurred because cervical smears and the appearance of the cervix led to underestimation of the severity of the lesion. One progressed to invasion in spite of cone biopsy. Reluctance on the patient's part to undergo surgery contributed to the delay in three cases, while in a fourth case full treatment was delayed until after childbirth. The others were asymptomatic.

Delay in presentation

Among the 68 women who had apparently never been screened there were 25 whose symptoms, at the time of presentation, had lasted over three months (11 women's symptoms had lasted over six months) and a further four with chronic mental illness and advanced cervical cancer for whom symptom duration was not known. Chronic ill-health (in seven cases), fear and embarrassment (in six cases), dependency of invalid children (in three cases), belief that symptoms were due to the menopause (in one case), Christian Science faith (in one case), and lack of command of the English language (in one case) were factors recorded in their notes which may be relevant in explaining the delay.

Cases discovered in association with pregnancy

Seven cases were diagnosed during pregnancy or within 10 weeks of parturition in women having their second or third child. They have been included in previous sections of this paper since all had had previous smear tests, but it may be valuable to regard them as a special group and so their details are summarized in Table 3.

Table 3. *Cases associated with pregnancy*

Age of patient (years)	Stage of carcinoma	Comments
28	1B	Discovered 10 weeks postpartum. Previous normal smears, last two years earlier
32	1B	Discovered after miscarriage. Previous smears normal, last one taken six years earlier
31	1	Discovered six weeks postpartum. Previous normal smears, last three years earlier
36	2 (adeno-carcinoma)	Polyp with carcinoma *in situ* biopsied at booking clinic. Invasive carcinoma discovered postpartum. Previous smear two and a half years earlier showed endocervical inflammation
31	1B (endocervical)	Discovered after miscarriage. Inflammatory smear in first pregnancy five years earlier
36	1A	Discovered nine weeks postpartum. Mild dyskaryosis in pregnancy four years earlier, not followed up
39	1B (endocervical)	Discovered in late pregnancy. Class 5 smear, polypectomy and cautery three years earlier. Histology: fragments of endometrium. Subsequent intermenstrual bleeding treated with Primolut; no further smears taken

Endocervical adenocarcinoma

The total proportion of the cases which were described as endocervical or as adenocarcinoma of the cervix was 16 per cent. Among those women with a history of a previous cervical smear test the proportion was higher (26 per cent) in accordance with the supposition that such lesions are less likely to be accessible to early cytological diagnosis.

Failure of the cervical screening programme are summarized in Table 4.

Table 4. *Summary of failures of the cervical screening programme. (Number of missed opportunities for screening, during gynaecological or rectal examination, in parentheses.)*

	Number of cases	
No record of previous screening	68	(12)
Inadequate follow-up of previous abnormal smear	13	(1)
Last smear normal but taken more than five years before diagnosis	10	(2)
Last smear normal and taken within five years:		
a) False-negative report associated with inadequate elicitation of symptoms at time of screening	2	(0)
b) Possibly false-negative report or possibly rapidly progressive lesion	7	(0)

Discussion

The risk of contracting invasive cervical cancer rises with age to a peak in the sixth decade of life. The comparatively small number of cases involving women in their fifth and sixth decades that were found in this study is consistent with larger analyses showing that women born in England between 1920 and 1940 carry a reduced risk compared with preceding and subsequent cohorts.[3] The deficit cannot be primarily attributed to screening but screening may be partly responsible.

The results of this study indicate that strategies to reduce the incidence of carcinoma of the cervix should have different emphases for women above and below the age of 40 years. Among women over 40 years of age, in 87 per cent of the cases there had never been any screening, and the prime aim must therefore be to reach unscreened women. Mass screening for cervical cancer began about 1964 and increased rapidly in volume. In spite of advice to concentrate screening on those aged over 35 years, the majority of tests have been done on younger women,[4] those seeking contraceptive or obstetric care. Women who had completed their families by the late 1960s are less likely to have had screening unless they expressly sought it; and unfortunately those at higher risk tend not to do so. Had the 68 unscreened women been screened at some time in the last 10 years, it is reasonable to expect that in 80 per cent of cases their condition would have been diagnosed at an earlier, perhaps pre-invasive stage. It might have been difficult to persuade many of them to undergo cervical screening, as is indicated by the reasons mentioned for delay, but on the other hand in several cases opportunities arose for easy screening at an earlier date. There is little information about the proportion of women in the general public who have been screened: a recent survey of women aged 45–64 years in part of this region found that only 53 per cent of the sample recalled having had a cervical smear test within the last five years; a further 15 per cent had had one longer ago. It would be complacent to accept low compliance for cervical screening when in the areas now showing some evidence of the programme's effectiveness 90 per cent of the women have been screened.[5–7]

Among younger women, the majority had been screened at some previous date. Increasing publicity for screening services would not therefore have much effect on cancer rates in this age group. While ultimately dependent on finding acceptable means of primary prevention,

early detection will for the present depend on improving the efficiency of the screening and follow-up systems.

Thirty-one of the 100 cases of invasive cancer that were studied involved women who had been previously screened. This figure should not be over-dramatized as evidence of screening ineffectiveness, for it must be considered in the context of the number of cases which are presumably prevented through screening: about 1,000 cases showing severe dyskaryosis or carcinomatous cells (smear class 4 and 5) are reported annually from cytology laboratories in this area and about 300 cases are histologically confirmed as carcinoma *in situ*.[8] It may be considered the tip of a large iceberg of disease in younger women, the majority of whom are treated before the invasive stage.

In previous reviews of screening history in cervical cancer patients, emphasis has been placed on the number of non-suspicious reports.[5,9,10] They have considered the extent to which negative reporting may have been erroneous, the result of technical failings in taking or reading the smears, or alternatively may have been due to the fast-growing nature of some lesions, such as to render five-yearly screening inadequate.

Less attention in the literature has been drawn to failures of follow-up of suspicious results: Morell[9] excluded such cases from analysis; Clarke and Anderson,[11] in a discussion of a case control study of screening histories, promised a separate paper on such failures; without discussing the frequency of their occurrence, Kinlen and Spriggs[12] used follow-up failures to assess the natural fate, without intervention, of women with severely abnormal smears. In the present study, follow-up failures were numerically more important than false negatives in causing delay in diagnosis, probably allowing some cases to progress from the pre-invasive to the invasive stage.

Follow-up failures arose for varied reasons and involved women who had been screened by laboratories both within and outside this region. The majority were only mildly dyskaryotic at screening and clearly, when requesting a patient to return in three months for a repeat smear test, it is difficult to ensure compliance without causing excessive anxiety. In view of the fact that probably more than two thirds of such cases would revert to normal even if untreated,[13] the patient should perhaps be told that she needs to be screened more frequently than other women because she is at somewhat increased risk, rather than that she has an abnormality. Memory and communication can be enhanced by maintenance of a good record system, a system that will alert doctors, repeatedly if necessary, to failures of follow-up so that non-attenders are traced and further counselled if necessary.

The DHSS Working Party on Cervical Cancer Screening recommends continuation of five-yearly screening for normal asymptomatic women, yet others, such as the International Academy of Cytology,[14] advocate annual screening. Since the present distribution of different frequencies is unknown, it is not possible from the present study to forecast the effect of a five-year interval on women currently being screened more frequently. However, if the screening intervals had been three years instead of five years, only two further cases might have been treated earlier. Thus increased screening of women already complying with current guidelines would have less beneficial effect on the present situation than more careful follow-up of suspected cases of cervical cancer.

Cervical smears taken either routinely from pregnant women or in the investigation of vaginal bleeding persisting after pregnancy yielded seven cases of invasive cancer. This indicates a discovery rate for invasive cervical cancer among women receiving obstetric care during pregnancy and for three post-parturition months two-and-a-half times the yearly discovery rate for all women in the area aged 20–40 years. Invasion occurred in five of the seven cases in spite of screening within the previous five years. It would therefore seem wise to continue the practice of screening multiparous women in pregnancy even though pregnancy may be an inopportune time to discover cervical cancer.

Conclusion

From the failures in prevention which this study has considered and which are summarized in Table 4, it is concluded that efforts should be directed most urgently towards reducing the proportion of women over 40 years of age who have never been screened and towards ensuring that women with abnormal cervical pathology are followed up with persistence even though reported only as mild dyskaryosis.

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Doubtful benefits of 'low-tar' cigarettes

The consumption of low-yield (ie. low-tar, low nicotine) cigarettes increased dramatically in the United States in the 1970s and early 1980s, due primarily to changes in cigarette marketing and an increased public perception that high-yield cigarettes are hazardous. It remains to be determined, however, whether low-yield cigarettes actually reduce smoking risks. In this study to determine the use and possible health risks of low-yield cigarettes, the authors ascertained the cigarette brands and serum thiocyanate levels of 2,561 adult smokers (aged 25-74 years) in population-based samples of seven upper Mid-western communities during 1980-82. Brands were coded according to December 1981 Federal Trade Commission ratings for 'tar', nicotine, and carbon monoxide.

Compared to 1980 data from the National Center for Health Statistics for the United States as a whole, a greater proportion of smokers in these communities smoked low-yield brands. More people with higher education than lesser and more women than men smoked low-yield cigarettes. Greater proportions of older people (aged 65-75 years) than younger people (aged < 65 years) smoked cigarettes in the highest and lowest brand yield categories. Serum thiocyanate levels, adjusted for number of cigarettes smoked and for sex, was only weakly associated with brand ratings for 'tar' ($r = +0.12$), nicotine ($r = +0.11$), and carbon monoxide ($r = +0.15$). Furthermore, the gradient in serum thiocyanate between lowest and highest quintiles of brand strength was less than 16 per cent—much lower than the 300-500 per cent gradient in smoke components implied by Federal Trade Commission ratings. These data add to the evidence that smoking low-yield cigarettes may not be less hazardous than smoking high-yield brands.

Source: Folsom AR, Pechacek TF, Gaudemaris R de, *et al.* Consumption of 'low-yield' cigarettes: its frequency and relationship to serum thiocyanate. *AM J Public Health* 1984; **74:** 564-568.