0959-8049(93)E0135-Q

Cervical Cancer Screening. Human Benefits and Human Costs in the Evaluation of Screening Programmes

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INTRODUCTION

THE SCIENTIFIC evidence of the effectiveness of screening for cervical cancer in reducing the incidence and mortality is well established and acknowledged by the scientific community [1, 2]. Screening programmes are applicable as public health policy [1, 2]. However, although screening is widespread in European countries, the potential benefits of screening have not been achieved. This is partly because smears are not distributed in an optimal way, and partly because the standards of screening vary across countries.

Homogenous standards are necessary in order to make comparable evaluations of the effectiveness and quality of different screening programmes. Quality assurance guidelines have to be adopted for increasing the potential benefits and, no less important, for reducing the potential adverse effects of cervical cancer screening.

The scientific evidence concerning human benefits and human costs of cervical screening form the background for the evaluation of effectiveness and for the definition of quality assurance standards. From the ethical point of view, the duty of carefully evaluating the adverse effects of screening is strengthened by the fact that screening addresses healthy people.

HUMAN BENEFITS

Prevented deaths

Mortality from cancer of the cervix uteri in the countries of the European Community (EC) was estimated to be 13 212 deaths per year in the period 1980–1984, representing the sixth most frequent cause of death from cancer among women and accounting for 4% of all cancer deaths. The cumulative risk (in the age span 0–74 years) of dying from this disease ranges from 0.3% in Luxembourg to 0.8% in Denmark, and the age-standardised rate (world population per 100 000) ranges from 2.5 in Luxembourg to 7.6 in Denmark. With the exception of Spain and Greece, both the incidence of and mortality from cervical cancer are decreasing in EC countries [3].

With a screening period of 30 years and based on an attendance rate of 80%, mortality can be reduced by between 49 and 63%, depending on the screening policy and the model of the natural history of the disease [4]. In Iceland, the mortality rate in 1986 was 28% of that observed in 1964 [5]. For Danish women aged 30–59, mortality from cervical cancer was reduced by 32% 5 years after the introduction of an organised screening programme [6].

Cumulative mortality rates between 1965 and 1982 among all females, aged 0–74 years, in the Nordic countries fell by 25% in Denmark, 50% in Finland, 80% in Iceland, 50% in Sweden, but only 10% in Norway where only 5% of the population was invited to participate in organised screening, compared to 40% in Denmark and 100% in the other countries [7].

Reducing the incidence of invasive cancer

In the period 1978–1982, the highest age-standardised incidence rate of invasive cervical cancer in the EC countries was 19.5 per 100 000 in Denmark. The lowest was 8.9 per 100 000 in Spain, the overall incidence in EC countries was 10.4 per 100 000 and the absolute number of cases was 22 054 per year [3].

The effect of different screening policies on reducing the rates of invasive cervical cancer has been estimated to be no less than 69.6% for screening six times every 5 years between the ages of 35–64 years, and no less than 93.3% for screening every year between 20 and 64 years of age [8]. The reduction in the incidence of cervical cancer associated with organised screening programmes has been convincingly substantiated [2].

Any further reduction in the incidence of invasive cervical cancer in EC countries depends on the (further) coverage of the female population. It has been estimated that in Italy 17% of women have a Papanicolaou (Pap) test at least every year [9] and that 30% of women in the north of the country (aged 18–69 years) have a test at least every 3 years [10]. Increasing the percentage of women who have a Pap test every 3 years from 30 to 60%, and screening 13 times between the ages of 25 and 64 would prevent about 1000 cases of invasive cancer per year. In countries where the percentage of women under surveillance is higher (e.g. 70–80% of women under the age of 54 in Netherlands), it has been suggested that the age range be extended to 65 years and that the interval between screens be widened to 5 years [11]. A survey of a sample of 12 400 women within the 12 EC countries showed that 51% of women 25–54 years old have a smear at least every 5 years and 44% every 3 years [12].

Years of life gained

The most important health effect of cervical cancer screening is a reduction in mortality, which can be expressed as number of years of life gained, thus giving more weight to deaths avoided among young people. The number of years of life gained per 1000 individuals has been estimated to be 13–68 in the Netherlands, depending on the policy used and attendance rates [13]. In England and Wales, person-years of life lost are reduced by 70% when comparing no screening with 3-yearly screening of women of 25–65 years of age [4].

HUMAN COSTS

Psychological problems

Many women undergo a screening test without understanding what the test is for, the accuracy of the test and the implications of the test result [14]. Women often believe that the function of a smear is to detect cancer rather than to prevent it [15]. The importance of counselling before screening is often acknowledged, but there are few data to show what information partici-

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pants should be given to ensure informed uptake and to minimise adverse emotional and behavioural consequences of participation [16]. High levels of anxiety have been reported in patients participating in screening programmes [14].

For some women, receiving an invitation to participate in a screening programme induced anxiety and was misinterpreted as evidence that their GP knew they had cancer [17]. In a controlled trial of women with dyskaryosis, 19 out of 31 women who did not receive a leaflet, explaining that most smears showing dyskaryosis do not indicate cervical cancer, thought that they had cancer. In the control group, who received a leaflet, only 1 out of 29 cases of dyskaryosis believed they had cancer [15]. The mean measured level of anxiety in the women not sent a leaflet was similar to that provoked by very stressful situations. Anxiety may remain for months or even years after a false positive result [14].

Adverse psychosexual sequelae associated with conservative treatment of pre-invasive cervical disease have been reported [18]. In order to reduce psychological costs of a screening programme, it has been suggested that a written protocol should be prepared, including details of how interactions with women should be conducted at the moment of invitation, as a preparation before performing the test and giving the results [14].

Unnecessary treatment

Unnecessary treatment occurs for true positive cases which would remain asymptomatic during their life or for false positive cases, as a consequence of diagnostic misclassification. Model-based analysis of the Dutch data lead to estimates of regression rate of pre-invasive disease of 60% and the mean duration of preclinical stages of 17 years [19]. The range of progression rates varies from 25 to 70% with the lowest at 12.2% [20]. The mean duration of CIS is in the 5- to 10-year range for most data sets and models. However, analysis of British Columbia data in two models yielded values of 20–25 years [21]. The regression probability and duration of CIS appear to vary inversely with age, particularly in the more recent comprehensive model [21]. The proportion of unnecessary treatment for cervical cancer lies between 88 and 30%. Unfortunately, it is not at present possible to distinguish between lesions which will progress to invasive cancer from the other lesions [22]. The incidence of detected CIN is determined by the frequency of screening and, therefore, the likelihood of unnecessary treatment increases with the number of smears during life. Given the mean duration of pre-invasive stages and the small proportion, at most 10% of CIS cases, of short duration and rapid progression [21], it seems important to adopt strategies of screening programmes with the lowest number of smears during life compatible with a substantial reduction of rates of invasive cancer.

The overall agreement of individual histological reports of 12 consultant hystopathologists with the majority category [23] was equal to 74% for no CIN, 49% for CIN I, 52% for CIN II and 87% for CIN III. Out of 100 consecutive, cervical biopsies [24] the proportion of CIN III ranged from 7 to 32%, and that of CIN I-III from 36 to 67% among eight hystopathologists. De Vet [25] reported the diagnoses of four experienced hystopathologists. Of 106 slides, severe dysplasia or CIS were diagnosed in between 20 and 45% of the cases. Given this large diagnostic variability, the chances of both overtreatment and undertreatment have to be taken into account in the evaluation of screening.

Overtreatment

Overtreatment occurs when pre-invasive lesions are treated as invasive cancer, or when low-grade pre-invasive lesions are treated instead of being followed. In eight Dutch hospitals between 1982–1986 and in the region of Nijmegen between 1981 and 1984 11 and 48%, respectively, of women with CIN III had hysterectomies [26]. Sixty per cent of women with less than CIN III in the same study have been treated, 30% with conisation. In the 1980s about 10% of women with CIN III in British clinics had total hysterectomies, 60–70% conserving treatment and 20–30% conisations [26]. In the period 1978–1982, some 480 hysterectomies and 2050 conisations were carried out for precursion lesions in Denmark per year [22].

Undertreatment

Cases of invasive cervical cancer, diagnosed as mild and moderate dyskaryosis and followed by cytology, were reported by Campion [18] and Fletcher [27] in the U.K. Colposcopical surveillance [18, 28] or randomised controlled trials to evaluate the optimum management of these patient [27] have been suggested.

Side-effects

As for the side-effects, a study from Norway used register linkage to identify live births in women following conisation, and to identify live births in a control group. They found the relative risk, following conisation, to be 9.4 for perinatal mortality and 4.9 for low birth weight [29].

CONCLUSIONS

From a non-exhaustive list of human costs and benefits, it follows that each screening programme should adopt evaluation protocols that consider not only the effectiveness of the programme, but also the adverse effects of the programme itself. If it is expected that the benefits of an organised screening programme should exceed the disadvantages, this does not release us from the obligation of minimising the adverse effects. There is a need for adopting screening policies which are coherent with the natural history of cervical cancer, and there is a requirement for improving the accuracy of the screening test, and of the diagnostic and follow-up protocols. Means to achieve this are quality assurance guidelines, tailored schedules for screening, conservative therapy and better information on the screening programme in order to reduce anxiety and psychological problems.

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0959-8049(94)E0136-R

Breast Cancer Screening: Methods, Human Benefits, Human Costs

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INTRODUCTION

IN THEIR renowned *Monograph on Screening for Disease*, Wilson and Jungner [1] began their list of requirements for justification of a population screening programme by emphasising that the disease under scrutiny should be an important public health problem, i.e. the disease should be relatively frequent and have serious consequences. Breast cancer is the commonest form of cancer in women in Europe and it has been estimated that in one single year (1980) there were approximately 135 000 incident cases [2].

There is, however, considerable variation in the incidence of breast cancer within Europe [3]. The highest incidence rates recorded in Europe around the mid-1980s were in Geneva, where the age-adjusted incidence rate was 73.5 per 100 000 and in Eindhoven (72.7 per 100 000). In sharp contrast, the lowest recorded incidence rates were in Kyrgyzstan (19.6 per 100 000) and Nowy Sacz (22.5 per 100 000) and Warsaw (22.9 per 100 000) in Poland [3]. There are also extremely low incidence rates reported in republics of the former U.S.S.R. [4].

This variation is sufficient that any discussion on the issue of whether to undertake a breast cancer programme should take into account the national incidence or mortality rates. Cost–benefit in relation to screening clearly depends on the prevalence and thus the detection rate of breast cancer. Recent experience of screening in southern Europe suggests that the detection rate at initial screening in women aged 50–64 years is lower than the 6–7 per 1000 found in northern and western Europe. A further factor which must be kept in mind is that the economic situation in many parts of eastern and southern Europe would exclude implementation of breast cancer screening programmes on the simple grounds of costs and priorities.

A broad understanding has been reached about the causes of breast cancer in that western habits of reproduction and, possibly, nutrition are involved in determining the risk of this form of cancer. It appears from our current knowledge that even if we

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