1. Introduction

1.1 RELEVANT BACKGROUND INFORMATION ABOUT CERVICAL CANCER

CANCER OF the uterine cervix is a common gynaecological cancer which occurs worldwide. The risk factors for the disease are related to sexual activity. The incidence at present reflects both exposure to risk factors and level of screening activity. The highest incidence is found in certain areas of Latin America (age standardised rate *ca.* 55 per 100 000 women) and a low incidence is found in for example Israel (*ca.* 3 per 100 000 women). In populations where screening has had little effect the incidence of the disease follows a particular age pattern rising rapidly with age until about 40 years, peaking at 45–54 and then levelling off. The disease is rare below the age of 25. With screening this age pattern changes.

There are two main types of cancer of the cervix. This document is concerned mainly with the commonest form of cervical cancer, namely squamous cancer of the cervix.

Numerous studies indicate that invasive squamous cervical cancer is usually preceded by an asymptomatic preinvasive stage of the disease where precancerous cells are confined to the epithelium of the cervix. This precancerous stage has been designated cervical intraepithelial neoplasia (CIN). The time span for the progression of CIN to invasive squamous cancer is variable and may be as long as 15 years. If precancerous lesions are diagnosed and treated, there is strong evidence that invasive cancer can be prevented by identifying and treating the preinvasive stages.

For the past 50 years, the Papanicolaou smear test has been used to screen for precancerous and early invasive squamous cancer in asymptomatic women. This test involves removing a sample of cells from the epithelium of the cervix, and examining the cells using a light microscope. Abnormal cells present in the sample can be recognised by an experienced cytologist. Thus women with precancerous lesions can be identified and treated and invasive disease prevented. There is now strong evidence that organised screening of a target population using the Papanicolaou test to detect cervical cancer is a very effective way of reducing morbidity and mortality from this disease.

1.2 THE EFFECTIVENESS OF ORGANISED SCREENING PROGRAMMES

The most persuasive evidence that screening for squamous cancer of the cervix is effective comes from comparison of time trends in incidence and mortality in populations which introduced mass screening with different intensities at different points in time. Supportive evidence for the effectiveness of cervical screening comes from case control and cohort studies in which incidence and mortality rates are compared between screened and unscreened women. However, bias cannot always be eliminated from such studies and the evidence is not as convincing as that obtained from studies on time trends of cancer incidence.

In this respect, the Nordic countries have provided the clearest data. The five Nordic countries, with uniformly high levels of medical care, adopted very different policies towards screening and have shown sharply contrasting trends both in incidence and in mortality from cervical cancer since the mid 1960s, when organised mass screening started. Table 1.1 shows the change in mortality between 1963 and 1967, where screening had little or no impact, and between 1978 and 1982, when the full effect of organised screening should have been revealed.

Table 1.1. *Change* (%) *in mortality from cervical cancer between* 1963–1967 *and* 1978–1982 *in the Nordic countries by age group*

Country	Target age group (years)	% Target age group covered nationally by organised screening	Change in mortality (%) by age group			
			30–39	40–49	50–59	60–69
Iceland	25–69	80	−100	−77	−66	−66
Finland	30–55	75	−172	−77	−60	−32
Sweden	30–49	70	−59	−63	−40	+7
Denmark	30–50	35	−61	−53	−26	+1
Norway	25–60	3	−48	−23	−2	+14

Table 1.2. *Number of smears used, number of women aged* 25–64 *years, and annual number of smears per women in the EC-countries.* 1990 *or most recent year*

	Number of smears in millions per year	Number of women aged 25–64 in millions	Smears per woman per year
Belgium	0.92	2.6	0.35
Denmark	0.6	1.3	0.46
Germany	7.32	17.2	0.43
Greece	?	2.6	—
Spain	?	9.8	—
France	5	14.4	0.35
Ireland	0.16	0.8	0.2
Italy	3.5–4.0	15.4	0.23–0.26
Luxembourg	0.03	0.1	0.3
Netherlands	0.85	3.9	0.22
Portugal	?	2.6	—
United Kingdom	3	14.5	0.21

The relationship between the extent of organised mass screening and the degree of reduction in mortality for women over 40 years is striking. Because these are not the results of randomised trials, it is always possible to propose alternative explanations for these figures, but the most obvious interpretation is that the variation in mortality is the direct effect of the different levels of organised screening. In the age group below 40 years a slight reduction in cervical cancer mortality is seen even in the absence of organised screening. This probably reflects the effect of opportunistic screening in this age group.

Thus there is sound scientific evidence that the incidence and mortality from squamous cancer of the cervix can be reduced by a well organised screening programme.

Table 1.3. *Cervical cancer mortality and incidence in the EC-countries. Mortality*: 1990 *or most recent year. Incidence*: *around* 1983–1987, *and estimated for all EC-countries for* 1978–1982

	Cervical cancer ICD-8 180 ICD-9 180 Mortality Annual number of deaths	Age-standardised rate	Cervical cancer ICD-9 180 Incidence Annual number of cases	Age-standardised rate	Cancer of uterus unspec. ICD-9 179 Incidence† Annual number of cases	Age-standardised rate
Belgium	234	2.6	NA	NA	NA	NA
Denmark	237	5.4	556	15.93	30	0.66
Germany, previous Democratic Republic	792	5.8	2540	22.54	25	0.14
Germany, previous Federal Republic	1884	3.2	NA	NA	NA	NA
Saarland	NA	NA	92	10.79	15	1.13
Greece	97	1.3	NA	NA	NA	NA
Spain	436	1.5	NA	NA	NA	NA
Basque Country	NA	NA	81	5.93	22	1.30
Granada	NA	NA	30	6.46	7	1.03
Murcia	NA	NA	43	7.09	10	1.48
Navarra	NA	NA	25	8.73	3	0.47
Tarragona	NA	NA	30	8.37	2	0.35
Zaragossa	NA	NA	29	4.78	10	1.28
France	840	1.9	NA	NA	NA	NA
Bas Rhin	NA	NA	66	10.90	3	0.49
Doubs	NA	NA	28	9.18	<1	0.12
Isere	NA	NA	58	9.55	5	0.67
Somme	NA	NA	52	15.63	4	1.03
Tarn	NA	NA	22	7.72	3	1.21
Ireland	66	3.1	NA	NA	NA	NA
Southern	NA	NA	23	8.54	3	0.76
Belgium	234	2.6	NA	NA	NA	NA
Italy	431	0.9	NA	NA	NA	NA
Latina	NA	NA	26	9.94	—	—
Parma	NA	NA	23	6.41	6	1.14
Ragusa	NA	NA	21	11.41	3	1.23
Romagna	NA	NA	36	11.28	—	—
Torino	NA	NA	73	8.32	6	0.36
Tuscany	NA	NA	74	7.25	7	0.46
Varese	NA	NA	43	7.23	2	0.20
Luxembourg	9	3.2	NA	NA	NA	NA
Netherlands	305	2.6	NA	NA	NA	NA
Eindhoven	NA	NA	32	6.16	0	0
Maastricht	NA	NA	42	7.33	<1	0.06
Portugal	169	2.3	NA	NA	NA	NA
V.N. de Gaia	NA	NA	23	17.80	5	3.69
United Kingdom	2116	4.7	NA	NA	NA	NA
England and Wales	NA	NA	4014	11.96	431	0.93
Birmingham	NA	NA	457	13.87	36	0.84
Mersey	NA	NA	258	16.08	10	0.42
North Western	NA	NA	382	13.81	82	2.39
Oxford	NA	NA	158	10.28	<1	0.04
Yorkshire	NA	NA	384	16.46	37	1.07
Scotland	NA	NA	454	13.21	50	1.04
East Scotland	NA	NA	32	11.33	2	0.41
N.E. Scotland	NA	NA	48	13.71	2	0.38
North Scotland	NA	NA	22	15.12	<1	0.30
S.E. Scotland	NA	NA	120	15.17	6	0.51
West Scotland	NA	NA	233	12.35	40	1.54
All EC-countries	7616	—	22 054*	10.4*	NA	NA

*Estimate for 1978–1982.
†Mortality data not available for this site of the WHO data bank.
Sources: WHO mortality data bank, and IARC cancer incidence in five continents, Vol VI (in press).

Table 1.4 *Recommendations of the committee of cancer experts on cervix uteri cancer screening* 6 *April* 1992

The Committee recommends that the following criteria be respected by any project intending to implement a cervix cancer screening programme:

1. Effectiveness
   The effectiveness of well-organised screening programmes in reducing morbidity and mortality from cervical cancer is now widely established. In successful programmes recruitment and recall to screening have been by personal invitation of women by means of population register and the quality of smear-taking, cytological examination and organisation of follow-up have been monitored.
   Screening by invitation should be promoted. Even where this is not available and screening is provided on the initiative of the patient or carried out opportunistically, the quality of screening should be monitored and controlled.

2. Inequalities in risk and use of screening
   Women of lower socio-economic status are at higher risk of dying of cervical cancer, but make less use of screening services, especially if attendance requires individual initiative. Efforts must be directed at ensuring that all women, including those of lower socio-economic status, are offered screening programmes.

3. Target populations
   Priority should be given at the start of a mass screening programme to the age group in which the incidence of invasive cervical cancer is highest. In most populations this will be between 35 and 60 years. An optimal screening programme should aim at the population aged 25–65 years, thus aimed also at the preinvasive stages.

4. Information and participation
   The success of mass screening depends on achieving and maintaining a high level of participation. A high participation rate can be obtained by personal invitation. The public needs a basic understanding of the nature of this cancer, its causes and the purpose of screening. Women also need practical information about the screening service and where it is available. Back-up for a screening programme through dissemination of information by newspapers, television and leaflets in public buildings and hospitals is helpful.

5. Screening text and training
   Detailed information about the screening programme for health professionals, especially general practitioners, gynaecologists, pathologists and others who take smears is especially important so that they can advise patients.
   The recommended method of screening is the Papanicolaou smear. The quality of smear-taking, as well as smear-reading, must be assured; organisation of training programmes, proficiency-testing and systems of quality control are needed. A uniform nomenclature for both cytology and histopathology between Member States is recommended.

6. Screening interval
   In order to make best use of available screening resources, the interval between screening should be controlled. The additional benefit to be gained by screening more frequently than 3-yearly is very small. Three to 5-yearly screening is therefore generally recommended, depending on the resources available and the relative importance of the disease in the population.

7. Follow-up of abnormal smears
   Every screening programme should designate an individual as responsible for its management. A detailed protocol for managing women with abnormal results should be drawn up for each programme. It should indicate what options are acceptable for the diagnostic investigation of screen-detected abnormalities and for their treatment follow-up. Ablative treatment should always be preceded by histological biopsy.

8. Monitoring
   Evaluation and appropriate adaptation of a screening programme depend on monitoring. For registration of samples and follow-up, person-based registers are of main importance. Comprehensive person-based records of invitation, screening attendance, screening results and follow-up provide the following advantages:
   (a) A fail-safe mechanism for ensuring that abnormal smears are followed up can be incorporated.
   (b) Screening invitation can be regulated to ensure that the laboratories receive an even flow of work; overfrequent screening can be discouraged and efforts concentrated on recruiting those who under-utilise the service.
   (c) Evaluation of cervical screening as a means of reducing the incidence of invasive cancer.
   (d) Review of false negative smears, which provides a means for continuing self-education for cytology staff as well as a means for monitoring quality.

9. Exchange of information
   Exchange of information between centres starting pilot projects is desirable. Areas of special interest are the success of different strategies for increasing participation in screening and assessment of cost-effectiveness. Studies of cost-effectiveness should take into account disadvantages, such as those of over-treatment, as well as the financial costs.

10. Optimal use of resources
    Screening of asymptomatic women every 3 years has proved to be an efficient means for reducing incidence and mortality from cervical cancer; on a population basis, the most efficient use of given resources is therefore achieved, if all women in the relevant age groups are offered screening every 3 years. Use of the public health care resources on annual screening should be avoided. To ensure that sufficient resources are available for a 3-year population screening, both GPs and the public should be informed about the good results obtained with 3-year screening intervals for asymptomatic women.

1.3 CURRENT SCREENING ACTIVITIES IN EC-COUNTRIES

Cervical screening was introduced into Europe over 30 years ago. Much of the screening was opportunistic although a few countries offered an organised screening programme. The first organised screening programmes in Europe started in Østfold county in Norway in 1959, and in the Grampian region of Scotland in 1960. The dissemination of the Papanicolaou smear test depended both on the professional interest and on the method of payment. A major increase in use was thus seen in Denmark after 1969 where smears taken by GPs on the request of the individual women were paid for through a public health insurance scheme.

A survey undertaken in 1991 indicated that the number of Papanicolaou smears taken to date in the EC-countries was sufficient to screen all women aged 25–65 years (Table 1.2). The number of smears in Denmark and Germany was almost enough for every woman to have a smear taken every second year. The number of smears in Belgium, France and Luxembourg was sufficient for screening every third year, and in Ireland, the Netherlands, and the U.K. for screening every fifth year.

Despite this extensive and costly screening effort approximately 22 000 new cases of cervical cancer are diagnosed each year in the EC-countries and 13 000 women die from the disease (Table 1.3). The reasons for this are 2-fold. Firstly, the smears are not distributed in an optimal way. This is illustrated by the fact that a substantial proportion of the smears are used for screening of women below the age of 25 years and frequent rescreening (e.g. annual screening) of the same women occurs. This suboptimal distribution of smears can be seen at present in Denmark which recommends that screening be offered at 3 yearly intervals from the age of 23 until the age of 75 years. A Danish county without an organised programme at present uses 14% of the smears for screening of women below the age of 23, and 28% of the smears for short interval rescreening of women aged 23–75 years. Thus in total, 42% of the screening resources of the county are not used in accordance with the national recommendations emphasising the waste of resources in this county.

Secondly, although screening is widespread in the EC, a recent survey undertaken by the European Commission Training Programme for Cervical Cancer Screening (ECTP.CCS) shows that standards of screening throughout the EC are very variable. In many EC-countries there are no specified training requirements for personnel participating in cervical screening and no test of proficiency of cytoscreeners who examined the smears. Moreover, there are no nationally or internationally recognised standards for monitoring the effectiveness of the programme, the coverage of the population at risk or the quality of the service.

Thus although the technology for cervical cancer screening is well established and a major part of the resources required to screen the female population at risk is available already, (in certain countries even in excess) the potential benefits of screening have not been achieved in the EC-countries. Improvement in the efficiency of the service by redistribution of resources, increased coverage of the population and the introduction of quality assurance in all its aspects is badly needed.

1.4 AIM OF THE DOCUMENT

This report was commissioned by the committee of cancer experts of the Europe Against Cancer programme with the aim of improving the quality of cervical screening. It also has the aim of increasing coverage and optimising use of resources thereby contributing to a decrease in the incidence and mortality from cervical cancer in the EC-countries. It is written in general terms to be intelligible to a broad range of readers, including administrators, scientists, medical and non-medical personnel. It is intended to be of value for decision making at the national, regional and local level. It should also be used as a basis for subvention proposals to the EC for support for cervical cancer screening programmes, and for preparation of progress reports for supported programmes.

The basis for these guidelines is the recommendations for cervical cancer screening proposed by the committee of cancer experts of the "Europe Against Cancer" programme, as summarised in Table 1.4. The scientific basis for these recommendations is not the subject of this report.

The report is divided into a number of sections. The infrastructure necessary for successful screening is discussed in the section on "organisation of the programme". Then follows a section on "screening methodology". A short section on "management of women with abnormal smears" is included, in spite of the fact that there is great variation in the approach to treatment of women with abnormal smears. This section points to areas where further collaborative research needs to be carried out.

The next section describes the "monitoring of the programme" in terms of essential data necessary to evaluate the effect of screening both in terms of short term and long term parameters. Advice is given on how these data can be obtained. A section is dedicated to the training of medical and non-medical personnel participating in screening. Finally, procedures for internal and external quality assurance in the cytology laboratory are described.

A precondition of quality assurance is the establishment of standards. The aim of a quality assurance programme is to ensure that these standards are met. However, because of the diversity of health care systems it is not possible to indicate a single approach to how quality assurance activities should be organised at the national level. It is necessary to use methods which on the one hand allow existing systems in individual countries to operate and on the other hand make it possible to monitor and compare the outcome between countries. In view of the need for flexibility, we have kept these guidelines as simple as possible so that they can be widely applied throughout the EC.