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EFFECT OF SCREENING FOR CANCER IN THE NORDIC COUNTRIES ON DEATHS, COST AND QUALITY OF LIFE UP TO THE YEAR 2017

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BACKGROUND

Aims of this study

Screening is practised for cancer at many sites using several different screening tests (3). However, most of these lack scientific evidence of their effectiveness, i.e., in reducing mortality. Only for breast cancer, cervical cancer and colorectal cancer can the results be regarded as sufficient evidence for screening to be run as a public health policy. In this monograph there are estimates on the effects of screening for cancer supplemented by economic and quality of life evaluation. The effects are based on all those tried and tested screening methods which are or can be recommended to become a public health policy. Estimated effects of mammography on breast cancer mortality are based on randomized preventive trials as well as those of fecal occult blood test on mortality from colorectal cancer. Screening for cervical cancer was never shown to be effective by a randomized preventive trial, but the Nordic screening programmes provide convincing evidence of effectiveness. Other screening modalities are not recommended for application as public health policy because of lack of evidence of the effect or because of sufficient evidence of ineffectiveness. Background information and details on design and methods are given by Hristova (4).

In the Nordic countries these screening modalities are at different phases of development. Screening for cervical cancer has been in operation since the mid-1960s. Owing to variations in screening policy between the Nordic countries, different reductions in incidence of and mortality from the disease were reached. Breast cancer screening started as randomized trials in Sweden (5) and as public health policy gradually in the late 1980s in Finland (6), Iceland (7) and Sweden (8). Even though the trials showed reduction in mortality, there is so far no reliable evidence of the effect of this screening as a public health policy. Colorectal cancer screening is at an early stage of evaluation. Three randomized screening trials have been published (9–11) on the basis of which it is likely that screening results in some reduction in mortality. However, nowhere in the Nordic countries was the screening for colorectal cancer practised as a public health policy.

The aim of this study was to evaluate the potential effects of screening for cancer in the Nordic countries. The effects were measured in terms of mortality reduction, costs for the society and quality of life. Following aspects were assessed in particular:

1) The effect of cervical cancer mass-screening if the Finnish programme had been applied and the potential effect of breast and colorectal cancer screening programmes on mortality from these three cancers in the period up to 2017.
2) The costs of such screening programmes, taking into account the direct costs of screening and savings from the treatment of advanced disease and terminal care.
3) The impact of mass-screenings on the quality of life at population level by taking into account the effect of screening and the indirect effects of prolongation of life.

On the basis of the predicted number of deaths prevented, effects on quality of life and costs, costs per life year saved and per quality adjusted life years saved due to screening in 1993–2012 will be predicted.

Incidence of cancer in the Nordic countries

In each of the Nordic countries there is a population-based cancer registry. The Nordic cancer registries receive reports from hospitals, physicians, pathological and cytological laboratories (except in Denmark), and institutions with hospital beds. Information is also collected from death certificates. Cases based solely on death certificates are not registered in Sweden. Notification of cancer cases is compulsory in all the Nordic countries with the exception of Iceland. The multiple sources of information guarantee an almost 100% coverage of all cancer cases in every Nordic country. The following items are used for routine

From the Finnish Cancer Registry (L. Hristova, M. Hakama), University of Tampere School of Public Health (L. Hristova, M. Hakama), Bulgarian Cancer Registry (L. Hristova).

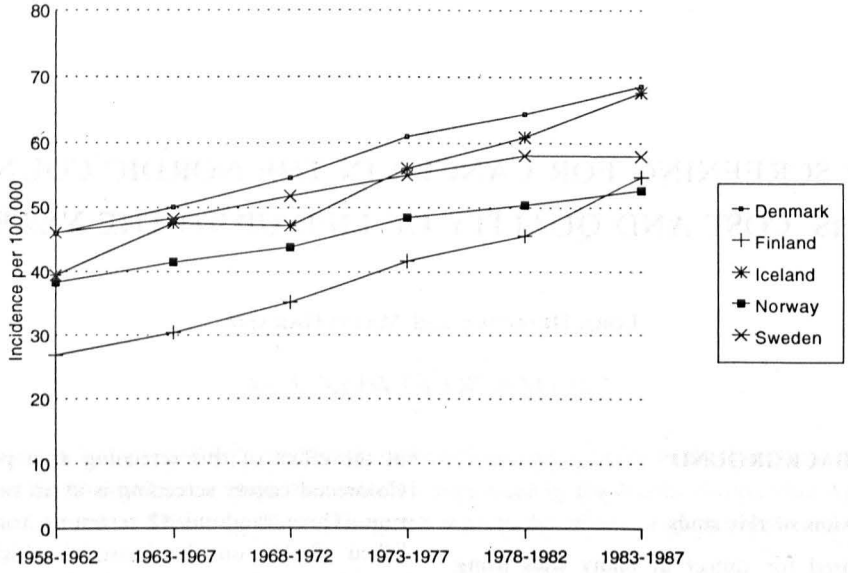


Fig. 1. Age-adjusted incidence rates of breast cancer in the Nordic countries.

statistical reporting: primary site of the tumour, date of diagnosis, verification of diagnosis, and place of residence. The Nordic cancer registries collaborate in the fields of routine statistics, epidemiology and public health.

Breast cancer has been reported as the most frequent form of cancer among females in the Nordic countries since the 1960s, and in the period 1983–1987 it accounted for 24% of all new cancers in females. The incidence rate of breast cancer was lowest in Finland and highest in Denmark (1) (Fig. 1).

Through the Nordic countries the incidence has increased in all age groups and by all birth cohorts during the period 1955–1990. The slope of the trend was similar in all the Nordic countries by the end of the 1970s (12). Since the early 1980s the increase in the incidence of breast cancer has been greatest in Finland and the trend is expected to remain unchanged in the next 20 years. During the period 1958–1987 the increase in the age-adjusted incidence rate was 28% in Sweden (the lowest) and 104% in Finland (the highest) (1).

Before 1965 the age-adjusted incidence rate for *cervical cancer* in Denmark was about 28 per 100 000 woman-years, 16–17 per 100 000, in Sweden and Norway and in Finland 14 per 100 000. In Denmark, Norway and Sweden

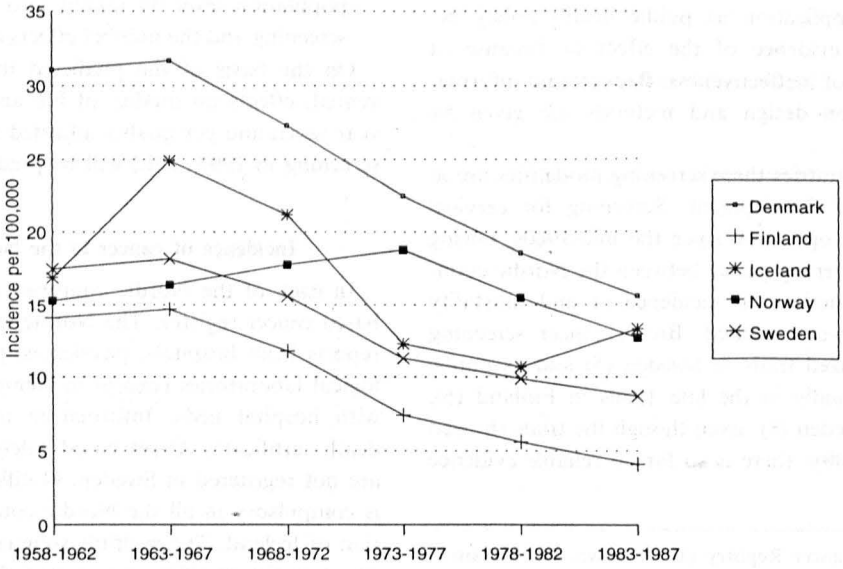


Fig. 2. Age-adjusted incidence rates of cervical cancer in the Nordic countries.

the incidence was highest in the age group 40–49 years. In Iceland and Finland the highest incidence rate was observed in the age group 50–59 (13). In the period 1983–1987, 41% of cases in the Nordic countries were between 30 and 54 years of age (1).

During the past two decades the incidence rates have decreased in all the Nordic countries (Fig. 2). Towards the end of the 1980s, the age-adjusted rates were 50% lower in Denmark and Sweden and 70% lower in Finland compared with those in the late 1960s. In Finland the maximum decrease in the age-specific incidence rates was observed in the 30–49 years age group. There was no decline in incidence in the 20–29 years age group (1).

In all the Nordic countries the incidence rates of *colon cancer* were approximately similar in both males and females, while for *rectal cancer* the rates were higher in males (Figs. 3–6). The incidence of colorectal cancer increased with age. In the Nordic countries the incidence rates have been highest in Denmark and lowest in Finland, and an increasing trend has been observed in all the Nordic countries, with the exception of Denmark (1).

Screening for cancer

Screening can be defined as identification of preclinical disease by a relatively simple test. The aim of screening for cancer is to reduce mortality and to improve quality of life (14). Incidence rate can be reduced by screening if the disease has a detectable in situ phase which is curable.

There are wide variations between screening programmes, but in principle the success of a screening programme depends on the following prerequisites (14–16).

1) A *disease* is suitable for screening if:
   - it is an important health problem justifying the efforts of screening
   - there is a long enough detectable asymptomatic preclinical phase
   - the proportion of lesions found in this preclinical phase that would progress to clinical lesions is significant
   - an acceptable treatment is available, which can improve patients' prognosis after earlier diagnosis.
2) The *test* should be valid and identify the disease in its preclinical phase. The test should be acceptable for the population—easy to apply, painless and without side effects.
3) A screening *programme* should make it possible to identify the disease in its preclinical phase or at an early stage in the target population, and treatment facilities should be available. A screening programme is well organized when:
   - the target population is identified
   - individuals in the target population are identifiable
   - high coverage and attendance rate can be guaranteed
   - there are the facilities for conducting the tests
   - there is a designed and agreed referral system
   - there is an organized quality control system.

Validity of a screening test is defined in terms of sensitivity and specificity. Sensitivity of a screening test is the proportion of true positives from all persons with the disease. High sensitivity means few false negatives. Specificity is the proportion of true negatives from all persons without the disease. High specificity means few false positives. Sensitivity of a particular screening round can be defined as the proportion of screen-detected cancers in

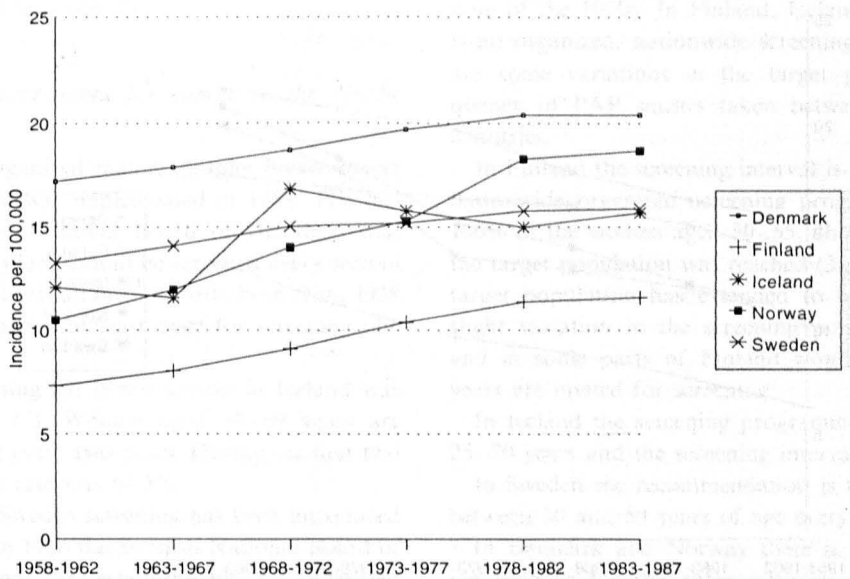


Fig. 3. Age-adjusted incidence rates of colon cancer in females in the Nordic countries.

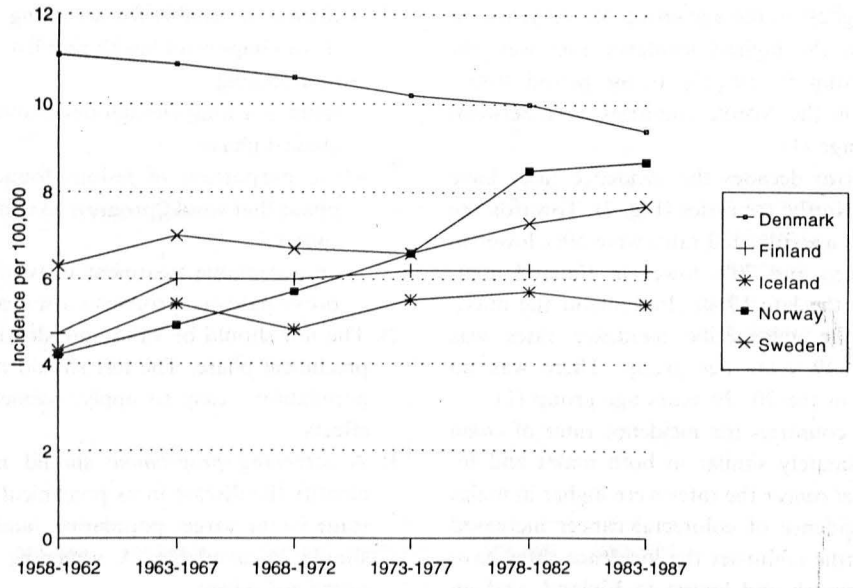


Fig. 4. Age-adjusted incidence rates of rectal cancer in females in the Nordic countries.

this round out of the screen-detected plus interval cancers (17).

Physical examination and mammography are the most frequently used methods for detection of breast cancer. The sensitivity of mammography is higher in older age groups and in bigger tumours. The specificity is about 97%, and 50% to 90% of all the cancers are diagnosed at screening (18–22).

In 1941 Papanicolaou published a method for collection, smearing, staining, and interpretation of exfoliated cells from the cervix uteri (PAP test). This test involves the removal of a sample of cells from the epithelium of the transformation zone of the cervix on the basis of which a cytological diagnosis is made. Between 1% and 5% of smears indicate suspicious cells and further diagnostic measures and follow-up of women with these findings are required (23). Evaluation of the sensitivity and specificity of the PAP test to identify preclinical phases of cervical cancer is difficult because pre-invasive lesions are usually asymptomatic and the total number of women with these lesions is unknown. Both the sensitivity and specificity of the PAP test are high

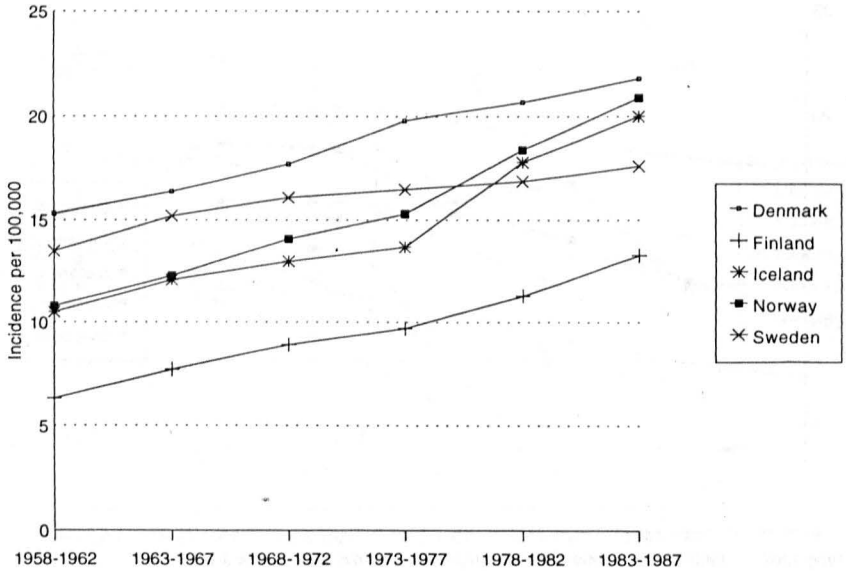


Fig. 5. Age-adjusted incidence rates of colon cancer in males in the Nordic countries.

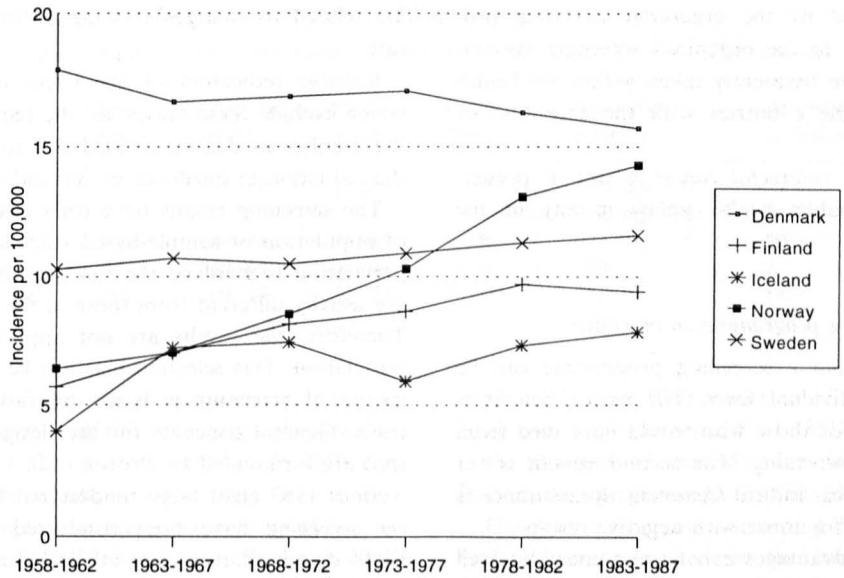


Fig. 6. Age-adjusted incidence rates of rectal cancer in males in the Nordic countries.

and more than 90% also for the public health policy (24).

Biochemical tests for fecal occult blood (FOBT) are the only non-invasive methods of screening asymptomatic subjects for early diagnosis of colorectal cancer. Sensitivity of non-hydrated FOBT varied in different studies from 52% to 80% and specificity was estimated to be between 96% and 98%. Rehydration of the slides increased the sensitivity to more than 90% (25) for neoplastic lesions, but resulted in lower specificity, 90–94% (26).

There are other tests available to screening for these cancers but in a randomized preventive trial it was shown that none of them was effective or the cost precluded effective use of such tests (26–28).

Mass-screening programmes for cancer in the Nordic countries

In Finland, an organized mammography *breast cancer screening* programme was implemented in 1987. The recommendation of the National Board of Health is that women aged 50–69 years should be screened every second year. By the end of 1991, all birth cohorts born from 1928 to 1941 had been invited at least once for screening (29, 30).

Nationwide screening for breast cancer in Iceland was introduced in 1987 (7). Women aged 40–69 years are invited for screening every two years. During the first two years the attendance rate was 64.3%.

In Denmark and Sweden screening has been introduced in selected regions. In 1986 the Swedish National Board of Health recommended the establishment of organized screening programmes in 18 counties. The recommendation was to screen all women aged 40–74 years according to the following schedule: from 40 to 54 years every 18 months and from 55 to 74 years every 24 months. In 1988, after a meta-analysis based on all randomized trials in Sweden, the National Board of Health gave a recommendation to screen all women between 50 and 69 years of age every two years, and as far as the limited capacity allows, to screen all women between 40 and 70 years (31). Norway has decided for the time being not to run any organized screening programme for breast cancer.

During the 1960s different kinds of *screening programmes for cervical cancer* were initiated in the Nordic countries, reaching their maximal coverage at the beginning of the 1970s. In Finland, Iceland and Sweden there is an organized, nationwide screening programme. There are some variations in the target population and frequency of PAP smears taken between different Nordic countries.

In Finland the screening interval is 5 years. By 1970 the nationwide organized screening programme had covered 100% of the women aged 30–55, and 75% compliance of the target population was reached (32, 33). Since 1987 the target population has extended to 60 years. There is a slight variation in the screening policy by municipality, and in some parts of Finland women younger than 30 years are invited for screening.

In Iceland the screening programme covers age groups 25–70 years and the screening interval is 2–3 years (24).

In Sweden the recommendation is to screen all women between 30 and 50 years of age every 4 years (33, 34).

In Denmark and Norway there is no common screening practice for the entire country. About 40% of the female population in Denmark (35) and only 5% in Nor-

way (36) are covered by the organized screening programme. In addition to the organized screening spontaneous PAP smears are frequently taken within the health care in all the Nordic countries with the exception of Iceland.

Mass-screening for colorectal cancer is not at present implemented as a public health policy in any of the Nordic countries.

Effect of a screening programme on mortality

Several benefits from a screening programme can be measured on an individual level. The major benefit is prolongation of life for those who would have died from the disease without screening. The second benefit is for those who will need less radical treatment. Reassurance is an important benefit for those with negative results.

A number of disadvantages can be mentioned as well (15, 37). For false positives and borderline abnormalities there is unnecessary morbidity and overtreatment. For all true positives, independently of whether they will die from the disease or not, there is a lead time morbidity. A short-term psychological morbidity and the potential hazard of a screening test itself are also associated with screening.

There are several approaches to evaluating the results of a screening programme on population and group level. Benefits for the population can be measured in terms of:

- change in incidence
- change in stage distribution
- change in survival time
- change in mortality rate
- change in the distribution of the indicators of quality of life
- cost—effectiveness.

A review of different models for estimation of the effect of screening depending on the natural history of the disease and the screening practice was presented by Miller et al. (16, 38). Incidence rate is an appropriate end point when preinvasive lesions are detectable by screening and are curable, as in the case of dysplasias and carcinoma in situ of the cervix uteri. The changes in stage distribution or in survival time due to screening are not good indicators of the effect of a screening programme, because both are influenced by some kind of bias.

Four types of bias are mentioned in the assessment of the results of screening (37, 39). A number of cases which would never surface as invasive disease in the absence of screening are diagnosed (overdiagnosis bias). Screening tests detect the disease earlier than would have been the case if diagnosed without screening (lead time bias) (40), and are more effective in the detection of lesions with a prolonged natural history and better prognosis than in that of diseases with a higher malignancy potential (length bias) (41). Lead time and length biases are related to changes in stage distribution and survival rate.

Reliable indicators of the effect of cancer screening which exclude these biases are the reduction in mortality, the number of deaths avoided due to the screening, and the reduction in incidence of cervical cancer.

The screening results have been evaluated on the basis of population or sample-based studies. When a volunteer population is involved the risk factors and the incidence are usually different from those in the general population. Therefore, the results are not applicable for the whole population. This selection bias can be avoided if the evaluation of screening is based on randomized controlled trials. General concepts for the design and control of a trial are formulated by Prorok (42).

Since 1963 eight large randomized trials of *breast cancer screening* have been conducted in different countries—five in Europe, one in the US and two in Canada. Nearly 500 000 women have been included in these trials. The aim of the trials was to evaluate the effectiveness of breast cancer screening in general and separately in different age groups. The screening test used was mammography alone or in addition to physical examination (5, 17, 43–44).

In the Health Insurance Plan (HIP) study in the US mortality reduction from breast cancer in the total screened group was 30% during the first 10 years and about 25% by the end of follow-up, i.e., 18 years after entry into the trial (45).

Four randomized trials have been carried out in Sweden to investigate the efficiency of mammography breast cancer screening in reducing mortality—in Malmö, in Kopparberg-Östergötland (Two-County Trial), in Stockholm and in Gothenburg. All the trials were population based. Some details of the Swedish trials are presented in Table 1.

Meta-analysis on all randomized Swedish trials was conducted in 1987 by the Swedish Cancer Society. Its aim was to check the quality of the follow-up information and to assess the overall efficacy of breast cancer mammography screening. In total, 282 777 women were included—156 911 in the study group and 125 866 in the control group. The relative risk (RR) of dying from breast cancer was significantly lower in the study group (RR = 0.77, 95% CI 0.66–0.88). Mortality reduction varied by age, although the heterogeneity test between groups was not significant. The conclusion was that the greatest effect (29%) of screening was achieved in women aged 50–69 years. In the 40–49 and 70–74 years age groups, the cumulative breast cancer mortality rate was almost similar in the study and control groups (46).

The UK Trial of Early Detection of Breast Cancer (Edinburgh Trial) was organized as a comparison between two screening programmes (mammography, BSE) and a control group in different geographical regions.

Table 1

Basic characteristics of the Swedish randomized breast cancer screening trials (43, 46)

Study	Year begun	Age at entry	Study group	Control group	Screening interval	Attendance rate at first round
Malmö	1976	45–69	21 088	21 195	18m age < 50 24m age > 50	74%
Two-County	1977	40–74	78 085	56 782	24, 33m	89%
Stockholm	1981	40–64	39 164	19 943	28m	82%
Gothenburg	1982	40–59	20 724	28 809	18m	84%

After 6–7 years of follow-up a mortality reduction of about 20% was reported in the mammography screened group compared with the control group but the difference was not statistically significant. Mortality in the BSE group was similar to that in the control group (17).

Two Canadian National Breast Cancer Screening Studies were initiated in 1980. Their aim was to evaluate the effect of a combination of annual mammography, physical examination and teaching of breast self-examination. Screening with mammography and physical examination every year detected considerably more small and node-negative tumours than the usual health care or screening with physical examination only, but during the first 7 years of follow-up no mortality reduction in breast cancer was observed in either of the study groups (47–49).

A summary of the results from randomized trials for breast cancer screening was presented by Fletcher et al. (43) and Wald et al. (44) (Table 2). It can be concluded that screening for breast cancer based on mammography results in a reduction of about 30% in the risk of deaths from breast cancer in ages 50 to 69.

The first *screening programme for cervical cancer* commenced in 1949 in British Columbia, Canada. Data on the occurrence of clinical invasive cervical cancer in Canada have been available since 1955, and a national cancer registry was established in 1969. The incidence of invasive cervical cancer in age group 35–64 years decreased from 30 to about 10 per 100 000 woman-years during the period 1957–1972, while the proportion of screened women aged 20 or over increased from 5% to 55%. An increasing trend in the incidence of cervical cancer was observed in 1969–1975 in the age group 20–34 (50, 51).

Table 2

Relative risk of breast cancer mortality in women of 50–70 years invited for mammographic screening compared with those not invited (43, 44)

Trial	RR	95% CI
Health Insurance Plan (HIP)	0.79	0.62–0.99
Edinburgh	0.85	0.65–1.12
Swedish Two Counties	0.78	0.65–0.93
Malmö	0.81	0.62–1.07
Stockholm	0.76	0.50–1.14
Gothenburg	0.78	0.70–0.87
Total Swedish trials	0.77	0.67–0.88
All trials	0.78	0.70–0.87

The results from mass-screening for cervical cancer in Finland were estimated on the basis of data from the Finnish Cancer Registry and the Mass-screening Registry 1963–1971 according to the recommendation of the National Board of Health in Finland. The cohorts between 40 and 54 years of age were most frequently screened. The probability of contracting invasive cervical cancer during one's lifetime was 0.010 for a woman aged 30–59 before the screening programme, and 0.002 after the first screening, which implied an 80% effect (52).

Screening for cervical cancer has been introduced to a different extent in the Nordic countries since the late 1960s. Before the screening programmes were initiated, about 2 500 new cases of cervical cancer were diagnosed every year. In the 1980s the number of new cases of invasive disease had decreased to about 1 700. A strong correlation has been found between the extent of the screening programmes and reduction in the incidence of invasive cervical cancer and mortality from cervical cancer (6, 23, 33, 35, 53–56).

Organized population screening programmes for cervical cancer are currently run in other European countries or regions, too. In Florence cytological screening for women aged 18 to 60 was started in 1980 (57). In England and Wales nationwide cervical screening was introduced in the mid-1960s (58).

Five controlled randomized trials have been initiated to investigate the potential effect of *screening for colorectal cancer*.

In the New York trial, a total of 21 756 participants aged 40 or over were enrolled from 1975 to 1979 (11, 59). A total of 12 deaths occurred among the screened group versus 22 expected ($p = 0.06$) during a 10-year follow-up (Winawer et al. 1991).

The Minnesota trial was initiated in 1975. By 1978, 46 550 participants between 50 and 80 years of age were randomly assigned into three groups. The study groups were offered FOBT every year or every two years, the third group constituted a control group without screening.

The mortality rate ratio from colorectal cancer after 13 years of follow-up was 0.67 (95% CI 0.50–0.87) in the annually screened group and 0.95 (non-significant) in the group screened every two years (10, 60).

A population-based randomized controlled clinical trial was initiated in Nottingham, UK, in 1984. By 1989 about 156 000 persons between 50 and 74 years of age were randomly included in the study and control groups. The study group subjects were offered FOBT every two years. No reduction in the mortality rate attributable to screening has been demonstrated so far (61–63).

The Gothenburg controlled trial was started in 1982, and 27 700 inhabitants of Gothenburg aged 60 to 64 were enrolled in the study by 1987. Subjects were randomly assigned to a test and a control group. Mortality reduction attributable to the screening has not been reported so far (25, 64).

A randomized controlled screening trial was initiated in Denmark in 1985. In this study 62 000 persons between 45 and 74 years of age were randomly allocated to screening and control groups. Reduction in mortality rate within the whole study group compared with the control group was 27% but non-significant over the short follow-up period (9, 65).

The reasons for non-participation in screening for colorectal cancer have been investigated by Dent et al. (66). They can be summarized as follows: indifference, procrastination, absence of complaints or preference for one's own doctor to do the test. Females, single, separated or divorced and those with personal knowledge of colorectal cancer patients are more likely to participate in screening.

Attempts at screening have been made for lung cancer, ovarian cancer, stomach cancer, prostate cancer and cancers at some other primary sites, but there is no scientific evidence of the effectiveness of these programmes. A review of publications on screening for cancer was published by Miller et al. (4). Screening for lung cancer based on cytological or roentgenological tests has shown that it is not effective in mortality reduction and cannot be regarded as an alternative to primary prevention (67, 68). The screening tests for ovarian cancer are based on tumour markers and ultrasound. Studies carried out so far have failed to obtain sufficient sensitivity and specificity. Further development of the screening technique and a randomized controlled trial are needed to prove the potential effect of ovarian cancer screening (69). Studies evaluating the screening programme for stomach cancer in Japan suggest that mortality rate could be reduced in regions with high incidence (70). However, there are no results available on reduction in mortality based on randomized preventive trials. Prostate cancer screening may result in serious over-diagnosis and over-treatment in the oldest ages when any possible extension of life is likely to be short and of poor quality (71). At present, screening for cancer as public health policy cannot be recommended for any primary site listed above except for breast, cervix and colorectum cancer.

Effect of a screening programme on quality of life

'The term *quality of life* might suggest an abstract and philosophical approach, but most approaches used in medical contexts do not attempt to include more general notions such as life satisfaction or living standards and tend rather to concentrate on aspects of personal experience that might be related to health and health care' (72). During the past decade quality of life measurement has become an essential part of assessing the results of any health care intervention. Different dimensions of quality of life (QoL) can be considered depending on the purpose of evaluation, but several of them are included in most of the measurement tools: physical function, emotional function, social function (or role performance) and pain (or other disease-specific symptoms) (72, 73).

There are various types of tools for measuring quality of life (73–75). In general, they can be divided into two groups: generic (applicable in a wide range of research settings), and specific (designed for a specific disease or treatment). Specific QoL tools for cancer can be divided into 'cancer-specific' questionnaires, those which can be used for all types of cancer, and 'specific cancer' questionnaires, for one particular type of cancer (76).

Some of the questionnaires are constructed for self-assessment and some of them are to be completed by medical professionals. The evaluation and expression of QoL are subjective and therefore the main respondent should always be the patient. When the patient's health status does not allow him to respond adequately, experts' opinion can be submitted (77).

For assessment of the results of a screening programme it is important to estimate not only the costs and duration of life but also the quality of the possibly gained life years. The adjustment for quality of life is a way of linking the exactly measured but not always sufficiently informative 'survival time' with a subjective quality of life (78–80).

The priority of different dimensions of quality of life varies among individuals, and depends on the disease and phase of the disease. When QoL is assessed at the diagnostic phase, psychological consequences are measured, whereas when QoL of terminal stage is assessed, the ability to cope with self-care, other physical functions and pain becomes highly significant.

Effect of screening for cancer on QoL can be defined as:

- short-term effect—for all screened individuals during the screening tests and diagnostic confirmation of false positives,
- long-term effect—for those diagnosed as cancer patients.

To assess the short-term effect, a study of 132 women with a normal test result in the Edinburgh breast cancer screening trial was carried out 6 months after the trial. No excess psychiatric morbidity related to the screening was found in the study group compared with the control group (81). The emotional, social and physical dysfunction of women after the first round of breast cancer screening was studied by Cockburn et al. (82) in Australia. Women in the recall group showed significant emotional ($p < 0.001$) and physical ($p < 0.05$) dysfunction one week after obtaining a negative result compared with those with a negative result in the initial mammography test (at comparable times from the screening) and the control group (non-screened). The difference between the groups had disappeared eight months later (82).

The long-term effect can be divided into three phases related to the screening programme: 1) lead time phase—from the diagnosis of the disease by screening test to the theoretical clinical surfacing of the disease without screening; 2) clinical phase—from clinical diagnosis to theoretical death without screening; 3) life time gained due to the screening.

When the overall effect of a screening programme is assessed the psychological morbidity during the diagnostic period on population level (short-term effect) can be included in the lead time phase.

For the assessment of the long-term effect of a screening programme on QoL of patients diagnosed by screening, the following steps were determined (83):

1) Definition of the disease/treatment phases
2) Definition of the duration of each of these phases
3) Quantitative evaluation of the quality of life in each phase, i.e., attaching utility to each of them.

Utility refers to the value of a specific health status and can be measured by individuals' (patients' or health care experts') preferences for any particular set of health outcomes.

de Koning et al. (84) calculated the overall effect of the screening programme in terms of quality adjusted life years (QALY) by multiplying the mean QoL value of each phase by the mean duration of the phase and the number of persons surviving this phase. Quality adjustment was estimated to reduce the effect of screening (increase in life years gained) for breast cancer by 3.2%.

Some aspects of quality of life in the oldest age unrelated to cancer were studied by Katz et al. (85), Hofman et al. (86), Skoog et al. (87), Roelands et al. (88), Grimby & Wiklund (89) and Holmen et al. (90). The active life expectancy or independence in the daily life activities such as bathing, dressing, transfer and eating in the elderly was investigated by Katz et al. (85). Seventy-one per cent and 54% of the total remaining life for men and women respectively is expected to be lived independently by people aged 65–69 years. At 80–84 years the corresponding proportions of active years remaining are 65% and 49% respectively. Roelands et al. (88) investigated the dementia-free life expectation in the oldest age in Belgium. Three levels of dementia were distinguished: mild, moderate and severe. Moderate dementia was defined as 'living independently is risky and some supervision is necessary'. Severe dementia was defined as health status requiring continued supervision. The authors found out that 7% of the remaining life at age 65 will be lived in moderate or severe dementia, and at the age of 85 this proportion is 26%. A significant difference was found by sex (Table 3).

In this study quality of life not directly related to cancer was also assessed, because not all the life years gained by screening will be active and with good quality.

Economic evaluation of a screening programme

A necessary extension of an evaluation in health care is economic evaluation, which incorporates both costs and effects. During the past decade the number of publications in this field has grown rapidly (91).

From the viewpoint of society, both the effects and the costs can be presented as direct and indirect (92):

- The direct benefits of a screening programme are savings in treatment costs attributable to the screening.
- Indirect benefits are savings in loss of work time.
- Direct costs include all the organizing and operating costs.
- Indirect costs are costs due to time lost from work.

An estimate of the direct treatment costs of breast cancer during the five first years of follow-up in Tampere University Hospital was made by Holli et al. (93). Their estimates of the costs by stage are presented in Table 4.

An overall estimate of primary treatment costs for advanced breast cancer in The Netherlands was obtained by de Koning et al. (94). Costs included in the estimation are listed in Table 5.

The purpose of an economic evaluation is to link the costs of the health programme under consideration to the consequences, and to identify the most favourable alternative. Economic analysis is useful when deciding on health care resource allocation. It is important for decision-making on whether or not a screening programme is cost-effec-

Table 3

Life expectancy (LE) and dementia-free life expectancy (DFLE) according to age and sex in Belgium in 1991 (88)

Sex	Age	LE	DFLE	LE-DFLE	DFLE/LE
Men	65	14.0	13.4	0.6	95.7
	75	8.3	7.7	0.6	92.8
	85	4.5	3.4	0.9	75.6
Women	65	18.3	16.7	1.6	91.3
	75	10.9	9.2	1.7	84.4
	85	5.6	3.9	1.7	69.6

Table 4

Costs of breast cancer treatment and follow-up in patients diagnosed in 1977–1980 in Tampere University Hospital (93)

Stage of disease	Overall costs per patient ($)
I	7 700
II	16 000
III–IV	16 000

tive, and to what extent the additional benefits justify the additional costs (95).

There are four main types of economic evaluation technique (92). If the outcome of two programmes is identical and the lower cost alternative is sought, the analysis is called a cost-minimization analysis. When a cost-effectiveness analysis (CEA) is performed the effect of the programmes is measured in single well-defined natural units, e.g., life years gained, number of correctly diagnosed cases, and so on. Furthermore, costs per unit of effect are compared between the alternative programmes. CEA has the restriction that only one type of effect can be assessed. The specificity of cost-benefit analysis (CBA) is that both effects and costs are measured in terms of money. Effects may be single or multiple, and not necessarily common to both alternatives. However, it is difficult to evaluate all the events in health care in terms of money and this is the reason why the applicability of CBA is limited.

When the outcome is measured in more general terms, such as QALY, the evaluation of cost-effectiveness is known as cost-utility analysis (CUA) (96–98). In this form of analysis the effects of a programme are measured in time units adjusted by health utility weights. CUA is a relatively new technique, it is particularly important when the considered treatment methods are aggressive and prolongation of life is achieved at the expense of side effects, as in cancer treatment. The outcome of interest, usually measured in life years gained, is adjusted for quality of life and expressed in the corresponding number of healthy life years gained.

Table 5

Medical costs for women treated for advanced breast cancer based on 68 patient files in The Netherlands (in US dollars) (94)

Procedure	Costs per woman $
Hospital nursing	10 575
Diagnostic procedure	1 700
Radiation treatment	1 625
Nursing home	1 250
Hormonal treatment	760
Specialists	640
Chemotherapy	550
Total	17 100

Usually the aim of cost-effectiveness and cost-utility analyses of screening programmes referred to in the literature was to compare the advantages and disadvantages of different policies in a specific situation or under a particular set of assumptions (84, 94, 99–102). Most of those studies have been based on complicated indicator-based theoretical models aiming at simulation of the results of a possible mass-screening. This approach is employed when different variants of screening policies are discussed in order to choose a proper policy for a particular practical situation. The set of assumptions can be changed in order to discover the most effective programme.

de Koning et al. (84, 94) examined the cost-effectiveness of different breast cancer screening policies in The Netherlands 1990–2017. The overall result of the analysis summarized in Table 6 shows that mammography screening of women aged 50–70 every second year is the most effective in terms of the number of life years saved and cost per life year saved.

An overview of the reported cost-effectiveness analysis of the mammography breast cancer screening in women over the age of 50 (HIP, Two County, Dutch trials) shows that, depending on the different screening policies and base-line assumptions, the cost per life year saved would vary between $5 400 and $140 000 (103). Studies conducted in the US, where clinical breast examination was included in the screening test, reported higher costs compared with European studies which were based on mammography only. The costs of the screening tests are significantly higher in the US when two-view mammography or two-view mammography plus clinical breast examination were applied, and although the incidence of and mortality rates for breast cancer are higher the cost-effect ratios are unfavourable compared with those in the European studies (103).

Most cost-effectiveness estimates of breast cancer screening reported costs per life year gained between $3 825 (The Netherlands) and $6 200 (Two County Trial) (83, 84, 94, 103, 104). A cost-effectiveness analysis of breast cancer screening in Germany was published recently (105). The method of evaluation was similar to that applied by de Koning et al. (84). All the factors related to the effectiveness of a screening programme vary widely between countries due to differences in population size to be screened, incidence and mortality rates, and other features of the particular health care systems. A cost-effectiveness analysis of breast cancer screening in Spain, France, the UK and The Netherlands revealed that the relative effect of screening on mortality was greatest in the UK and smallest in Spain (106).

The total cost of screening tests is proportional to the population size while the cost per test declines when the size of screened population increases. Diagnostic and

Table 6

Effects of different breast cancer screening policies in The Netherlands in 1990–2017 (mil $) (84)

	Age and intervals of screening				
	50–70 2 yr	40–70 2 yr	50–70 1.3 yr	57–75 2 yr	50–65 3 yr
Deaths prevented*	17 000	17 800	19 800	19 450	10 800
Life years gained*	260 000	290 000	310 000	275 000	180 000
Cost of screening	300	457	405	310	185
Cost of assessment	−10	−62	−12	2	−12
Cost of primary treatment	50	57	55	71	26
Cost of follow-up	22	25	25	27	14
Cost of advanced disease	−128	−131	−145	−145	−80
Difference in costs	233	346	328	265	133
Deaths prevented	6 000	6 115	6 780	6 790	3 770
Life years gained	61 000	64 000	70 000	64 500	41 000
QALYs gained	57 500	59 500	66 000	59 500	39 300
Cost per life years gained	3 825	5 385	4 670	4 100	3 235
Cost per QALYs gained	4 050	5 815	5 000	4 450	3 400

* not discounted

treatment costs are related to the incidence rate and stage distribution, and savings from advanced disease treatment are proportional to the mortality rates. The comparison showed that in 2015, the cost per life year gained is expected to be more than three times higher in France, and more than five times higher in Spain, where the populations are much bigger and both incidence and mortality rates are lower than in The Netherlands (106).

MATERIAL

Data for breast cancer (ICD7 170), cervical cancer (ICD7 171) and colorectal cancer (ICD7 153 + 154) were employed to assess the results of the mass-screening programmes for these three cancers. The *observed numbers of new cancer cases* from 1958 to 1992, grouped into five-year calendar periods and five-year age groups (0–4, 5–9, . . . , 80–84, 85+), were obtained from the Cancer Registries of Denmark, Finland, Iceland, Norway and Sweden. The predicted numbers of incident cases of breast and colorectal cancer for the next four 5-year periods, from 1993 to 2012, published in 'Prediction of cancer incidence in the Nordic countries up to the years 2000 and 2010' (1) were employed in this study.

The *observed numbers of cancer deaths* were employed to predict future number of deaths from cancer. The observed numbers of deaths from cancer by site, sex, 5-year calendar period (1953–1992 for Denmark and Finland, 1958–1992 for Iceland and Sweden, 1968–1992 for Norway) and five-year age group (same as above) were obtained from the Nordic Cancer Registries.

The observed (1953–1992) and predicted (1993–2017) *population data* by sex, calendar period and age group (as above) were provided by the Nordic Statistical Offices and employed to predict future mortality rates and to calculate the costs of screening tests up to 2012 for Norway and up to 2017 for the other Nordic countries.

Stage distribution of new cancer cases in Finland for the period 1961–1992 by site, sex and the same age groups as above was provided by the Finnish Cancer Registry and employed in the calculation of treatment costs in the absence of screening and when the potential effect of screening was approximated. In this study, Stages I and II were combined and referred to as 'localized', and Stages III and IV 'non-localized'. Stage 'unknown' was considered to be non-localized.

Survival rates by age and calendar period in Finland were employed to estimate the proportion of number of deaths among cases diagnosed during the screening period out of the total number of deaths (which consists of cases diagnosed during the period the screening was practised and before that period). The immediate reduction in mortality attributable to the screening programme in the screened age group is only a fraction of the total ultimate effect, because many of the deaths occur in patients diagnosed before the start of screening. Cumulative relative survival rates (107) for breast, cervical and colorectal cancer patients in Finland by sex, calendar period (1974–1980 and 1981–1987) and age group (0–44, 45–64, 65–74, 75+) were obtained from the Finnish Cancer Registry and employed to estimate the immediate mortality reduction due to the screening programme in the screened age groups.

Life expectation data for the general population were taken from Statistics Finland. The life expectation data for the patients were taken from the Finnish Cancer Registry, estimated by the method proposed by Hakama and Haku-

linen (108). The data were employed in the calculation of the average number of life years gained due to the screening. The mean ages at diagnosis of patients with breast, cervical, or colorectal cancer in the period 1980–1986, within the screened age groups were used to estimate at what age the life years gained will occur. Life expectations were considered by the site of the cancer, sex and age as above (109).

The *cost* of PAP smear tests and mammography is the average charge per woman in the agreements on organizing the screening between individual municipalities and the Cancer Society of Finland, $10 per PAP smear and $40 per mammography. The cost per FOBT was assumed at $5 (101).

METHODS

Predictions

For mortality prediction, age-cohort and age-cohort-period multiplicative models were fitted to the observed mortality rates (1, 110, 111). The choice of models was justified by a wish to avoid difficulties arising from the problem of non-identifiability and to employ models allowing risk to be distinguished by birth-cohort or age groups. Particular age groups and observed periods (112, 113) were included in the models according to the following considerations:

1) the natural history of the disease: deaths from breast, cervical and colorectal cancer are rare before the age of 25 (cervix) or 30 (breast, colorectum),
2) changes in health policy, such as the establishment of mass-screening for cervical cancer, which have changed the pattern of mortality,
3) goodness of fit of the model (114, 115).

The number of deaths was predicted by the following scheme: 1) observed mortality rates were used to forecast future mortality rates, 2) number of deaths was calculated from the predicted population and predicted mortality rate.

Five-year birth cohorts were defined synthetically. For example, the birth cohort which was 0–4 years old in 1938–1942 was aged 30–34 in 1963–1967, and aged 35–39 in 1968–1972. In the figures the cohorts are indicated by the mid-year of birth.

Table 7

Models chosen for the predictions

Country	Site	Model	Observed period	Age groups	Predicted period
Denmark	Breast	Aa + Cc multipl.	1968–1992	30–85+	1993–2017
	Cervical	Aa + Cc multipl.	1953–1967	25–85+	1968–2017
		Aa + Cc multipl.	1968–1992	25–85+	1993–2017
	Colorectal				
	females	Aa + Cc + Pp multipl.	1953–1992	30–85+	1993–2017
	males	Aa + Cc + Pp multipl.	1953–1992	30–85+	1993–2017
Iceland	Breast	Aa multipl.	1958–1992	35–85+	1993–2017
	Cervical	Aa + Cc multipl.	1958–1992	35–85+	1993–2017
	Colorectal				
	females	Aa multipl.	1958–1992	50–85+	1993–2017
	males	Aa multipl.	1958–1992	50–85+	1993–2017
Finland	Breast	Aa + Cc multipl.	1953–1987	30–85+	1988–2017
	Cervical	Aa + Cc multipl.	1953–1967	25–85+	1968–2017
		Aa + Cc multipl.	1968–1992	25–85+	1993–2017
	Colorectal				
	females	Aa + Cc + Pp multipl.	1953–1992	30–85+	1993–2017
	males	Aa + Cc multipl.	1953–1992	30–85+	1993–2017
Norway	Breast	Aa + Cc multipl.	1963–1992	30–85+	1993–2012
	Cervical	Aa + Cc multipl.	1963–1992	25–85+	1993–2012
	Colorectal				
	females	Aa + Cc + Pp multipl.	1963–1992	30–85+	1993–2012
	males	Aa + Cc + Pp multipl.	1968–1992	30–85+	1993–2012
Sweden	Breast	Aa + Cc + Pp multipl.	1963–1992	30–85+	1993–2017
	Cervical	Aa + Cc multipl.	1968–1992	25–85+	1993–2017
	Colorectal				
	females	Aa + Cc + Pp multipl.	1963–1992	30–85+	1993–2017
	males	Aa + Cc + Pp multipl.	1963–1992	30–85+	1993–2017

Aa = age component; Cc = cohort component, Pp = period component.

The statistical package GLIM was used for the predictions (115). The models shown in Table 7 were chosen for the predictions.

Age-adjusted ('world standard population') mortality was calculated on the basis of the age groups included in the prediction models, assuming zero mortality rate in the youngest age groups, which were excluded from the prediction models.

Evaluation of mortality reduction due to screening

Usually when a screening programme is initiated as a public health policy, screening covers the target population gradually and the immediate effect on the entire population takes place slowly. At the onset of a screening programme deaths from cancer in any particular screened group are a combination of deaths from cancer diagnosed before the establishment of screening and deaths from cancer diagnosed by the screening programme. The proportion of deaths from cancer diagnosed by screening increases gradually during the first time periods until the optimal effect of the screening programme is reached. Mortality reduction as a result of screening can be expected only in those patients whose cancer is diagnosed by screening.

In this study an attempt was made to assess the gradual effect of screening on mortality during the period up to 2017, when it was assumed that the ultimate effect would be reached.

Breast cancer. The background for the reduction in mortality was derived from the Swedish trials. Biannual screening between ages 50–69 was assumed. According to the results of the Swedish trials, mortality reduction in the invited group during the first five years after the establishment of a screening programme was about 30%, in the next 5 years it was 28% and again 30% from the 10th to the 13th year. These mortality reduction percentages were applied to numbers of breast cancer cases detected by screening.

The percentage of breast cancer deaths occurring in the first 5 years after diagnosis were estimated on the basis of the 5-year survival rate of breast cancer patients in Finland and the assumption that about 50% of women with invasive breast cancer, diagnosed within the normal clinical practice, will die from the disease (101). It was calculated that about 28% of deaths in the age group 50–54 are from breast cancer diagnosed after the age of 50. The mortality reduction reported from Swedish trials was applied to this subgroup only. Furthermore, the same approach was used to calculate the number of screen-diagnosed cases who will die from breast cancer in the next age groups.

During the first five years after the start of the screening programme an 8.4% reduction in breast cancer mortality was calculated. From the 6th to the 10th year this reduction is 17.4%. For those women who belong to a cohort screened for 10 to 15 years, mortality is estimated to be 28.2% lower than in the non-screened group. The optimal effect of 30% mortality reduction is estimated after the 15th year of the screening programme. The assumption was that after the age of 69 preventive effects by cohorts will remain at the same level as during the last screening period and will later decrease gradually.

If the nationwide breast cancer screening programme had started in 1988 and had covered 80% of women between 50 and 69 years of age, the scheme shown in Table 8 for breast cancer mortality reduction can be assumed.

Cervical cancer. The observed mortality is affected by the mass-screening as practised in each country. Therefore, an approximation was made of what the mortality rates would have been without screening and if the Finnish screening programme had been applied. Finnish rates were considered as a reference, since the effect due to screening in Finland is the largest of all the Nordic countries. In Finland the organized screening programme starts at the age of 25 or 30 years and ends at 55 or 60 years. The interval between the screening rounds in 5 years and the participation rate varies between 70% and 80%.

Mortality rates in the absence of screening were assumed to follow the same trend as those in the period 1953–1967, i.e., before the establishment of the screening programmes. Numbers of deaths from cancer in this period were available for Denmark, and Danish data from 1953 to 1967 were used to predict mortality rates in the period 1968–1992 without mass-screening. The age-cohort model shown in Table 7 was chosen for the prediction. The Danish cohort estimates of the model were applied for the other countries. The age log-rates of the Danish model were corrected by the

Table 8

Percentage reduction in breast cancer mortality by age and calendar period if screening had been established in 1988 and had covered 80% of women aged 50–69

Period	50–54	55–59	60–64	65–69	70–74	75–79	80–84	85+
1988–92	8.4	8.4	8.4	8.4	–	–	–	–
1993–97	8.4	17.4	17.4	17.4	10.0	–	–	–
1998–02	8.4	17.4	28.2	28.2	20.0	10.0	–	–
2003–07	8.4	17.4	28.2	30.0	30.0	20.0	10.0	–
2008–12	8.4	17.4	28.2	30.0	30.0	30.0	10.0	–
2013–17	8.4	17.4	28.2	30.0	30.0	30.0	20.0	–

logarithms of the age-specific mortality rate ratios of Denmark and each of the other Nordic countries:

$$\text{Log}(A_{ci}) = \text{Log}(A_{Di}) - \text{Log}(m_{Di}/m_{ci})$$

where i is the age group, A_{ci} is estimated age component for country c (excluding Denmark), A_{Di} is the estimated age component for Denmark, m_{Di} is mortality rate in Denmark in age group i, and m_{ci} is mortality rate in country c (except Denmark). Norwegian age rates were applied for Finland in the age groups over 50.

A linear trend was applied to the age components of the model for Iceland to avoid fluctuation due to small numbers.

The predicted number of deaths for 1968–1992 for each country was employed as 'observed' in the prediction model for the future calendar period, from 1993 to 2017.

An approximation of what the mortality from cervical cancer in 1968–1992 would have been in Denmark, Iceland, Norway and Sweden if Finnish screening policy had been applied was made on the basis of the observed mortality in Finland in the period. The same cohort estimates as those for the observed cohorts in Finland were included in the models for the other Nordic countries. Furthermore, age estimates for each of the Nordic countries except Finland were corrected in a similar way as in the models without screening:

$$\text{Log}(A_{ci}) = \text{Log}(A_{Fi}) - \text{Log}(m_{Fi}/m_{ci})$$

where i is the age group, A_{ci} is age estimation for country c (excluding Finland), A_{Fi} is age coefficient for Finland, m_{Fi} is mortality rate in Finland in age group i and m_{ci} is mortality rate in country c (excluding Finland). Norwegian age estimates were employed to predict mortality from cervical cancer in Iceland.

Predictions for the future period 1993–2017 were made for each of the countries, based on the estimated numbers of deaths for the previous period 1968–1992.

Colorectal cancer. Results of the randomized Minnesota (10, 60) trial revealed that a yearly fecal occult blood test (FOBT) from 50 to 74 years reduced mortality from colorectal cancer in the invited group by 25% from the 5th to 10th years and by 30% after the 10th year to the end of follow-up after 13 years. The attendance rate was 75%. No reduction was observed in mortality rate during the first 5 years after implementation of the screening programme. The results of the Minnesota trial were applied in this study with some additional assumptions:

1. Attendance rate in a mass-screening programme is expected to be lower than that in a randomized trial based on volunteers. If we assume 50% attendance rate, the reduction in mortality rate is considered to be 0% in the first 5 years, 15% from the 5th to 10th years and 20% after the 10th year.
2. The influence of survivors from the previous age group can be ignored and the reduction in mortality rates and number of deaths is directly applicable to the corresponding age-specific death rates and number of deaths. This assumption is justified on the basis of the following:
   - the difference in the incidence rate between age groups is large
   - the 5-year survival rate is comparatively low—about 52% for females and 53% for males
   - the survival rate of colorectal cancer patients after 7–8 years is stabilized and reaches the point of cure
   - the reduction in mortality rate from colorectal cancer due to screening is 0 during the first 5 years of screening.
3. The reduction in mortality rate will remain at the same level as in the last screening period at least 5 years after the end of screening, and thereafter will decrease gradually.

On the basis of these assumptions the following scheme of reduction in the number of deaths from colorectal cancer was presumed if screening had been established in 1993 (Table 9).

Estimation of treatment costs

Cost estimation of breast cancer treatment in Tampere University Hospital assessed by Holli et al. (93) was applied. Treatment costs for cervical and colorectal cancer were approximated on the basis of breast cancer treatment costs and the proportions between costs by site and stage described by Eddy (101) and Koopmanschap et al. (116).

Table 9

Percentage reduction in colorectal cancer mortality by age and calendar period if screening had been established in 1993 and had covered 50% of the population aged 50–74 years

Period	50–54	55–59	60–64	65–69	70–74	75–79	80–84	85+
1993–97	–	–	–	–	–	–	–	–
1998–02	–	15	15	15	15	15	–	–
2003–07	–	15	20	20	20	20	15	–
2008–12	–	15	20	20	20	20	20	15
2013–17	–	15	20	20	20	20	20	15

Table 10

Proportion of treatment costs by site and stage

Site of cancer test ($)	Cost of screening test ($)	Treatment costs ($)		
		in situ	localized	non-localized
Breast	40	–	8 000	16 000
Cervix	10	4 000	20 000	32 000
Colorectum	6	–	16 000	24 000

The costs applied are listed in Table 10. Terminal care costs were included as a part of the costs by stage.

The basis of the cost calculations was the average treatment costs for localized breast cancer which was assumed to be $8 000. These costs and proportions were assumed to remain unchanged during the study period.

Estimation of costs with and without screening

The total, or additional, costs of a screening programme can be presented as the difference between the direct costs of the screening and savings in treatment costs attributable to screening. Direct costs of a screening programme included the cost of the screening tests, the cost of consecutive diagnostic confirmation of positive screen results and the cost of excess treatment of preinvasive lesions. The estimation of the costs is given in terms of formulas in the footnotes of Tables 20 to 22 and in Appendix 5. Total costs of the screening test were calculated as the product of number of persons to be screened according to the particular health care policy and costs per test. Savings from treatment costs were equal to the difference between treatment costs with screening and those in the absence of screening. Some features of cost evaluation by site are specified below.

Incidence rates for breast and colorectal cancer were obtained from the Finnish Cancer Registry and 'Prediction of cancer incidence in the Nordic countries up to the years 2000 and 2010' (1) because it refers to the incidence without screening. Instead, incidence predictions without screening had to be made for cervical cancer because the rates observed in 1953–1992 and predicted for 1993–2017 include the effect of screening.

The incidence of invasive cervical cancer (ICC) was assumed to have remained at the same level as that before the start of the mass-screening in 1958–1962. The age-specific number of new cases would thus have depended on the population size only. The expected number of new invasive cancers was calculated by applying the incidence rate 1958–1962 to the population in the subsequent calendar periods:

$$I_{58-62} = N_{58-62}/P_{58-62} \quad \text{and} \quad N_p = I_{58-62} \times P_p$$

where I_{58-62} is incidence rate 1958–1962, N_{58-62} is number of new cases 1958–1962, P_{58-62} is number of women and p is calendar period (1963–1967 to 2008–2012). The ratio of invasive cervical cancer to carcinoma in situ or severe dysplasia (ICC/CIN) before implementation of the 1958–1962 screening, was assumed to be one to two, and it was assumed that this ratio and the risk of contracting CIN remained unchanged during the following calendar periods. Total costs without screening, which are equal to the treatment costs for ICC, were calculated according to the stage distribution of 50% localized and 50% non-localized cancers.

Numbers of CIN lesions in situ with screening were calculated as the difference between approximated number of invasive cancers and CIN lesions if no screening was established and the observed (or predicted) number of new cancers with screening. The cost of treatment of CIN lesions thus includes the cost of additional diagnostic procedures and the overtreatment of CIN lesions which were unlikely to progress into invasive disease. Total cost with screening was calculated as the sum of cost of treatment of new cases assuming screening and cost of screening test and cost of treatment of CIN lesions. The cost of treatment of ICC assuming screening was calculated according to the observed stage distribution in Finland during the period 1963–1972. This stage distribution reached in 1973 remained the same until the end of the observation period, and was applied for the prediction period up to 2017 (Table 11).

Treatment costs for breast and colorectal cancer in the absence of screening were calculated on the basis of the observed (or predicted) number of new cases and the same stage distribution in Finland as in the last observed period without screening: 1983–1987 for breast cancer and 1988–1992 for colorectal cancer (Table 12).

The proportional costs for diagnostic confirmation were estimated on the basis of results from randomized trials and mass-screening for breast cancer in Europe (117) and Finnish data. For breast and colorectal cancer, costs for additional diagnostic procedures and treatment of preinvasive lesions were calculated taking into account the percentage of positive results after the first screening test and costs for diagnostic procedures and treatment of preinvasive lesions. A coefficient of 1.1 was applied to the cost of screening tests for breast cancer and 1.2 for colorectal

Table 11

Stage distribution (%) of new cases of cervical cancer applied for Finland by calendar period

Stage	Calendar period			
	1958–1962	1963–1967	1968–1972	1973–2017
Localized	50	72	70	60
Non-localized	50	28	30	40
Total	100	100	100	100

Table 12

Stage distribution (%) of new cases of breast and colorectal cancer in Finland in 1983–1987

Stage (both sexes)	Breast cancer		Colorectal cancer	
	Without screening	With screening	Without screening	With screening
Localized	50	66	43	59
Non-localized	50	34	57	41
Total	100	100	100	100

cancer screening, thus indicating costs of diagnostic confirmation of the false positives.

Costs for treatment of preinvasive lesions and overtreatment of invasive cases which were unlikely to have progressed into the clinical stage were included in the treatment costs as an increase in number of new cases, with 10% for breast cancer and 20% for colorectal cancer, due to the screening programme.

Savings in treatment costs attributable to screening for breast and colorectal cancer were assumed to be related only to improvement in stage distribution of new cases. The differences between the the stage distributions in screened and in non-screened populations estimated on the basis of results from randomized trials are presented in Table 12 (63, 118).

The treatment costs were assumed according to the scheme shown in Table 10.

Estimation of quality of life and cost-utility

Costs may be considered as 'patient' and 'society' costs. Direct society costs have been mentioned already. Patient costs, such as time investments and travelling expenses, and indirect society costs, such as loss of production and health care expenses during the life years gained, are difficult to measure and they were not taken into consideration in this study. Non-monetary costs for patients were considered as 'quality of life' (95).

The benefits of the screening programmes were assessed in terms of life years gained due to the screening. The number of life years gained was calculated as the product of the number of deaths avoided and the difference between life expectancy of the general population and that of cancer patients in Finland. The difference between life expectancy was assessed on the basis of Finnish data (109, 119) by age and gender, specifically for each of the three sites of cancer.

The loss of life years gained (LYG) after adjustment for quality of life (QALYG) for breast cancer patients was assumed to be 3% (84). For cervical and colorectal cancer the values for QALY gained (QALYG) were assumed to be 1% and 5% respectively, less than total LYG. An additional adjustment for dementia-free life years gained was performed. Moderate and severe dementia were included in the term 'dementia' in this study. The assumption was that females over 75 years of age will live 85% of their remaining life dementia-free, and at the same ages males will live 93% of their remaining life free of dementia (87). LYG with good quality were defined as dementia-free life years out of those adjusted for quality of life.

Finally, cost-utility was estimated as costs per QALYG, per dementia-free life years gained and per life years with good quality.

RESULTS

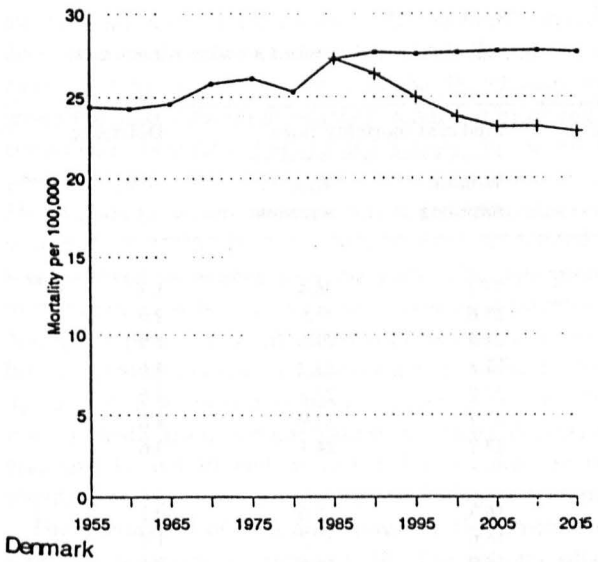
Mortality predictions

Breast cancer

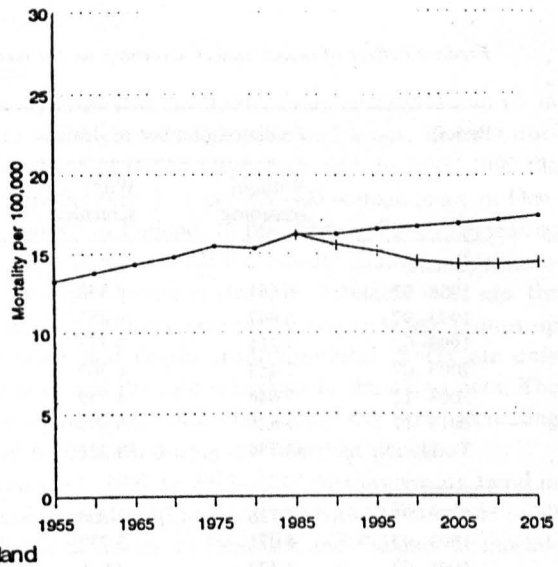
Since the cancer registration in the Nordic countries was established, mortality from breast cancer has been increasing in Denmark and Finland, but has remained relatively stable in Iceland, Norway and Sweden (Appendix 1A). A trend toward increase was observed in the 50 to 74 years age groups in Denmark and in all ages in Finland. Breast cancer mortality is strongly correlated with age. The mortality rates have been increasing with age during all the periods and the highest mortality rates are found in the oldest ages.

In all the Nordic countries except Finland, mortality from breast cancer was predicted to remain stable in the period 1993–2017 (2012) (Appendix 1B). Following the observed trend of stabilization in the younger age groups, the mortality rate in Finland in 1988–1992 was predicted to remain approximately on the same level as that in 1983–1987 with some variation by age group. The highest age-adjusted mortality rate was predicted in Denmark, about 27.7 per 100 000 woman-years over the predicted period. The age-adjusted mortality rate from breast cancer in Finland was forecast to reach about 17.5 by the end of the period (2013–2017). In Iceland and Norway mortality was predicted to remain unchanged, 20.3 and 18.5 respectively. The mortality rates increase with age in the Nordic countries, and in the 70–74 years age group they are about twice as high as in the 50–54 years age group in both observed and predicted periods. The highest mortality rate is expected in women over 85 years.

The prediction of what the mortality rate would be if mass-screening for breast cancer, covering the ages from 50 to 69, had been established in 1987, and had reached the optimal effect is shown in Appendix 1C. The reduction in the total age-adjusted breast cancer mortality is negligible in the first 5-year period, 0.7 per 100 000 woman-years, but becomes larger in the subsequent intervals. At the end of the period the expected difference between mortality rates without screening and with screening is between 4.8 (Denmark) and 2.9 (Finland) (Table 13). Although the reduction in the age-adjusted mortality rates attributable to mass-



Denmark



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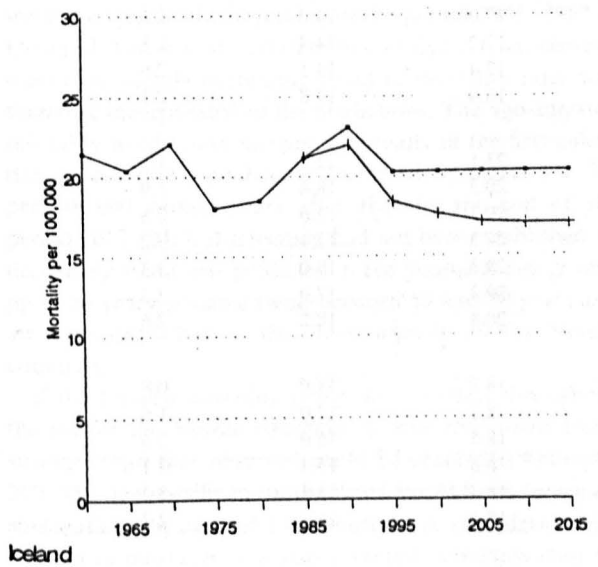

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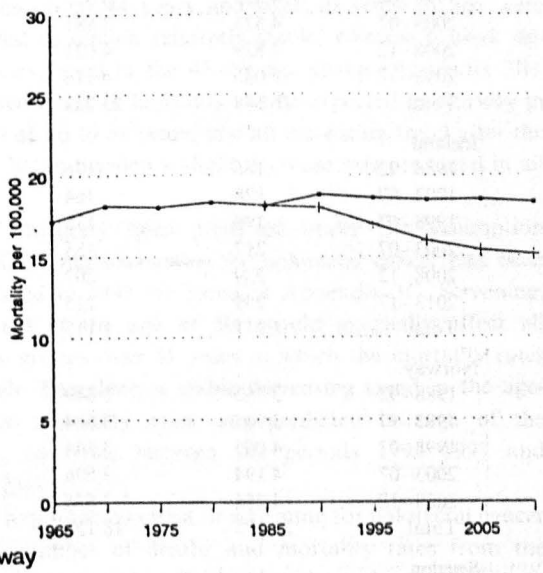

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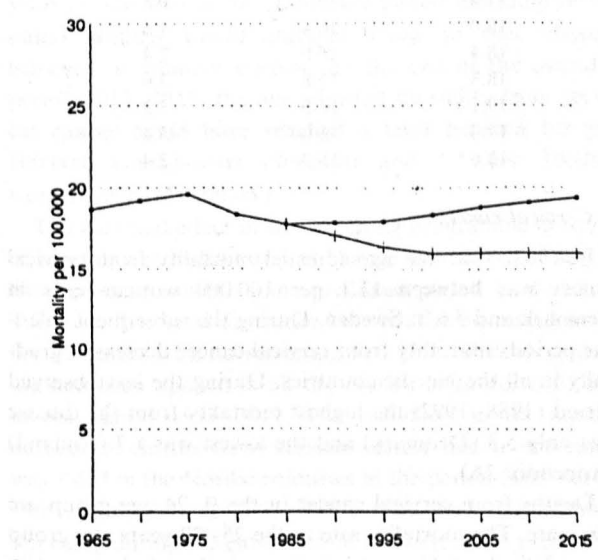


Sweden

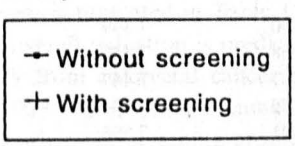


Fig. 7. Age-adjusted mortality rates for breast cancer with and without screening in the Nordic countries.

Table 13

Predicted effect of breast cancer screening on the number of deaths and age-adjusted ('world standard population') mortality rates

Period	Predicted number of deaths		Difference	Predicted mortality rates		Difference
	Without screening	With screening		Without screening	With screening	
Denmark						
1988–92	6 651	6 430	221	27.7	26.4	1.3
1993–97	6 947	6 457	490	27.6	25.0	2.6
1998–02	7 211	6 373	838	27.7	23.8	3.9
2003–07	7 453	6 307	1 146	27.8	23.2	4.6
2008–12	7 646	6 359	1 287	27.8	23.2	4.6
2013–17	7 826	6 395	1 431	27.7	22.9	4.8
Total	43 734	38 321	5 413	27.7	24.1	3.6
Finland						
1988–92	3 736	3 606	130	16.3	15.6	0.7
1993–97	4 071	3 778	293	16.6	15.2	1.4
1998–02	4 322	3 825	497	16.8	14.6	2.2
2003–07	4 575	3 881	694	17.0	14.4	2.6
2008–12	4 829	4 021	808	17.2	14.4	2.8
2013–17	5 045	4 116	929	17.4	14.5	2.9
Total	26 578	23 227	3 351	16.9	14.8	2.1
Iceland						
1988–92	186	176	10	23.1	22.0	1.1
1993–97	178	164	14	20.3	18.4	1.9
1998–02	198	175	23	20.3	17.6	2.8
2003–07	217	185	32	20.3	17.1	3.2
2008–12	239	202	37	20.3	17.0	3.3
2013–17	259	215	44	20.3	17.0	3.3
Total	1 277	1 117	160	20.8	18.2	2.6
Norway						
1988–92	3 755	3 649	106	18.8	18.0	0.8
1993–97	3 905	3 664	241	18.6	17.0	1.6
1998–02	4 065	3 644	421	18.5	16.0	2.6
2003–07	4 194	3 596	598	18.5	15.4	3.1
2008–12	4 256	3 575	681	18.3	15.1	3.2
Total	20 175	18 128	2 047	18.5	16.3	2.2
Sweden						
1988–92	7 590	7 349	241	17.9	17.1	0.8
1993–97	7 968	7 448	520	18.0	16.4	1.6
1998–02	8 347	7 447	900	18.4	16.0	2.4
2003–07	8 678	7 394	1 284	18.8	15.8	3.0
2008–12	9 001	7 508	1 493	19.1	15.9	3.2
2013–17	9 341	7 603	1 738	19.4	16.0	3.4
Total	50 925	44 749	6 176	18.6	16.2	2.4

screening for breast cancer is relatively low, the number of deaths which can be avoided is substantial and will increase due to the increasing population size in the oldest ages. A total of 16 439 deaths from breast cancer in the Nordic countries were estimated as avoidable in the period 1988–2017. The reduction in the annual number of deaths from breast cancer due to screening was 861 in the years 2008–2012 (when the screening programme was predicted to have its ultimate effect). The observed age-adjusted mortality from breast cancer and the predicted mortality rates with and without mass-screening are presented in Fig. 7.

Cervical cancer

In 1963–1967 the age-adjusted mortality from cervical cancer was between 11.1 per 100 000 woman-years in Denmark and 5.6 in Sweden. During the subsequent calendar periods mortality from cervical cancer decreased gradually in all the Nordic countries. During the last observed period (1988–1992) the highest mortality from the disease was only 5.3 (Denmark) and the lowest was 1.7 (Finland) (Appendix 2A).

Deaths from cervical cancer in the 0–24 age group are very rare. The mortality rate in the 25–29 years age group was relatively stable and low through the whole period in

all the countries with the exception of Denmark, where a decreasing trend was observed, from 4.2 in the period 1953–1957 to 1.0 in 1988–1992. In the 35–59 years age group the most substantial mortality reduction by calendar period was observed in Finland and Sweden. In the 60–74 years age group the reduction started later than in the 35–44 years age group, and there was no reduction observed in ages over 75. In Denmark and Norway no reduction was observed in women over 60 years. The age-specific mortality rates by birth cohorts have changed substantially during the period. For the oldest cohorts that have never been covered by an organized screening programme, mortality rates of a given cohort have increased with age. The risk of death from cervical cancer has been decreasing gradually by cohort and by age within a cohort in the populations completely covered by a screening programme.

The prediction of mortality rates in the absence of screening is shown in Appendix 2B. The cohorts which were youngest at the beginning of the period 1953–1967 in Denmark had a lower relative risk of dying from cervical cancer. A slightly decreasing trend in mortality rates was therefore incorporated in the predictions. The age-adjusted mortality would have increased annually in the first calendar periods and would have decreased by about 1.0–2.0 per 100 000 woman-years after that by the end of the period 2012–2017, if screening had not been established. A decreasing trend was predicted in the youngest age groups up to 50 years, a stable trend between 50 and 80 years and an increasing trend in the oldest ages in all the Nordic countries.

If the Finnish screening policy were applied throughout the rest of the Nordic countries, a total decreasing trend stronger than that observed could be expected (Appendix 2C). The age-specific mortality rates would have decreased substantially in each of the countries. A considerable reduction in mortality was also expected in women over 60 years of age, and at the end of the period mortality in the oldest women would stabilize close to that already achieved in younger women. By the end of the calendar period 2013–2017, the age-adjusted mortality from cervical cancer could have reached a level between 0.2 per 100 000 woman-years (Iceland) and 1.1 per 100 000 woman-years (Denmark).

The maximal effect of the screening programme in terms of mortality reduction and as change in number of deaths from cervical cancer in the predicted period is shown in Table 14. The total difference between the estimated number of deaths with no screening and if the Finnish screening had been applied in all the Nordic countries is 33 572 in the period 1993–2017. The reduction in the annual number of deaths from cervical cancer due to screening was 1 453 in the Nordic countries in the period 2008–2012. The overall pattern of mortality rates with and without screening during the entire period (observed and predicted) is shown in Fig. 8.

Colorectal cancer

Females

The age-adjusted mortality from colorectal cancer in females was highest in Denmark and lowest Finland during the observed period (Appendix 3A). In 1988–1992 the rates were between 17.1 per 100 000 woman-years in Denmark and 8.5 in Finland. In the 1980s a slightly decreasing trend was observed in all the Nordic countries. Mortality from colorectal cancer is strongly correlated with age: the disease was extremely rare in the youngest age groups up to 29 years and deaths from colorectal cancer are only occasional, and the rate is highest in the oldest ages. The risk of dying from colorectal cancer has been decreasing slightly by cohorts during the observed period.

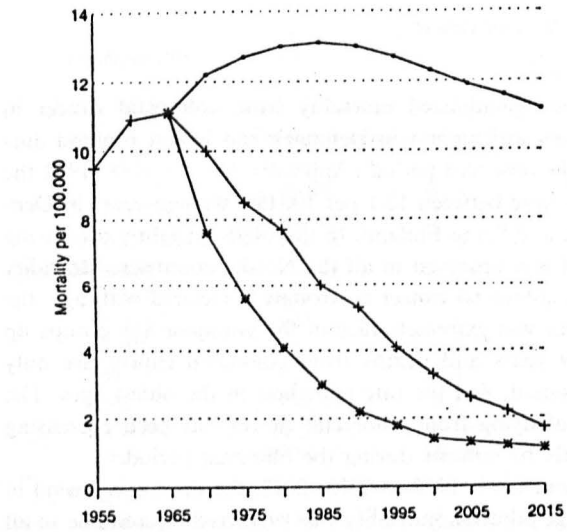
From 1993–1997 to 2013–2017, the decreasing trend in the age-adjusted mortality was predicted to continue in all the Nordic countries. In Denmark and Finland the mortality rates up to 44 years and over 70 years of age were predicted to remain relatively stable, whereas a weak decline is expected in the 45–69 age group (Appendix 3B). Some reduction in mortality can be expected in Norway in women of up to 54 years, and an increasing trend after the age of 70. In Sweden a slight decrease was predicted in all ages.

The mortality rates predicted under the assumption that FOBT mass-screening for colorectal cancer had been established in 1993 are listed in Appendix 3C. Screening, if started at the age of 50, would gradually affect all the age groups over 55 years in which the mortality rates are high. Therefore, a stable decreasing trend in the age-adjusted mortality rates was predicted in each of the Nordic countries between the periods 1993–1997 and 2012–2017.

The hypothetical effect of screening for colorectal cancer on the number of deaths and mortality rates from the disease is presented in Table 15 and graphically in Fig. 9. An overall reduction is predicted in the age-adjusted mortality from colorectal cancer in females between 2.7 per 100 000 woman-years, Denmark, and 1.3 per 100 000, Sweden, when the screening programme reaches full scope, in the period 2013–2017. A total of 10 376 deaths from the disease would be avoided during the whole predicted period in the Nordic countries.

Males

The age-adjusted mortality from colorectal cancer in males has been increasing during the observed period in all the Nordic countries with the exception of Sweden, where there has been a decreasing trend since the late 1970s (Appendix 4A). In the period 1988–1992 the highest mortality rate was observed in Denmark, 22.5 per 100 000 man-years, and the lowest rate was in Finland, 12.2. Mortality from colorectal cancer has been increasing with age, and the time trends were different in different age groups. In the 35 to 54 age groups, the mortality rates



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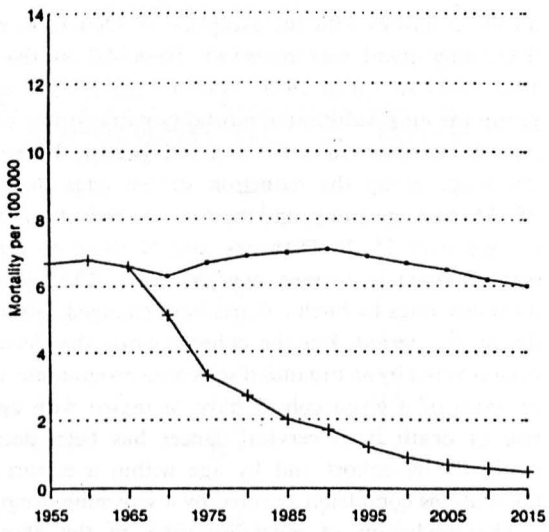
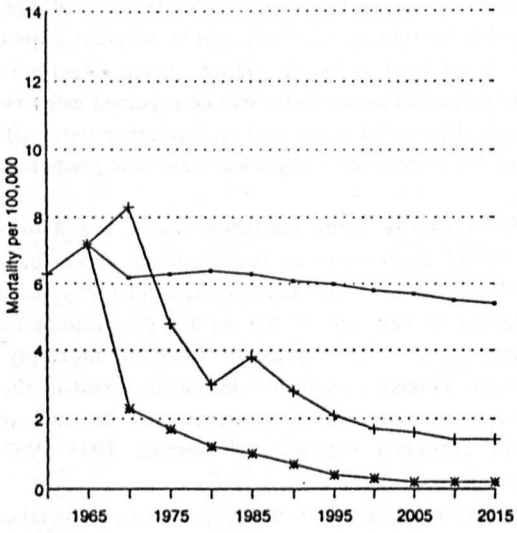


Finland



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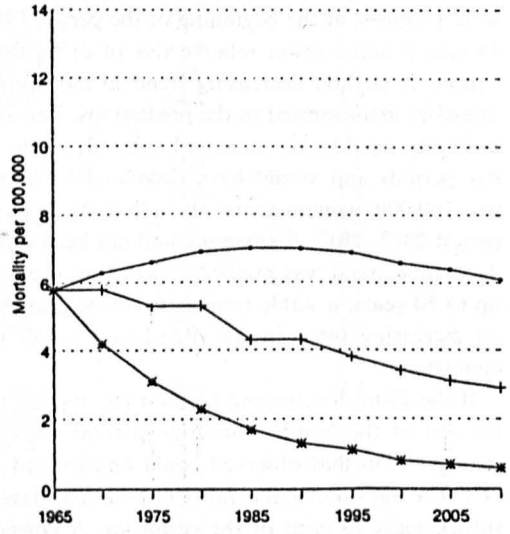

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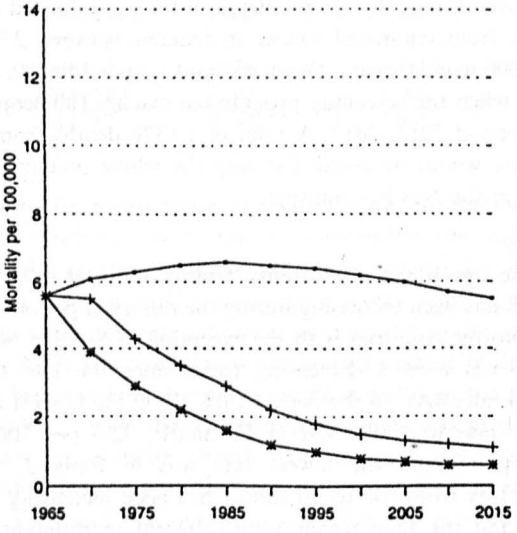


Sweden

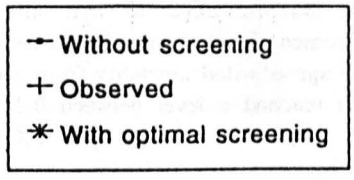


Fig. 8. Age-adjusted mortality rates for cervical cancer without screening, observed and with the optimal screening in the Nordic countries.

Table 14

Predicted effect of screening for cervical cancer on the number of deaths and age-adjusted ("world standard population") mortality rates

Period	Predicted number of deaths		Difference	Predicted mortality rates		Difference
	Without screening	With screening		Without screening	With screening	
Denmark						
1993–97	2 649	436	2 213	12.7	1.8	10.9
1998–02	2 678	345	2 333	12.3	1.4	10.9
2003–07	2 694	283	2 411	11.9	1.3	10.6
2008–12	2 704	237	2 467	11.6	1.2	10.4
2013–17	2 673	202	2 471	11.2	1.1	10.1
Total	13 398	1 503	11 895	11.9	1.4	10.5
Finland						
1993–97	1 444	335	1 109	6.9	1.2	5.7
1998–02	1 506	259	1 247	6.7	0.9	5.8
2003–07	1 548	196	1 352	6.5	0.7	5.8
2008–12	1 564	152	1 412	6.2	0.6	5.6
2013–17	1 555	122	1 433	6.0	0.5	5.5
Total	7 617	1 064	6 553	6.5	0.8	5.7
Iceland						
1993–97	55	5	50	6.0	0.4	5.6
1998–02	59	3	56	5.8	0.3	5.5
2003–07	64	2	62	5.7	0.2	5.5
2008–12	65	1	64	5.5	0.2	5.3
2013–17	69	1	68	5.4	0.2	5.2
Total	312	12	300	5.7	0.3	5.4
Norway						
1993–97	1 241	242	999	6.9	1.1	5.8
1998–02	1 274	186	1 088	6.6	0.8	5.8
2003–07	1 300	154	1 146	6.4	0.7	5.7
2008–12	1 306	122	1 146	6.1	0.6	5.5
Total	5 121	704	4 417	6.5	0.8	5.7
Sweden						
1993–97	2 374	509	1 865	6.4	1.0	5.4
1998–02	2 442	401	2 041	6.2	0.8	5.4
2003–07	2 470	331	2 139	6.0	0.7	5.3
2008–12	2 435	259	2 176	5.7	0.6	5.1
2013–17	2 386	200	2 186	5.5	0.6	4.9
Total	12 107	1 700	10 407	6.0	0.7	5.3

were relatively stable throughout the period, and found to have increased in the over 55 age groups in Denmark, Finland and Iceland. An increasing trend was also observed in men of over 50 years in Norway. In Sweden there was a slight decrease in mortality from colorectal cancer in men younger than 45, and a stable mortality in older ages.

In the future (1993–2017), a decrease in mortality from colorectal cancer in men was predicted in Denmark and Sweden, with no changes in the mortality rates in Finland and Iceland, while an increase from 21.8 per 100 000 man-years to 27.4 was predicted in Norway (Appendix 4B). In the last predicted period the highest mortality rate was expected in Norway, 27.4 per 100 000 man-years, and the lowest was in Iceland and Sweden, 11.7 and 11.8 respectively.

The predicted mortality rates from colorectal cancer in males, assuming that screening was started in 1993, are listed in Appendix 4C. The increase in the mortality rate in the oldest age group could be suspended and a slight reduction was predicted. When the ultimate effect of screening was reached the mortality was predicted to be between 22.9 (Norway) and 9.6 (Iceland).

In Table 16 and Fig. 10 the effect of a hypothetical screening for colorectal cancer in males is shown. The expected reduction in mortality rate would be between 4.5 per 100 000 man-years in Norway (2008–2012) and 2.0 in Sweden (2013–2017), when the results of the screening programme are ascertained. The number of deaths avoided would be proportionally larger than the reduction in mortality due to the ageing of the population. A total of 11 119 deaths from colorectal cancer in males could be

Table 15

Predicted effect of screening for colorectal cancer on the number of deaths and age-adjusted ('world standard population') mortality rates, females

Period	Predicted number of deaths		Difference	Predicted mortality rates		Difference
	Without screening	With screening		Without screening	With screening	
Denmark						
1993–97	5 661	5 661	–	17.0	17.0	–
1998–02	5 879	5 434	445	17.1	15.5	1.7
2003–07	5 962	5 206	756	17.0	14.7	2.4
2008–12	5 964	4 928	1 036	16.7	14.0	2.7
2013–17	6 097	5 038	1 059	16.5	13.8	2.7
Total	29 563	26 267	3 296	16.9	15.0	1.9
Finland						
1993–97	2 880	2 880	–	8.8	8.8	–
1998–02	3 019	2 793	226	8.7	7.9	0.8
2003–07	3 123	2 727	396	8.6	7.7	1.4
2008–12	3 254	2 686	568	8.4	7.0	1.4
2013–17	3 335	2 752	583	8.2	6.8	1.7
Total	15 611	13 838	1 773	8.5	7.5	1.0
Iceland						
1993–97	115	115	–	9.6	9.6	–
1998–02	124	113	11	9.6	8.6	1.0
2003–07	136	117	19	9.6	7.7	1.9
2008–12	148	122	26	9.6	7.5	2.1
2013–17	160	132	28	9.6	7.5	2.1
Total	683	599	84	9.6	8.2	1.4
Norway						
1993–97	3 877	3 877	–	14.0	14.0	–
1998–02	4 174	3 855	319	14.3	12.8	1.5
2003–07	4 397	3 850	547	14.2	12.1	2.1
2008–12	4 540	3 673	867	13.9	11.5	2.4
Total	16 988	15 255	1 733	14.1	12.6	1.5
Sweden						
1993–97	6 472	6 472	–	10.4	10.4	–
1998–02	6 557	6 071	486	10.0	9.0	1.0
2003–07	6 531	5 732	799	9.4	8.1	1.4
2008–12	6 388	5 270	1 118	8.7	7.3	1.5
2013–17	6 101	5 029	1 072	7.9	6.6	1.3
Total	32 049	28 573	3 476	9.3	8.3	1.0

prevented during the study period in the Nordic countries. The reduction in the annual number of deaths from colorectal cancer due to screening was 1 461 (723 in females and 738 in males) in the Nordic countries in the period 2008–2012, when the screening programme was predicted to reach its ultimate effect.

Summary

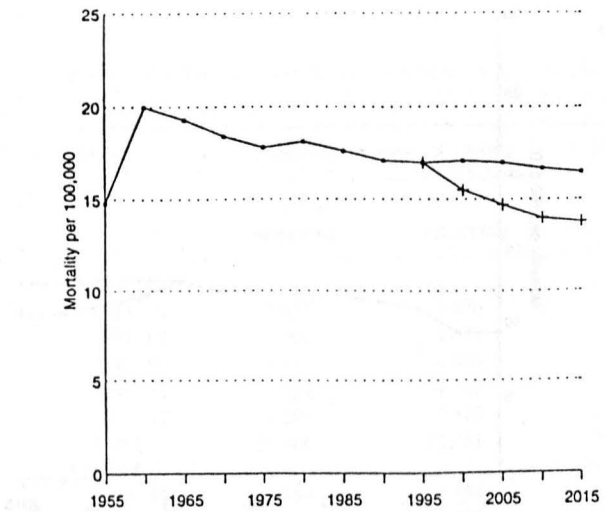
Without screening, a total of 348 581 deaths was predicted to occur in the Nordic countries in the period 1993–2017 from these three types of cancer – 121 000 from breast cancer, 38 555 from cervical cancer and 189 026 from colorectal cancer. This number would be 21% smaller (71 506 cancer deaths less) with screening as described in this study for cervical and breast cancer, and assumed for colorectal cancer.

In the period 2013–2017 the annual number of deaths will be 15 280 (5 345 from breast cancer, 1 598 from cervical cancer and 8 337 from colorectal cancer) assuming no screening had taken place (Table 17). If the full effect screening had been started in 1963–1967 for cervical cancer, in 1988 for breast cancer and in 1993 for colorectal cancer, the predicted number of deaths would be 11 370 (4 381 from breast cancer, 129 from cervical cancer and 6 860 from colorectal cancer), which is 26% less than assuming no screening. Those percentages are 18, 91 and 18 for breast, cervical and colorectal cancer screenings, respectively.

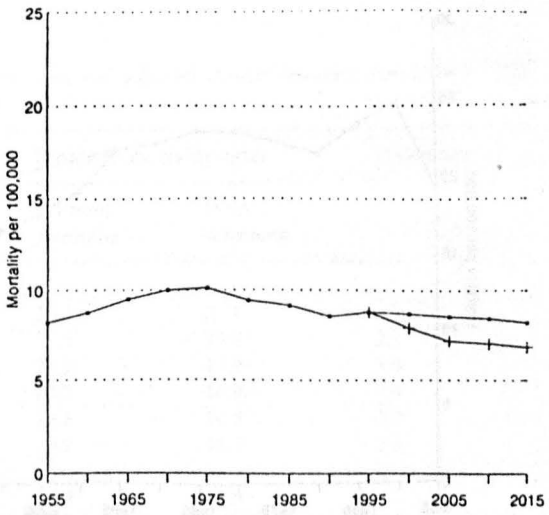
Costs

Breast cancer

The costs of the breast cancer screening programme are highly dependent on the population size and structure



Denmark



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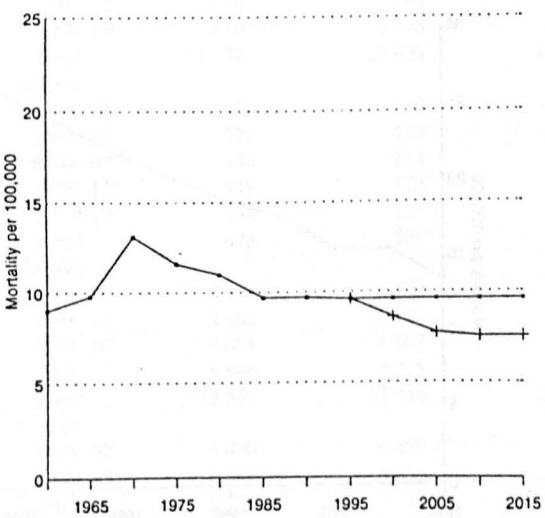

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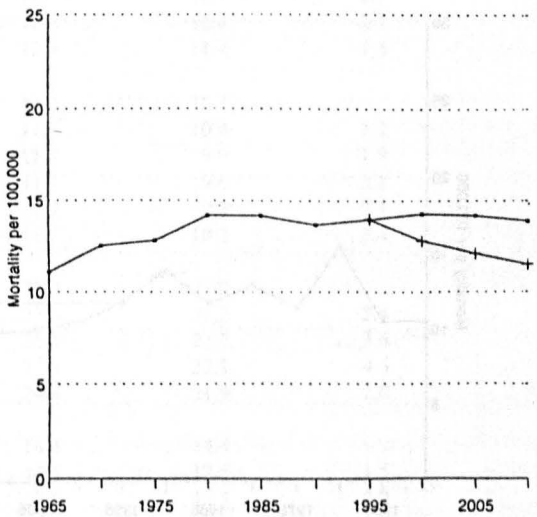
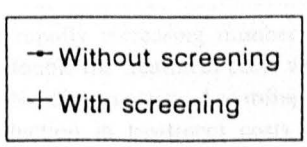
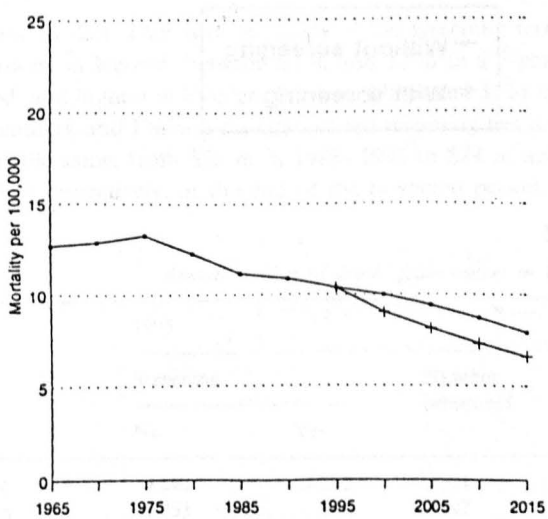


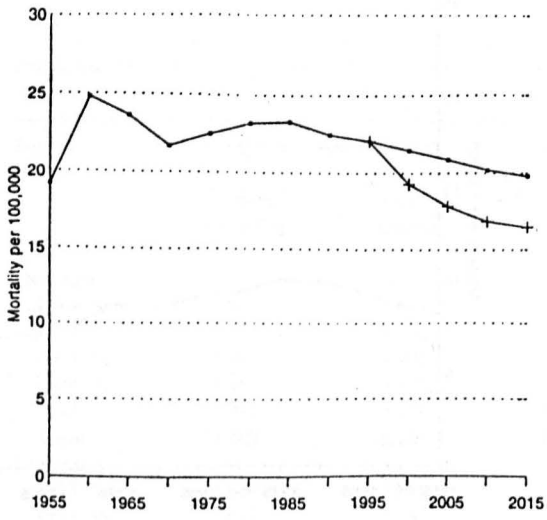
Norway



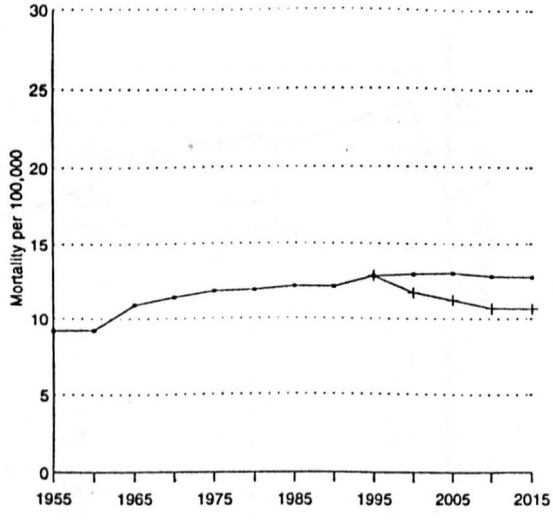


Sweden

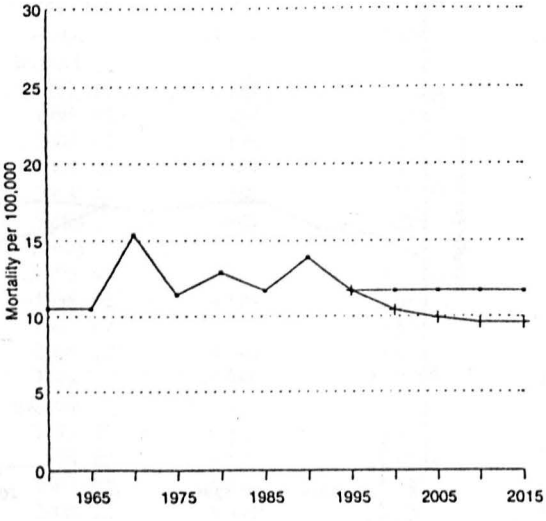
Fig. 9. Age-adjusted mortality rates for colorectal cancer with and without screening in the Nordic countries, males.



Denmark



Finland



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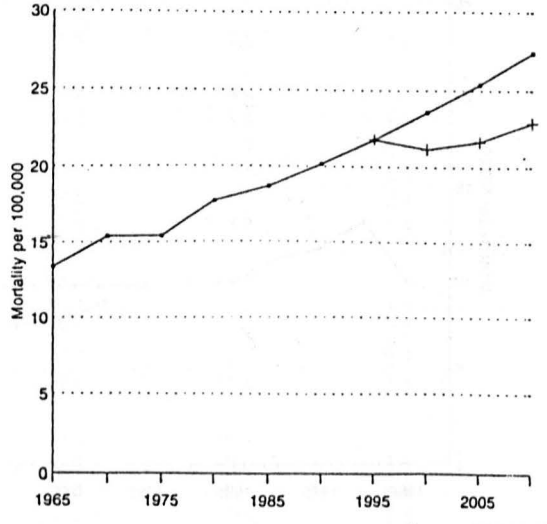

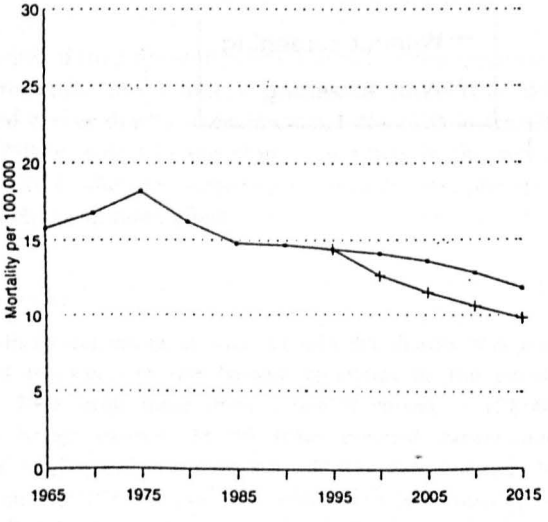

Sweden

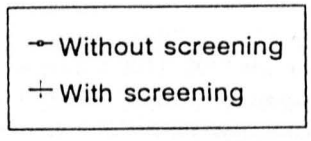

Fig. 10. Age-adjusted mortality rates for colorectal cancer with and without screening in the Nordic countries, females.

Table 16

Predicted effect of screening for colorectal cancer on the number of deaths and age-adjusted ('world standard population') mortality rates, males

Period	Predicted number of deaths		Difference	Predicted mortality rates		Difference
	Without screening	With screening		Without screening	With screening	
Denmark						
1993–97	5 070	5 070	–	22.1	22.1	–
1998–02	5 099	4 622	477	21.5	19.3	2.2
2003–07	5 147	4 406	741	20.9	17.9	3.0
2008–12	5 194	4 290	904	20.2	16.9	3.4
2013–17	5 296	4 373	923	19.8	16.5	3.3
Total	25 806	22 761	3 045	20.9	18.5	2.4
Finland						
1993–97	2 354	2 354	–	12.9	12.9	–
1998–02	2 634	2 383	251	13.0	11.8	1.2
2003–07	2 948	2 516	432	13.1	11.3	1.8
2008–12	3 267	2 689	578	12.9	10.7	2.2
2013–17	3 595	2 956	639	12.8	10.6	2.2
Total	14 798	12 898	1 900	12.9	11.4	1.5
Iceland						
1993–97	110	110	–	11.7	11.7	–
1998–02	121	110	11	11.7	10.4	1.2
2003–07	134	114	20	11.7	9.9	1.8
2008–12	149	122	27	11.7	9.6	2.1
2013–17	164	135	29	11.7	9.6	2.1
Total	678	591	87	11.7	10.2	1.4
Norway						
1993–97	4 174	4 174	–	21.8	21.8	–
1998–02	4 602	4 187	415	23.6	21.2	2.4
2003–07	5 075	4 367	708	25.4	21.7	3.6
2008–12	5 686	4 718	968	27.4	22.9	4.5
Total	19 537	17 446	2 091	24.5	21.9	2.6
Sweden						
1993–97	6 490	6 490	–	14.4	14.4	–
1998–02	6 647	6 045	602	14.1	12.6	1.5
2003–07	6 723	5 758	965	13.6	11.5	2.0
2008–12	6 744	5 528	1 216	12.8	10.6	2.2
2013–17	6 709	5 495	1 214	11.8	9.8	2.0
Total	33 313	29 317	3 996	13.4	11.8	1.6

(Tables 18–22). Therefore the costs of the screening tests are lowest in Iceland, between $2 m and $3 m in a 5-year period, and highest in Sweden, between $98 m and $124 m. In Denmark and Finland the costs of the screening test are about the same, from $58 m in 1988–1992 to $74 m and $77.5 m respectively, at the end of the predicted period.

The rapidly increasing number of new cases leads to about double the treatment costs without screening in each of the Nordic countries. According to the assumption that the reduction in treatment costs results solely from the change in the stage distribution in the screened group, treatment costs with screening were predicted to increase

Table 17

Annual number of deaths from cancer in 1993–1997 and 2013–2017 in the Nordic countries

Site	1995				2015			
	Screening		Number prevented	%	Screening		Number prevented	%
	No	Yes			No	Yes		
Breast	4 613	4 302	311	7	5 345	4 381	964	18
Cervix	1 553	306	1 247	80	1 598	129	1 469	91
Colorectum	7 441	7 441	0	0	8 337	6 860	1 477	18
Total	13 607	12 049	1 558	11	15 280	11 370	3 910	26

in proportion to the treatment costs without screening. The difference between the total treatment costs with and without screening is relatively small because screening affects a relatively small proportion of patients. The difference was predicted to increase slowly, depending on the number of new cases, by between $1 m and $2 m over the period in all the countries except Iceland, where the difference was between $50 000 and $73 000. This difference is the only compensation for the costs of the screening test. Therefore, the difference between the two alternatives remains much smaller than the total cost of the screening test, and the cost of the screening programme is about the same as the cost of the screening test.

Cervical cancer

Although the number of new cases of invasive cervical cancer with screening was predicted to decrease in the last predicted 5-year period (Appendix 5), the predicted number of new cases without screening would have increased in all the Nordic countries. In the period after the starting of the screening programme, a number of cases which would have surfaced later as clinical diseases were diagnosed by the PAP test. Thus, an increase in the number of new cases was estimated. In the period 1963–1967, when the first screening measures were initiated, the number of new invasive cervical cancers was higher than in the previous and subsequent periods.

Table 18

Estimated cost difference between situation without screening for breast cancer and with mammographic screening of women aged 50–69 years every second year, Denmark

Period	Woman–years (50–69)	Cost of screening and confirmation	No. of new cases without screening	Cost of treatment without screening	No. of new cases with screening	Cost of treatment with screening	Difference between costs with and without screening
1988–92	2 656 000	58 439 000	6 666	79 992 000	7 333	78 605 000	57 053 000
1993–97	2 794 000	61 479 000	6 986	83 832 000	7 685	82 379 000	60 026 000
1998–02	3 055 000	67 215 000	8 247	98 964 000	9 072	97 249 000	65 499 000
2003–07	3 244 000	71 371 000	9 447	113 364 000	10 392	111 399 000	69 406 000
2008–12	3 380 000	74 359 000	10 220	122 640 000	11 242	120 514 000	72 233 000

Table 19

Estimated cost difference between situation without screening for breast cancer and with mammographic screening of women aged 50–69 years every second year, Finland

Period	Woman–years (50–69)	Cost of screening and confirmation	No. of new cases without screening	Cost of treatment without screening	No. of new cases with screening	Cost of treatment with screening	Difference between costs with and without screening
1988–92	2 681 000	58 991 000	5 170	62 040 000	5 687	60 965 000	57 915 000
1993–97	2 745 000	60 381 000	6 037	72 444 000	6 641	71 188 000	59 125 000
1998–02	3 020 000	66 440 000	7 165	85 980 000	7 882	84 490 000	64 950 000
2003–07	3 314 000	72 899 000	8 081	96 972 000	8 889	95 291 000	71 218 000
2008–12	3 526 000	77 572 000	8 873	106 476 000	9 760	104 630 000	75 726 000

Table 20

Estimated cost difference between situation without screening for breast cancer and with mammographic screening of women aged 50–69 years every second year, Iceland

Year	Woman–years (50–69)	Cost of screening and confirmation	No. of new cases without screening	Cost of treatment without screening	No. of new cases with screening	Cost of treatment with screening	Difference between costs with and without screening
1988–92	101 000	2 219 000	224	2 688 000	246	2 641 000	2 172 000
1993–97	107 000	2 356 000	240	2 880 000	264	2 830 000	2 306 000
1998–02	119 000	2 614 000	261	3 132 000	287	3 078 000	2 560 000
2003–07	136 000	2 989 000	299	3 588 000	329	3 526 000	2 927 000
2008–12	158 000	3 485 000	351	4 212 000	386	4 139 000	3 412 000

Table 21

Estimated cost difference between situation without screening for breast cancer and with mammographic screening of women aged 50–69 years every second year, Norway

Period	Woman–years (50–69)	Cost of screening and confirmation	No. of new cases without screening	Cost of treatment without screening	No. of new cases with screening	Cost of treatment with screening	Difference between costs with and without screening
1988–92	2 033 000	44 728 000	3 393	40 716 000	3 732	40 010 000	44 022 000
1993–97	2 032 000	44 714 000	3 516	42 192 000	3 868	41 461 000	43 982 000
1998–02	2 229 000	49 028 000	3 834	46 008 000	4 217	45 211 000	48 231 000
2003–07	2 462 000	54 166 000	4 311	51 732 000	4 742	50 835 000	53 269 000
2008–12	2 701 000	59 429 000	4 753	57 036 000	5 228	56 047 000	58 440 000

Table 22

Estimated cost difference between situation without screening for breast cancer and with mammographic screening of women aged 50–69 years every second year, Sweden

Period	Woman–years (50–69)	Cost of screening and confirmation	No. of new cases without screening	Cost of treatment without screening	No. of new cases with screening	Cost of treatment with screening	Difference between costs with and without screening
1988–92	4 499 000	98 983 000	10 954	131 448 000	12 049	129 170 000	96 705 000
1993–97	4 661 000	102 547 000	9 317	111 804 000	10 249	109 866 000	100 609 000
1998–02	5 092 000	112 029 000	10 377	124 524 000	11 415	122 366 000	109 870 000
2003–07	5 431 000	119 488 000	11 398	136 776 000	12 538	134 405 000	117 117 000
2008–12	5 661 000	124 553 000	12 384	148 608 000	13 622	146 032 000	121 977 000

The cost estimate of the screening programme for cervical cancer in the Nordic countries is presented in Tables 23–27 and in Appendix 5. The costs of treatment of ICC were calculated for both alternatives, i.e., with and without screening (Appendix 5), according to the number of new cases and the stage distribution of incident cases shown in Table 11. The number of new ICCs without screening would have increased until the early 1990s and stabilized after that in all the Nordic countries with the exception of Iceland, where a decrease was predicted and where it would continue until the end of the period 2013–2017 (Appendix 5). The total cost without screening is equal to the treatment cost of all cases that would have progressed to the invasive stage in the absence of screening. This would have increased in the period 1968–1997 and would remain stable in the next predicted 5-year periods.

Table 23

Estimated cost difference between situation without screening for cervical cancer and with screening of women aged 25–59 years every fifth year, Denmark

Period	Woman–years (25–59)	Cost of screening	Total cost without screening	Total cost with screening	Difference between cost with and without screening
1963–67	5 180 000	10 360 000	95 161 000	126 315 000	31 154 000
1968–72	5 320 000	10 639 000	97 728 000	110 601 000	12 873 000
1973–77	5 534 000	11 068 000	101 668 000	86 361 000	−15 307 000
1978–82	5 675 000	11 350 000	104 258 000	77 718 000	−26 540 000
1983–87	5 797 000	11 593 000	106 493 000	74 272 000	−32 221 000
1988–92	6 051 000	12 102 000	111 168 000	74 864 000	−36 303 000
1993–97	6 324 000	12 647 000	116 174 000	76 377 000	−39 797 000
1998–02	6 474 000	12 948 000	118 939 000	78 195 000	−40 744 000
2003–07	6 361 000	12 723 000	116 867 000	76 833 000	−40 034 000
2008–12	6 074 000	12 147 000	111 580 000	73 357 000	−38 223 000

Table 24

Estimated cost difference between situation without screening for cervical cancer and with screening of women aged 25–59 years every fifth year, Finland

Period	Woman–years (25–59)	Cost of screening	Total cost without screening	Total cost with screening	Difference between cost with and without screening
1963–67	5 032 000	10 065 000	37 931 000	56 259 000	18 327 000
1968–72	5 060 000	10 119 000	38 138 000	49 063 000	10 925 000
1973–77	5 373 000	10 745 000	40 497 000	40 734 000	237 000
1978–82	5 655 000	11 310 000	42 625 000	38 290 000	−4 334 000
1983–87	5 867 000	11 735 000	44 226 000	37 609 000	−6 617 000
1988–92	6 041 000	12 083 000	45 537 000	37 753 000	−7 785 000
1993–97	6 212 000	12 424 000	46 825 000	38 036 000	−8 789 000
1998–02	6 184 000	12 368 000	46 612 000	37 787 000	−8 825 000
2003–07	6 210 000	12 421 000	46 812 000	37 895 000	−8 917 000
2008–12	5 974 000	11 947 000	45 028 000	36 616 000	−8 412 000

Table 25

Estimated cost difference between situation without screening for cervical cancer and with screening of women aged 25–59 years every fifth year, Iceland

Period	Woman–years (25–59)	Cost of screening	Total cost without screening	Total cost with screening	Difference between cost with and without screening
1963–67	175 000	351 000	1 367 000	2 017 000	650 000
1968–72	186 000	372 000	1 452 000	1 858 000	406 000
1973–77	203 000	405 000	1 580 000	1 576 000	−4 500
1978–82	223 000	445 000	1 735 000	1 549 000	−185 000
1983–87	248 000	496 000	1 931 000	1 632 000	−299 000
1988–92	275 000	549 000	2 142 000	1 759 000	−383 000
1993–97	297 000	595 000	2 318 000	1 866 000	−452 000
1998–02	321 000	642 000	2 504 000	2 016 000	−488 000
2003–07	339 000	678 000	2 644 000	2 129 000	−515 000
2008–12	350 000	701 000	2 731 000	2 199 000	−532 000

Table 26

Estimated cost difference between situation without screening for cervical cancer and with screening of women aged 25–59 years every fifth year, Norway

Period	Woman–years (25–59)	Cost of screening	Total cost without screening	Total cost with screening	Difference between cost with and without screening
1963–67	3 964 000	7 928 000	34 929 000	50 490 000	15 560 000
1968–72	3 998 000	7 997 000	35 234 000	44 036 000	8 802 000
1973–77	4 140 000	8 279 000	36 478 000	35 294 000	−1 184 000
1978–82	4 255 000	8 509 000	37 492 000	32 376 000	−5 116 000
1983–87	4 398 000	8 795 000	38 752 000	31 604 000	−7 148 000
1988–92	4 648 000	9 296 000	40 957 000	32 419 000	−8 538 000
1993–97	4 978 000	9 956 000	43 865 000	34 019 000	−9 846 000
1998–02	5 250 000	10 499 000	46 259 000	35 875 000	−10 383 000
2003–07	5 309 000	10 618 000	46 782 000	36 281 000	−10 501 000
2008–12	5 234 000	10 467 000	46 119 000	35 767 000	−10 352 000

Table 27

Estimated cost difference between situation without screening for cervical cancer and with screening of women aged 25–59 years every fifth year, Sweden

Period	Woman–years (25–59)	Cost of screening	Total cost without screening	Total cost with screening	Difference between cost with and without screening
1963–67	8 646 000	17 292 000	91 746 000	129 086 000	37 339 000
1968–72	8 820 000	17 639 000	93 592 000	113 371 000	19 779 000
1973–77	9 068 000	18 136 000	96 226 000	89 398 000	−6 828 000
1978–82	9 198 000	18 396 000	97 606 000	80 529 000	−17 077 000
1983–87	9 243 000	18 486 000	98 083 000	76 215 000	−21 868 000
1988–92	9 582 000	19 165 000	101 686 000	76 574 000	−25 112 000
1993–97	10 035 000	20 069 000	106 484 000	78 483 000	−28 001 000
1998–02	10 318 000	20 636 000	109 492 000	80 700 000	−28 792 000
2003–07	10 189 000	20 379 000	108 128 000	79 695 000	−28 433 000
2008–12	9 897 000	19 794 000	105 022 000	77 406 000	−27 616 000

In Denmark and Finland the total cost of screening tests was estimated to be between $10 m in the period 1968–1972 and $12 m in the period 1988–1992, and the cost was predicted to remain unchanged by the end of the studied period, 2008–2012. In Iceland the cost of screening test increased from $400 000 to $700 000 in the same period, and from $8 m to $10 m in Norway. Screening tests in Sweden were the most expensive, $18 m to $20 m over the period. The treatment of carcinoma in situ, including excess diagnostic work-up and overtreatment of preinvasive lesions, was the most expensive component of the screening policy, according to the set of assumptions applied in this study. Treatment costs of invasive cervical cancer decreased during the screening period in all the Nordic countries. According to the prediction, costs remained constant in Denmark, Finland, Norway and Sweden in the period 1993–2012. The total cost of the screening programmes was predicted to be lower than the treatment costs of invasive disease without screening. The total cost of the screening programmes, including the test costs and the treatment costs of CIN and invasive cancers, was estimated to decrease in the period. Screening for cervical cancer is expensive during the first years, but when the full intensity of the programme is reached and the number of new invasive cancers is substantially reduced it could be considered as cost-saving in each of the Nordic countries. The savings amounted to $38.2 m, $8.4 m, $0.5 m, $10.3 m and $27.6 m in the period 2008–2012, in Denmark, Finland, Iceland, Norway and Sweden, respectively.

Colorectal cancer

The cost estimates for colorectal cancer screening are listed in Tables 28–32. According to the Nordic incidence predictions for 1988–2012, the number of new cases of colorectal cancer in the 50–74 years age group will increase in both sexes (1). Males are more often affected by the disease, and although the female population is somewhat bigger in this age group in all the Nordic countries, more new cases occur among males. The total

Table 28

Estimated cost difference between situation without screening for colorectal cancer and with screening of population aged 50–74 years every year, Denmark

Period	Woman–years (50–69)	Cost of screening and confirmation	No. of new cases without screening	Cost of treatment without screening	No. of new cases with screening	Cost of treatment with screening	Difference between costs with and without screening
Females							
1993–97	3 373 000	20 239 000	3 948	81 171 000	4 738	91 341 000	30 409 000
1998–02	3 592 000	21 549 000	4 023	82 713 000	4 828	93 076 000	31 913 000
2003–07	3 764 000	22 581 000	4 183	86 002 000	5 020	96 778 000	33 357 000
2008–12	3 936 000	23 616 000	4 401	90 485 000	5 281	101 822 000	34 953 000
Males							
1993–97	3 138 000	18 829 000	4 730	97 249 000	5 676	109 433 000	31 013 000
1998–02	3 407 000	20 442 000	4 798	98 647 000	5 758	111 007 000	32 802 000
2003–07	3 594 000	21 566 000	4 929	101 340 000	5 915	114 037 000	34 263 000
2008–12	3 761 000	22 567 000	5 215	107 220 000	6 258	120 654 000	36 001 000

Table 29

Estimated cost difference between situation without screening for colorectal cancer and with screening of population aged 50–74 years every year, Finland

Period	Woman–years (50–69)	Cost of screening and confirmation	No. of new cases without screening	Cost of treatment without screening	No. of new cases with screening	Cost of treatment with screening	Difference between costs with and without screening
Females							
1993–97	3 326 000	19 957 000	2 415	49 652 000	2 898	55 873 000	26 178 000
1998–02	3 612 000	21 675 000	2 473	50 845 000	2 968	57 215 000	28 045 000
2003–07	3 877 000	23 260 000	2 599	53 435 000	3 119	60 130 000	29 955 000
2008–12	4 109 000	24 655 000	2 840	58 390 000	3 408	65 706 000	31 971 000
Males							
1993–97	2 867 000	17 203 000	2 725	56 026 000	3 270	63 046 000	24 222 000
1998–02	3 279 000	19 672 000	2 958	60 816 000	3 550	68 436 000	27 292 000
2003–07	3 608 000	21 648 000	3 172	65 216 000	3 806	73 387 000	29 819 000
2008–12	3 855 000	23 130 000	3 368	69 246 000	4 042	77 922 000	31 806 000

Table 30

Estimated cost difference between situation without screening for colorectal cancer and with screening of population aged 50–74 years every year, Iceland

Period	Woman–years (50–69)	Cost of screening and confirmation	No. of new cases without screening	Cost of treatment without screening	No. of new cases with screening	Cost of treatment with screening	Difference between costs with and without screening
Females							
1993–97	128 000	767 000	104	2 138 000	125	2 406 000	1 035 000
1998–02	141 000	847 000	109	2 241 000	131	2 522 000	1 127 000
2003–07	159 000	951 000	119	2 447 000	143	2 753 000	1 258 000
2008–12	180 000	1 081 000	135	2 776 000	162	3 123 000	1 429 000
Males							
1993–97	123 000	739 000	129	2 652 000	155	2 985 000	1 072 000
1998–02	139 000	831 000	125	2 570 000	150	2 892 000	1 153 000
2003–07	157 000	944 000	139	2 858 000	167	3 216 000	1 302 000
2008–12	180 000	1 078 000	160	3 290 000	192	3 702 000	1 490 000

Table 31

Estimated cost difference between situation without screening for colorectal cancer and with screening of population aged 50–74 years every year, Norway

Period	Woman–years (50–69)	Cost of screening and confirmation	No. of new cases without screening	Cost of treatment without screening	No. of new cases with screening	Cost of treatment with screening	Difference between costs with and without screening
Females							
1993–97	2 547 000	15 282 000	3 451	70 953 000	4 141	79 842 000	24 171 000
1998–02	2 678 000	16 070 000	3 414	70 192 000	4 097	78 986 000	24 865 000
2003–07	2 868 000	17 207 000	3 578	73 564 000	4 294	82 781 000	26 424 000
2008–12	3 118 000	18 700 000	3 909	80 369 000	4 691	90 439 000	28 775 000
Males							
1993–97	2 368 000	14 210 000	4 301	88 429 000	5 161	99 508 000	25 289 000
1998–02	2 554 000	15 323 000	4 309	88 593 000	5 171	99 693 000	26 423 000
2003–07	2 769 000	16 612 000	4 581	94 185 000	5 497	105 986 000	28 413 000
2008–12	3 022 000	18 132 000	4 968	102 142 000	5 962	114 940 000	30 930 000

Table 32

Estimated cost difference between situation without screening for colorectal cancer and with screening of population aged 50–74 years every year, Sweden

Period	Woman–years (50–69)	Cost of screening and confirmation	No. of new cases without screening	Cost of treatment without screening	No. of new cases with screening	Cost of treatment with screening	Difference between costs with and without screening
Females							
1993–97	5 755 000	34 531 000	5 719	117 583 000	6 863	132 315 000	49 263 000
1998–02	6 082 000	36 494 000	5 724	117 685 000	6 869	132 430 000	51 239 000
2003–07	3 363 000	38 175 000	5 966	122 661 000	7 159	138 029 000	53 543 000
2008–12	6 653 000	39 917 000	6 378	131 132 000	7 654	147 561 000	56 347 000
Males							
1993–97	5 440 000	32 637 000	6 370	130 967 000	7 644	147 376 000	49 046 000
1998–02	5 846 000	35 074 000	6 204	127 554 000	7 445	143 536 000	51 055 000
2003–07	6 169 000	37 014 000	6 304	129 610 000	7 565	145 849 000	53 253 000
2008–12	6 464 000	38 785 000	6 677	137 279 000	8 012	154 479 000	55 985 000

cost of the screening tests and confirmation of the diagnoses is expected to be higher for females than for males over the predicted period. The treatment costs per patient were assumed to be equal for men and women, and the total treatment cost without screening depended on the predicted numbers of new cases and on the stage distribution of the cancers. Thus the highest treatment costs were predicted for Sweden, between $280 m and $302 m, about twice those in Finland, while the lowest cost was predicted for Iceland. The costs of treatment without screening were estimated to increase in both sexes in each of the Nordic countries. Owing to the smaller number of predicted new cases in females and, thus, lower treatment costs, the overall screening programmes were estimated to be less expensive in males than in females. The cost difference between the two alternatives (with and without screening) was more favourable in men compared with that in women (Tables 28–32). The total cost of the colorectal cancer screening programme was predicted to be $71 m in Denmark, $64 m in Finland, $2.9 m in Iceland, $60 m in Norway, and $112 m in Sweden in 2008–2012.

Table 33

Summary of estimated cost in millions of dollars. Screening compared with no screening in 1995 and 2010 by primary site. All Nordic countries combined

Year, Primary site	Screening		
	No	Yes	Difference
Year 1995			
Breast	62.6	109.3	46.7
Cervix	63.1	45.8	−17.3
Colorectum, females	64.3	72.3	8.0
Colorectum, males	75.1	84.5	9.4
Total	265.1	311.9	46.8
Year 2010			
Breast	87.8	154.1	66.2
Cervix	62.1	45.1	−17.0
Colorectum, females	72.6	103.3	30.7
Colorectum, males	83.8	115.0	31.2
Total	306.3	417.5	111.2

Summary

The cost estimates in 1995 and 2010 are presented in Table 33 for the Nordic countries combined. Cost of screening for colorectal cancer would be the most expensive, $157 m in 1995. The difference between cost with screening and cost without screening was the greatest for breast cancer, $47 m, however. After full maturation of the programmes, as estimated for the year 2010, the relative position of colorectal screening becomes less favourable: the difference in cost between screening and no screening is the same, more than $60 m, for both breast and colorectal cancer. Colorectal cancer screening will cover both sexes, however. Screening for cervical cancer is cost-saving, about 17 m a year and the savings are stable over time. In the year 2010 screening for these three primary sites is assumed to be $111 m more than would be the resources without screening in the Nordic countries combined.

Quality of life

In Table 34, we find the overall number of deaths avoided and life years gained (LYG) due to breast cancer screening in the Nordic countries. In 1993–1997, a total of 233 life years, out of 7 790 years gained, can be considered as 'lost' after adjustment for quality of life related to the screening programme. In all, 1 200 of the LYGs will be lived in moderate or severe dementia, independent of cancer. In the last column of Table 34, 'LYG with good quality' (GQLYG), dementia-free life years gained (DFLYG) out of QALYG are presented. The total number of GQLYG will rise from 6 424 in 1993–1997 to 17 752 in 2008–2012. According to the scheme for calculating QALYG, DFLYG and GQLYG increase in propor-

Table 34

Total life years gained due to screening for breast cancer, life years gained (LYG) discounted for quality of life (QALYG) and life years free of dementia in the Nordic countries

Country	Period	Deaths avoided	Life years gained	QALYG	Dementia-free LYG	LYG with good quality
Denmark	1993–97	490	2 450	2 377	2 083	2 020
	1998–02	838	4 190	4 064	3 562	3 455
	2003–07	1 146	5 730	5 558	4 871	4 724
	2008–12	1 287	6 435	6 242	5 470	5 306
Finland	1993–97	293	1 465	1 421	1 245	1 208
	1998–02	497	2 485	2 410	2 112	2 049
	2003–07	694	3 470	3 366	2 950	2 861
	2008–12	808	4 040	3 919	3 434	3 331
Iceland	1993–97	14	70	68	60	58
	1998–02	23	115	112	98	95
	2003–07	32	160	155	136	132
	2008–12	37	185	179	157	153
Norway	1993–97	241	1 205	1 169	1 024	994
	1998–02	421	2 105	2 042	1 789	1 736
	2003–07	598	2 990	2 900	2 542	2 465
	2008–12	681	3 405	3 303	2 894	2 807
Sweden	1993–97	520	2 600	2 522	2 210	2 144
	1998–02	900	4 500	4 365	3 825	3 710
	2003–07	1 284	6 420	6 227	5 457	5 293
	2008–12	1 493	7 465	7 241	6 345	6 155

tion to an increasing number of deaths that would have occurred during the period but were avoided due to the screening programme.

The results of cervical cancer screening in terms of life years gained are shown in Table 35. The predicted number of deaths from cervical cancer avoided due to the screening programme are predicted to increase slightly during the period 1993–2012 in all the Nordic countries. A total of 43 652 person-years of life would have been 'gained' due to deaths avoided in the period 1993–1997 because of cervi-

Table 35

Total life years gained due to screening for cervical cancer, life years gained (LYG) discounted for quality of life (QALYG) and life years free of dementia in the Nordic countries

Country	Period	Deaths avoided	Life years gained	QALYG	Dementia-free LYG	LYG with good quality
Denmark	1993–97	2 213	15 491	15 026	13 167	12 772
	1998–02	2 333	16 331	15 841	13 881	13 465
	2003–07	2 411	16 877	16 371	14 345	13 915
	2008–12	2 467	17 269	16 751	14 679	14 238
Finland	1993–97	1 109	7 763	7 530	6 599	6 401
	1998–02	1 247	8 729	8 467	7 420	7 197
	2003–07	1 352	9 464	9 180	8 044	7 803
	2008–12	1 412	9 884	9 587	8 401	8 149
Iceland	1993–97	50	350	350	298	289
	1998–02	56	392	380	333	323
	2003–07	62	434	421	369	358
	2008–12	64	448	435	381	369
Norway	1993–97	999	6 993	6 783	5 944	5 766
	1998–02	1 088	7 616	7 388	6 474	6 279
	2003–07	1 146	8 022	7 781	6 819	6 614
	2008–12	1 146	8 022	7 781	6 819	6 614
Sweden	1993–97	1 865	13 055	12 663	11 097	10 764
	1998–02	2 041	14 287	13 858	12 144	11 780
	2003–07	2 139	14 973	14 524	12 727	12 345
	2008–12	2 176	15 232	14 775	12 947	12 559

Table 36

Total life years gained due to screeing for colorectal cancer, life years gained (LYG) discounted for quality of life (QALYG) and life years free of dementia in the Nordic countries, females

Country	Period	Deaths avoided	Life years gained	QALYG	Dementia-free LYG	LYG with good quality
Denmark	1998–02	445	3 560	3 382	3 026	2 875
	2003–07	756	6 048	5 746	5 141	4 884
	2008–12	1 036	8 288	7 874	7 045	6 693
Finland	1998–02	226	1 808	1 718	1 537	1 460
	2003–07	396	3 168	3 010	2 693	2 558
	2008–12	568	4 544	4 317	3 862	3 669
Iceland	1998–02	11	88	84	75	71
	2003–07	19	152	144	129	123
	2008–12	26	208	198	177	168
Norway	1998–02	319	2 552	2 424	2 169	2 061
	2003–07	547	4 376	4 157	3 720	3 534
	2008–12	867	6 936	6 589	5 896	5 601
Sweden	1998–02	486	3 888	3 694	3 305	3 140
	2003–07	799	6 392	6 072	5 433	5 162
	2008–12	1 118	8 944	8 497	7 602	7 222

cal cancer screening, and this number would increase to 50 855 in the period 2008–2012. Although the target age group for cervical cancer screening (30–59 years) is much younger than that for breast cancer, the LYG occur at the same age, and the same effect of ageing was considered. After adjustment for quality of life due to screening and discounting for dementia-free life years, the total number of person-years with good quality of life that would be gained would increase from 36 039 in the period 1993–1997 to 42 795 in 2008–2012.

Tables 36 and 37 show the life years gained due to avoidance of colorectal cancer by sex. During the first five years of the screening programmes, 1993–1997, no reduction in the number of deaths from the disease was assumed, and according to the scheme applied, no change in the quality of life was predicted either. In the next three 5-year periods the total number of life years gained would increase gradually in both sexes from 11 896 to 28 920 in females and from 12 292 to 25 851 in males. Although the predicted number of LYG at the end of the period was

Table 37

Total life years gained (LYG) due to screeing for colorectal cancer and life years gained discounted for quality of life (QALYG) and life years free of dementia in the Nordic countries, males

Country	Period	Deaths avoided	Life years gained	QALYG	Dementia-free LYG	LYG with good quality
Denmark	1998–02	477	3 339	3 172	3 105	2 696
	2003–07	741	5 187	4 928	4 824	4 189
	2008–12	904	6 328	6 012	5 885	5 110
Finland	1998–02	251	1 757	1 669	1 634	1 419
	2003–07	432	3 024	2 873	2 812	2 442
	2008–12	578	4 046	3 844	3 763	3 267
Iceland	1998–02	11	77	73	72	62
	2003–07	20	140	133	130	113
	2008–12	27	189	180	176	153
Norway	1998–02	415	2 905	2 760	2 702	2 346
	2003–07	708	4 956	4 708	4 609	4 002
	2008–12	968	6 776	6 437	6 302	5 472
Sweden	1998–02	602	4 214	4 003	3 919	3 403
	2003–07	965	6 755	6 417	6 282	5 455
	2008–12	1 216	8 512	8 086	7 916	6 873

Table 38

Summary of estimated life years gained in 2010 due to screening by primary site. All Nordic countries combined

Life years gained	Breast	Cervix	Colorectum		Total
			Females	Males	
Deaths avoided	861	1 453	723	739	3 776
LYG	4 306	10 171	5 784	5 170	25 431
QALYG	4 176	10 069	5 495	4 912	24 652
DFLYG	3 659	8 645	4 916	4 808	22 028
GQLYG	3 549	8 559	4 670	4 175	20 953

somewhat higher in females than in males, the difference was partly compensated when dementia-free life years gained were calculated. This was due to the fact that men spend a smaller proportion of their remaining life over the age of 75 in dementia than women. Finally, 23 353 and 20 875 life years gained with good quality were estimated, respectively, in women and men in the period 2008–2012 if a screening programme for colorectal cancer had been established in 1993 in all the Nordic countries (Tables 36 and 37).

Table 38 summarizes the life years gained for all the Nordic countries in 2010. The LYGs varied from 4300 for breast cancer to 10 200 for cervical cancer. The total number of LYG was 25 400 which decreased to 21 000 GQLYG after adjusting for quality of life and dementia.

Cost-utility analysis

Breast cancer

As the breast cancer screening programme in the Nordic countries has not reached its optimal intensity, the number of deaths avoided is expected to increase rapidly during the predicted period (Table 39). Breast cancer screening does not save money: in Sweden additional costs of up to $122 m in the period 2008–2012 were predicted to be attributable to the programme. Despite the predicted increase in the total additional costs of the screening programme, the additional costs per life years gained are expected to decrease, and at the end of the period the predicted costs per life years gained will only be half those in 1993–1997 (Table 39). The additional costs per life years gained attributable to the programme in the period 2008–2012 are predicted to be between $11 000 in Denmark and $19 000 in Finland. The predicted difference between the additional costs per life years gained and additional costs per quality-adjusted life years gained decreased over time; from $1 200 in 1993–1997 the cost will fall to $580 in 2008–2012. The additional costs per dementia-free life years gained were approximated between $47 000 in Finland and $29 000 in Denmark in the period 1993–1997. At the end of the predicted period these costs were predicted to decrease to 22 000 and 13 000, respectively. The additional costs per LYG with good quality are slightly higher than those per dementia-free LYG, and this

Table 39

Cost-utility estimation for breast cancer screening in the Nordic countries

Country	Period	Deaths avoided	Life years gained	Additional costs (AC)	AC per LYG	QALYG	AC per QALYG	Dementia-free LYG	AC per dementia-free LYG	AC per death avoided	LYG with good quality	AC per LYG with good quality
Denmark	1993–97	490	2 450	60 026 000	24 000	2 377	25 000	2 083	29 000	122 000	2 020	30 000
	1998–02	838	4 190	65 500 000	16 000	4 064	16 000	3 562	18 000	78 000	3 455	19 000
	2003–07	1 146	5 730	69 406 000	12 000	5 558	12 000	4 871	14 000	61 000	4 724	15 000
	2008–12	1 287	6 435	72 233 000	11 000	6 242	12 000	5 470	13 000	56 000	5 306	14 000
Finland	1993–97	293	1 465	59 126 000	40 000	1 421	42 000	1 245	47 000	202 000	1 208	49 000
	1998–02	497	2 485	64 950 000	26 000	2 410	27 000	2 112	31 000	131 000	2 049	32 000
	2003–07	694	3 470	71 218 000	21 000	3 366	21 000	2 950	24 000	103 000	2 861	25 000
	2008–12	808	4 040	75 726 000	19 000	3 919	19 000	3 434	22 000	94 000	3 331	23 000
Iceland	1993–97	14	70	2 306 000	33 000	68	34 000	60	39 000	165 000	58	40 000
	1998–02	23	115	2 560 000	22 000	112	23 000	98	26 000	111 000	95	27 000
	2003–07	32	160	2 927 000	18 000	155	19 000	136	22 000	91 000	132	22 000
	2008–12	37	185	3 412 000	18 000	179	19 000	157	22 000	92 000	153	22 000
Norway	1993–97	241	1 205	43 982 000	36 000	1 169	38 000	1 024	43 000	182 000	994	44 000
	1998–02	421	2 105	48 231 000	23 000	2 042	24 000	1 789	27 000	115 000	1 736	28 000
	2003–07	598	2 990	53 269 000	18 000	2 900	18 000	2 542	21 000	89 000	2 465	22 000
	2008–12	681	3 405	58 440 000	17 000	3 303	18 000	2 894	20 000	86 000	2 807	21 000
Sweden	1993–97	520	2 600	100 609 000	39 000	2 522	40 000	2 210	46 000	193 000	2 144	47 000
	1998–02	900	4 500	109 870 000	24 000	4 365	25 000	3 825	29 000	122 000	3 710	30 000
	2003–07	1 284	6 420	117 117 000	18 000	6 227	19 000	5 457	21 000	91 000	5 293	22 000
	2008–12	1 493	7 465	121 977 000	16 000	7 241	17 000	6 345	19 000	82 000	6 155	20 000

Table 40

Cost-utility estimation for cervical cancer screening in the Nordic countries

Country	Period	Deaths avoided	Life years gained	Additional costs (AC)	AC per LYG	QALYG	AC per QALYG	Dementia-free LYG	AC per dementia-free LYG	AC per death avoided	LYG with good quality	AC per LYG with good quality
Denmark	1993–97	2 213	15 491	39 797 000	2 600	15 026	2 600	13 167	3 000	18 000	12 772	3 100
	1998–02	2 333	16 331	40 744 000	2 500	15 841	2 600	13 881	2 900	17 500	13 465	3 000
	2003–07	2 411	16 877	40 034 000	2 400	16 371	2 400	14 345	2 800	16 600	13 915	2 900
	2008–12	2 467	17 269	38 223 000	2 200	16 751	2 300	14 679	2 600	15 500	14 238	2 700
Finland	1993–97	1 109	7 763	8 789 000	1 100	7 530	1 200	6 599	1 300	7 900	6 401	1 400
	1998–02	1 247	8 729	8 825 000	1 000	8 467	1 000	7 420	1 200	7 100	7 197	1 200
	2003–07	1 352	9 464	8 917 000	900	9 180	1 000	8 044	1 100	6 600	7 803	1 100
	2008–12	1 412	9 884	8 412 000	900	9 587	900	8 401	1 000	6 000	8 149	1 000
Iceland	1993–97	50	350	452 000	1 300	340	1 300	298	1 500	9 000	289	1 600
	1998–02	56	392	488 000	1 200	380	1 300	333	1 500	8 700	323	1 500
	2003–07	62	434	515 000	1 200	421	1 200	369	1 400	8 300	358	1 400
	2008–12	64	448	532 000	1 200	435	1 200	381	1 400	8 300	369	1 400
Norway	1993–97	999	6 993	9 846 000	1 400	6 783	1 500	5 944	1 700	9 900	5 766	1 700
	1998–02	1 088	7 616	10 383 000	1 400	7 388	1 400	6 474	1 600	9 500	6 279	1 700
	2003–07	1 146	8 022	10 501 000	1 300	7 781	1 300	6 819	1 500	9 200	6 614	1 600
	2008–12	1 146	8 022	10 352 000	1 300	7 781	1 300	6 819	1 500	9 000	6 614	1 600
Sweden	1993–97	1 865	13 055	28 001 000	2 100	12 663	2 200	11 097	2 500	15 000	10 764	2 600
	1998–02	2 041	14 287	28 792 000	2 000	13 858	2 100	12 144	2 400	14 100	11 780	2 400
	2003–07	2 139	14 973	28 433 000	1 900	14 524	2 000	12 727	2 200	13 300	12 345	2 300
	2008–12	2 176	15 232	27 616 000	1 800	14 775	1 900	12 947	2 100	12 700	12 559	2 200

Table 41

Cost-utility estimation for colorectal cancer screening in the Nordic countries, females

Country	Period	Deaths avoided	Life years gained	Additional costs (AC)	AC per LYG	QALYG	AC per QALYG	Dementia-free LYG	AC per dementia-free LYG	AC per death avoided	LYG with good quality	AC per LYG with good quality
Denmark	1998–02	445	3 560	31 913 000	9 000	3 382	9 000	3 026	11 000	72 000	2 875	11 000
	2003–07	756	6 048	33 357 000	6 000	5 746	6 000	5 141	6 000	44 000	4 884	7 000
	2008–12	1 036	8 288	34 953 000	4 000	7 874	4 000	7 045	5 000	34 000	6 693	5 000
Finland	1998–02	226	1 808	28 045 000	16 000	1 718	16 000	1 537	18 000	124 000	1 460	19 000
	2003–07	396	3 168	29 955 000	9 000	3 010	10 000	2 693	11 000	76 000	2 558	12 000
	2008–12	568	4 544	31 971 000	7 000	4 317	7 000	3 862	8 000	56 000	3 669	9 000
Iceland	1998–02	11	88	1 127 000	13 000	84	13 000	75	15 000	102 000	71	16 000
	2003–07	19	152	1 258 000	8 000	144	9 000	129	10 000	66 000	123	10 000
	2008–12	26	208	1 429 000	7 000	198	7 000	177	8 000	55 000	168	9 000
Norway	1998–02	319	2 552	24 865 000	10 000	2 424	10 000	2 169	11 000	78 000	2 061	12 000
	2003–07	547	4 376	26 424 000	6 000	4 157	6 000	3 720	7 000	48 000	3 534	7 000
	2008–12	867	6 936	28 775 000	4 000	6 589	4 000	5 896	5 000	33 000	5 601	5 000
Sweden	1998–02	486	3 888	51 239 000	13 000	3 694	14 000	3 305	16 000	105 000	3 140	16 000
	2003–07	799	6 392	53 543 000	8 000	6 072	9 000	5 433	10 000	67 000	5 162	10 000
	2008–12	1 118	8 944	56 347 000	6 000	8 497	7 000	7 602	7 000	50 000	7 222	8 000

Table 42

Cost-utility estimation for colorectal cancer screening in the Nordic countries, males

Country	Period	Deaths avoided	Life years gained	Additional costs (AC)	AC per LYG	QALYG	AC per QALYG	Dementia-free LYG	AC per dementia-free LYG	AC per death avoided	LYG with good quality	AC per LYG with good quality
Denmark	1998–02	477	3 339	32 802 000	10 000	3 172	10 000	3 105	11 000	69 000	2 696	12 000
	2003–07	741	5 187	34 263 000	7 000	4 928	7 000	4 824	7 000	46 000	4 189	8 000
	2008–12	904	6 328	36 001 000	6 000	6 012	6 000	5 885	6 000	40 000	5 110	7 000
Finland	1998–02	251	1 757	27 292 000	16 000	1 669	16 000	1 634	17 000	109 000	1 419	19 000
	2003–07	432	3 024	29 819 000	10 000	2 873	10 000	2 812	11 000	69 000	2 442	12 000
	2008–12	578	4 046	31 806 000	8 000	3 844	8 000	3 763	8 000	55 000	3 267	10 000
Iceland	1998–02	11	77	1 153 000	15 000	73	16 000	72	16 000	105 000	62	19 000
	2003–07	20	140	1 302 000	9 000	133	10 000	130	10 000	65 000	113	12 000
	2008–12	27	189	1 490 000	8 000	180	8 000	176	8 000	55 000	153	10 000
Norway	1998–02	415	2 905	26 423 000	9 000	2 760	10 000	2 702	10 000	64 000	2 346	13 000
	2003–07	708	4 956	28 413 000	6 000	4 708	6 000	4 609	6 000	40 000	4 002	7 000
	2008–12	968	6 776	30 930 000	5 000	6 437	5 000	6 302	5 000	32 000	5 472	6 000
Sweden	1998–02	602	4 214	51 055 000	12 000	4 003	13 000	3 919	13 000	85 000	3 403	15 000
	2003–07	965	6 755	53 253 000	8 000	6 417	8 000	6 282	8 000	55 000	5 455	10 000
	2008–12	1 216	8 512	55 985 000	7 000	8 086	7 000	7 916	7 000	46 000	6 873	8 000

difference decreases with time. In the last predicted period the difference between costs per LYG and costs per LYG with good quality was approximately half that in the period 1993–1997.

Cervical cancer

According to the treatment costs employed in this study, screening for cervical cancer was estimated as cost-saving (Table 40). Costs saved per life years gained were predicted to be between $2 600 in Denmark and $1 100 in Finland in the period 1993–1997 but a decrease in cost savings was predicted in the next 5-year period. The overall financial savings per cervical cancer death avoided varied by country, and was twice as high in Denmark (the highest) than in Finland (the lowest). The ranking was the same for savings per LYG with good quality, ranging from $2 700 in Denmark, to $1 000 in Finland, in the period 2008–2012.

Colorectal cancer

In Tables 41 and 42 the cost-utility estimations for colorectal cancer screening programmes in the Nordic countries by sex are presented. The additional costs per life years gained are expected to decline rapidly and the trend is similar in both sexes. At the end of the predicted period, the years 2008–2012, the highest additional cost attributable to colorectal cancer screening is expected in Iceland ($7 000 and 8 000) and the lowest in Norway ($4 000 and 5 000), in females and males, respectively.

The additional costs per dementia-free life years out of the screening prolonged lifespan in females are about the same as or slightly higher than those for males in all the Nordic countries in the period 1998–2002, but the decreasing trend is also stronger in females. However, the difference between costs per LYG and costs per LYG with good quality remained slightly less favourable in males than in females except in Norway, where the difference was similar in both sexes (Tables 41 and 42). In the period 2008–2012 the additional costs per death avoided are predicted to be lowest in Norway at $33 000 and 32 000, and highest in Finland at $56 000 and 55 000, and within $55 000 in Iceland in both females and males.

Summary

Table 43 presents a summary of all the Nordic countries combined in the year 2010. The additional cost per deaths avoided by means of the three screening programmes is

Table 43

Summary of cost (in US dollars) utility analysis in the year 2010 due to screening by primary site. All Nordic countries combined

Additional cost ($) per	Primary site				Total
	Breast	Cervix	Colorectum		
			Females	Males	
Death avoided	77 073	−11 700	42 434	42 246	29 465
LYG	15 414	−1 671	5 304	6 036	4 375
QALYG	15 891	−1 688	5 583	6 353	4 515
DFLYG	18 135	−1 966	6 240	6 489	5 053
GQLYG	18 696	−1 986	6 569	7 473	5 312

about $30 000 and about $5 300 per GQLYG. Screening for breast cancer is the most expensive, $77 000 per deaths prevented and $18 700 per GQLYG. The cost saved by screening for cervical cancer was $11 700 per deaths prevented and $2 000 per GQLYG.

DISCUSSION

Mortality predictions

The most reliable measure of the effect of a screening programme for cancer is the reduction in the number of deaths from cancer. For the purpose of this study, the predicted number of deaths was assumed to follow the same age, period and cohort trends as the observed number of deaths from 1953 to the beginning of screening. Another approach was applied in the mortality predictions of the KiN-project published by Engeland et al. (2). They estimated the number of deaths from cancer in the Nordic countries in the period 1968–1987 as a function of the observed incidence rates and relative survival rates. For the period 1953–1957, they did not estimate the number of deaths due to cancer. The estimates for the periods 1958–1962 and 1963–1967 included only those cases of death due to cancer that occurred in patients with tumours diagnosed after 1957. Therefore, the number of deaths in these periods was underestimated and the underestimation decreased with time, making the estimated number of deaths unsuitable as reference values.

The estimate of what the mortality rate would have been if screening for cervical cancer had not been established is based on the observed mortality data from Denmark in the period 1953–1967 and on the assumption that the mortality rate would have followed the same trend as that observed before the establishment of the screening programme. A biased estimate of the base-line mortality for these periods would introduce bias in the future mortality trends. An increasing trend was observed in the oldest birth cohorts in the beginning of the period (1953–1962), which may be partly due to improved quality of defining the cause of death in these age groups rather than to a real increase in mortality rates. Such a bias affecting only early periods and advanced ages will have only a small effect on the predictions, however. On the basis of the observed mortality, a slightly declining trend was predicted for the number of deaths from cervical cancer after 1967 in the absence of screening. A similar pattern of cervical cancer mortality was observed in countries where there was no organized screening policy or where the effect of screening was shown to be small (36, 120).

The age-cohort model was fitted to the observed breast cancer mortality data in the period up to 1987 to predict mortality rates and number of deaths without screening. The last observed period (1988–1992) was not included in the model for breast cancer in Finland because the fit of the model based on the observed period 1953–1987 was substantially better than that based on the period 1953–1992. A comparison between the mortality from breast cancer in the Nordic countries predicted in this study and the results from the Nordic mortality predictions for the years 1993–2012 (2) reveals that the difference between these two predictions increases with calendar time (Table 44). The number of deaths increases with calendar time in both predictions but the trends differ considerably. The greatest differences appear in age groups in which the highest level of mortality reduction attributable to screening is expected. Thus the effect of mammography is larger and the cost-effectiveness ratio smaller if the Engeland et al. (2) predictions are to be assumed.

Similar comparisons between the predictions of deaths from cervical cancer cannot be made for any other country except Finland. In Finland the number of deaths from cervical cancer has been continuously declining since the screening programme was established, and the trends are similar in both predictions. Although the number of deaths varies over time, there is no difference between the overall mortality trends.

Table 44

Mortality predictions for Finland based on the observed mortality data (present study) and on the joint effect of incidence and survival rates (2)

Site, age group	Period	Number of deaths	
		Based on observed number of deaths	Based on incidence and survival
Breast			
30–85+	1983–1987	3 488*	3 518**
	1993–1997	4 071	4 744
	1988–2002	4 322	5 475
	2003–2007	4 575	6 264
	2008–2012	4 829	7 061
Cervical			
25–85+	1983–1987	478*	536**
	1993–1997	335	302
	1998–2002	259	238
	2003–2007	196	199
	2008–2012	152	179
Colorectal,			
females 30–85+	1983–1987	2 474*	303**
	1993–1997	2 880	2 669
	1998–2002	3 019	2 804
	2003–2007	3 123	2 970
	2008–2012	3 254	3 098
Colorectal,			
males 30–85+	1983–1987	1 862*	1 750**
	1993–1997	2 354	2 210
	1998–2002	2 634	2 472
	2003–2007	2 948	2 762
	2008–2012	3 267	3 020

* Observed
** Estimated

The number of colorectal cancer deaths will increase by calendar period according to both compared predictions. The number of deaths estimated by Engeland et al. (2) on the basis of incidence and survival is slightly less than that observed in the period 1983–1987, but the same difference remains over the predicted period and the trends are similar in females and males.

Mortality reduction

In this study mammography screening of women aged 50 to 69 years every two years was predicted to reduce the number of deaths from breast cancer in the Nordic countries by about 15 000, which is 12% of all breast cancer deaths in women 30 years of age and over, during the total predicted period, 1993–2017. Ultimately, in the year 2015 it is predicted that about 1 000 deaths from breast cancer will be prevented in the Nordic countries. This is about 18% of all breast cancer deaths predicted in 2015. In The Netherlands, where both the incidence of and mortality from breast cancer are higher, de Koning et al. (84) estimated that mortality from breast cancer in the total female population can be reduced by a maximum of 16% in the period 1990–2017, if women aged 50–70 were screened mammographically every second year. An analysis of the data from the Swedish breast cancer screening trials by counties was published recently by Törnberg et al. (8). They estimated that 10 years after the onset of the programme, mortality in the 50–74 years age group would have been 19% lower if 100% of the population of that age had been invited and participated in screening. Mortality reduction due to breast cancer screening in Sweden was calculated as a product of the proportion of women invited to screening and the presumed full effect on mortality: 0% during the first 5 years of follow-up; 50% from the 5th to the 10th year; and 100% after the 10th year. This assumption was based on data from the Stockholm Regional Cancer Registry, and these figures correspond fully with those assumed in the present study. The summary report (44) on six randomized trials of breast cancer screening showed an overall attendance rate of 70% in the 50–74 years age group leading to a 24% reduction in mortality in the invited group.

The ultimate mortality reduction observed in the Swedish trials was applied directly on the population affected by screening in the Nordic countries, thus assuming the same participation rate, sensitivity of test and other indicators of the programme. These assumptions are crude but avoid the possible errors arising from the inevitable differences between the empirical results from mass-screening as well as those arising from the assumptions of specific theoretical models. The wide variations between the assumptions employed in the models indicate that it would be difficult to define any one of them more clearly than the other.

The predicted reduction in the number of deaths from colorectal cancer during the period 1998–2017 was about 13.6% in females and about 14.6% in males, compared with the situation without screening. This reduction is somewhat higher than the estimated mortality reduction from breast cancer. The total number of deaths that can be prevented by screening (21 500) is larger for colorectal than for breast cancer because of the large total number of deaths predicted (152 000). In 2015 the predicted number of deaths prevented is 1 500, which is 18% of the total number of deaths from colorectal cancer. Only limited data on the overall effect of screening on population level are available, and the validity of these results is difficult to verify.

The effect of screening for cervical cancer can be presented in terms of incidence reduction and in terms of mortality reduction. The reduction in the number of deaths from cervical cancer due to screening over the predicted period, 1993–2017, was estimated to be 89%. A total of 33 600 deaths from cervical cancer would be prevented in the Nordic countries out of 37 600 estimated in the absence of screening. The effect of cervical cancer screening in terms of preventable deaths is equal to the combined effect of screening programmes for breast and colorectal cancers. The decrease in the number of invasive cervical cancers in Finland comes close to that predicted in the literature as an optimal decline attributable to an organized screening programme. Day (121) predicted that the cumulative incidence rate would decrease by about 82% if 100% of the population aged 25–64 years is screened every 5 years. The observed number of cases in Finland in 1988–1992 was about 17% of that estimated without screening. In the predicted period 1993–2017, the expected reduction in the number of new cases is approximately 85%. Ultimately, in the year 2015 the number of deaths prevented would be 1 500 out of 1 600 expected deaths (91%). To a large extent the reduction in mortality from cervical cancer can be considered to be a consequence of the substantial reduction in the incidence of the disease (6, 33, 35, 56). The estimated numbers of invasive new cases in Finland in the period 1958–1992 compared with the period before the establishment of the screening programme, 1958–1962, are presented in Table 45. An increase of 9% in the number of new cases was observed in

Table 45

Incidence of cervical cancer in the 25–59 age group (%) from that observed in 1958–1962 in Finland

Calendar period	New cases	
	No.	%
1958–62	1 349	100
1963–67	1 462	109
1968–72	1 087	80
1973–77	564	42
1978–82	390	29
1983–87	310	23
1988–92	275	20

the first 5-year calendar period after the start of screening, followed by a considerable fall in the number of invasive diseases in the subsequent calendar periods. The decreasing trend was stronger during the first time intervals, and diminished later when screening reached its full coverage.

The NCI of the US estimated that a reduction of between 25% and 50% in total mortality from cancer can be achieved in the US as a result of a combination of prevention, screening and treatment by the year 2000 (99). According to the same study the estimated reduction in mortality due to prevention alone was about 13% in both sexes. The potential contribution of treatment only was 10% in males and 8% in females and that of screening was 3% in the female population due to screening for breast and cervical cancers. Hakama (30) estimated that a 3% potential reduction in mortality can be expected in a European female population as a result of screening for cervical cancer only. Results of the present study are more optimistic compared with those of the NCI project (99) and similar to those suggested by Hakama (30). The total predicted mortality in the period 2008–2012 can be found in Engeland et al. (2). The prediction is based on the observed trends in incidence, therefore the effect of screening for cervical cancer is incorporated. The difference caused by these two approaches is small in predictions for total mortality from cancer, and therefore the estimate of the total mortality by Engeland et al. (2) can be used in the estimation of the ultimate proportion of deaths. In the period 2008–2012, when breast cancer screening is expected to reach its full extent, of those deaths in females which were predicted by Engeland et al. (2), 5% were estimated in this study to be avoidable due to screening for breast and cervical cancers. In addition, a reduction in mortality of 1.8% in females and 1.6% in males was predicted in this study as a result of screening for colorectal cancer in the same period.

Extrapolation of the Engeland (2) results and assumption of the results on mortality of this study will predict mortality reduction due to screening to be 5.7% of the total predicted mortality in 2013–2017 (9.7% in females and 2.0% in males) (Table 46).

Table 46

Estimated mortality reduction due to screening for breast, cervical and colorectal cancers in the Nordic countries in 2013–2017

	Total annual number of deaths from cancer*	Mortality reduction**	
		Annual number	%
Females	32 600	3 270	9.7
Males	36 300	740	2.0
Total	68 900	3 910	5.7

* Predicted on basis of Engeland et al. (2)

** Annual number of deaths from breast, cervical and colorectal cancers predicted in this study.

The potential effect of screening on mortality reduction is relatively small compared with the estimated impact of prevention and treatment, but it has been empirically tried and tested at population level by cervical cancer mass-screening and by randomized screening trials for breast and colorectal cancer.

Costs

The wide range of cost-effectiveness and cost-utility estimates can be referred to in correspondence with the broad set of assumptions employed. However, several reasons for the incomparability of the direct results from the present study with those from other studies on cost-effectiveness of screening for cancer can be pointed out.

A serious uncertainty in the evaluation of cost-effectiveness is the estimation of costs. The organization of health care in the Nordic countries does not allow differentiation between all the treatment costs by stage of the disease. This was the reason for approximating the costs, admitting all the risks and uncertainties that are likely to appear in such an estimation.

The cost per screening test for cervical cancer in Finland is approximately $10. Costs of sending an invitation letter and letter of result information, registration, smear-taking and cytological examination are all included in this cost. In some of the studies referred to the cost per PAP test is considerably higher. For instance, in The Netherlands the costs per PAP test were assumed to be $16–18, and the total cost of screening per smear was $21–29 (100). Eddy (101) stated that in the US the laboratory fees for PAP smears were approximately $3, but when the high fees of private physicians or clinicians were included the total charge varied from $34 to more than $100. The cervical cancer screening programme covers a wide age group of the female population and, corresponding to the number of smears taken, a possible underestimation of the costs can influence significantly the cost-effectiveness ratio of the whole programme. Although the cost per screening test (PAP test) in Finland is lower than that mentioned above, it can be considered relatively reliable, due to the well-organized programme. Therefore, the cost of screening tests in Finland was not likely to be seriously underestimated and it was applied for all the Nordic countries.

The costs per breast cancer screening test referred to in literature vary between $40 (84) and $46 (101) per single-view mammography, and are close to the two-view mammography in Finland, $40. Costs per FOBT vary between $2 (102) and approximately $5 (122). An average $5 per test (101) was employed in the present study.

The definition of the treatment costs depends on the standard treatment procedures in a particular stage of a given cancer. When the costs of cervical cancer screening were estimated, the diagnostic work-up of all positives after the first PAP test, overtreatment due to screening and

treatment of CIN were included in the calculations as 'costs of treatment of in situ cases'. These costs were applied to the difference between the estimated cases of CIN and invasive cancer in the absence of screening and the number of new cases with screening. A similar scheme for estimation of the potential effect of cervical cancer screening was applied in the model to project cancer mortality in the year 2000 in the US (99). The authors considered the total number of CIN and invasive cancers unchanged over the period and estimated the potential effect of screening as a change in the stage distribution as follows: the ratio CIN/invasive cancers is 4/1 in the absence of screening and it is changed to 9/1 when the maximum programme effect is reached. One out of 3 CIN lesions would probably have progressed into invasive cancer if not subjected to treatment (52). Owing to the difference in the ratios between the studies, a slight difference in the estimated reduction of the number of invasive diseases can be seen. The number of new invasive cancers with screening is half that without screening according to the NCI model (99), and the reduction estimated for the Finnish screening programme was about 57% (52). The assumption for the change in the stage distribution of invasive cancers with screening in the NCI model was that the percentage of localized cancers is likely to increase, but the observed data from Finland show the reverse to be true. The screen-detected cases will be diagnosed mainly as CIN. Therefore, the new invasive cancers are mainly interval cancers which can be considered as fast-growing tumours or that they appear in women who did not attend the screening, or that they are false negatives. This accounts for the slight increase in the percentage of non-localized cancers during the period the screening was implemented in Finland. The costs of the diagnostic confirmation were included in the treatment costs.

For breast and colorectal cancer the estimate is only a crude one for the additional diagnostic procedures due to false positive screening tests and the number of cancers in the preclinical stage which would never have surfaced as clinical disease in the absence of screening (overdiagnosis). Several approaches to these problems have been employed in different studies. An optimistic assumption is that breast and colorectal cancers have an identifiable preclinical stage when the disease can already be diagnosed by a screening test and cured successfully, and the incidence rates thus reduced. Such an assumption was employed in the cost-effectiveness analyses of colorectal cancer screening carried out in Japan (102). This scheme was based on the assumption that 50% of colorectal cancers are derived from adenomas and 3% of all adenomas progress to invasive cancers. Costs applied for Japan were as follows: colonoscopy $120, biopsy $75, complications $5 000, polypectomy $2 170, and initial treatment for cancer $8 600. These costs are lower than those estimated in the Nottingham trial (122) and those employed in the evaluation models in the US (123), but they support the assumption that the expenses caused by false positives and overdiagnosis due to screening are close to those of the initial treatment of cancer (101). This scheme of estimation of the impact of screening is uncertain until there is evidence of to what extent the progress of adenomas to invasive cancer can be prevented by early detection and treatment. In the present study a similar approach to considering the excess costs of false positives and overdiagnosis was used. The test is sensitive to adenomas, and thus a considerable increase in the number of persons undergoing excess diagnostic procedures and treatment of adenomas (or early stage invasive disease) is expected. These additional diagnostic procedures and treatment of adenomas are included in the treatment costs by assuming a 20% increase in the number of new cases. As far as the relationship between the preinvasive lesions and invasive cancers has not been quantatively assessed for colorectal cancer, it is difficult to estimate the effect of treatment of preinvasive lesions as a part of a screening programme on the forecast of decrease in incidence rates or on the cost of the programme.

The specificity of the FOBT is 98%, i.e., the proportion of false positives in randomized screening trials is 2% (101). The cost of additional diagnostic procedures (approximately $50) of false positives (2%) is included in the cost of screening tests. The difference between treatment costs for localized and non-localized colorectal cancer is estimated to be as much as half of the costs for localized colorectal cancer. This ratio was proposed by Eddy (101) and Brown et al. (123).

The increase in the number of new cases diagnosed by screening and the change in the stage distribution of new cases are greatest in the first round. For example, the maximum increase in the number of newly diagnosed breast cancers compared with the situation without screening was estimated to be about 17%, falling later to a 3.5% excess in number of new cases (84). de Koning et al. (84) showed that the costs per years of life gained are expected to be lower after the first rounds, whereas later the increase in the number of new cases is expected to diminish, which will result in a less favourable cost-effectiveness ratio.

This study is based on the assumption that the reduction in mortality from breast and colorectal cancers is expected to appear due to reduction in the number of advanced and terminal stage cases and that no temporary increase in the number of new cases was considered after the prevalence round. By this approach the favourable effect, in terms of cost-effectiveness ratio, is overestimated. The costs of additional diagnostic procedures for false positives after the first screening test for breast cancer are approximately $120 and they were included as part of the screening tests costs. Greenwald and Sondik suggested a 10% increase in the number of early diagnosed new cases in the long run of the screening programme for breast cancer (99). Therefore, the additional diagnostic procedures of the true positives

and the additional treatment were included in the treatment expenses in the form of assuming an increase of 10% in the number of invasive cases. The difference is non-significant between treatment costs of localized breast cancer detected through normal clinical practice and preclinical disease (101). Elixhauser (124) applied the same assumption in the cost-effectiveness estimation of breast cancer screening in the US, a 10% increase in the number of new cases compared with the situation without screening in the long term. Brown (125) discussed that a 10% overdiagnosis due to screening, if treated similarly to early-stage cancer, could increase the cost-effectiveness ratio by 27%.

The costs of histological analysis of biopsy specimens were assumed to remain unchanged by the screening programme and were included in the treatment costs (84, 94).

The treatment costs estimated for breast cancer patients during the first 5 years of follow-up in Tampere University Hospital were employed in the analysis: $8 000 for localized and $16 000 for non-localized breast cancer (93). This estimation of treatment costs is supported by several studies on breast cancer screening (83, 84, 94, 101, 103). A similar model for estimating the results of breast cancer screening was applied by the US Office of Technology Assessment (126). They assessed the costs of a breast cancer screening programme as the difference between costs of the screening test and the reduction in costs for treatment and terminal care. The estimate was calculated over the period 1987–2020, based on assumptions of 30% participation rate, 50% mortality reduction at 5 years among participants, gradually falling to 30% at 20 years. The following costs were assumed: mammography and physical examination $83, diagnostic work-up for a false-positive $1 500, terminal care $18 000, $2 000 less expenses for early-stage breast cancer treatment than for late-stage disease during the initial three months of treatment. In the present analysis the costs of terminal care were included in the treatment costs of non-localized cases and thus the total cost reduction was accounted for by the change in the stage distribution.

Non-medical direct costs such as travel expenses and time loss for participants are minimal in an organized screening programme. However, they were not assumed to be society costs and therefore they were not included in the estimate.

Results of screening for cancer arise in the oldest age group when indirect society benefits, such as savings in lost work time, cannot be achieved. This limitation is likely to have an unfavourable effect on a comparison between cancer screening programmes and other health programmes affecting younger populations. Therefore, the indirect society costs, such as loss of production, are not considered, either. If indirect costs only, but not the indirect benefits, had been included in the estimate, the overall cost of the programme would have been higher.

The evaluation of health care expenses during the life years gained is technically difficult. Moreover, if costs of future health care are incorporated, benefits should also be attributed to the life years gained. However, it is impossible to assess the value of life in terms of money. These costs or benefits are not taken into consideration in most cost-effectiveness estimates. In this study an attempt to evaluate the prolongation of life was made by the QALYs and by taking into account the expected duration of senility, but no excess health care costs were included. According to Taplin et al. (125) at the age of 80 and older the total cost of continuing care is about the same for colon cancer patients, for breast cancer patients and for any individual free of these two diseases. Furthermore, the cancer patient cost was relatively independent of age. Therefore, it is likely that the net costs of screening will be equal to the screening costs and the cost of the resultant cancer treatment in prevention of cancer death.

A practical feature of this evaluation is the assessment of the main benefits from a screening programme. Some of the screening programmes have covered age groups other than those in the Nordic countries, or the intervals between the screening rounds were different, or different screening tests were applied and thus the expected effect of screening varied. The number of life years gained per death avoided was calculated as the product of number of deaths avoided and average prolongation of patients' life attributed to the earlier diagnoses of the disease. The average prolongation of life for patients who would avoid death from breast cancer in Finland according to the data available (109) is significantly shorter than that assumed by de Koning et al. (84) (Table 6). The average age of diagnosing breast cancer in the 50–69 age group in Finland is 59.8 years, and patients have 16.9 years of life expectancy, which is 5 years less than the population life expectancy at that age (109). The same problem occurs in cervical and colorectal cancer screening estimation. In a number of studies the assumed prolongation of life per deaths avoided is 16 years or more (102, 128), which is approximately the total expected length of life for the general population at the same age as the patients. However, in this study the difference between the life expectancy of the general population and that of the patients was applied as life years gained per deaths avoided. This could be one of the reasons that the cost per life years gained in The Netherlands was much lower than that estimated for the Nordic countries.

While most base-line assumptions in the present study are similar to those employed in the assessment of the results from breast cancer screening in The Netherlands, the variation in the overall cost-effect ratios can be explained by different approaches in the estimate of life years gained per death avoided and the discount rate of 5%. In the most cost-effectiveness estimates a 5% discount is applied to both effects and costs. According to the results

of the US Office of Technology Assessment (103) the 5% discount in breast cancer screening analyses leads to about a 20% increase in cost per life year saved, but a comparison of the results of analyses of cervical cancer screening (100, 129) indicated that the difference could be much bigger. In this study it is considered that deaths prevented at present are as valuable as those in the future, whereas the idea of discounting 5% is that deaths prevented at present are more valuable. If this is accepted, the clinical medicine which gives results immediately should be evaluated as more important than preventive medicine, and such an attitude would be particularly misleading when comparisons are made between prevention, screening and clinical treatment. From an ethical point of view it is equally important to invest in the future. Russell (130) suggested that the cost evaluation of life years saved should be utilized only when the total medical care expenses are planned, but not as an argument about whether a preventive policy is a good investment. However, about 5% discount is not likely to change the order of primary sites as to the costs of the screening programmes.

The effect of correct specification of assumptions and modelling on the cost-effectiveness is routinely evaluated by sensitivity analysis in health economics (92). In this study no detailed formulation was available on treatment costs and on other clinical information, which has been consistent and comparable between the primary sites. The screening costs were estimated as one entity and the effect of changing the cost of tests on the cost-effectiveness could be directly estimated. In this study no formal sensitivity analysis was made.

If it is assumed, as in the experimental models, that screening will be stopped, the savings in treatment costs will continue for the next 15 years and the average cost-effectiveness ratio will be more favourable. This strategy is not a subject for discussion in public health policy, but it should be taken into consideration when cost-effect rates are compared with those reported in similar studies.

Although the colorectal cancer incidence rate is much lower than that of breast cancer and the screening interval was annual for colorectal and biannual for breast cancer, the total estimated cost per years of life saved in colorectal cancer is about 30–40% of that in breast cancer screening. Regardless of the bigger population size and shorter screening interval, the total cost of screening and confirmation of colorectal cancer is about 30% less than that for breast cancer. Furthermore, the difference in treatment costs between the situation with and without screening for colorectal cancer remains stable over the period and much higher than the difference in treatment costs for breast cancer. Finally, total additional costs attributed to the screening programme were lower for colorectal cancer than those for breast cancer.

The estimates of the cost-effectiveness of cervical cancer screening may seem unexpected, therefore some features of the model should be discussed. The observed reduction in the number of new cases in Finland was accepted for this estimation model as the optimal, real effect of the screening programme on incidence of the disease, whereas the estimations found in the literature were based on theoretical, indicator-based, or on sample-based approximations of the effect of screening (100, 101, 131–133). The observed stage distribution was also applied. The number of new cases without screening is unlikely to be overestimated regarding the incidence trend in Norway and other European countries where there are no organized screening programmes (36, 120) (Appendix 5). Treatment costs were approximated, and some uncertainty can be assumed taking into consideration the wide variation between different estimates of treatment costs.

The substantial difference in the approach to the three primary sites in the present study and the differences in the models from the literature explain the wide variation between the estimated cost-effectiveness. The overall cost-saving effect of the programme for cervical cancer could be substantially changed if more data were available. However, in this study mass-screening for cervical cancer was assessed as financially beneficial for society, whereas screening for colorectal cancer and especially that for breast cancer will need substantial additional resources.

Quality of life

Prolongation of patients' life is accepted as the basic measurement of the favourable effect of any treatment but it is often attained by more aggressive treatment methods, resulting in lower quality of life during the prolonged lifetime. If a better rate of survival can be achieved with screening, less aggressive treatment and an improved quality of life can also be achieved. The measurement of the benefits and possible unfavourable effects of screening cannot be completed without taking into consideration the effect on quality of life. In some cases the improvement in the quality of life may be the only or the main effect of a screening programme.

Measurement of QoL in breast cancer patients performed by Koning et al. (84) and Haes et al. (83) was applied in this study. QoL in each phase of the disease was evaluated by 13 medical experts: 3 surgical oncologists, 3 medical oncologists, 2 radiotherapists, 1 radiologist and 2 epidemiologists. The estimates were given on a visual analogue scale from 0 (the worst) to 1 (the best) (83). For each of the phases physical, psychological and social status were estimated. Questionnaires concerning QoL during subsequent phases were sent to 31 breast cancer clinical experts: screening examination, assessment (biopsy), primary surgery, primary radiotherapy, adjuvant systematic therapy, first year after mastectomy, first year after breast conserving therapy, disease-free interval after mastectomy, disease-free interval after conserving therapy, and ad-

Table 47

Duration and utilities of the phases related to screening for breast cancer (83)

Phase*	Utility	1-utility	Duration
Terminal illness	0.288	0.712	1 month
Palliative + chemotherapy	0.531	0.469	4 months
Palliative + radiotherapy	0.591	0.419	1 month
Palliative + surgery	0.617	0.383	5 weeks
Palliative + hormonal therapy	0.663	0.337	14 months
Initial chemotherapy	0.717	0.283	6 months
Initial radiotherapy	0.803	0.197	2 months
Initial hormonal therapy	0.820	0.180	2 years
2 months–1 yr after mastectomy	0.844	0.156	10 months
Initial surgery	0.867	0.133	2 months
Diagnostic phase	0.895	0.105	5 weeks
2 months–1 yr after breast-conserving therapy	0.914	0.086	10 months
Disease-free > 1 yr after mastectomy	0.947	0.053	Life expectancy
Disease-free > 1 yr after breast-conserving therapy	0.960	0.040	Life expectancy
Screening attendance	0.994	0.006	1 week

* Phases are ranged according to the value of the utility attributed

vanced disease (treatment episodes/terminal care). QoL was valued on a visual analogue scale from 0 to 100. The duration of health states and utility estimated for each of them (83, 84) are presented in Table 47.

Since the target group of mass-screening is the entire population at a particular age, the effect of screening on QoL should be investigated at population level. For the purpose of measuring QoL, the population liable to screening can be divided into subgroups according to results from screening tests, age, change in long-term prognosis due to the programme, and treatment practice.

The only part of the programme which affects the entire screened population is the screening test. The effect of this phase on QoL has been assessed in several studies, referred to in the review of the literature section, and is usually included in the estimate when the total effect of a screening programme on QoL is evaluated. The duration of the screening phase was estimated to be one week (83), which is the period of receiving the results of the mammography, and less than 1% loss in utility was attributed to the screening test itself (83).

Furthermore, the QoL in four separate categories should be measured in accordance with the results from a screening test. In each of these four categories basic differences in relation to influence on QoL can be ascertained. When QoL is measured, the group always considered is that with a positive result from a screening test. In this group there are several subgroups, all of which have not received equal attention in relation to QoL measurement.

QoL in false positives (FP) is measured in the interval between a positive test result and receiving a negative result from subsequent diagnostic procedures. The influence of screening on this group is relatively short. de Haes et al. (83) assumed 5 weeks' duration of diagnostic phase for breast cancer patients. The QoL in this group was evaluated, first, in the time interval between the positive result from mammography and following biopsy, which is the most widespread method for diagnostic confirmation at present, and then in the time interval between carrying out the biopsy and receiving the result. The losses in utility were estimated to be 10% for all the women during the diagnostic phase.

The group of true positives (TP) has always been the major object of interest when QoL is measured. Most of the attention of researchers has been focused on this group, but in spite of this QoL has not been studied adequately in some subgroups. The benefit from screening is optimal for patients who are likely to avoid advanced and terminal stages and death from the disease. Those are patients included in the category 'deaths avoided'. They remain longer in the health status in which QoL is higher and thus escape the advanced and terminal stages of the disease when QoL is significantly lower.

Although the duration of advanced stages, estimated by de Koning et al. (84) on the basis of 68 women who died from breast cancer, cannot be expected to change significantly as a result of screening, an issue to be discussed is the duration of earlier health states. According to the main aim of any screening programme, a certain prolongation of earlier phases should be expected for screen-diagnosed cases. The obvious cause of extension of the life span in the earlier phases for screen-detected cases is the lead bias. Furthermore, it can be supposed that there will be a difference between the duration of some of these phases in symptomatically detected cases and those diagnosed by screening.

For those who will die from the disease despite screening, longer morbidity because of lead time results has a negative effect on QoL. It has been reported that when a standard gamble technique is used to measure patients'

preferences for quality and quantity of life, the estimate varies depending on the long-term prognosis (134). Therefore some variation in utility estimate could be expected in this group.

In the case of overdiagnosis, patients would never die from the disease independently of screening, and the effect of screening in terms of mortality reduction or deaths avoided cannot be assumed in this group. The impact of this group on QoL was not taken into consideration in the model applied by de Koning et al. (84). According to that model, no long-term increase in the number of new cases was assumed to be attributable to screening programme and cases of overdiagnosis were not included when the utilities were calculated. As far as these cases could be called long-term false positives, they receive excess diagnostic procedures and overtreatment and their QoL is unjustifiably diminished. Screening can be considered as negatively modifying QoL in this group and the percentage of the total reduction of QoL attributable to the programme will increase.

Those who have a true negative (TN) result from the screening test make up the largest group within the total screened population. However, sufficient attention has not been paid to the QoL in this group. Even though this effect is assumed to be relatively small, it concerns a large population and the total estimate should not be neglected. Because the negative effect of screening tests at population level is often included in the estimate of QoL, the positive effect of a negative test result should also be taken into consideration. According to Kauppinen et al. (135) a major section of the participants (72%) attend screening for cervical cancer in order 'just to be sure' that they are healthy. Since the expectation of a negative result is the strongest motive for most of the individuals, a certain positive effect of a negative test result on QoL must be included in the evaluation. However, no studies on this topic have been found and the probable duration and utility of this effect are unknown. This viewpoint on QoL related to screening was not included in the estimation of QoL in this study.

The number of false negatives (FN) is strongly related to the test itself and to the technical quality of the test applied. A rough assumption is that there is no change in their health status and QoL related to screening. These individuals do not receive health care before the disease has reached a symptomatic, clinical stage, after which time the model of treatment is not significantly different from that without screening, given the same stage. The QoL in FN in the interval between the test and diagnosis may be considered equal to that in TN and after that it is similar to QoL without screening. If the estimation is more precise, it should stress the fact that after a negative screening result people are less likely to pay attention to symptoms and they may either never seek treatment or obtain it later than they would if the test had not been performed. The consequences from the delay could be a poorer prognosis and thus a lower QoL compared to cases diagnosed without screening. Interval cases, independently of whether they are FN or faster growing cancers with higher malignant potential, from the point of view of QoL, can be included in this group. False negatives were included in the model applied as interval cases but no unfavourable effect was attributed to the programme.

The scheme of measuring the effect of screening on the quality of life in TP was considered similar for the three primary sites studied.

When the effect of screening on QoL in FP is estimated, a significant difference by site can be expected. In the case of cervical cancer screening, the lesion diagnosed by a PAP test is not called 'cancer', which has been found to influence patients' assessments when a standard gamble technique was applied for estimation of QoL. It is well known that CIN is curable, therefore a minimal negative effect of the positive (or FP) test results on QoL can be attributed to a cervical cancer screening programme. For breast and colorectal screening, some short-term negative effects can be expected after an FP test result. The specificity of diagnostic procedures should also be taken into account when QoL of FP is estimated. Furthermore, the positive effect of a TN result on QoL can be considered as an inverse proportion to the negative effect after an FP result. The unfavourable effect of screening in FN, including effect on QoL, could be considered as being strongly related to the duration of the preclinical phase of the disease. If the period of progression of CIN to invasive disease is more than ten years, then at least two PAP smears will be taken in this time interval and the conditional probability of obtaining an FN result from both tests is practically negligible. Consequently, the negative effect of FN results on QoL in cervical cancer screening can be ignored. But for breast and colorectal cancer all the negative consequences in FN mentioned above are applicable.

A simplification in the evaluation of results from screening is always to assume that the earlier the disease is detected, the better the results, the lower the costs and the better the cost-effectiveness ratio, or the less radical the treatment, the better the QoL. Conservative breast cancer surgery is applied in order to improve QoL, although it does not affect survival rate (136). Nevertheless, psychological morbidity in women who have undergone conservative surgery and in those who have had radical treatment is not essentially different (137, 138). According to the opinion of the experts' (84) employed in this study, the effect of breast-conserving therapy was assessed to have a 7% higher utility 3 to 12 months after the surgery compared with those who underwent mastectomy, and a 1% higher utility later.

Cancer is a disease that affects mainly the oldest age groups, and the effect of ageing, unrelated to cancer,

should be taken into consideration when the quality of the cancer patient's life is being assessed. It has been reported that the age of the individual is related in many ways to the estimation of QoL (134). No studies on the direct relation of age factor on QoL assessment in cancer patients have been found. Therefore population sample-based estimations of age-related QoL in the oldest were employed in this study to discount life years gained for life years spent in severe or moderate dementia. As far as the estimate based on the experts' opinion of QoL was applied in the calculation of QALY, there was justification for applying an estimate of dementia-free life expectancy at population level in order to obtain a more objective assessment of the benefit from screening for society. To the best of our knowledge such an adjustment has never been applied in studies on the effect of disease on quality and length of life. Estimation of QoL should be made in the future based on self-assessment of individuals from all the categories concerned above and after incorporation of a method for age-adjustment. The viewpoints of society and the individual on the benefit of a screening programme are complementary rather than contradictory. They have different applications. The estimate of the benefits to society should not be employed as an argument in decision-making on whether to screen or not to screen but as a basis for comparison between the cost-utility rates of different health policies and as an argument when resources are allocated.

SUMMARY AND CONCLUSIONS

The aim of this study was to evaluate the effects of screening for cancer in the Nordic countries. There is sufficient scientific evidence to conclude that screening for cervical cancer, breast cancer and colorectal cancer will result in a reduction in mortality. The effects on mortality were predicted for the future up to the year 2017 assuming that the Nordic countries are covered by screening as a nation-wide population-based public health policy and comparing the predicted mortality trends with those assuming no screening programmes.

For cervical cancer the programme as practised in Finland was used as a point of reference. For breast cancer and for colorectal cancer the results of randomized preventive trials were assumed in the absence of detailed results based on any public health policy, i.e., a reduction of 30% in mortality from breast cancer and 20% in mortality from colorectal cancer. The assumed ages and frequencies of screening ranged from 25 to 59 years at 5-year intervals for cervical cancer, from 50 to 69 at 2-year intervals for breast cancer and annual screening from 50 to 74 years for colorectal cancer.

Data on incidence and incidence predicted up to the year 2012, mortality, survival and size of the general population were employed in the estimation. Age-cohort and age-period-cohort log-linear models were applied in predicting future mortality rates with and without screening. The choice of the models depended on the age distribution of deaths from each particular site of cancer, on changes in public health policy, such as establishment of mass-screening, and on the goodness of fit of the model.

The screening policy assumed would result in 1 600 annual deaths prevented out of the potential 13 600 deaths in the Nordic countries in 1995, corresponding to 11% of the deaths from the three primary sites. Only after the year 2010 will the ultimate effect of such a screening policy have as full an effect and in 2013–2017 the annual number of cancer deaths prevented will be 3 900 out of 15 000 potential deaths, i.e., a 26% reduction. This is equal to 5.7% of all cancer deaths in the Nordic countries in 2013–2017 (2.0% for males and 9.7% for females).

The predicted numbers of annual deaths prevented in 2013–2017 are 1 500 for cervical cancer, 1 000 for breast cancer and 1 500 for colorectal cancer. Most (91%) of the cervical cancers can be prevented, whereas the proportion of breast cancer deaths (18%) and colorectal cancer deaths (18%) prevented will be much smaller.

Costs of the screening programmes were estimated taking into consideration the direct costs of screening and savings from advanced disease treatment and terminal care. The total cost of screening for cervical, breast and colorectal cancer in the Nordic countries in the year 2010 is estimated to be $111 m. Cervical cancer screening is estimated to save $17 m yearly in the period 2008–2012. Screening for cervical cancer is approaching a phase when both the effect and costs are relatively stable and it was estimated to be cost-saving. The effect of screening for breast and colorectal cancers is expected to become apparent gradually during the predicted period due to the increasing number (and percentage) of patients diagnosed by screening. When the screening programmes are assumed to achieve the optimal effect, the reduction in mortality will increase and treatment costs fall, resulting in a substantial decrease in the cost-effectiveness ratio. In the last considered period (2008–2012) the costs per life year gained (breast cancer $15 400, colorectal cancer $5 700) are approximately one half of those at the onset of screening. The differences in the costs per LYG were relatively small between the Nordic countries and mainly dependent on the differences in baseline risk of cancer. The total cost of the three screening programmes was estimated at $4 400 per life years gained in the year 2010.

The impact of mass-screening on the quality of life at population level was estimated including the psychological consequences of screening tests, adverse effect of false positives and the advantages for those who would avoid radical treatment and advanced stage disease. The reduction in the number of life years gained (LYG) after adjustment for quality of life (QALYG) was relatively small. Not all the life years gained are of good quality and

the prolongation of life will not take place without medical cost. The costs due to ill health during the life years gained were not estimated. Instead, a further adjustment for senility during the life years gained was estimated and adjusted for. Senility adjustment had a greater effect on LYG than the traditional adjustment for quality of life. The difference between quality- and dementia-adjusted LYG is small in men, due to the fact that men spend a shorter period of their remaining life in dementia, partly due to the shorter life expectancy. The life years gained due to screening after adjusting both for the traditional quality of life and for dementia are called good quality life years gained (GQLYG). The total number of GQLYG in the year 2010 was 18 500 instead of 25 400 life years gained.

Finally, cost-utility analyses were performed. The estimated costs per GQLYG were $18 700 for breast cancer and $6 700 for colorectal cancer screening in the period 2008–2012. The savings per GQLYG were $2 000 for cervical cancer.

Two screening programmes are run in most of the Nordic countries as organized public health policy, screening for cervical cancer and screening for breast cancer. Screening based on the PAP-smear is inexpensive and effective in reducing cervical cancer mortality. Its positive and negative effects on quality of life are relatively small. Mammography is a more expensive technology, screening is more intensive (with shorter intervals between the rounds), and the effect in deaths prevented and in reducing mortality is smaller than that of screening for cervical cancer. Screening for colorectal cancer may occupy an intermediate position even if experience is limited. Compared to cancer prevention or treatment of cancer, the effect of screening may seem modest in total cancer control (5.7% of all cancer deaths). However, the effectiveness is tried and tested, whereas many of the health service activities have never been subjected to rigorous scientific evaluation. Any screening programme will have an impact on length of life, quality of life and cost. Any of these components may be a basis of decision on whether to screen or not to screen. Unfortunately, the effects (on length, quality, cost) may be contradictory. The relative importance of these components cannot be scientifically proven. Therefore, there is no unique combination i.e. relative weighting or utilities which would be inevitably true or correct. Therefore, there is neither a scientific proof to support the decision whether to run or not to run an organized programme but value judgements are also needed in deciding whether to screen or not to screen for cancer.

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Appendix 1. Breast cancer

Appendix 1A

Observed age-specific and age-adjusted ('world standard' population) mortality rates per 100 000 by calendar period

Country/ Period	30–34	35–39	40–44	45–49	50–54	55–59	60–64	65–69	70–74	75–79	80–84	85+	WS
Denmark													
1953–57	3.5	10.5	25.2	41.7	62.6	71.3	87.4	105.8	129.3	177.6	232.3	265.0	24.4
1958–62	3.4	10.0	24.5	41.2	61.6	70.1	81.4	108.8	123.0	176.9	233.3	347.4	24.3
1963–67	5.4	12.8	23.4	40.6	61.6	78.6	87.1	103.2	132.4	176.9	201.2	281.1	24.6
1968–72	5.6	13.4	28.2	47.7	67.6	82.9	94.2	103.7	130.5	154.9	194.7	273.8	25.8
1973–77	6.1	12.6	28.4	46.7	70.0	85.1	99.2	105.5	128.2	153.9	190.7	271.0	26.1
1978–82	5.0	10.9	25.1	41.3	63.5	85.6	100.0	100.3	135.3	154.1	198.5	293.7	25.3
1983–87	4.4	11.0	25.3	48.4	75.4	91.5	101.8	117.0	137.8	161.4	206.1	316.9	27.3
1988–92	4.0	12.9	27.9	42.7	70.6	98.4	103.0	125.5	145.8	167.7	203.3	295.1	27.7
Finland													
1953–57	2.8	7.3	15.6	28.2	38.0	33.5	47.1	61.7	61.2	76.6	88.6	124.2	13.3
1958–62	2.5	9.2	16.8	25.5	38.6	42.6	46.9	64.4	66.9	74.5	88.4	114.0	13.8
1963–67	3.0	7.3	14.3	30.6	37.1	45.5	49.6	52.8	73.4	88.5	102.4	181.4	14.3
1968–72	3.3	8.5	16.2	25.8	39.3	53.3	57.3	51.9	68.0	90.8	116.6	150.4	14.8
1973–77	3.0	8.4	15.8	25.9	40.6	51.4	56.5	73.1	70.5	80.3	132.8	171.0	15.5
1978–82	3.5	7.8	16.8	30.7	38.3	48.6	54.1	60.2	81.2	86.1	110.8	184.0	15.3
1983–87	3.2	8.2	15.6	27.9	41.7	50.6	61.2	64.8	87.8	112.5	134.0	183.5	16.3
1988–92	2.9	9.5	17.7	36.8	46.1	49.7	64.3	71.2	77.4	101.9	119.8	179.4	17.1
Iceland													
1958–62		8.0	29.0	46.0	81.0	68.0	87.0	78.0	39.0	104.0	153.0	125.0	21.5
1963–67		11.0	27.0	47.0	70.0	84.0	30.0	80.0	95.0	96.0	128.0	211.0	20.4
1968–72		11.0	29.0	31.0	44.0	96.0	60.0	115.0	149.0	38.0	172.0	180.0	22.1
1973–77		7.0	36.0	15.0	56.0	76.0	60.0	35.0	120.0	71.0	156.0	92.0	18.0
1978–82		16.0	19.0	36.0	34.0	73.0	65.0	85.0	90.0	98.0	115.0	167.0	18.5
1983–87		20.0	19.0	45.0	44.0	80.0	67.0	84.0	99.0	121.0	170.0	219.0	21.2
1988–92		17.0	20.0	53.0	42.0	105.0	94.0	80.0	124.0	123.0	136.0	150.0	23.1
Norway													
1963–67	2.4	9.2	18.2	32.0	42.0	58.7	64.2	70.2	87.6	102.1	124.8	186.3	17.2
1968–72	5.2	9.6	17.3	31.1	47.0	61.6	70.7	76.0	91.6	106.6	128.2	171.4	18.1
1973–77	5.5	7.6	17.1	28.4	47.0	61.6	75.6	73.3	89.8	107.1	129.4	182.1	18.0
1978–82	2.9	8.3	17.6	24.4	45.5	59.2	78.7	81.4	102.6	121.2	144.1	175.7	18.3
1983–87	2.9	10.1	18.8	29.9	40.8	57.2	69.0	78.5	97.7	120.0	152.6	201.5	18.1
1988–92	3.4	8.9	20.5	34.1	43.9	58.4	67.8	76.9	104.0	122.0	158.0	225.6	18.8
Sweden													
1963–67	2.2	7.8	17.6	31.2	50.1	65.2	71.3	82.5	94.1	118.0	140.3	188.1	18.7
1968–72	2.6	8.5	17.2	31.3	49.7	66.9	71.1	79.1	104.8	130.6	161.8	201.7	19.2
1973–77	4.8	7.3	20.7	29.9	49.0	61.7	71.9	87.6	102.9	130.6	161.1	245.0	19.6
1978–82	3.0	9.0	15.7	30.7	42.3	59.8	71.1	83.2	100.9	116.6	161.6	218.9	18.4
1983–87	3.9	9.1	17.0	27.9	43.9	62.2	69.1	77.1	95.0	111.4	134.8	185.4	17.8
1988–92	2.7	10.9	18.7	33.0	42.7	56.2	68.2	75.3	94.1	110.5	137.0	180.3	17.9

Appendix 1B

Predicted age-specific and age-adjusted ('world standard' population) mortality rates per 100 000 for the period 1988– 2017 in the situation without screening

Country/ Period	30–34	35–39	40–44	45–49	50–54	55–59	60–64	65–69	70–74	75–79	80–84	85+	WS
Denmark													
1993–97	5.3	12.0	26.9	44.7	65.3	92.0	110.7	118.4	151.8	175.5	212.0	311.4	27.6
1998–02	5.3	12.0	26.8	45.0	68.0	85.2	107.2	126.0	149.9	182.7	225.3	318.8	27.7
2003–07	5.3	12.0	26.8	44.9	68.4	88.9	99.3	122.1	159.6	180.4	234.6	338.8	27.8
2008–12	5.3	12.0	26.8	44.9	68.3	89.4	103.6	113.1	154.6	192.0	231.6	352.8	27.8
2013–17	5.3	12.0	26.8	44.9	68.3	89.2	104.2	117.9	143.2	186.0	246.5	348.2	27.7

Appendix 1B (continued)

Country/ Period	30–34	35–39	40–44	45–49	50–54	55–59	60–64	65–69	70–74	75–79	80–84	85+	WS
Finland													
1988–92	3.2	8.6	16.8	27.3	41.5	52.8	56.7	68.0	84.8	104.7	148.8	190.1	16.3
1993–97	3.3	8.7	17.1	29.4	39.5	51.8	61.4	66.4	85.6	106.6	145.5	224.3	16.6
1998–02	3.3	8.9	17.2	29.9	42.4	49.3	60.3	71.9	83.6	107.7	148.1	219.3	16.8
2003–07	3.4	9.0	17.6	30.0	43.2	53.0	57.4	70.7	90.5	105.0	149.6	223.2	17.0
2008–12	3.4	9.1	17.7	30.7	43.5	54.0	61.7	67.2	89.0	113.8	146.0	225.5	17.2
2013–17	3.4	9.1	17.9	31.0	44.3	54.3	62.8	72.3	84.6	111.9	158.2	220.0	17.5
Iceland													
1993–97		13.6	25.0	39.1	51.3	83.8	67.7	79.4	105.3	95.0	146.9	167.0	20.3
1998–02		13.6	25.0	39.1	51.3	83.8	67.7	79.4	105.3	95.0	146.9	167.0	20.3
2003–07		13.6	25.0	39.1	51.3	83.8	67.7	79.4	105.3	95.0	146.9	167.0	20.3
2008–12		13.6	25.0	39.1	51.3	83.8	67.7	79.4	105.3	95.0	146.9	167.0	20.3
2013–17		13.6	25.0	39.1	51.3	83.8	67.7	79.4	105.3	95.0	146.9	167.0	20.3
Norway													
1993–97	3.4	8.2	17.0	32.7	49.2	59.2	65.8	74.6	99.6	129.1	160.5	221.8	18.6
1998–02	3.4	8.2	16.5	28.2	48.9	65.9	70.4	71.2	96.3	123.0	166.7	226.9	18.5
2003–07	3.4	8.2	16.5	27.4	42.2	65.4	78.4	76.1	91.9	119.0	158.9	235.6	18.5
2008–12	3.4	8.2	16.5	27.5	41.1	56.4	77.4	84.7	98.2	113.4	153.7	224.6	18.3
Sweden													
1993–97	3.2	8.7	22.9	32.6	49.6	54.2	65.6	73.9	90.3	108.1	138.8	187.3	18.0
1998–02	3.2	8.7	18.6	40.2	49.6	64.9	61.1	73.9	88.5	106.0	134.7	187.3	18.4
2003–07	3.2	8.7	18.6	32.6	61.1	64.9	73.2	68.9	88.5	103.8	132.0	181.8	18.8
2008–12	3.2	8.7	18.6	32.6	49.6	80.1	73.2	82.5	82.5	103.8	129.4	178.2	19.1
2013–17	3.2	8.7	18.6	32.6	49.6	64.9	90.3	82.5	98.8	96.8	129.4	174.7	19.4

Appendix 1C

Predicted age-specific and age-adjusted ('world standard' population) mortality rates per 100 000 for the period 1988–2017 if women aged 50–69 years are screened by mammography every second year

Country/ Period	30–34	35–39	40–44	45–49	50–54	55–59	60–64	65–69	70–74	75–79	80–84	85+	WS
Denmark													
1988–92	4.0	12.9	27.9	42.7	64.7	90.1	94.4	115.0	145.8	167.7	203.3	295.1	26.4
1993–97	5.3	12.0	26.9	44.7	59.8	76.0	91.4	97.8	136.6	175.5	212.0	311.4	25.0
1998–02	5.3	12.0	26.8	45.0	62.3	70.4	77.0	90.5	119.9	164.4	225.3	318.8	23.8
2003–07	5.3	12.0	26.8	44.9	62.6	73.4	71.3	85.5	111.7	144.3	211.1	338.8	23.2
2008–12	5.3	12.0	26.8	44.9	62.6	73.8	74.4	79.2	108.2	134.4	208.4	352.8	23.2
2013–17	5.3	12.0	26.8	44.9	62.6	73.7	74.8	82.5	100.2	130.2	197.2	348.2	22.9
Finland													
1988–92	3.2	8.6	16.8	27.3	38.0	48.3	51.9	62.3	84.8	104.7	148.8	190.1	15.6
1993–97	3.3	8.7	17.1	29.4	36.2	42.8	50.7	54.8	77.5	106.6	145.5	224.3	15.2
1998–02	3.3	8.9	17.2	29.9	38.9	40.7	43.3	51.6	67.0	96.9	148.1	219.3	14.6
2003–07	3.4	9.0	17.6	30.0	39.6	43.8	41.2	49.5	63.4	84.0	134.7	223.2	14.4
2008–12	3.4	9.0	17.7	30.7	39.8	44.6	44.3	47.0	62.3	79.7	131.4	225.5	14.4
2013–17	3.4	9.1	17.9	31.0	40.6	44.8	45.1	50.6	59.2	78.3	126.5	220.0	14.5
Iceland													
1988–92		17.0	20.0	53.0	38.5	96.2	86.1	73.3	124.0	123.0	136.0	150.0	22.0
1993–97		13.6	25.0	39.1	47.0	69.2	55.9	65.6	94.8	95.0	146.9	167.0	18.4
1998–02		13.6	25.0	39.1	47.0	69.2	48.6	57.0	84.2	85.5	146.9	167.0	17.6
2003–07		13.6	25.0	39.1	47.0	69.2	48.6	55.6	73.7	76.0	132.2	167.0	17.1
2008–12		13.6	25.0	39.1	47.0	69.2	48.6	55.6	73.7	66.5	132.2	167.0	17.0
2013–17		13.6	25.0	39.1	47.0	69.2	48.6	55.6	73.7	66.5	117.5	167.0	17.0
Norway													
1988–92	3.4	8.9	20.5	34.1	40.2	53.5	62.1	70.4	104.0	122.0	158.0	225.6	18.0
1993–97	3.4	8.2	17.0	32.7	45.1	48.9	54.4	61.6	89.6	129.1	160.5	221.8	17.0
1998–02	3.4	8.2	16.5	28.2	44.8	54.4	50.6	51.1	77.0	110.7	166.7	226.9	16.0
2003–07	3.4	8.2	16.5	27.4	38.7	54.0	56.3	53.3	64.3	95.2	143.0	235.6	15.4
2008–12	3.4	8.2	16.5	27.5	37.6	46.6	55.6	59.3	68.7	79.4	138.3	224.6	15.1

Appendix 1C (continued)

Country/ Period	30–34	35–39	40–44	45–49	50–54	55–59	60–64	65–69	70–74	75–79	80–84	85+	WS
Sweden													
1988–92	2.7	10.9	18.7	33.0	39.1	51.5	62.5	69.0	94.1	110.5	137.0	180.3	17.1
1993–97	3.2	8.7	22.9	32.6	45.4	44.8	54.2	61.2	81.2	108.1	138.8	187.3	16.4
1998–02	3.2	8.7	18.6	40.2	45.4	53.6	43.9	53.1	70.8	95.4	134.7	187.3	16.0
2003–07	3.2	8.7	18.6	32.6	56.0	53.6	52.5	48.2	61.9	83.1	118.8	181.8	16.0
2008–12	3.2	8.7	18.6	32.6	45.4	66.1	52.5	57.8	57.8	72.7	116.5	178.2	16.0
2013–17	3.2	8.7	18.6	32.6	45.4	53.6	64.8	57.8	69.2	67.8	103.5	174.7	16.0

Appendix 2. Cervical cancer

Appendix 2A

Observed and predicted (assuming the observed rates) age-specific and age-adjusted ('world standard' population) mortality rates per 100 000 by calendar period

Country/ Period	25–29	30–34	35–39	40–44	45–49	50–54	55–59	60–64	65–69	70–74	75–79	80–84	85+	WS
Denmark														
1953–57	4.2	9.7	14.0	20.8	27.6	25.3	22.9	23.4	23.6	28.6	21.1	33.6	16.1	9.5
1958–62	3.1	8.5	18.0	24.1	27.0	32.7	29.9	28.2	30.0	27.2	24.5	35.2	31.4	10.9
1963–67	2.0	9.0	17.5	26.4	32.3	30.3	29.3	28.8	28.9	30.7	26.8	24.8	31.6	11.1
1968–72	1.9	6.3	14.0	20.3	28.2	32.6	26.5	27.0	26.1	28.2	29.8	25.5	36.6	10.0
1973–77	1.6	5.4	8.3	12.2	21.0	24.1	27.4	30.9	27.8	31.1	27.0	29.9	30.6	8.5
1978–82	1.5	4.9	5.5	9.7	18.0	20.7	23.6	30.3	27.7	28.1	32.6	35.9	31.1	7.7
1983–87	1.9	4.3	3.7	7.2	9.4	12.5	21.0	25.1	23.7	25.6	34.4	29.0	32.5	6.0
1988–92	1.0	2.1	4.0	6.4	8.5	11.0	17.1	19.5	25.9	28.0	28.2	33.7	26.3	5.3
1993–97	0.9	2.4	3.1	5.2	6.6	7.5	9.5	15.3	18.9	24.5	30.8	31.0	31.1	4.1
1998–02	0.7	2.0	2.7	3.7	5.9	6.1	7.2	9.8	14.2	19.7	26.7	31.9	29.8	3.3
2003–07	0.6	1.7	2.3	3.2	4.3	5.5	5.9	7.4	9.1	14.8	21.5	27.7	30.7	2.6
2008–12	0.5	1.4	1.9	2.7	3.7	4.0	5.3	6.0	6.9	9.5	16.2	22.3	26.6	2.1
2013–17	0.4	1.1	1.5	2.2	3.1	3.4	3.8	5.4	5.6	7.1	10.4	16.7	21.4	1.7
Finland														
1953–57	1.0	4.2	10.1	10.4	16.5	21.2	21.4	20.0	16.5	26.5	19.5	22.1	12.1	6.7
1958–62	0.6	2.4	7.1	13.8	13.4	20.8	20.7	19.0	23.3	28.6	28.1	30.5	33.2	6.8
1963–67	0.1	3.3	3.8	9.7	14.6	20.5	22.1	22.0	21.9	28.2	28.2	38.8	34.6	6.6
1968–72	0.4	1.1	3.5	5.1	10.9	14.8	17.3	20.8	18.4	20.4	27.9	31.4	29.0	5.1
1973–77	0.3	0.8	1.2	1.5	4.9	7.3	11.1	14.0	17.7	18.8	17.1	29.0	34.5	3.3
1978–82	0.3	0.6	1.2	1.7	3.4	4.4	9.8	11.5	13.1	18.1	17.7	21.1	30.7	2.7
1983–87	0.3	0.4	0.8	0.9	2.2	3.7	3.4	7.2	11.4	17.3	21.1	18.8	23.4	2.0
1988–92	0.2	0.8	1.2	1.4	1.8	2.9	2.4	4.5	8.8	13.0	15.9	24.5	27.3	1.7
1993–97	0.3	0.6	1.1	1.3	1.4	1.4	1.9	2.6	3.9	8.4	12.2	17.7	26.3	1.2
1998–02	0.3	0.6	1.1	1.7	1.4	1.3	1.3	1.8	2.5	4.3	8.3	13.7	20.5	0.9
2003–07	0.3	0.6	1.1	1.7	1.4	1.2	1.2	1.2	1.7	2.8	4.2	9.3	15.9	0.7
2008–12	0.3	0.6	1.1	1.7	1.4	1.2	1.1	1.1	1.2	1.9	2.7	4.7	10.7	0.6
2013–17	0.3	0.6	1.1	1.7	1.4	1.2	1.1	1.0	1.0	1.3	1.9	3.0	5.5	0.5
Iceland														
1958–62			8.0	21.0	23.0	10.0	17.0	0.0	42.0	10.0	0.0	44.0	31.0	6.3
1963–67			4.0	34.0	13.0	9.0	26.0	6.0	40.0	16.0	12.0	0.0	30.0	7.2
1968–72			11.0	14.0	16.0	31.0	38.0	5.0	32.0	37.0	38.0	17.0	0.0	8.3
1973–77			7.0	11.0	15.0	4.0	13.0	15.0	23.0	21.0	18.0	13.0	23.0	4.8
1978–82			0.0	0.0	11.0	7.0	12.0	14.0	11.0	6.0	25.0	12.0	0.0	3.0
1983–87			5.0	3.0	11.0	4.0	23.0	4.0	25.0	0.0	8.0	0.0	12.0	3.8
1988–92			4.0	3.0	6.0	4.0	4.0	4.0	9.0	11.0	34.0	10.0	32.0	2.8
1993–97			2.9	4.9	4.3	2.1	6.7	2.9	13.6	7.9	18.8	9.2	9.9	2.1
1998–02			2.9	4.9	4.4	2.6	3.4	2.2	8.8	7.2	12.7	8.6	12.4	1.7
2003–07			2.9	4.9	4.4	2.7	4.3	1.1	6.5	4.7	11.6	5.8	11.5	1.6
2008–12			2.9	4.9	4.4	2.7	4.4	1.4	3.3	3.4	7.5	5.3	7.8	1.4
2013–17			2.9	4.9	4.4	2.7	4.4	1.4	4.1	1.7	5.5	3.4	7.1	1.4

Appendix 2A (continued)

Country/ Period	25–29	30–34	35–39	40–44	45–49	50–54	55–59	60–64	65–69	70–74	75–79	80–84	85+	WS
Norway														
1963–67	1.2	3.0	9.6	10.6	15.0	14.4	17.9	18.2	14.5	22.1	17.9	21.0	25.1	5.8
1968–72	1.8	2.4	7.3	10.6	15.9	16.1	16.8	15.2	20.7	22.3	21.8	20.5	11.2	5.8
1973–77	0.9	3.5	6.2	8.4	9.9	14.0	19.5	17.3	18.0	20.7	23.5	19.2	20.7	5.3
1978–82	1.2	2.3	4.8	8.8	11.1	14.8	16.5	18.0	19.6	20.0	24.4	21.9	25.7	5.3
1983–87	1.4	2.8	5.0	5.8	8.0	10.2	10.4	15.3	16.1	21.7	21.0	19.8	25.1	4.3
1988–92	0.9	3.5	4.5	4.9	10.2	11.2	9.7	15.3	16.7	16.8	19.8	19.3	21.7	4.3
1993–97	1.0	2.3	4.6	5.8	8.0	9.2	9.9	10.9	13.7	17.6	20.1	19.3	20.8	3.8
1998–02	0.9	2.0	4.2	5.7	7.3	8.4	9.2	10.1	11.4	14.5	18.8	18.2	21.7	3.4
2003–07	0.9	1.9	3.8	5.1	7.1	7.7	8.4	9.4	10.5	12.1	15.5	17.1	20.5	3.1
2008–12	0.8	1.9	3.6	4.6	6.4	7.4	7.7	8.5	9.8	11.2	12.9	14.1	19.2	2.9
Sweden														
1963–67	0.8	3.7	8.5	12.0	16.4	16.1	15.7	15.7	12.7	13.9	18.6	15.7	12.8	5.6
1968–72	1.4	2.9	6.2	11.8	13.8	15.3	18.4	16.6	14.9	18.4	18.3	18.2	13.0	5.5
1973–77	0.8	2.1	3.9	7.3	9.4	10.0	13.9	13.2	17.6	19.1	20.0	19.4	25.0	4.3
1978–82	0.9	2.6	2.5	4.3	5.5	8.0	10.9	14.1	16.8	15.8	15.9	19.7	18.0	3.5
1983–87	1.1	1.8	2.7	3.1	6.1	5.7	8.3	10.9	12.9	14.7	15.2	16.2	12.9	2.9
1988–92	1.0	1.6	2.9	3.8	2.8	4.1	5.4	5.8	10.5	11.3	15.5	14.2	13.7	2.2
1993–97	0.9	1.8	2.3	3.3	3.3	2.4	3.7	4.5	7.1	9.5	12.5	14.2	13.8	1.8
1998–02	0.9	1.8	2.4	2.9	3.0	2.7	2.3	3.3	4.7	6.8	9.5	11.7	13.0	1.5
2003–07	0.9	1.8	2.4	3.0	2.6	2.4	2.6	2.1	3.4	4.5	6.8	9.0	10.7	1.3
2008–12	0.9	1.8	2.4	3.0	2.7	2.1	2.3	2.3	2.1	3.3	4.5	6.4	8.2	1.2
2013–17	0.9	1.8	2.4	3.0	2.7	2.2	2.0	2.1	2.4	2.0	3.3	4.2	5.8	1.1

Appendix 2B

Predicted age-specific and age-adjusted ('world standard' population) mortality rates per 100 000 for the period 1968–2017 without screening

Country/ Period	25–29	30–34	35–39	40–44	45–49	50–54	55–59	60–64	65–69	70–74	75–79	80–84	85+	WS
Denmark														
1968–72	3.2	8.2	15.8	27.1	36.9	35.4	30.6	34.0	34.0	33.9	28.2	30.5	29.6	12.2
1973–77	3.0	7.8	15.1	25.0	36.4	41.1	35.5	33.5	38.9	38.5	30.2	34.8	30.6	12.7
1978–82	2.9	7.4	14.3	23.9	33.6	40.6	41.2	38.9	38.3	43.9	34.3	37.2	35.0	13.0
1983–87	2.8	7.0	13.6	22.7	32.2	37.4	40.7	45.1	44.5	43.4	39.1	42.3	37.4	13.1
1988–92	2.6	6.7	13.0	21.6	30.6	35.8	37.6	44.6	51.7	50.4	38.6	48.3	42.5	13.0
1993–97	2.5	6.9	12.8	20.6	29.2	34.1	35.5	41.2	51.2	58.4	40.0	47.6	48.5	12.7
1998–02	2.5	6.4	12.7	19.9	27.7	32.4	34.2	38.9	47.2	57.9	52.0	49.4	47.8	12.3
2003–07	2.5	6.4	11.7	20.1	26.8	30.9	32.6	37.5	44.6	53.4	51.5	64.2	49.6	11.9
2008–12	2.5	6.4	11.7	18.6	27.1	29.9	31.0	35.7	43.0	50.4	47.5	63.6	64.4	11.6
2013–17	2.5	6.4	11.7	18.6	25.0	30.2	30.0	34.0	40.9	48.6	44.9	58.6	63.8	11.2
Finland														
1968–72	0.9	3.0	6.4	11.5	16.8	18.2	18.2	21.4	21.0	21.2	21.9	21.2	22.7	6.3
1973–77	0.8	2.9	6.1	10.6	16.6	21.1	21.1	21.2	23.9	24.1	23.5	24.2	23.5	6.7
1978–82	0.8	2.7	5.8	10.1	15.3	20.9	24.5	24.6	23.6	27.5	26.6	25.9	26.8	6.9
1983–87	0.8	2.6	5.6	9.6	14.6	19.3	24.2	28.5	27.4	27.2	30.4	29.4	28.6	7.0
1988–92	0.7	2.5	5.3	9.1	13.9	18.4	22.4	28.2	31.8	31.5	30.0	33.6	32.5	7.1
1993–97	0.7	2.4	4.9	8.8	13.1	17.5	21.4	26.0	31.4	36.6	34.9	33.3	37.3	6.9
1998–02	0.7	2.3	4.7	8.1	12.6	16.5	20.3	24.8	29.0	36.2	40.4	38.6	36.8	6.7
2003–07	0.7	2.3	4.7	7.8	11.7	15.9	19.3	23.6	27.7	33.4	40.0	44.7	42.7	6.5
2008–12	0.7	2.3	4.6	7.8	11.3	14.8	18.5	22.4	26.3	31.9	36.9	44.3	49.6	6.2
2013–17	0.7	2.3	4.6	7.7	11.2	14.2	17.2	21.5	24.9	30.3	35.3	40.9	49.1	6.0
Iceland														
1968–72			8.3	10.6	12.9	17.1	21.1	21.1	22.2	24.9	26.6	28.6	32.7	6.2
1973–77			7.9	10.1	12.3	15.8	20.9	24.5	25.8	24.6	30.4	32.5	35.0	6.3
1978–82			7.5	9.6	11.7	15.1	19.3	24.2	30.0	28.5	30.0	37.2	39.7	6.4
1983–87			7.1	9.1	11.2	14.3	18.4	22.4	29.6	33.1	34.9	36.7	45.4	6.3

Appendix 2B (continued)

Country/ Period	25–29	30–34	35–39	40–44	45–49	50–54	55–59	60–64	65–69	70–74	75–79	80–84	85+	WS
1988–92			6.8	8.7	10.6	13.6	17.5	21.4	27.3	32.7	40.4	42.6	44.8	6.1
1993–97			6.4	8.9	9.2	12.7	19.0	20.2	25.3	29.5	43.4	47.1	57.1	6.0
1998–02			6.4	8.8	9.3	12.4	15.8	21.0	25.0	27.7	39.3	46.8	68.6	5.8
2003–07			6.4	8.8	9.2	12.6	15.4	17.5	26.0	27.4	37.0	42.4	68.2	5.7
2008–12			6.4	8.8	9.2	12.4	15.6	17.0	21.6	28.5	36.6	39.9	61.7	5.5
2013–17			6.4	8.8	9.2	12.4	15.4	17.3	21.1	23.7	38.0	39.5	58.1	5.4
Norway														
1968–72	1.4	3.9	8.7	10.9	17.1	16.8	18.8	19.2	17.2	24.4	18.9	21.2	23.6	6.3
1973–77	1.4	3.7	8.3	10.1	16.9	19.5	21.8	19.0	19.6	27.7	20.2	24.2	24.4	6.6
1978–82	1.3	3.5	7.9	9.6	15.6	19.3	25.3	22.0	19.3	31.7	22.9	25.9	27.9	6.9
1983–87	1.2	3.4	7.5	9.1	14.9	17.8	25.0	25.5	22.4	31.3	26.2	29.4	29.8	7.0
1988–92	1.2	3.2	7.1	8.7	14.2	17.0	23.1	25.2	26.1	36.3	25.8	33.6	33.9	7.0
1993–97	1.1	3.0	6.7	8.2	13.4	16.2	22.0	23.3	25.8	42.0	29.9	33.2	38.6	6.9
1998–02	1.1	3.0	6.3	7.8	12.7	15.3	20.8	22.3	23.8	41.6	34.7	38.6	38.1	6.6
2003–07	1.1	2.9	6.2	7.3	12.0	14.5	19.7	21.2	22.8	38.4	34.3	44.7	44.3	6.4
2008–12	1.1	2.9	6.1	7.2	11.2	13.7	18.7	20.0	21.6	36.7	31.7	44.3	51.3	6.1
Sweden														
1968–72	1.2	3.4	7.7	12.3	18.7	18.7	16.3	18.5	14.9	15.4	19.6	19.2	12.0	6.1
1973–77	1.1	3.2	7.3	11.3	18.5	21.8	18.9	18.2	17.0	17.5	21.0	21.9	12.4	6.3
1978–82	1.1	3.0	7.0	10.8	17.1	21.5	22.0	21.1	16.8	20.0	23.9	23.5	14.1	6.5
1983–87	1.0	2.9	6.6	10.3	16.3	19.8	21.7	24.5	19.5	19.7	27.3	26.6	15.1	6.6
1988–92	1.0	2.8	6.3	9.8	15.5	19.0	20.0	24.2	22.6	22.9	26.9	30.4	17.2	6.5
1993–97	0.9	2.6	6.1	9.4	14.8	18.1	19.1	22.4	22.4	26.6	31.2	30.0	19.5	6.4
1998–02	0.9	2.6	5.8	9.0	14.1	17.2	18.3	21.4	20.6	26.3	36.2	34.8	19.3	6.2
2003–07	0.9	2.5	5.6	8.5	13.5	16.4	17.3	20.4	19.7	24.3	35.9	40.4	22.3	6.0
2008–12	0.9	2.5	5.6	8.3	12.8	15.7	16.6	19.4	18.8	23.1	33.1	40.0	25.9	5.7
2013–17	0.9	2.5	5.5	8.2	12.4	14.8	15.8	18.5	17.9	22.1	31.6	36.9	25.6	5.5

Appendix 2C

Predicted age-specific and age-adjusted ('world standard' population) mortality rates per 100 000 for the period 1968–2012 if the Finnish screening policy had been applied

Country/ Period	25–29	30–34	35–39	40–44	45–49	50–54	55–59	60–64	65–69	70–74	75–79	80–84	85+	WS
Denmark														
1968–72	0.3	2.7	12.2	11.0	23.2	20.4	21.4	25.3	22.8	29.5	24.9	19.6	26.5	7.6
1973–77	0.3	1.9	8.5	7.0	11.9	13.8	16.6	19.8	24.6	20.8	25.3	18.8	32.5	5.6
1978–82	0.3	1.6	5.7	4.9	7.6	7.0	11.2	15.3	19.2	22.4	17.8	19.1	31.1	4.1
1983–87	0.4	1.6	5.1	3.3	5.3	4.5	5.7	10.4	14.8	17.5	19.2	13.5	31.6	3.0
1988–92	0.2	2.1	4.8	2.9	3.6	3.1	3.7	5.3	10.0	13.6	15.0	14.6	22.3	2.2
1993–97	0.3	1.6	4.9	2.8	3.2	2.1	2.6	3.4	5.2	9.2	11.6	11.3	24.0	1.8
1998–02	0.3	1.6	4.9	2.8	3.0	1.9	1.8	2.4	3.3	4.7	7.9	8.8	18.7	1.4
2003–07	0.3	1.6	4.9	2.8	3.1	1.8	1.6	1.6	2.3	3.0	4.0	6.0	14.6	1.3
2008–12	0.3	1.6	4.9	2.8	3.1	1.9	1.5	1.4	1.6	2.1	2.6	3.0	9.9	1.2
2013–17	0.3	1.6	4.9	2.8	3.1	1.9	1.5	1.4	1.4	1.4	1.8	1.9	5.0	1.1
Finland														
1968–72	0.4	1.1	3.5	5.1	10.9	14.8	17.3	20.8	18.4	20.4	27.9	31.4	29.0	5.1
1973–77	0.3	0.8	1.2	1.5	4.9	7.3	11.1	14.0	17.7	18.8	17.1	29.0	34.5	3.3
1978–82	0.3	0.6	1.2	1.7	3.4	4.4	9.8	11.5	13.1	18.1	17.7	21.1	30.7	2.7
1983–87	0.3	0.4	0.8	0.9	2.2	3.7	3.4	7.2	11.4	17.3	21.1	18.8	23.4	2.0
1988–92	0.2	0.8	1.2	1.4	1.8	2.9	2.4	4.5	8.8	13.0	15.9	24.5	27.3	1.7
1993–97	0.3	0.6	1.1	1.3	1.4	1.4	1.9	2.6	3.9	8.4	12.2	17.7	26.3	1.2
1998–02	0.3	0.6	1.1	1.7	1.4	1.3	1.3	1.8	2.5	4.3	8.3	13.7	20.5	0.9
2003–07	0.3	0.6	1.1	1.7	1.4	1.2	1.2	1.2	1.7	2.8	4.2	9.3	15.9	0.7
2008–12	0.3	0.6	1.1	1.7	1.4	1.2	1.1	1.1	1.2	1.9	2.7	4.7	10.7	0.6
2013–17	0.3	0.6	1.1	1.7	1.4	1.2	1.1	1.0	1.0	1.3	1.9	3.0	5.5	0.5

Appendix 2C (continued)

Country/ Period	25–29	30–34	35–39	40–44	45–49	50–54	55–59	60–64	65–69	70–74	75–79	80–84	85+	WS
Iceland														
1968–72			3.2	2.0	3.5	3.4	6.9	9.7	9.6	16.2	11.9	16.2	24.7	2.3
1973–77			2.8	1.3	2.5	2.1	3.5	6.5	7.5	12.6	12.9	11.4	25.1	1.7
1978–82			2.7	1.2	1.7	1.5	2.2	3.3	5.0	9.8	10.0	12.3	17.7	1.2
1983–87			3.7	1.1	1.5	1.0	1.6	2.1	2.6	6.6	7.8	9.6	19.1	1.0
1988–92			2.1	1.5	1.4	0.9	1.1	1.5	1.6	3.4	5.3	7.4	14.9	0.7
1993–97			2.1	0.4	0.3	0.1	0.1	0.1	0.5	3.1	3.6	5.3	12.8	0.4
1998–02			2.1	0.4	0.1	0.1	0.1	0.1	0.1	0.7	2.1	4.4	7.4	0.3
2003–07			2.1	0.4	0.1	0.1	0.1	0.1	0.1	0.1	0.4	2.5	6.1	0.2
2008–12			2.1	0.4	0.1	0.1	0.1	0.1	0.1	0.1	0.1	0.5	3.5	0.2
2013–17			2.1	0.4	0.1	0.1	0.1	0.1	0.1	0.1	0.1	0.1	0.7	0.2
Norway														
1968–72	0.3	0.9	6.7	4.4	10.8	9.7	13.1	16.0	11.4	21.2	16.6	16.6	21.0	4.2
1973–77	0.3	0.6	4.7	2.8	5.5	6.6	10.1	12.5	12.3	15.0	16.9	15.9	25.8	3.1
1978–82	0.3	0.6	3.2	2.0	3.5	3.4	6.9	9.7	9.6	16.2	11.9	16.2	24.7	2.3
1983–87	0.4	0.5	2.8	1.3	2.5	2.1	3.5	6.5	7.5	12.6	12.9	11.4	25.1	1.7
1988–92	0.2	0.7	2.7	1.2	1.7	1.5	2.2	3.3	5.0	9.8	10.0	12.3	17.7	1.3
1993–97	0.3	0.5	4.0	1.1	1.4	1.0	1.5	2.1	2.5	6.6	7.8	9.6	19.2	1.1
1998–02	0.3	0.6	2.6	1.6	1.4	0.9	1.0	1.5	1.6	3.3	5.3	7.5	14.9	0.8
2003–07	0.3	0.6	2.9	1.1	2.0	0.8	0.9	1.0	1.1	2.1	2.7	5.1	11.6	0.7
2008–12	0.3	0.6	2.9	1.2	1.3	1.2	0.9	0.9	0.8	1.5	1.7	2.5	7.9	0.6
Sweden														
1968–72	0.3	11	5.9	5.0	11.2	10.8	11.5	13.8	10.0	13.4	17.3	12.4	29.2	3.9
1973–77	0.3	0.8	4.1	3.2	5.7	7.3	8.9	10.8	10.8	9.4	17.6	11.9	35.8	2.9
1978–82	0.3	0.7	2.8	2.2	3.7	3.7	6.0	8.4	8.4	10.2	12.4	12.1	34.2	2.2
1983–87	0.4	0.6	2.5	1.5	2.5	2.4	3.1	5.7	6.5	7.9	13.4	8.5	34.8	1.6
1988–92	0.2	0.9	2.4	1.3	1.7	1.7	2.0	2.9	4.4	6.1	10.4	9.2	24.6	1.2
1993–97	0.3	0.5	3.1	1.3	1.5	1.1	1.4	1.9	2.3	4.2	8.1	7.1	26.7	1.0
1998–02	0.3	0.7	1.7	1.7	1.4	1.0	0.9	1.3	1.5	2.1	5.5	5.6	20.8	0.8
2003–07	0.3	0.7	2.4	0.9	1.9	0.9	0.8	0.9	1.0	1.4	2.8	3.8	16.2	0.7
2008–12	0.3	0.7	2.4	1.3	1.0	1.2	0.8	0.8	0.7	0.9	1.8	1.9	11.0	0.6
2013–17	0.3	0.7	2.4	1.3	1.5	0.7	1.0	0.7	0.6	0.7	1.2	1.2	5.6	0.6

Appendix 3. Colorectal cancer, females

Appendix 3A

Observed age-specific and age-adjusted ('world standard' population) mortality rates per 100 000 by calender period

Country/ Period	30–34	35–39	40–44	45–49	50–54	55–59	60–64	65–69	70–74	75–79	80–84	85+	WS
Denmark													
1953–57	1.6	3.2	6.9	10.8	20.0	33.5	44.1	75.7	119.0	162.9	271.2	340.2	14.8
1958–62	2.2	4.2	6.3	13.2	24.8	44.7	66.4	94.4	162.0	247.2	384.5	461.2	20.0
1963–67	1.7	4.4	8.8	13.6	29.3	40.1	61.2	95.2	153.3	225.0	353.4	429.6	19.3
1968–72	1.1	3.1	8.9	14.6	29.5	41.5	65.3	90.8	138.3	203.4	304.0	394.8	18.4
1973–77	1.5	3.4	8.2	13.1	22.5	39.2	61.0	85.5	140.4	212.9	315.6	409.7	17.8
1978–82	1.1	3.1	6.7	13.8	20.0	37.4	67.0	90.6	139.0	211.2	309.2	449.6	18.1
1983–87	1.1	3.2	4.9	12.0	24.2	42.3	59.1	90.5	142.4	200.4	304.2	395.7	17.6
1988–92	1.2	2.1	5.6	13.0	22.1	38.3	62.0	84.6	144.3	199.9	258.5	392.2	17.1
Finland													
1953–57	0.9	1.5	4.5	5.3	10.6	15.1	27.5	40.8	68.3	103.2	134.0	184.8	8.2
1958–62	0.5	0.9	4.0	6.1	8.5	14.2	25.0	48.4	86.2	106.8	173.7	190.0	8.7
1963–67	0.6	1.5	3.7	6.1	9.9	16.1	27.1	48.9	92.3	130.6	165.1	226.8	9.5
1968–72	1.0	3.0	4.9	6.0	12.1	16.5	26.5	45.8	71.1	135.6	210.6	318.8	10.0
1973–77	1.1	2.2	3.6	8.1	12.9	17.4	27.2	53.7	68.5	104.9	201.6	351.7	10.1
1978–82	0.9	1.2	3.8	4.7	12.5	19.0	26.8	40.3	75.8	98.0	177.4	346.2	9.4
1983–87	0.6	1.7	3.8	7.3	9.9	16.2	26.2	45.0	74.0	110.7	160.5	282.7	9.1
1988–92	0.2	1.5	2.8	5.3	11.0	14.8	22.7	42.8	66.8	119.5	177.0	241.5	8.5

Appendix 3A (continued)

Country/ Period	30–34	35–39	40–44	45–49	50–54	55–59	60–64	65–69	70–74	75–79	80–84	85+	WS
Iceland													
1958–62					5.0	34.0	6.0	28.0	79.0	118.0	284.0	219.0	9.0
1963–67					19.0	10.0	24.0	73.0	79.0	121.0	107.0	211.0	9.8
1968–72					9.0	33.0	49.0	64.0	104.0	125.0	241.0	359.0	13.1
1973–77					16.0	18.0	40.0	76.0	85.0	142.0	182.0	301.0	11.6
1978–82					7.0	24.0	33.0	53.0	109.0	147.0	196.0	274.0	11.0
1983–87					26.0	11.0	29.0	50.0	58.0	136.0	170.0	207.0	9.7
1988–92					15.0	26.0	47.0	49.0	65.0	130.0	117.0	140.0	9.7
Norway													
1963–67	1.0	2.2	5.4	8.2	12.4	21.8	36.9	54.8	95.6	139.5	193.7	237.6	11.1
1968–72	0.6	2.8	4.7	11.6	15.6	25.8	44.3	57.0	105.8	149.8	208.4	272.8	12.5
1973–77	1.1	2.2	6.5	10.6	22.6	29.4	41.8	61.4	92.1	153.6	206.8	263.2	12.8
1978–82	1.1	3.0	7.2	11.2	15.0	32.0	48.5	71.6	109.6	150.3	249.5	356.2	14.2
1983–87	1.2	1.6	5.3	12.6	17.8	31.8	52.1	71.1	113.5	153.0	242.8	313.3	14.2
1988–92	0.8	0.9	4.9	10.0	19.5	27.3	55.6	68.9	107.5	143.5	209.2	339.0	13.7
Sweden													
1963–67	1.7	3.0	5.9	9.7	17.6	26.2	40.0	66.7	101.7	149.8	219.2	257.6	12.7
1968–72	2.0	2.2	5.6	8.3	16.6	25.6	42.3	64.2	100.0	158.0	228.9	323.8	12.9
1973–77	0.8	3.4	4.4	8.7	16.7	27.0	41.8	64.8	103.4	160.6	248.1	367.2	13.3
1978–82	0.8	1.6	4.8	9.1	13.4	29.6	40.6	60.8	95.8	141.6	213.0	323.4	12.3
1983–87	0.5	1.4	3.2	8.9	15.5	25.1	40.0	60.0	85.3	120.5	183.9	277.1	11.2
1988–92	0.7	1.9	3.4	7.8	14.3	26.8	38.5	56.6	83.6	123.8	175.8	255.1	10.9

Appendix 3B

Predicted age-specific and age-adjusted ('world standard' population) mortality rates per 100 000 by calendar period 1993–2017 without screening

Country/ Period	30–34	35–39	40–44	45–49	50–54	55–59	60–64	65–69	70–74	75–79	80–84	85+	WS
Denmark													
1993–97	1.2	2.8	5.6	10.5	21.1	35.7	60.2	88.8	135.8	212.7	302.8	378.8	17.0
1998–02	1.2	2.8	5.6	10.5	19.7	35.1	56.0	89.7	145.0	204.6	320.5	412.8	17.1
2003–07	1.2	2.8	5.6	10.5	19.7	32.8	55.1	83.5	146.5	218.5	308.2	437.0	17.0
2008–12	1.2	2.8	5.6	10.4	19.7	32.8	51.4	82.2	136.3	220.7	329.3	420.3	16.7
2013–17	1.2	2.8	5.6	10.4	19.6	32.8	51.5	76.7	134.2	205.4	332.6	449.0	16.5
Finland													
1993–97	0.7	1.4	3.1	4.9	9.6	17.1	22.8	43.9	72.4	107.0	173.4	280.4	8.8
1998–02	0.7	1.4	3.1	4.9	8.8	14.4	26.9	39.8	72.0	110.8	170.1	280.2	8.7
2003–07	0.7	1.4	3.1	4.9	8.7	13.3	22.7	46.9	65.4	110.3	176.2	274.9	8.6
2008–12	0.7	1.4	3.1	4.9	8.7	13.1	20.9	39.6	77.0	100.1	175.5	284.7	8.4
2013–17	0.7	1.4	3.1	4.9	8.7	13.1	20.5	36.5	65.0	117.9	159.3	283.6	8.2
Iceland													
1993–97					14.2	22.3	33.9	55.9	81.7	133.3	178.2	226.5	9.6
1998–02					14.2	22.3	33.9	55.9	81.7	133.3	178.2	226.5	9.6
2003–07					14.2	22.3	33.9	55.9	81.7	133.3	178.2	226.5	9.6
2008–12					14.2	22.3	33.9	55.9	81.7	133.3	178.2	226.5	9.6
2013–17					14.2	22.3	33.9	55.9	81.7	133.3	178.2	226.5	9.6
Norway													
1993–97	0.6	1.4	4.1	8.7	16.9	33.0	49.4	73.1	123.1	160.9	229.6	312.7	14.0
1998–02	0.6	1.3	3.6	7.7	14.4	29.2	56.8	71.4	123.9	181.1	246.6	329.4	14.3
2003–07	0.5	1.1	3.2	6.8	12.8	24.9	50.2	82.1	121.1	182.3	277.6	353.8	14.2
2008–12	0.4	1.0	2.9	6.1	11.4	22.2	42.8	72.6	139.2	178.2	279.4	398.3	13.9
Sweden													
1993–97	0.7	1.4	3.0	5.5	11.2	25.6	38.2	54.8	85.9	121.9	174.7	250.4	10.4
1998–02	0.7	1.3	2.6	5.4	9.3	19.0	38.2	57.0	80.9	123.1	174.7	245.4	10.0
2003–07	0.6	1.3	2.5	4.7	9.2	15.8	28.3	57.0	84.9	115.9	176.4	245.4	9.4
2008–12	0.6	1.2	2.4	4.5	8.0	15.7	23.6	42.2	84.9	120.6	166.2	247.9	8.7
2013–17	0.6	1.2	2.4	4.4	7.7	13.5	23.4	35.3	62.4	120.6	172.9	233.4	7.9

Appendix 3C

Predicted age-specific and age-adjusted ('world standard' population) mortality rates per 100 000 for the period 1993–2017 if screening had been established in 1993

Country/ Period	30–34	35–39	40–44	45–49	50–54	55–59	60–64	65–69	70–74	75–79	80–84	85+	WS
Denmark													
1993–97	1.2	2.8	5.6	10.5	21.1	35.7	60.2	88.8	135.8	212.7	302.8	378.8	17.0
1998–02	1.2	2.8	5.6	10.5	19.7	29.8	47.6	76.2	123.2	173.9	320.5	412.8	15.5
2003–07	1.2	2.8	5.6	10.5	19.7	27.9	44.1	66.8	117.2	174.8	262.0	437.0	14.7
2008–12	1.2	2.8	5.6	10.4	19.7	27.9	41.1	65.8	109.0	176.6	263.4	357.3	14.0
2013–17	1.2	2.8	5.6	10.4	19.6	27.9	41.2	61.4	107.4	164.3	266.1	381.6	13.8
Finland													
1993–97	0.7	1.4	3.1	4.9	9.6	17.1	22.8	43.9	72.4	107.0	173.4	280.4	8.8
1998–02	0.7	1.4	3.1	4.8	8.8	12.2	22.8	33.8	61.2	94.2	170.1	280.2	7.9
2003–07	0.7	1.4	3.1	4.9	8.7	11.3	18.1	37.5	52.3	88.3	149.7	274.9	7.2
2008–12	0.7	1.4	3.1	4.9	8.7	11.1	16.8	31.6	61.6	80.1	140.4	242.0	7.0
2013–17	0.7	1.4	3.1	4.9	8.7	11.2	16.4	29.2	52.0	94.3	127.4	241.0	6.8
Iceland													
1993–97					14.2	22.3	33.9	55.9	81.7	133.3	178.2	226.5	9.6
1998–02					14.2	19.0	28.8	47.5	69.4	113.3	178.2	226.5	8.6
2003–07					14.2	19.0	27.1	44.7	65.4	106.6	151.5	226.5	7.7
2008–12					14.2	19.0	27.1	44.7	65.4	106.6	142.6	192.5	7.5
2013–17					14.2	19.0	27.1	44.7	65.4	106.6	142.6	192.5	7.5
Norway													
1993–97	0.6	1.4	4.1	8.7	16.9	33.0	49.4	73.1	123.1	160.9	229.6	312.7	14.0
1998–02	0.6	1.3	3.6	7.7	14.4	24.8	48.3	60.7	105.3	153.9	246.6	329.4	12.8
2003–07	0.5	1.1	3.2	6.8	12.8	21.2	40.2	65.7	96.9	145.4	236.0	353.8	12.1
2008–12	0.4	1.0	2.9	6.1	11.4	18.9	34.2	58.1	111.4	142.6	223.5	338.6	11.5
Sweden													
1993–97	0.7	1.4	3.0	5.5	11.2	25.6	38.2	54.8	85.9	121.9	174.7	250.4	10.4
1998–02	0.7	1.3	2.6	5.4	9.3	16.1	32.5	48.4	68.8	104.6	174.7	245.4	9.0
2003–07	0.6	1.3	2.5	4.7	9.2	13.5	22.6	45.6	67.3	92.7	150.0	245.4	8.1
2008–12	0.6	1.2	2.4	4.5	8.0	13.3	18.9	33.8	67.3	96.5	132.9	210.7	7.3
2013–17	0.6	1.2	2.4	4.4	7.7	11.5	18.7	28.2	49.9	96.5	138.4	198.4	6.6

Appendix 4. Colorectal cancer, males

Appendix 4A

Observed age-specific and age-adjusted ('world standard' population) mortality rates per 100 000 by calendar period

Country/ Period	30–34	35–39	40–44	45–49	50–54	55–59	60–64	65–69	70–74	75–79	80–84	85+	WS
Denmark													
1953–57	1.6	2.1	5.2	10.6	18.5	38.0	65.16	106.4	186.2	235.5	347.0	398.0	19.2
1958–62	0.8	4.7	5.5	12.6	22.9	45.1	76.11	140.6	215.5	328.9	460.4	653.6	24.8
1963–67	1.6	3.4	6.6	11.9	24.8	44.2	77.44	128.2	215.6	303.7	437.4	532.9	23.6
1968–72	1.8	2.8	7.3	11.9	21.7	43.8	77.97	121.9	184.1	278.6	372.1	465.1	21.7
1973–77	1.2	3.8	6.8	14.3	27.0	43.3	73.10	126.0	182.5	283.6	405.4	530.7	22.5
1978–82	1.7	2.9	6.0	16.6	27.1	46.0	75.20	104.7	203.8	306.8	415.3	598.3	23.2
1983–87	1.3	3.8	6.0	11.2	22.4	44.5	77.39	135.0	199.8	295.2	400.4	592.2	23.3
1988–92	1.8	2.7	5.3	11.5	20.7	44.2	78.05	131.7	199.6	290.1	357.3	525.3	22.5
Finland													
1953–57	1.3	2.3	3.5	5.4	8.4	12.2	33.5	50.3	101.9	111.4	130.0	180.6	9.2
1958–62	1.0	1.0	3.0	7.2	10.6	17.5	26.8	52.7	77.7	133.0	154.0	192.3	9.2
1963–67	1.7	2.3	4.6	6.6	12.1	19.6	31.4	49.9	97.7	140.1	204.0	301.5	10.9
1968–72	1.9	3.1	4.1	4.5	12.4	20.5	32.0	57.1	88.8	170.2	215.5	328.8	11.4
1973–77	1.0	2.6	3.2	7.6	14.1	21.4	34.7	62.0	89.5	119.3	242.4	397.8	11.9
1978–82	1.3	2.2	3.3	6.8	12.6	18.1	34.5	59.6	103.6	158.3	199.5	387.9	11.9
1983–87	0.9	2.3	2.6	5.4	13.4	19.0	37.2	69.6	99.8	168.4	220.9	343.2	12.2
1988–92	0.9	1.4	3.3	7.6	10.0	24.3	39.6	65.1	105.6	149.0	203.5	349.0	12.2

Appendix 4A (continued)

Country/ Period	30–34	35–39	40–44	45–49	50–54	55–59	60–64	65–69	70–74	75–79	80–84	85+	WS
Iceland													
1958–62					15.0	22.0	13.0	54.0	102.0	169.0	440.0	117.0	10.5
1963–67					14.0	21.0	36.0	29.0	63.0	102.0	395.0	316.0	10.5
1968–72					22.0	49.0	62.0	74.0	70.0	175.0	298.0	338.0	15.4
1973–77					16.0	32.0	32.0	70.0	112.0	124.0	196.0	182.0	11.4
1978–82					7.0	29.0	54.0	53.0	141.0	142.0	262.0	251.0	12.9
1983–87					4.0	27.0	26.0	76.0	97.0	181.0	190.0	326.0	11.7
1988–92					8.0	34.0	60.0	72.0	144.0	116.0	197.0	396.0	13.9
Norway													
1963–67	1.0	2.1	4.7	8.4	15.5	23.8	45.7	76.7	113.0	190.0	235.5	238.6	13.4
1968–72	0.6	2.6	5.0	11.1	15.5	30.2	51.5	86.7	127.1	197.6	289.5	325.0	15.4
1973–77	0.4	1.7	5.2	10.1	19.0	31.4	51.2	83.0	120.9	203.4	284.0	342.0	15.4
1978–82	1.1	2.1	3.9	9.3	18.9	33.7	57.6	91.0	150.2	233.7	319.6	484.4	17.7
1983–87	1.3	2.6	4.3	11.6	19.8	37.0	62.3	105.6	165.6	228.4	319.9	433.4	18.7
1988–92	1.2	3.4	3.4	12.2	24.6	44.7	74.5	110.7	160.1	254.8	343.4	442.0	20.2
Sweden													
1963–67	1.6	3.2	4.0	9.5	15.4	29.4	48.0	83.6	138.2	219.2	293.8	375.0	15.8
1968–72	1.4	2.6	5.2	10.6	15.9	29.4	53.2	85.8	138.0	228.8	327.2	456.5	16.8
1973–77	1.1	2.5	6.5	9.7	17.3	30.2	56.0	95.4	155.6	230.5	350.1	523.2	18.2
1978–82	0.8	2.8	3.5	7.9	16.4	30.7	49.2	84.9	137.0	210.0	328.1	442.7	16.2
1983–87	0.7	1.6	3.3	8.2	17.7	28.2	50.9	78.7	125.8	182.4	260.1	390.9	14.8
1988–92	0.7	1.9	3.7	7.0	16.0	29.4	51.2	78.2	129.3	185.6	241.3	371.6	14.7

Appendix 4B

Predicted age-specific and age-adjusted ('world standard' population) mortality rates per 100 000 for the period 1993–2017 without screening

Country/ Period	30–34	35–39	40–44	45–49	50–54	55–59	60–64	65–69	70–74	75–79	80–84	85+	WS
Denmark													
1993–97	1.5	3.3	5.8	11.7	20.3	37.8	75.3	126.7	197.5	290.3	370.2	532.7	22.1
1998–02	1.5	3.2	5.8	11.6	21.2	36.4	65.0	121.7	199.1	290.9	385.3	506.7	21.5
2003–07	1.5	3.2	5.8	11.6	21.0	38.0	62.6	105.0	191.3	293.2	386.0	527.4	20.9
2008–12	1.5	3.2	5.8	11.5	21.0	37.7	65.4	101.1	165.0	281.7	389.1	528.4	20.2
2013–17	1.5	3.2	5.8	11.5	20.8	37.7	64.8	105.7	158.8	243.0	373.9	532.7	19.8
Finland													
1993–97	1.2	2.1	3.2	6.4	11.9	18.2	42.0	69.0	107.5	174.0	230.8	397.4	12.9
1998–02	1.2	2.1	3.2	6.0	11.8	19.8	33.3	75.4	114.7	171.0	250.9	400.0	13.0
2003–07	1.2	2.1	3.2	6.0	11.1	19.7	36.2	59.8	125.3	182.4	246.6	435.0	13.1
2008–12	1.2	2.1	3.2	6.0	11.1	18.5	36.0	65.0	99.4	199.3	263.0	427.4	12.8
2013–17	1.2	2.1	3.2	6.0	11.1	18.5	33.8	64.8	108.0	158.1	287.4	455.8	12.8
Iceland													
1993–97					11.7	30.7	41.7	62.6	107.1	143.7	257.7	293.2	11.7
1998–02					11.7	30.7	41.7	62.6	107.1	143.7	257.7	293.2	11.7
2003–07					11.7	30.7	41.7	62.6	107.1	143.7	257.7	293.2	11.7
2008–12					11.7	30.7	41.7	62.6	107.1	143.7	257.7	293.2	11.7
2013–17					11.7	30.7	41.7	62.6	107.1	143.7	257.7	293.2	11.7
Norway													
1993–97	1.3	3.4	5.8	13.9	23.8	43.8	76.2	124.6	181.0	266.8	375.1	484.8	21.8
1998–02	1.5	3.8	6.4	15.4	26.3	46.0	79.9	132.8	202.5	293.4	393.6	527.0	23.6
2003–07	1.6	4.2	7.1	17.0	29.0	50.8	83.9	139.4	216.0	328.3	432.9	553.0	25.4
2008–12	1.8	4.6	7.9	18.8	32.1	56.2	92.8	146.3	226.6	350.1	484.4	608.2	27.4
Sweden													
1993–97	0.6	1.5	3.1	6.2	12.7	26.1	52.1	81.7	129.4	183.6	258.0	362.5	14.4
1998–02	0.6	1.4	2.5	6.0	11.3	22.7	46.2	85.0	130.7	191.1	255.4	362.5	14.1
2003–07	0.6	1.4	2.4	4.9	10.8	20.1	40.2	75.4	136.0	193.0	265.8	358.8	13.6
2008–12	0.6	1.3	2.3	4.7	8.9	19.3	35.6	65.6	120.6	200.9	268.5	373.5	12.8
2013–17	0.6	1.3	2.2	4.5	8.5	15.8	34.2	58.1	104.9	178.2	279.5	377.3	11.8

Appendix 4C

Predicted age-specific and age-adjusted ('world standard' population) mortality rates per 100 000 for the period 1993–2017 if screening had been established in 1993

Country/ Period	30–34	35–39	40–44	45–49	50–54	55–59	60–64	65–69	70–74	75–79	80–84	85+	WS
Denmark													
1993–97	1.5	3.3	5.8	11.7	20.3	37.8	75.3	126.7	197.5	290.3	370.2	532.7	22.1
1998–02	1.5	3.2	5.8	11.6	21.2	30.9	55.2	103.4	169.2	247.3	385.3	506.7	19.3
2003–07	1.5	3.2	5.8	11.6	21.0	32.3	50.1	84.0	153.0	234.6	328.1	527.4	17.9
2008–12	1.5	3.2	5.8	11.5	21.0	32.0	52.3	80.9	132.0	225.4	311.3	449.1	16.9
2013–17	1.5	3.2	5.8	11.5	20.8	32.0	51.8	84.6	127.0	194.4	299.1	452.8	16.5
Finland													
1993–97	1.2	2.1	3.2	6.4	11.9	18.2	42.0	69.0	107.5	174.0	230.8	397.4	12.9
1998–02	1.2	2.1	3.2	6.0	11.8	16.8	28.3	64.1	97.5	145.4	250.9	400.0	11.8
2003–07	1.2	2.1	3.2	6.0	11.1	16.8	28.9	47.9	100.3	145.9	209.6	435.0	11.3
2008–12	1.2	2.1	3.2	6.0	11.1	15.8	28.8	52.0	79.5	159.5	210.4	363.3	10.7
2013–17	1.2	2.1	3.2	6.0	11.1	15.8	27.1	51.8	86.4	126.5	229.9	387.4	10.6
Iceland													
1993–97					11.7	30.7	41.7	62.6	107.1	143.7	257.7	293.2	11.7
1998–02					11.7	26.1	35.4	53.2	91.0	122.2	257.7	293.2	10.4
2003–07					11.7	26.1	33.4	50.1	85.7	115.0	219.0	293.2	9.9
2008–12					11.7	26.1	33.4	50.1	85.7	115.0	206.2	249.2	9.6
2013–17					11.7	26.1	33.4	50.1	85.7	115.0	206.2	249.2	9.6
Norway													
1993–97	1.3	3.4	5.8	13.9	23.8	43.8	76.2	124.6	181.0	266.8	375.1	484.8	21.8
1998–02	1.5	3.8	6.4	15.4	26.3	39.1	67.9	112.9	172.1	249.4	393.6	527.0	21.2
2003–07	1.6	4.2	7.1	17.0	29.0	43.2	67.1	111.5	172.8	262.6	368.0	553.0	21.7
2008–12	1.8	4.6	7.9	18.8	32.1	47.8	74.2	117.0	181.3	280.1	387.5	517.0	22.9
Sweden													
1993–97	0.6	1.5	3.1	6.2	12.7	26.1	52.1	81.7	129.4	183.6	258.0	362.5	14.4
1998–02	0.6	1.4	2.5	6.0	11.2	19.3	39.3	72.3	111.1	162.4	255.4	362.5	12.6
2003–07	0.6	1.4	2.4	4.9	10.8	17.1	32.1	60.3	108.8	154.4	226.0	358.9	11.5
2008–12	0.6	1.3	2.3	4.7	8.9	16.4	28.5	52.4	96.5	160.7	214.8	317.5	10.6
2013–17	0.6	1.3	2.2	4.5	8.5	13.5	27.4	46.5	83.9	142.6	223.6	320.7	9.8

Appendix 5

Estimated cost attributed to cervical cancer without screening and if the Finnish screening policy had been established

Country/ Period	Without screening		Cost of treatment	With Finnish screening policy						
	Woman-years (25–59)	No. of cases	=total cost	No. of cases	No. of invasive+ in situ cancers	Cost of screening	Cost of treatment of in situ cancers	Cost of treatment of invasive cancers	Total cost with screening	Cost difference
	(A)	(B)	(C)	(D)	(E)	(F)	(G)	(H)	(I)	(J)
Denmark										
58–62	5153048	3381	94668000	3381	10143	10306000	27048000	94668000	132022000	37354000
63–67	5179887	3399	95161000	3670	10196	10360000	26101000	89854000	126315000	31154000
68–72	5319620	3490	97728000	2792	10471	10639000	30715000	69247000	110601000	12873000
73–77	5534085	3631	101668000	1416	10893	11068000	37908000	37385000	86361000	−15307000
78–82	5675058	3723	104258000	968	11170	11350000	40810000	25558000	77718000	−26540000
83–87	5796708	3803	106493000	761	11410	11593000	42597000	20082000	74272000	−32221000
88–92	6051170	3970	111168000	675	11911	12102000	44943000	17819000	74864000	−36303000
93–97	6323661	4149	116174000	622	12447	12647000	47299000	16430000	76377000	−39797000
98–02	6474189	4248	118939000	637	12743	12948000	48425000	16821000	78195000	−40744000
03–07	6361399	4174	116867000	626	12521	12723000	47582000	16528000	76833000	−40034000
08–12	6073629	3985	111580000	598	11955	12147000	45429000	15781000	73357000	−38223000
Finland										
58–62	5011100	1349	37772000	1349	4047	10022000	10792000	37772000	58586000	20814000
63–67	5032300	1355	37932000	1462	4064	10065000	10404000	35790000	56259000	18327000

Appendix 5 (continued)

Country/ Period	Without screening		Cost of treatment = total cost	With Finnish screening policy						
	Woman-years (25–59)	No. of cases		No. of cases	No. of invasive + in situ cancers	Cost of screening	Cost of treatment of in situ cancers	Cost of treatment of invasive cancers	Total cost with screening	Cost difference
	(A)	(B)	(C)	(D)	(E)	(F)	(G)	(H)	(I)	(J)
68–72	5059700	1362	38138000	1087	4086	10119000	11986000	26958000	49063000	10925000
73–77	5372600	1446	40497000	564	4339	10745000	15010000	14890000	40734000	237000
78–82	5654900	1522	42625000	390	4567	11310000	16685000	10296000	38290000	−4334000
83–87	5867300	1579	44226000	310	4738	11735000	17690000	8184000	37609000	−6617000
88–92	6041300	1626	45537000	275	4879	12083000	18410000	7260000	37753000	−7785000
93–97	6212200	1672	46825000	248	5017	12424000	19065000	6547000	38036000	−8789000
98–02	6183900	1665	46612000	244	4994	12368000	18978000	6442000	37787000	−8825000
03–07	6210400	1672	46812000	243	5016	12421000	19059000	6415000	37895000	−8917000
08–12	5973700	1608	45028000	240	4824	11947000	18333000	6336000	36616000	−8412000
Iceland										
58–62	168814	47	1316000	47	141	338000	376000	1316000	2030000	714000
63–67	175394	49	1367000	53	146	351000	375000	1291000	2017000	650000
68–72	186247	52	1452000	41	156	372000	456000	1029000	1858000	406000
73–77	202693	56	1580000	22	169	405000	589000	581000	1576000	−5000
78–82	222531	62	1735000	16	186	445000	679000	425000	1549000	−185000
83–87	247760	69	1931000	14	207	496000	773000	364000	1632000	−299000
88–92	274727	76	2142000	13	229	549000	866000	343000	1759000	−383000
93–97	297292	83	2318000	12	248	595000	944000	328000	1866000	−452000
98–02	321181	89	2504000	13	268	642000	1019000	354000	2016000	−488000
03–07	339216	94	2644000	14	283	678000	1077000	374000	2129000	−515000
08–12	350378	98	2731000	15	293	701000	1112000	386000	2199000	−532000
Norway										
58–62	4025938	1267	35476000	1267	3801	8052000	10136000	35476000	53664000	18188000
63–67	3963910	1247	34929000	1347	3742	7928000	9581000	32981000	50490000	15560000
68–72	3998457	1258	35234000	1007	3775	7997000	11073000	24966000	44036000	8802000
73–77	4139612	1303	36478000	508	3908	8279000	13601000	13413000	35294000	−1184000
78–82	4254714	1339	37492000	348	4017	8509000	14675000	9191000	32376000	−5116000
83–87	4397691	1384	38752000	277	4152	8795000	15501000	7307000	31604000	−7148000
88–92	4647986	1462	40957000	249	4388	9296000	16558000	6565000	32419000	−8538000
93–97	4977958	1567	43865000	235	4700	9956000	17859000	6204000	34019000	−9846000
98–02	5249586	1652	46259000	248	4956	10499000	18834000	6542000	35875000	−10383000
03–07	5309013	1671	46782000	251	5012	10618000	19047000	6616000	36281000	−10501000
08–12	5233742	1647	46119000	247	4941	10467000	18777000	6523000	35767000	−10352000
Sweden										
58–62	8723235	3306	92568000	3306	9918	17446000	26448000	92568000	136462000	43894000
63–67	8645799	3277	91746276	3539	9830	17292000	25165000	86629000	129086000	37340000
68–72	8819727	3343	93591940	2674	10028	17639000	29415000	66317000	113371000	19779000
73–77	9067970	3437	96226210	1340	10310	18136000	35879000	35384000	89398000	−6828000
78–82	9197973	3486	97605758	906	10458	18396000	38206000	23927000	80529000	−17077000
83–87	9242974	3503	98083293	701	10509	18486000	39233000	18496000	76215000	−21868000
88–92	9582466	3632	101685867	617	10895	19165000	41110000	16299000	76574000	−25112000
93–97	10034613	3803	106483897	570	11409	20069000	43354000	15060000	78483000	−28001000
98–02	10318070	3910	109491846	587	11731	20636000	44579000	15485000	80700000	−28792000
03–07	10189506	3862	108127569	579	11585	20379000	44023000	15292000	79695000	−28433000
08–12	9896863	3751	105022141	563	11252	19794000	42759000	14853000	77406000	−27616000

$i = 1, 2, \ldots, 11$ calendar period

$B_i = B, {}^*A_i/A_1$

$C_i = 0.5 * B_i * 20000 + 0.5 * B_i * 36000$

$D_i = D_1 * P_i$ where P_i is the proportion given in Table 42

$E_i = 3 * B_i$

$F_i = 10 * A_i/5$

$G_i = (E_i - D_i) * 4000$

$H_i = D_i * K_i * 20000 + D_i * (1 - K_i) * 36000$ where K_i is the proportion of localized cases given in Table 11

$I_i = G_i + H_i$

$J_i = I_i - C_i$