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ORIGINAL ARTICLE

Trends in the survival of patients diagnosed with cancer in female genital organs in the Nordic countries 1964–2003 followed up to the end of 2006

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Abstract

Cancers of the female genital organs constitute more than 12% of all female cancers in the Nordic countries. The group includes cervix uteri, corpus uteri, ovary and other female genital organs including vulva and vagina, and in this study we compare the development in the Nordic countries regarding incidence, mortality and relative survival. *Material and methods*. Data were retrieved from the NORDCAN database for the period 1964 to 2003, grouped into eight 5-year periods. The patients were followed up until the end of 2006. Analyses comprised trends in 5-year relative survival, excess mortality and age-specific relative survival. *Results.* A substantial reduction of cervical cancer incidence followed the introduction of population-based screening in the 1970s and was also accompanied by a modest improvement in survival. Incidence trends in cancer of corpus uteri varied between the countries but the survival increased by around 20 percentage points during the study period in all countries. Ovarian cancer patients have the lowest survival among female genital cancers, but survival increased 10–15 percentage points over the 40 years of observation, while the incidence and mortality were rather stable throughout the observed period. Cancers of the other female genital organs, including vulva and vagina, are rare diagnoses and only small changes in incidence, mortality and survival have been observed over time. *Conclusion.* The declining trends in cervical cancer incidence and mortality, and improving survival of corpus uteri cancer patients, are in contrast with the rather poor prognosis associated with an ovarian cancer diagnosis. Cancer-specific differences between countries in the survival of female patients diagnosed with cancers of the cervix uteri, corpus uteri and other female genital organs are small.

Cancers of the female genital organs (cervix uteri, corpus uteri, ovary, and other female genital organs including vulva and vagina) constitute more than 12% of all female cancers in the Nordic countries. Cancer of corpus uteri is the most common in this group and the fourth most common among women with approximately 3 200 incident cases and 560 deaths per year during 1999–2003 in the Nordic countries [1]. The second most frequent, ovarian cancer, comprises almost 2 500 diagnoses and 1 700 deaths annually [1]. Since the mid-1960s, all Nordic countries have had organised screening programmes (Norway started approximately 10 years later) to identify precancerous lesions of the cervix uteri for women around the age-span 20–60. This has reduced cervical cancer incidence by more than 50% since the early 1960s and approximately 1 300 cases were diagnosed every year in the period 1999–2003 [1,2].

The aetiology of the diseases differs, but they share certain risk factors. Obesity, reproductive factors including nulliparity or late childbirth, and unopposed oestrogen HRT are risk factors for cancer of the ovaries and corpus uteri, while the use of combined oral contraceptives is likely protective [3–6]. Human Papilloma Virus (HPV) infection is a necessary but not sufficient cause of cervical cancer [7]. Smoking may modulate the risk of cervical cancer among HPV-positive women, but appears to reduce the risk of cancers of the corpus

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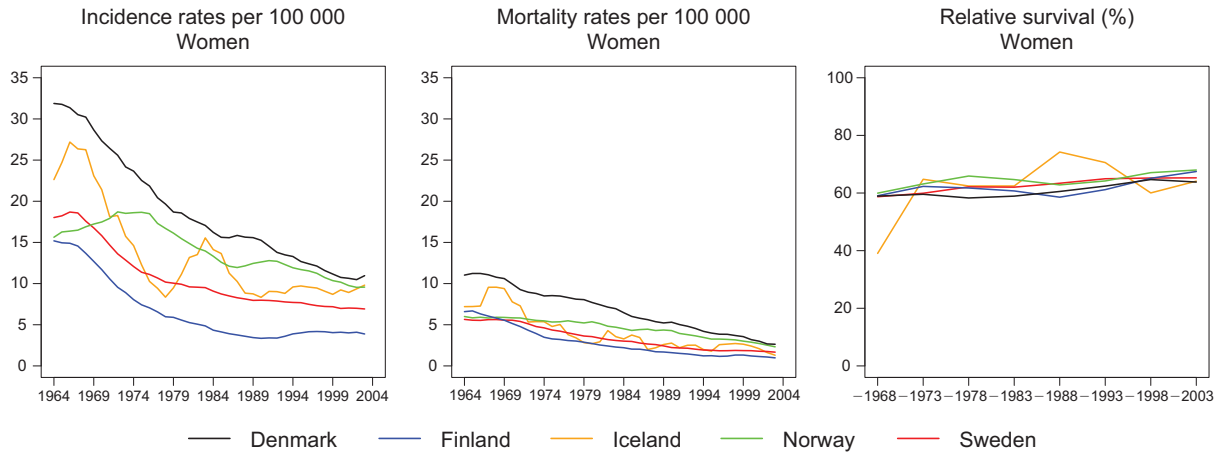

Figure 1. Trends in age-standardised (World) incidence and mortality rates per 100 000 and age-standardised (ICSS) 5-year relative survival for cancer of cervix uteri by country. Nordic cancer survival study 1964–2003.

uteri. HPV and smoking are also associated with cancer of other female genital organs such as vulva and vagina [8].

In the EUROCARE-4 study [9], the European age-standardised 5-year relative survival was 63% for cervical cancer, 76% for corpus uteri, 37% for ovaries, and 59% for vagina and vulva. A Nordic report from 1995 pointed out the importance of age at diagnosis on 5-year survival following cervical cancer. Patients below age 45 in the period 1983–1987 had a relative survival of 82% while the corresponding figure was 34% among women older than 75 years. The same study, based on patients diagnosed in 1958–1987, showed that 5-year relative survival after cancers of the corpus uteri increased steadily during that period in all Nordic countries except Iceland, where no increase was seen for patients diagnosed after 1978 [10]. Relative to the European average, the female genital cancer survival among Nordic patients was similar or higher than the European average with few exceptions [9].

The purpose of this study is to compare the trends in survival following diagnoses of cancer of the female genital organs, in relation to the corresponding incidence and mortality trends in each of the five Nordic countries, Denmark, Finland, Iceland, Norway, and Sweden over the period 1964–2003.

Material and methods

The data sources and methods are described in detail elsewhere [11]. In brief, the study is based on the core dataset in NORDCAN, a database with comparable data on cancer incidence and mortality in the Nordic countries delivered from the national cancer registries, with follow-up for death or emigration for each cancer patient through 2006. The study covers cancer of cervix uteri (ICD-10 C53), corpus uteri (ICD-10 C54), ovaries (ICD-10 C56, C57.0-C57.4) and other female genital organs including vulva and

Table I. Trends in survival for cancer of cervix uteri by country. Number of tumours (N) included and the 5-year age-standardised (ICSS) relative survival in percent with 95% confidence intervals (RS (CI)). Nordic cancer survival study 1964–2003.

	Denmark		Finland		Iceland		Norway		Sweden	
	N	RS (CI)	N	RS (CI)	N	RS (CI)	N	RS (CI)	N	RS (CI)
Women										
1964–1968	4 489	59 (57–61)	2 084	59 (56–62)	125	39 (31–49)	1 883	60 (57–63)	4 608	59 (57–61)
1969–1973	3 947	60 (58–61)	1 593	62 (59–65)	90	65 (54–78)	2 081	63 (61–66)	3 823	60 (58–62)
1974–1978	3 492	58 (56–60)	1 185	62 (59–65)	53	*62 (53–74)*	2 203	66 (64–68)	3 076	62 (60–64)
1979–1983	3 002	59 (57–61)	972	61 (57–64)	76	*62 (53–74)*	1 891	65 (62–67)	2 791	62 (60–64)
1984–1988	2 740	61 (59–63)	783	59 (55–62)	74	74 (61–90)	1 645	63 (60–65)	2 552	63 (61–65)
1989–1993	2 629	62 (60–64)	715	61 (58–65)	66	71 (59–84)	1 798	64 (62–67)	2 446	65 (63–67)
1994–1998	2 296	65 (62–67)	814	65 (62–69)	75	60 (48–75)	1 664	67 (65–70)	2 325	65 (63–67)
1999–2003	1 991	64 (62–66)	787	67 (65–70)	76	64 (54–76)	1 475	68 (66–70)	2 251	65 (64–67)

Numbers in *italics* indicate that two or more cells had to be combined to get sufficient number of patients to calculate survival.

Table II. Trends in 5-year age-specific relative survival in percent after cancer of cervix uteri by country. Nordic cancer survival study 1964–2003.

	Women					
Age	0–49	50–59	60–69	70–79	80–89	90+
Denmark						
1964–1968	70	60	60	46	23	0
1969–1973	74	63	56	43	24	0
1974–1978	72	61	57	40	26	0
1979–1983	78	57	52	44	22	0
1984–1988	81	57	54	43	27	28
1989–1993	81	65	57	40	28	0
1994–1998	82	65	61	47	26	16
1999–2003	83	68	54	44	26	9
Finland						
1964–1968	71	60	52	48	43	*
1969–1973	80	64	55	42	36	*
1974–1978	74	68	59	43	35	*
1979–1983	76	60	56	49	30	0
1984–1988	73	64	50	48	22	*
1989–1993	80	66	54	41	20	0
1994–1998	82	62	61	50	34	0
1999–2003	85	63	63	50	43	74
Iceland						
1964–1968	61	60	11	*14*	*14*	*
1969–1973	82	71	69	*28*	*28*	*
1974–1978	*79*	*60*	*66*	*35*	*35*	*
1979–1983	*79*	*60*	*66*	*35*	*35*	*
1984–1988	83	103	43	*67*	*67*	*
1989–1993	84	77	77	*37*	*37*	*
1994–1998	84	64	48	*31*	*31*	*
1999–2003	92	77	34	*40*	*40*	*
Norway						
1964–1968	75	64	60	40	15	*
1969–1973	78	67	59	47	25	*
1974–1978	83	69	58	47	35	*
1979–1983	81	67	60	42	41	0
1984–1988	78	64	60	42	36	0
1989–1993	80	66	61	47	30	41
1994–1998	84	68	62	51	30	65
1999–2003	85	70	64	47	32	52
Sweden						
1964–1968	75	64	54	35	32	*
1969–1973	76	65	58	35	30	0
1974–1978	81	66	56	38	33	0
1979–1983	83	55	57	46	26	0
1984–1988	82	62	54	43	47	17
1989–1993	85	68	54	44	33	17
1994–1998	86	68	55	45	26	0
1999–2003	86	69	54	47	29	10

Numbers in *italics* indicate that two or more cells had to be combined to get sufficient number of patients to calculate survival.
* Too few patients to calculate survival, see reference [11].

vagina (ICD-10 C51-C52, C57.7-C57.9). We calculated 5-year relative survival for each of the diagnostic groups in NORDCAN for eight 5-year periods from 1964–1968 to 1999–2003. For the last five-year period, hybrid analysis methods were used. Country specific population mortality rates were used for calculating the expected survival. Age-standardisation of relative survival used the ICSS-standard cancer patient populations [12]. We show age-standardised incidence and mortality (World standard), 5-year relative survival, and excess mortality rates for the follow-up periods: the first month, one to three months and two to five years following diagnosis, as well as age-specific 5-year relative survival by country and 5-year period.

Results

Cancer of cervix uteri

Incidence and mortality. The main observation with respect to the age-standardised incidence and mortality trends in cervical cancer was a continuous decline in each of the Nordic countries up to 2003 (Figure 1). Some deceleration in the rate of decrease in incidence was seen in recent decades, particularly in Finland and Sweden (Figure 1). In Finland, a transitory increase in cervical cancer incidence was observed beginning in the early 1990s, followed by a period of relative stability; this feature was less evident in the mortality trends, with continual declines in the latest years. Similarly, a short-lived increase in rates in the late-1980s was observed in Norway, and more notably in Iceland slightly earlier, followed by a subsequent period of uniform decline. The incidence and mortality rate in Denmark was twofold that in Finland, Norway, and Sweden in the early 1960s and although rates still varied threefold across the Nordic populations circa 2003 the relative ranking has changed little since the 1970s. Age-standardised incidence rates in 2003 were in the range four to 10 per 100 000 and mortality rates in the range one to three per 100 000, with rates highest in Denmark and lowest in Finland.

Survival

Cervical cancer survival ratios and trends were rather similar in the Nordic countries throughout the study period, including the latest diagnostic period 1999–2003. After a period where trends were quite stable or even decreasing (up to around 1985), small increments in survival of two to three percentage points were observed from the late-1980s to the present, although the absolute increases were somewhat greater in Finland (Figure 1 and Table I). The 5-year relative survival estimates remained quite comparable across populations for Nordic patients diagnosed 1999–2003 with ratios only varying between 64% and 68% (Table I). Age at diagnosis was evidently a major determinant of cancer survival, with 5-year relative survival among patients below age 50 years estimated at around 85–90% in the latest period, with survival steadily decreasing as age increased (Table II). The recent and minor increase in overall survival did not appear related to age, although

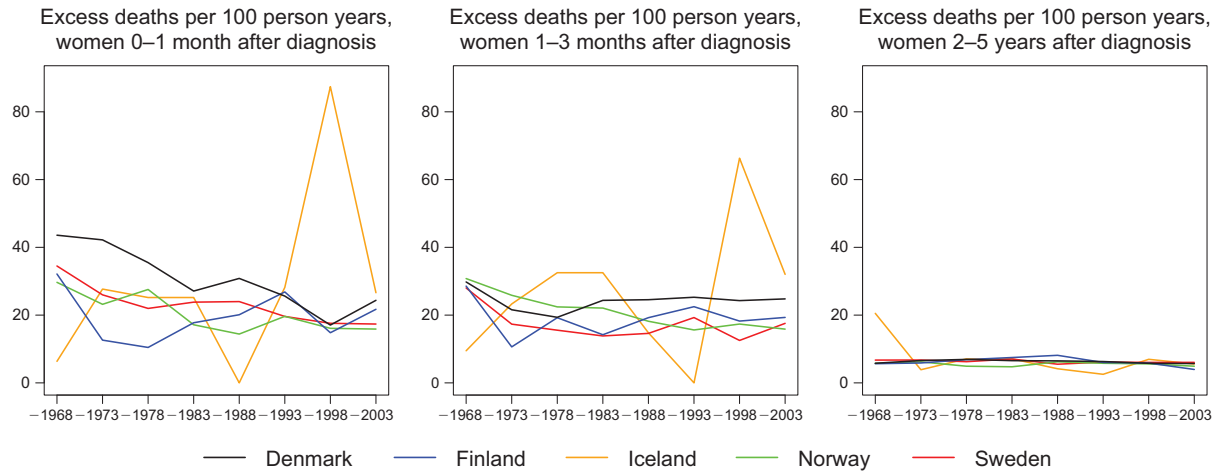

Figure 2. Trends in age-standardised (ICSS) excess death rates per 100 person years for cancer of cervix uteri by country and time since diagnosis. Nordic cancer survival study 1964–2003.

slight but continuous survival increases in patients aged under 50 were observed in the long-term trends.

The variability in excess death rates between countries appeared restricted to the first three months after diagnosis, within the first three months, with a slightly higher excess death rate in Denmark (Figure 2). A decrease in the excess mortality was found for follow-up in the first month in consecutive calendar periods 1964–2003, from about 40 to 20–25 deaths per 100 person years. At two to five years of follow-up after diagnosis the mortality rates were fairly constant at around six per 100 person years, with hardly any variation between countries.

Cancer of corpus uteri

Incidence and mortality. In Norway and Finland, incidence increased steadily during the study period (Figure 3) while a lesser increase was seen in Sweden. No overall changes were seen in Iceland, and in Denmark a decrease was observed since the 1980s, following a rather sharp increase in the preceding decade. In 2003, Denmark and Iceland had the lowest age-standardised incidence of cancer of the corpus uteri at about 13 cases per 100 000 women and Norway the highest (16 per 100 000). Mortality rates were rather stable, although some declines were apparent in Sweden and Iceland since the 1960s. Mortality rates were at a much lower level than incidence (range one to two per 100 000 in 2003), with Sweden having the lowest rate throughout the period.

Survival

In each Nordic country except for Iceland, the 5-year relative survival increased markedly during the

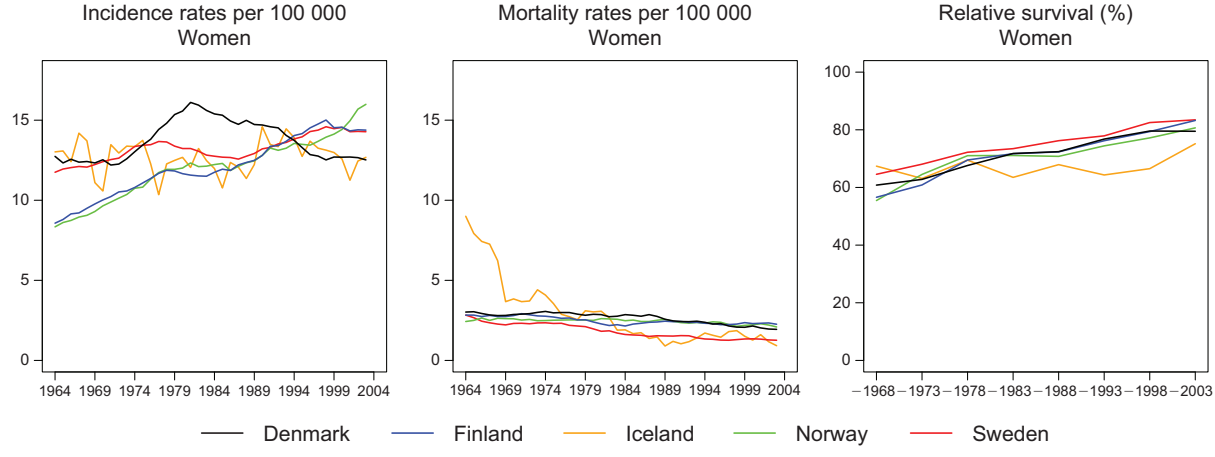

Figure 3. Trends in age-standardised (World) incidence and mortality rates per 100 000 and age-standardised (ICSS) 5-year relative survival for cancer of corpus uteri by country. Nordic cancer survival study 1964–2003.

Table III. Trends in survival for cancer of corpus uteri by country. Number of tumours (N) included and the 5-year age-standardised (ICSS) relative survival in percent with 95% confidence intervals (RS (CI)). Nordic cancer survival study 1964–2003.

	Denmark		Finland		Iceland		Norway		Sweden	
	N	RS (CI)	N	RS (CI)	N	RS (CI)	N	RS (CI)	N	RS (CI)
Women										
1964–1968	2 170	61 (58–64)	1 386	57 (53–60)	57	67 (51–89)	1 190	55 (52–60)	3 658	65 (62–67)
1969–1973	2 268	63 (60–66)	1 658	61 (57–65)	70	63 (50–79)	1 436	65 (61–69)	4 003	68 (66–70)
1974–1978	2 742	68 (65–70)	1 975	70 (66–73)	71	69 (57–85)	1 712	71 (68–74)	4 493	72 (70–74)
1979–1983	3 243	72 (70–74)	2 176	72 (69–75)	83	64 (54–75)	1 890	71 (68–74)	4 560	73 (72–75)
1984–1988	3 112	72 (70–75)	2 388	72 (70–75)	86	68 (56–82)	1 928	71 (68–73)	4 598	76 (75–78)
1989–1993	3 194	77 (75–79)	2 863	76 (74–78)	100	64 (54–77)	2 196	74 (72–77)	5 211	78 (76–79)
1994–1998	2 981	80 (77–82)	3 280	79 (77–81)	116	67 (57–77)	2 369	77 (75–79)	5 924	83 (81–84)
1999–2003	3 122	79 (78–81)	3 525	83 (82–85)	115	75 (68–84)	2 846	81 (79–82)	6 394	83 (82–84)

period, the increase amounting to 20 percentage points (Figure 3, Table III). In Iceland, no increase was apparent between 1978 and 1993, but thereafter an upward trend was seen, although survival remained considerably lower than in the other four countries after 1978. Among Nordic patients diagnosed in 1999–2003 the 5-year relative survival was in the range 75 to 83%, Sweden had the highest survival throughout the period.

Sweden also had the lowest excess death rates during the first year after diagnosis (not shown for months three to 12), but there was no difference in excess mortality between the countries two to five years after diagnosis (Figure 4). Iceland appeared to have the highest excess death rates one to three months after diagnosis, since 1978.

The general pattern in the age-specific relative survival was a decline with advancing age from the age group 50–59 in all countries. The youngest patients, aged below 50 years, had worse or similar survival to those aged 50–59 in all countries after 1989, with the exception of Norway (Table IV).

Ovarian cancer

Incidence and mortality. Ovarian cancer incidence and mortality rates slightly declined in the Nordic countries from the mid-1980s, although in Finland slightly later from the mid-1990s (Figure 5). The age-standardised incidence rate was around 12–14 cases per 100 000, although there was some variation between the countries. Finland has had lower rates than the other countries in terms of both incidence and mortality but these were fairly constant over the study period. In Denmark and Sweden, on the other hand, the incidence has been historically higher, at approximately 15–16 per 100 000 around 1970, but has constantly decreased subsequently, most notably in Sweden. Mortality followed incidence closely in the Nordic countries, although at a lower level, at approximately seven per 100 000 circa 2003. Mortality was higher in Denmark than in the other countries throughout the period.

Survival

Increasing trends in 5-year survival following ovarian cancer diagnoses were observed in all Nordic countries

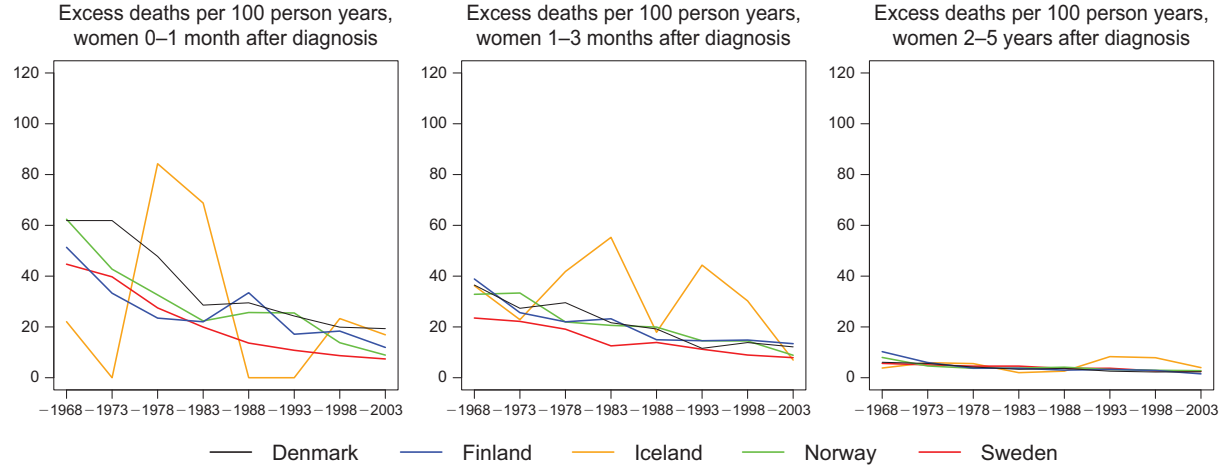

Figure 4. Trends in age-standardised (ICSS) excess death rates per 100 person years for cancer of corpus uteri by country and time since diagnosis. Nordic cancer survival study 1964–2003.

Table IV. Trends in 5-year age-specific relative survival in percent after cancer of corpus uteri by country. Nordic cancer survival study 1964–2003.

	Women					
Age	0–49	50–59	60–69	70–79	80–89	90+
Denmark						
1964–1968	88	79	65	51	31	*
1969–1973	86	79	66	53	39	*
1974–1978	85	86	75	55	44	0
1979–1983	84	87	80	64	46	0
1984–1988	90	84	80	66	43	43
1989–1993	88	88	81	73	55	32
1994–1998	82	87	82	78	69	30
1999–2003	83	87	83	76	69	36
Finland						
1964–1968	92	78	64	49	6	*
1969–1973	91	83	65	50	25	*
1974–1978	90	85	74	56	52	62
1979–1983	92	89	76	63	45	54
1984–1988	93	85	79	63	47	61
1989–1993	88	91	80	71	54	66
1994–1998	89	89	84	76	58	47
1999–2003	91	90	87	80	68	47
Iceland						
1964–1968	81	67	80	*56*	*56*	*
1969–1973	94	93	63	*43*	*43*	*
1974–1978	71	84	92	*50*	*50*	*
1979–1983	101	98	69	*36*	*36*	*
1984–1988	86	96	70	*51*	*51*	*
1989–1993	87	94	70	*43*	*43*	*
1994–1998	84	88	64	*55*	*55*	*
1999–2003	87	81	77	*69*	*69*	*
Norway						
1964–1968	82	78	61	49	13	*
1969–1973	92	81	70	48	47	0
1974–1978	87	85	73	63	55	*
1979–1983	91	86	77	60	49	0
1984–1988	89	85	77	63	45	55
1989–1993	91	88	79	70	47	25
1994–1998	93	89	83	72	51	37
1999–2003	91	89	85	77	63	70
Sweden						
1964–1968	93	86	67	51	39	65
1969–1973	94	87	72	57	39	0
1974–1978	93	89	75	64	48	54
1979–1983	92	92	82	63	42	70
1984–1988	94	91	82	68	50	23
1989-1993	91	90	83	71	57	45
1994–1998	90	91	87	77	69	58
1999–2003	90	92	87	78	73	56

Numbers in *italics* indicate that two or more cells had to be combined to get sufficient number of patients to calculate survival.

*Too few patients to calculate survival, see reference [11].

(Figure 5), with Denmark and Sweden having the lowest and highest ratios, respectively. Finland and Norway caught up with the Swedish survival in the most recent period while Danish patients still experienced a lower survival than patients in Finland, Norway and Sweden estimated at 33% compared to 41–44% in the other countries (Table V). The survival in Iceland was at about the same level as in Norway and Finland until the mid-1990s whereafter it dropped somewhat.

Large differences in the absolute level and a decrease over time were observed in the number of excess deaths by time since diagnosis (Figure 6). The excess mortality rates during the first month after diagnosis were high, starting in the 1960s at around 200 per 100 person years, except in Finland and Iceland where the rate was below 150, and decreased to 80 in the last period 1999–2003. In the follow-up interval of one to three months, excess rates started around 100 and fell to around 70. Denmark had the highest level of excess mortality in the first year following diagnosis, but differences decreased over calendar time, with rates in Sweden considerably lower. In the last follow-up interval, two to five years after diagnosis, the rates were relatively uniform at 10 to 14 per 100 person years, with few differences between countries.

Younger age was associated with higher survival in each of the Nordic countries, and the main increases over time were seen in women below the age of 70 years at diagnosis. Five-year survival in the age group 0–49 in the period 1999–2003 ranged from 63 (Denmark) to 71% (Finland) (Table VI).

Cancer of other female genital organs (vulva, vagina and other unspecified organs)

Incidence and mortality. The incidence rates of cancer in other female genital organs were at a fairly constant level over time, although with some random variation, at around two per 100 000, with a slightly decreasing trend observed in Finland. The vast majority of cases were vulva cancer constituting 71% of the cases in 1999–2003, while cancer of the vagina and other unspecified organs constituted 18% and 11%, respectively. Mortality rates were somewhat lower with trends declining throughout the observed period to less than one per 100 000 circa 2003 (Figure 7).

Survival

Some increases in survival were observed with 5-year other female genital survival increasing from around 50 to nearly 60% from 1964 to 2003 (Figure 7 and Table VII). The survival was slightly lower in Finland in the whole period, with Norway and Iceland exhibiting the highest survival in the last period at above 60% (although with wide confidence intervals), with the other countries close behind with survival at around 55–57% (Table VII). The excess death rates were around 40 in the first month of follow-up, 30 one to three months after diagnosis and about six deaths per 100 person years at two to five years follow-up, with

Table V. Trends in survival for ovarian cancer by country. Number of tumours (N) included and the 5-year age-standardised (ICSS) relative survival in percent with 95% confidence intervals (RS (CI)). Nordic cancer survival study 1964–2003.

	Denmark		Finland		Iceland		Norway		Sweden	
	N	RS (CI)	N	RS (CI)	N	RS (CI)	N	RS (CI)	N	RS (CI)
Women										
1964–1968	2 505	20 (18–23)	1 397	25 (22–28)	61	*18 (13–25)*	1 669	31 (28–35)	4 239	28 (26–30)
1969–1973	2 746	19 (17–20)	1 483	27 (24–30)	67	*18 (13–25)*	1 779	26 (24–29)	4 819	31 (30–33)
1974–1978	2 897	21 (20–23)	1 641	24 (22–27)	79	40 (28–58)	1 880	27 (25–30)	4 835	33 (32–35)
1979–1983	2 838	22 (20–23)	1 801	31 (28–33)	84	29 (20–42)	2 070	30 (28–33)	4 926	36 (34–37)
1984–1988	2 941	27 (25–29)	1 952	31 (29–33)	105	31 (23–43)	2 248	32 (30–35)	4 820	40 (38–41)
1989–1993	2 845	27 (25–29)	2 270	32 (30–34)	95	36 (27–47)	2 267	34 (32–36)	4 620	38 (37–40)
1994–1998	2 911	30 (28–32)	2 409	37 (35–39)	105	29 (21–40)	2 362	37 (35–39)	4 383	42 (40–44)
1999–2003	2 986	33 (31–34)	2 433	44 (42–45)	103	34 (28–42)	2 389	41 (39–42)	4 145	43 (42–45)

Numbers in *italics* indicate that two or more cells had to be combined to get sufficient number of patients to calculate survival.

a slight decline with time and little variation between countries (Figure 8). Survival decreased with age at diagnosis and increased with time (Table VIII).

Discussion

To summarise the main incidence trends established in this paper, there were large declines in cervical cancer in the Nordic countries, slight increases in cancer of corpus uteri, small decreases in ovarian cancer and little change in cancer of the other female genital organs. For all female genital cancers, mortality has been slightly decreasing while survival has tended to increase slightly. The Icelandic figures should be interpreted cautiously given large random variation due to small numbers.

The decline in cervical cancer incidence started in the mid-1960s in each of the Nordic countries with the exception of Norway, where the decrease started 10 years later. This is an observation attributed to differences in organised screening programmes for early detection of precancerous lesions [13]. The variations in rates and the relative extent of declines were shown to match the extent and intensity of population-based screening in the respective countries [2], providing substantial support for the effectiveness of early detection by organised programmes [14]. The temporary rise in incidence occurring in Iceland during the 1980s was due to an increase in the proportion of women ever attending the nationwide screening program through implementation of a new electronic invitation system. This focused first on women who had not attended the program within the past five years and resulted in rapidly rising three year attendance rates followed by the peak in incidence as a consequence [15]. Cytological screening for precancerous lesions and following treatment have been the major factor in the reduction of cervical cancer incidence and mortality in the Nordic countries, while in contrast, 5-year relative survival has remained largely stable at around 60% in each of the Nordic populations from the 1960s through to the 1980s [10]. Thereafter, a slight increase in survival has been observed.

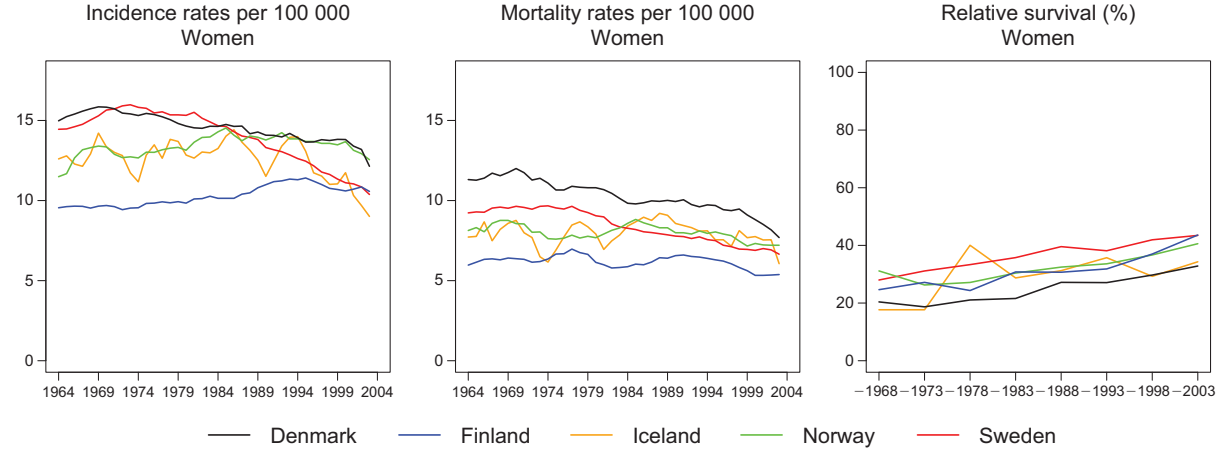

Figure 5. Trends in age-standardised (World) incidence and mortality rates per 100 000 and age-standardised (ICSS) 5-year relative survival for ovarian cancer by country. Nordic cancer survival study 1964–2003.

Table VI. Trends in 5-year age-specific relative survival in percent after ovarian cancer by country. Nordic cancer survival study 1964–2003.

	Women					
Age	0–49	50–59	60–69	70–79	80–89	90+
Denmark						
1964–1968	39	22	18	17	13	*
1969–1973	40	24	17	15	5	0
1974–1978	45	29	21	12	12	0
1979–1983	48	27	23	13	8	32
1984–1988	54	34	27	20	12	12
1989–1993	53	35	29	19	10	27
1994–1998	53	42	30	21	12	31
1999–2003	63	46	32	24	13	19
Finland						
1964–1968	51	30	24	17	14	*
1969–1973	46	35	28	24	8	*
1974–1978	49	33	22	20	8	*
1979–1983	58	39	29	22	21	0
1984–1988	61	42	30	19	17	0
1989–1993	62	40	31	26	12	14
1994–1998	69	50	41	22	19	27
1999–2003	71	58	48	32	20	9
Iceland						
1964–1968	*63*	*21*	*14*	*10*	*	*
1969–1973	*63*	*21*	*14*	*10*	*	*
1974–1978	62	40	22	42	51	*
1979–1983	50	34	16	35	16	*
1984–1988	95	22	26	13	36	*
1989–1993	82	40	26	34	15	*
1994–1998	56	30	40	10	25	82
1999–2003	68	38	56	12	6	*
Norway						
1964–1968	46	35	27	30	26	*
1969–1973	46	32	25	23	13	*
1974–1978	52	31	28	20	15	51
1979–1983	57	37	30	23	16	38
1984–1988	60	38	33	25	19	57
1989–1993	61	43	33	24	20	0
1994–1998	65	47	42	25	14	17
1999–2003	68	52	47	28	18	24
Sweden						
1964–1968	52	34	28	22	14	0
1969–1973	55	39	29	22	25	0
1974–1978	61	40	34	23	21	0
1979–1983	64	42	36	28	20	14
1984–1988	67	49	40	30	24	11
1989–1993	64	50	36	31	23	19
1994–1998	66	48	43	35	28	16
1999–2003	65	52	45	35	31	29

Numbers in *italics* indicate that two or more cells had to be combined to get sufficient number of patients to calculate survival.

*Too few patients to calculate survival, see reference [11].

A EUROCARE study published in 2007 indicated that the cervical cancer survival five years after diagnosis in the Nordic countries was among the highest in Europe [16]. Geographical and temporal variations in cervical cancer incidence and mortality in these populations however are mainly the product of two major and competing factors. One relates to the timing and extent of implementation of organised screening programs [2,14]. The second results from the changing pattern of sexual behaviour, with increasing transmission of oncogenic types of HPV and a higher prevalence of persistent infection increasing the risk of cancer of cervix uteri. The latter phenomenon is evident in successive birth cohorts in a number of European populations born 1930–1950 [17]. The historical declines in survival observed in certain populations may result from a selective prevention of slower-growing tumours via screening [18].

Clinical stage and age at diagnosis are clear prognostic factors for cervical cancer, but the relative survival increases in the Nordic patients among those diagnosed at early age are not particularly substantial relative to other age groups. Older women might have been diagnosed at a later stage since they never have been offered screening, and may have had co-morbidities leading to a choice of more conservative treatment options, while younger women, often diagnosed at earlier clinical stages, are more likely to receive and accept more aggressive treatments with a curative intent. It is still unclear as to the role of histological subtype in subsequent survival differences, despite much research activity [16,19–22]; some have reported a higher survival for squamous cell carcinoma, while others have reported no difference in prognosis. In a Finnish study it was shown that the incidence of squamous cell carcinoma of cervix uteri declined following the introduction of the screening programme while the incidence of adenocarcinoma was rather stable over time [23]. A possible interaction with age at diagnosis, with higher survival for both cervical adenocarcinoma in younger women, and cervical squamous cell carcinoma diagnosis among older women has also been noted [16].

The main symptom of cancer of the corpus uteri is bleeding and the disease is usually diagnosed at an early stage leading to a rather good prognosis. Icelandic patient survival has previously been reported to deviate from the other Nordic countries since around 1978 [10], and this result was confirmed and updated in this study. Swedish patients have a survival a few percentage points higher than patients in the other Nordic countries over the study period, although this was confined to the first three months after diagnosis, most notably during the first month.

Varying coding practices in the Nordic countries may also contribute to the country-specific differences in survival estimates from cancer of the corpus uteri; the category for "uterus other" (ICD-10 C55 & C58), associated with poorer survival, was seldom used in Iceland and has been used variably in the other countries, but most frequently in Sweden. On including this unspecified category with cancers of

Table VII. Trends in survival for cancer in other female genital organs by country. Number of tumours (N) included and the 5-year age-standardised (ICSS) relative survival in percent with 95% confidence intervals (RS (CI)). Nordic cancer survival study 1964–2003.

	Denmark		Finland		Iceland		Norway		Sweden	
	N	RS (CI)	N	RS (CI)	N	RS (CI)	N	RS (CI)	N	RS (CI)
Women										
1964–1968	433	53 (47–59)	328	43 (36–50)	9	*	306	52 (46–60)	709	47 (43–51)
1969–1973	416	61 (55–67)	341	40 (35–46)	9	*	330	55 (49–62)	742	50 (46–55)
1974–1978	525	57 (53–63)	371	49 (43–55)	11	*	429	50 (45–56)	711	56 (52–61)
1979–1983	622	58 (54–63)	375	55 (49–62)	11	*	439	50 (45–56)	797	56 (52–60)
1984–1988	539	60 (55–65)	400	46 (41–52)	18	*63 (46–86)*	432	52 (47–58)	866	56 (52–60)
1989–1993	621	58 (54–63)	420	54 (48–60)	10	*63 (46–86)*	453	54 (49–60)	940	58 (54–62)
1994–1998	665	59 (54–64)	480	54 (49–59)	15	*64 (48–85)*	546	58 (54–64)	998	58 (54–62)
1999–2003	631	57 (53–60)	550	55 (51–59)	16	*64 (48–85)*	491	63 (59–67)	1018	57 (54–60)

Numbers in *italics* indicate that two or more cells had to be combined to get sufficient number of patients to calculate survival.
*Too few patients to calculate survival, see reference [11].

corpus uteri to explore the impact of that more advanced cases incorrectly might have been classified as "uterus other", the relative survival ratios were lowered by one to four percentage points, most notably in Sweden, thus resulting in no changes in the relative ranking of survival between countries, except in Iceland, where women who still experienced a poorer survival by four to eight percentage points.

The use of HRT increased steadily in Iceland from the late 1970s [24] and a similar trend is likely to have occurred in all the Nordic countries. A Nordic report for the years 1995–2007 showed an increasing use of both unopposed oestrogens and in combination with progesterones between 1995 and 2000, and a decline thereafter in all countries [25]. The use of unopposed oestrogens is associated with a substantially increased risk of the diagnosis of endometrial cancer, without a corresponding increase in mortality [26]. The increasing use of HRTs in the Nordic countries during the last three decades may therefore explain part of the improved survival. Of the five Nordic countries, the lowest use of oestrogens was reported for Denmark [25] so the postulated effect on survival would have been smallest in Denmark.

Since treatment has not changed much during the last 30 years [27], factors behind the steadily increasing survival, besides earlier diagnosis and better peri-operative care, could be the increased oestrogen exposure (HRT) increasing the frequency of corpus uteri cancer diagnoses associated with better prognosis [26].

Ovarian cancer trends are encouraging with overall declines in both incidence and mortality as well as increasing survival. Nevertheless the prognosis is poor with 5-year relative survival around 40%. Due to diffuse early symptoms the majority of patients are diagnosed at an advanced stage, unless incidentally found during diagnostic procedures for other diseases. Tumour stage at diagnosis has been identified as an important prognostic factor [28,29]; in one report, Danish women with a localised ovarian can-

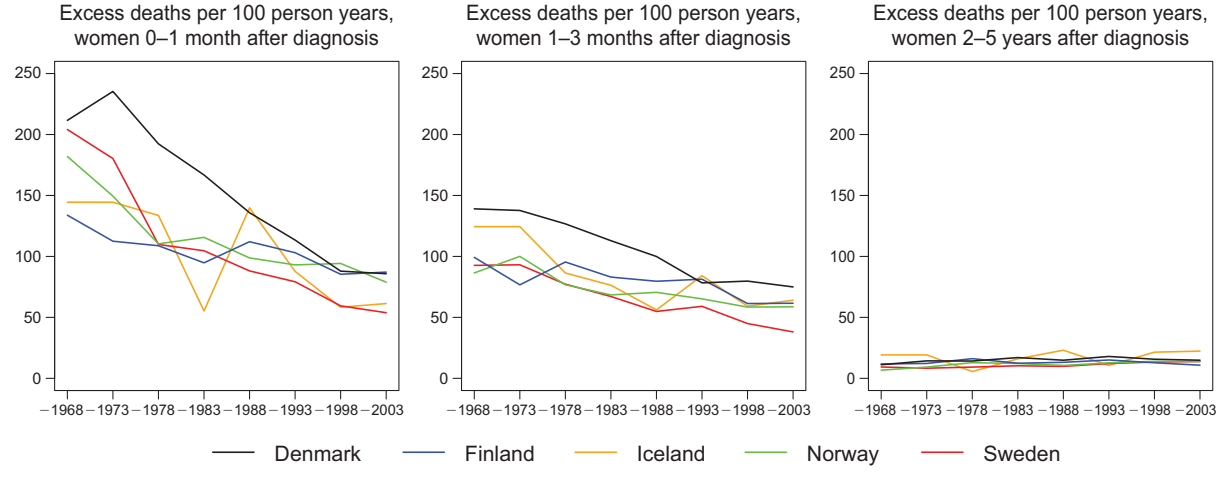

Figure 6. Trends in age-standardised (ICSS) excess death rates per 100 person years for ovarian cancer by country and time since diagnosis. Nordic cancer survival study 1964–2003.

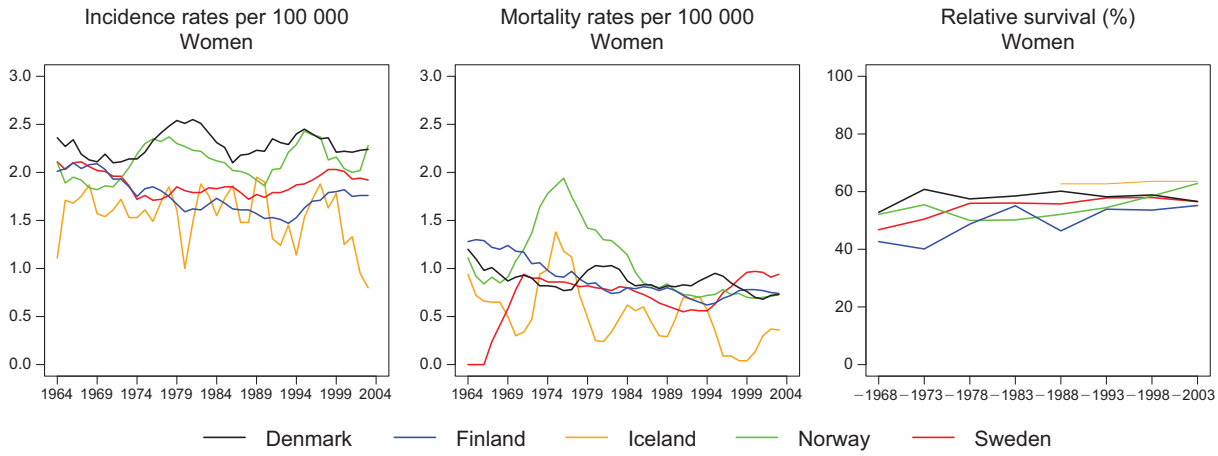

Figure 7. Trends in age-standardised (World) incidence and mortality rates per 100 000 and age-standardised (ICSS) 5-year relative survival for cancer of other female genital organs by country. Nordic cancer survival study 1964–2003.

cer had a significantly reduced relative excess mortality risk compared with those who were diagnosed with tumours with regional or distant metastases [29]. Unfortunately, the currently available screening methods do not have adequate sensitivity or specificity to justify organised programmes, and thus attentiveness among clinicians to women showing (vague) symptoms is important. Diagnosis and treatment of ovarian cancer patients in Denmark is yet to be restricted to specialised centres which in other countries has been shown to improve the results [30], and may be one factor behind the poorer Danish survival. Surgical removal of the ovaries and debulking of peritoneal metastases is the primary treatment, often combined with postoperative chemotherapy. Operating methods have improved with time and combined with more effective combinations of chemotherapy for women with advanced ovarian cancer may have contributed to improving survival [31,32].

There are no major differences between the Nordic countries regarding survival among women with cancer of the vulva, vagina and other unspecified genital organs. Vaginal and vulvar cancers are mainly of squamous cell type and have certain aetiologic features, such as being HPV- and smoke-related, in common with cervical cancer [8]. The development and introduction of HPV vaccine may consequently increase the prospect for prevention of both cervical as well as vaginal and vulvar cancer.

Death certificates have not been used as a source of cancer notification in Sweden and death certificate initiated cases tend to have an inferior survival compared to others which consequently could bias the results. This could partly explain the higher ovarian cancer survival in Sweden relative to elsewhere, especially since the excess mortality in the first three months was considerably lower than in the other countries. Studies of completeness of the Swedish

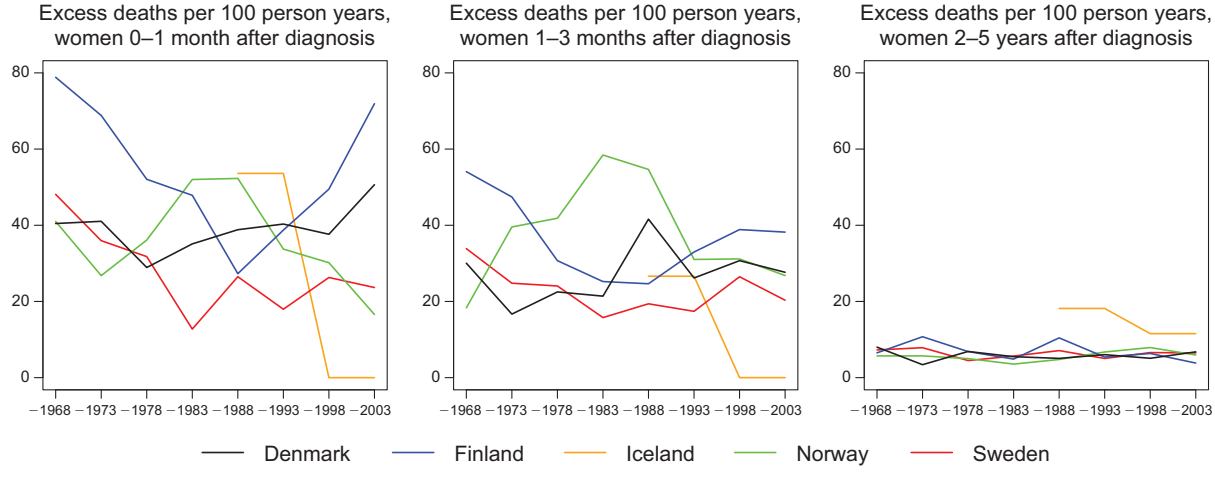

Figure 8. Trends in age-standardised (ICSS) excess death rates per 100 person years for cancer of other female genital organs by country and time since diagnosis. Nordic cancer survival study 1964–2003.

Table VIII. Trends in 5-year age-specific relative survival in percent after cancer in other female genital organs by country. Nordic cancer survival study 1964–2003.

	Women					
Age	0–49	50–59	60–69	70–79	80–89	90+
Denmark						
1964–1968	74	66	53	49	28	0
1969–1973	73	68	66	49	55	0
1974–1978	84	65	58	52	35	58
1979–1983	82	65	60	55	36	41
1984–1988	72	69	63	57	42	66
1989–1993	72	65	59	57	39	0
1994–1998	80	67	61	51	43	46
1999–2003	84	68	59	44	43	39
Finland						
1964–1968	60	45	42	41	31	*
1969–1973	76	58	40	31	9	0
1974–1978	74	54	54	44	22	0
1979–1983	82	53	63	44	44	0
1984–1988	77	44	59	40	15	24
1989–1993	81	60	54	48	36	40
1994–1998	69	65	57	47	35	0
1999–2003	76	65	58	45	42	22
Iceland						
1964–1968	*66*	*66*	*66*	*	*	*
1969–1973	*66*	*66*	*66*	*	*	*
1974–1978	*69*	*69*	*69*	*	*	*
1979–1983	*69*	*69*	*69*	*	*	*
1984–1988	*80*	*80*	*80*	*62*	*0*	*
1989–1993	*80*	*80*	*80*	*62*	*0*	*
1994–1998	*86*	*86*	*86*	*43*	*20*	*
1999–2003	*86*	*86*	*86*	*43*	*20*	*
Norway						
1964–1968	63	54	55	50	40	*
1969–1973	79	54	66	47	34	46
1974–1978	67	61	49	44	37	46
1979–1983	71	60	59	39	29	86
1984–1988	74	69	46	46	39	0
1989–1993	75	72	58	41	38	26
1994–1998	80	76	57	49	41	28
1999–2003	81	75	60	58	49	17
Sweden						
1964–1968	72	53	53	38	26	68
1969–1973	76	52	52	48	31	38
1974–1978	73	62	58	51	42	15
1979–1983	76	65	58	47	45	0
1984–1988	82	61	56	51	37	54
1989–1993	70	63	63	53	42	40
1994–1998	81	69	56	51	42	39
1999–2003	73	72	56	50	40	35

Numbers in *italics* indicate that two or more cells had to be combined to get sufficient number of patients to calculate survival.
*Too few patients to calculate survival, see reference [11].

Cancer Registry though, have demonstrated a high completeness for cases of the female genital organs, indicating that non-use of death certificate information has only a minor influence on the survival estimates [33,34].

In conclusion, this study points to encouraging trends for cancer of cervix uteri as the disease is becoming less common, and for corpus uteri where survival continues to improve. Prognosis is still poor for women diagnosed with ovarian cancer however, and there remain relatively large differences between countries. Cancer-specific differences between countries in the survival of female patients diagnosed with cancers of the cervix uteri, corpus uteri and other female genital organs are small relative to many other cancer sites.

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