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RESEARCH ARTICLE

Trends in gynecologic cancer among elderly women in Denmark, 1980–2012

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ABSTRACT

Background The aim of this analysis was to describe trends in incidence, mortality, prevalence, and survival in Danish women with gynecologic cancer from 1980–2012 comparing women aged 70 years or more with younger women.

Material and methods Gynecologic cancers included were ICD-10 codes C53 (cancer of the cervix uteri), C54 (corpus uteri cancer), C56 (ovarian cancer) and C57 (Fallopian tube cancer). Data derived from the NORDCAN database with comparable data on cancer incidence, mortality, prevalence and relative survival in the Nordic countries, where the Danish data are delivered from the Danish Cancer Registry and the Danish Cause of Death Registry with follow-up for death or emigration until the end of 2013.

Results For cervical cancer the incidence decreased among women aged less than 70 years and remained stable among the elderly. The mortality rates were clearly separated by age groups with a 2–3 fold higher mortality rate among 70 + years-old than younger women. The mortality rates, however, decreased in all age groups from 1980–2012.

For ovarian and Fallopian tube cancers the incidence was almost constant, whereas the average annual number of deaths decreased over time from 466 in 1980 to 396 in 2012. The mortality rates were clearly separated by age groups with mortality rates 3–4 times higher among the elderly. The mortality rate decreased among women less than 70 years during the entire period.

The average annual number of newly diagnosed corpus uteri cancer increased from 631 in 1980 to 773 in 2012. The mortality rates were clearly separated by age groups with much higher mortality rates among the 70+ years-old as compared with younger women. Overall the mortality rates decreased from 1980 to 2012.

Conclusion In gynecologic cancer both mortality rates and survival are age-dependent with a significantly shorter survival in the group of elderly.

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Gynecologic cancers comprise cancers of the cervix uteri, corpus uteri, ovaries, Fallopian tubes, vulva, and vagina, but the latter two are not included into this analysis and will not be mentioned further.

Cervical cancer is a sexually transmitted disease caused by human papilloma virus (HPV) in virtually all cases. The disease is more prevalent in lower socioeconomic groups and in women with multiple sexual partners. Smoking is an independent risk factor for squamous cell cervix uteri cancer [1].

Cervical cancer is the fourth most common cancer in women worldwide with an estimated 528.000 new cases in 2012 with approximately 85% occurring in low-resource countries. The incidence of cervical cancer is decreasing in high-resource countries, whereas in low-resource countries it is among the most common of all cancer types and accounts for the highest number of cancer deaths in women. In 2012, there was an estimated 266.000 deaths from cancer of the cervix with 87% occurring in low-resource countries [2].

In Denmark and other high-resource countries, cervical cancer is primarily diagnosed in women aged 25–70 years with a peak in the incidence at 30–40 years and a smaller peak at 75–80 years. Danish women aged 23–64 years are offered routine screening in a well-established national screening program with a cytology test of cell samples from the cervix. HPV vaccines can prevent infection with HPV 16 and HPV 18, which are known to cause at least 70% of cervical cancer cases. In Denmark, 12 years old girls are offered HPV vaccination free of charge. Because of the screening program the incidence of cervical cancer has decreased in Denmark during the past 50 years [3] and is expected to continue to decrease, also as a consequence of the vaccination program.

The cause of cancers of the ovaries and Fallopian tube cancer is multi-factorial and until recently basically unknown. Use of hormonal contraceptives for at least five years, multiple deliveries, and to a lesser degree breast feeding decrease the risk, whereas the number of years with ovulation is positively associated with an increased risk. A recent, large meta-analysis [4] concluded that use of menopausal hormones for 5 years increases the risk (RR 1.43, 95% CI 1.31-1.56, $P < 0.0001$).

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Approximately 5–10% of cases are inherited with BRCA mutations as the most important contributor.

Ovarian- and Fallopian tube cancer is most common in high-resource countries and is worldwide the sixth most common cancer in women with approximately 238.000 new cases and approximately 152.000 deaths in 2012 [2]. The disease is typically diagnosed between 35–75 years. The epithelial cancers are primarily diagnosed in women older than 50 years (peak incidence around 70 years) and germ cell tumors are primarily diagnosed in younger women. Danish women have the second highest incidence of ovarian- and Fallopian tube cancer world-wide [5].

Worldwide the incidence of corpus uteri cancer (endometrial cancer) almost displays the same geographical distribution as ovarian cancer and is most commonly diagnosed between the age of 40 and 75 years [2] with a peak incidence around 70 years in Denmark. The risk increases with age, nulliparity, diabetes, use of hormone replacement therapy, use of tamoxifen and in women with metabolic syndrome, probably primarily because of the central obesity component [6].

The aim of this analysis was to describe trends in incidence, mortality, prevalence, and survival in Danish women with gynecologic cancer from 1980–2012 comparing women aged 70 years or more with younger women.

Material and methods

Gynecologic cancers were defined as ICD-10 codes C53 (cervix uteri), C54 (corpus uteri), C56 (ovarian cancer) and C57 (Fallopian tube cancer). A more detailed description of the materials and methods appear elsewhere [7]. In brief, data derives from the NORDCAN database with comparable data on cancer incidence, mortality, prevalence and relative survival in the Nordic countries, where the Danish data are delivered from the Danish Cancer Registry and the Danish Cause of Death Registry with follow-up for death or emigration until the end of 2013. This study focuses on the group of elderly women categorized by age as 0–69, 70–79, 80–89 and 90+ years with one of the above-mentioned diagnoses.

The incidence and mortality, age group specific numbers and rates per 100,000 person years are shown in tables and graphs with calendar periods for time of diagnosis 1978–1982, 1988–1992, 1998–2002, 2003–2007, 2010, 2011 and 2012. Prevalence is defined as the number of cancer patients (including cured patients) alive and is shown in tables by the end of 1980, 1990, 2000, 2005, 2010, 2011 and 2012. Age specific 1- and 5-year relative survival proportion ratios were calculated for each of the diagnostic groups for the age groups 0–69, 70–79, 80–89 and 90+ years and for the 5-year intervals in the period 1968 to 2012. Relative survival for a group of cancer patients is calculated as the observed survival (where all causes of death are considered events) divided by the expected survival in a comparable Danish population with the same age and year of birth composition. Actuarial method is used for observed survival and Ederer II method for expected survival [8]. Relative survival can be interpreted as the survival if the cancer was the only cause of death. For the most recent period, 2008–2012, not all patients can be followed up for death in 5 years and we used hybrid methods where we supplement with survival experience from cancer patients diagnosed earlier years. If all patients die in the follow-up period resulting in zero survival, this is indicated as 0 (–) and if calculation for a cell results in a relative survival higher than 100%, the result is shown in tables, but restricted to 100% in graphs.

Results

Cancer of the uterine cervix

Incidence and mortality

The average annual number of newly diagnosed cancers of the uterine cervix decreased from 627 in 1980 to 356 in 2012. The proportion of patients diagnosed over the age of 70 years has remained constant in the entire period and with 18.0% in 1980 and 18.3% in 2012 (Table I). Table II shows that the average annual number of deaths from cervical cancer has decreased over time from 296 in 1980 to approximately 100 per year in 2012.

Adjusting for changes in population size and age, Figure 1 illustrates that the incidence rates decreased with time during the entire period from 1980 through 2012. The incidence was higher among women aged 70 years or more than among younger, but the age group 30-40 years had the highest incidence. The mortality rates (Figure 2) were clearly separated by age groups with a 2-3 fold higher mortality rate among women aged 70 years or more than in those aged less than 70 years. The mortality rates did, however, decrease in all age groups from 1980 through 2012.

Prevalence

Since 1980 the prevalence of cervix uteri cancer decreased from 11.904 in 1980 to 8.880 in 2012 (Table III). The proportion of persons alive after a diagnosis of cervix uteri cancer and

Table I. Average annual number of new cervical cancer cases in Denmark, 1980–2012.

	0–69 yr		70–74 yr		75–79 yr		80–84 yr		85–89 yr		90 + yr		All ages	
	cases (incidence)		cases (incidence)		cases (incidence)		cases (incidence)		cases (incidence)		cases (incidence)		cases (incidence)	
	N	%	*N*	%	*N*	%	*N*	%	*N*	%	*N*	%	*N*	%
1980	514	82.0	51	8.1	35	5.6	18	2.8	7	1.2	2	0.3	627	100
1990	436	78.6	46	8.3	34	6.1	25	4.5	11	1.9	3	0.6	554	100
2000	320	79.3	25	6.3	25	6.2	20	5.1	8	2.0	4	1.1	404	100
2005	312	80.4	23	5.9	24	6.1	16	4.1	9	2.4	4	1.1	388	100
2010	283	81.8	20	5.8	18	5.2	15	4.3	7	2.0	3	0.9	346	100
2011	335	83.3	20	5.0	15	3.7	14	3.5	10	2.5	8	2.0	402	100
2012	291	81.7	20	5.6	21	5.9	12	3.4	9	2.5	3	0.8	356	100

1980, 1990, 2000, 2005 indicate means for the 5-year period around the year.

aged 70 years or more has increased from 3.041 out of 11.904 (25.5%) in 1980 to 2.904 out of 8.880 (32.7%) in 2012.

Survival

Figure 3 shows that both the one- and five-year relative survival decreased with increasing age, although the group of 90 + years-olds was too small to draw any firm conclusions. In 2012, the one-year relative survival in the age groups of less than 70, 70–79, and 80–89 years was 94%, 72% and 71% respectively, and the corresponding figures for five-year relative survival were 80%, 41% and 31% respectively.

The one-year relative survival increased among 80–89 years-old from 58% in 1978–1982 to 71% in 2008–2012. In women aged less than 70 years, a minor increase was seen from 89% to 94%. The same trend was observed in the 5-year relative survival with an increase among women aged lees than 70 years from 66% if diagnosed in 1978–1982 to 80% for those diagnosed 2008–2012. A 10% numerical increase in 5-year relative survival was seen for patients (80–89 years) diagnosed between 1978 and 1982 versus 2008-2012 (from 21% to 31% respectively).

Ovarian and fallopian tube cancer

Incidence and mortality

The average annual number of newly diagnosed ovarian and Fallopian tube cancers was almost constant with 583 in 1980 and 565 in 2012 (Table IV). The proportion of patients diagnosed over the age of 70 years increased from 34.4% in 1980 to 41.9% in 2012 Table V shows that the average annual number of deaths from ovarian cancer has decreased over time from 466 in 1980 to 396 in 2012.

Adjusting for changes in population size and age, Figure 4 illustrates a slight decrease in incidence rates with time among women aged less than 70 years whereas a minor increase was seen in the group of 80–84 years-old. The incidence rates increased with age, the rates among women aged 70 years or more being about three times higher than among those aged less than 70 years. The mortality rates (Figure 5) were clearly separated by age groups with mortality rates 3–4 times as high among the elderly compared with younger women in whom the mortality rate decreased during the entire period.

Prevalence

Since 1980 the prevalence of ovarian cancer has increased substantially (Table VI). In 2012, 4,523 women (all ages) were alive in Denmark after a diagnosis of ovarian cancer compared with 2,706 in 1980 despite of almost constant incidence rates in the period. The proportion of persons aged 70 years or more has also increased from 32% in 1980 to 43% in 2012.

Survival

Relative survival increased steadily over time for all age groups, except the 90 + years-old (very few cases) (Table VI). Among

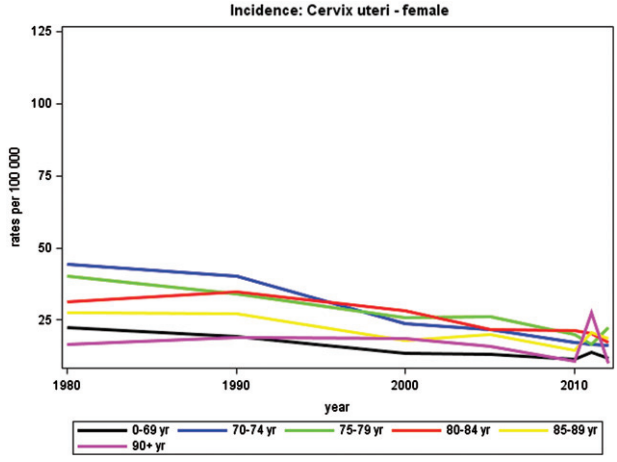

Figure 1. Incidence rates of cervical cancer in Denmark, 1980-2012, by age group.

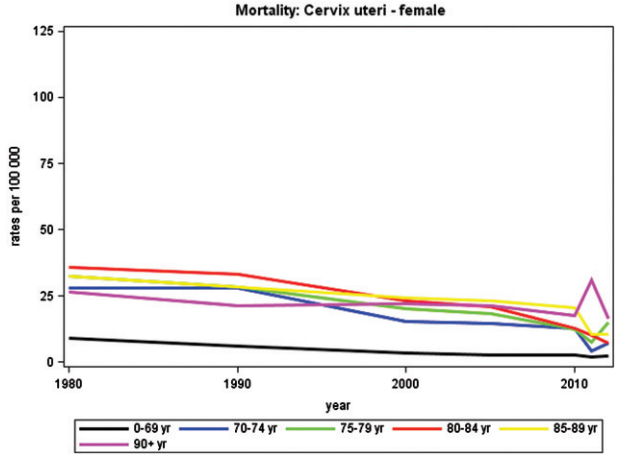

Figure 2. Mortality rates from cervical cancer in Denmark, 1980-2012, by age group.

Table II. Average annual number of deaths from cervical cancer in Denmark, 1980–2012.

	0–69 yr		70–74 yr		75–79 yr		80–84 yr		85–89 yr		90 + yr		All ages	
	cases (mortality)		cases (mortality)		cases (mortality)		cases (mortality)		cases (mortality)		cases (mortality)		cases (mortality)	
	N	%	*N*	%	*N*	%	*N*	%	*N*	%	*N*	%	*N*	%
1980	204	68.9	32	10.9	28	9.6	20	6.8	9	3.0	3	0.9	296	100
1990	138	58.4	32	13.5	28	11.8	24	10.1	11	4.6	4	1.5	237	100
2000	85	55.0	16	10.7	20	12.7	17	10.9	11	7.3	5	3.4	154	100
2005	66	50.8	15	11.9	17	12.8	16	12.0	11	8.2	6	4.3	130	100
2010	64	56.1	15	13.2	11	9.6	9	7.9	10	8.8	5	4.4	114	100
2011	45	57.7	5	6.4	7	9.0	7	9.0	5	6.4	9	11.5	78	100
2012	57	60.0	9	9.5	14	14.7	5	5.3	5	5.3	5	5.3	95	100

Table III. Annual number of persons alive with cervical cancer (ICD-10, C53) in Denmark by december 31, 1980–2012.

	0–69 yr		70–74 yr		75–79 yr		80–84 yr		85–89 yr		90+ yr		All ages	
	prev cases		prev cases		prev cases		prev cases		prev cases		prev cases		prev cases	
	N	%	*N*	%	*N*	%	*N*	%	*N*	%	*N*	%	*N*	%
1980	8863	74.5	1419	11.9	904	7.6	475	4.0	204	1.7	39	0.3	11904	100
1990	7252	63.0	1685	14.6	1275	11.1	834	7.2	340	3.0	127	1.1	11513	100
2000	6010	59.7	1156	11.5	1250	12.4	947	9.4	480	4.8	216	2.1	10059	100
2005	5889	62.4	925	9.8	921	9.8	911	9.7	541	5.7	244	2.6	9431	100
2010	5904	66.0	811	9.1	783	8.7	665	7.4	503	5.6	286	3.2	8952	100
2011	5990	67.0	797	8.9	735	8.2	643	7.2	481	5.4	292	3.3	8938	100
2012	5976	67.3	804	9.1	715	8.1	636	7.2	458	5.2	291	3.3	8880	100

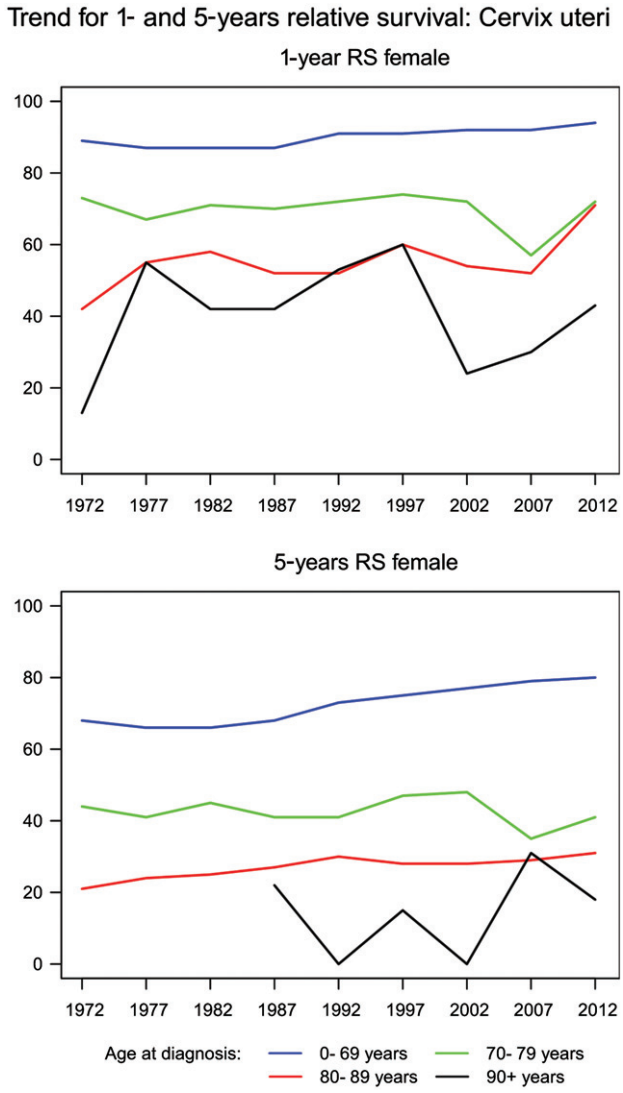

Figure 3. Age-specific relative survival after cervival cancer in Denmark.

patients aged less than 70 years, the five-year relative survival increased from 30% to 47% for those diagnosed from 1978–1982 to 2008–2012 respectively. Correspondingly, for patients aged 70–79 years, the five-year relative survival increased from 12% to 30%. The relative survival decreased with increasing age group. In the most recent period from 2008 to 2012, the relative one-year survival was 85%, 72%, 45% and 25% for women aged less than 70, 70–79, 80–89 and 90+ years respectively and the corresponding relative five-year survival was 47%, 30%, 17% and 10% respectively.

Cancer of the corpus uteri

Incidence and mortality

This analysis included only endometrial carcinomas (uterine sarcomas were excluded). The average annual number of newly diagnosed endometrial cancers has increased from 631 in 1980 to 773 in 2012. The proportion of patients diagnosed over the age of 70 years increased from 31% in 1980 to 42% in 2012 (Table VII). Table VIII shows that the average annual number of deaths from endometrial cancer has decreased over time from 148 in 1980 to 92 in 2012.

Adjusting for changes in population size and age, Figure 7 illustrates that the incidence rate has been unchanged in women less than 70 years from 1980 to 2012, whereas the incidence rates in women aged more than 70 years peaked around 2005 and then remained almost constant. The incidence increased with age, the rates among women aged 70 years or more being about three times higher than among those aged less than 70 years. The mortality rates (Figure 8) were much higher among women aged more than 70 years than in women aged less than 70 years. Overall, the mortality rates decreased from 1980 to 2012.

Prevalence

Since 1980, the prevalence of corpus uteri cancer has increased from 6,516 in 1980 to 10,138 in 2012 (Table IX). While the prevalence has been almost unchanged among women less than 70 years (3,436 in 1980 and 3,633 in 2012), the prevalence has increased in all other age groups. The proportion of women aged more than 70 years alive after a diagnosis of cancer of the corpus uteri comprised 47% of the entire group in 1980 increasing to 64% in 2012.

Survival

Relative survival increased over time for all age groups, but most pronounced among the 70 + years-old (Figure 9). Thus, for patients aged less than 70 years diagnosed from 1978 to 1982, the one-year relative survival increased from 92% to 96% for those diagnosed from 2008 to 2012 and the corresponding

Table IV. Average annual number of new ovarian and fallopian tube cancers in Denmark, 1980–2012.

	0–69 yr		70–74 yr		75–79 yr		80–84 yr		85–89 yr		90 + yr		All ages	
	cases (incidence)		cases (incidence)		cases (incidence)		cases (incidence)		cases (incidence)		cases (incidence)		cases (incidence)	
	N	%	*N*	%	*N*	%	*N*	%	*N*	%	*N*	%	*N*	%
1980	382	65.6	78	13.3	65	11.2	38	6.5	17	2.9	3	0.5	583	100
1990	383	65.7	77	13.2	57	9.8	42	7.2	18	3.2	5	0.9	583	100
2000	393	63.2	87	14.0	72	11.7	42	6.7	21	3.3	7	1.1	621	100
2005	359	63.0	68	12.0	63	11.1	50	8.7	23	4.1	6	1.1	570	100
2010	337	59.3	71	12.5	75	13.2	50	8.8	29	5.1	6	1.1	568	100
2011	337	58.4	79	13.7	76	13.2	54	9.4	24	4.2	7	1.2	577	100
2012	328	58.1	89	15.8	63	11.2	55	9.7	21	3.7	9	1.6	565	100

1980, 1990, 2000, 2005 indicate means for the 5-year period around the year.

Table V. Average annual number of deaths from ovarian and fallopian tube cancers in Denmark, 1980–2012.

	0–69 yr		70–74 yr		75–79 yr		80–84 yr		85–89 yr		90 + yr		All ages	
	cases (mortality)		cases (mortality)		cases (mortality)		cases (mortality)		cases (mortality)		cases (mortality)		cases (mortality)	
	N	%	*N*	%	*N*	%	*N*	%	*N*	%	*N*	%	*N*	%
1980	275	59.0	70	15.0	61	13.1	40	8.6	16	3.4	4	0.9	466	100
1990	253	55.0	67	14.5	64	14.0	45	9.7	24	5.2	7	1.6	461	100
2000	230	51.4	69	15.3	69	15.5	46	10.2	24	5.4	10	2.2	448	100
2005	196	49.2	56	14.0	60	15.0	50	12.6	27	6.7	10	2.5	399	100
2010	178	45.1	56	14.2	50	12.7	62	15.7	36	9.1	13	3.3	395	100
2011	171	44.8	65	17.0	50	13.1	51	13.4	35	9.2	10	2.6	382	100
2012	191	48.2	57	14.4	43	10.9	52	13.1	38	9.6	15	3.8	396	100

Table VI. Annual number of persons alive with ovarian and fallopian tube cancers in Denmark by december 31, 1980–2012.

	0–69 yr		70–74 yr		75–79 yr		80–84 yr		85–89 yr		90 + yr		All ages	
	prev cases		prev cases		prev cases		prev cases		prev cases		prev cases		prev cases	
	N	%	*N*	%	*N*	%	*N*	%	*N*	%	*N*	%	*N*	%
1980	1833	67.7	349	12.9	276	10.2	147	5.4	81	3.0	20	0.7	2706	100
1990	2086	63.3	446	13.5	336	10.2	262	8.0	120	3.6	44	1.3	3294	100
2000	2417	61.8	486	12.4	456	11.7	311	8.0	162	4.1	77	2.0	3909	100
2005	2591	61.5	524	12.4	447	10.6	355	8.4	204	4.8	91	2.2	4212	100
2010	2614	58.9	599	13.5	514	11.6	348	7.8	254	5.7	110	2.5	4439	100
2011	2627	58.3	622	13.8	521	11.6	353	7.8	268	5.9	115	2.6	4506	100
2012	2582	57.1	646	14.3	548	12.1	358	7.9	270	6.0	119	2.6	4523	100

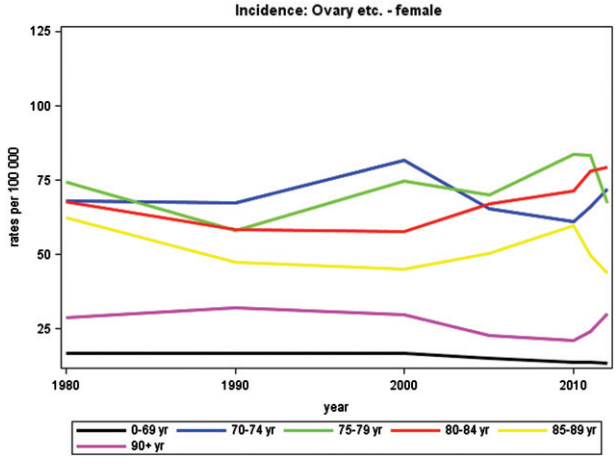

Figure 4. Incidence rates of ovarian- and Fallopian tube cancers in Denmark, 1980-2012, by age group.

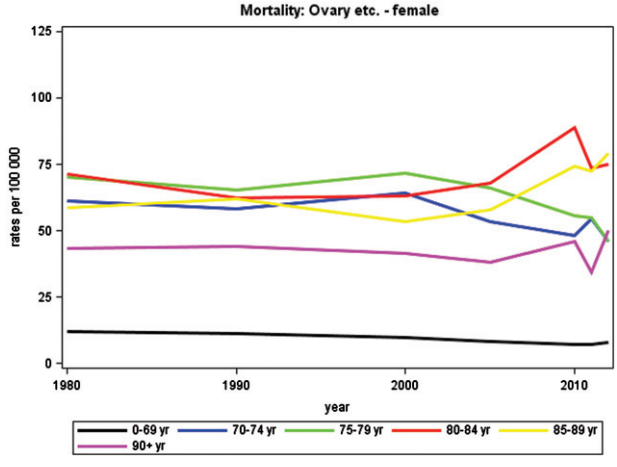

Figure 5. Mortality rates from ovarian- and Fallopian tube cancer in Denmark, 1980-2012, by age group.

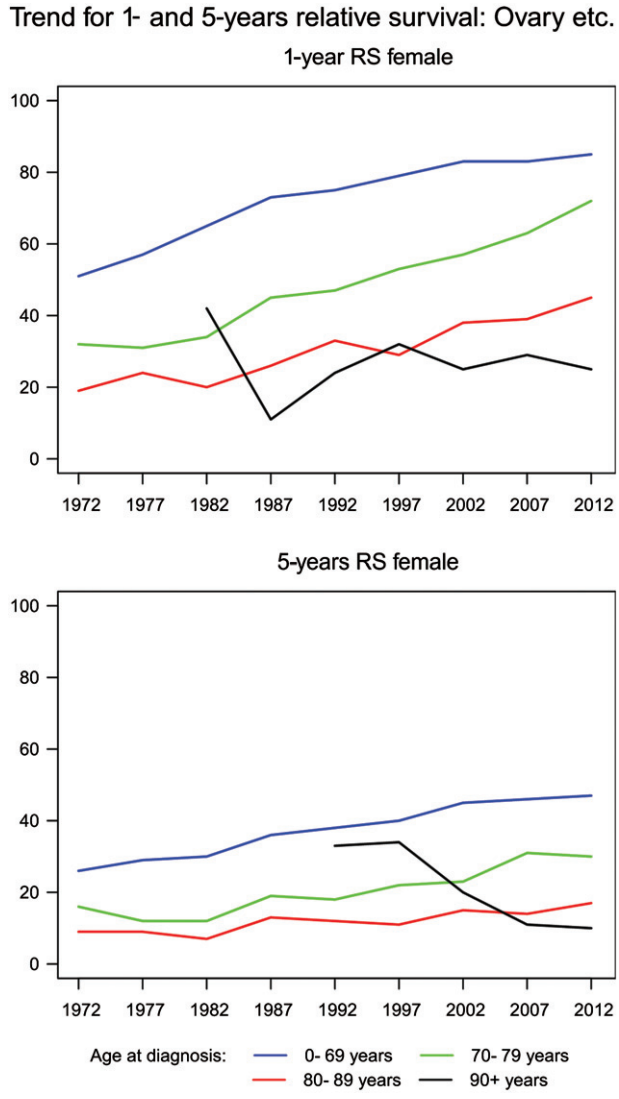

Figure 6. Age-specific relative survival after ovarian cancer in Denmark.

5-year relative survival was 83% and 85%, respectively. For patients aged 70–79 years and diagnosed from 1978 to 1982, the 1-year and 5-year relative survival increased from 81% and 61% to 92% and 76% respectively for those diagnosed 2008–2012. The same trend was observed among the oldest old (80 + years-old).

The relative survival decreased with increasing age group but the differences diminished with time, e.g. from 1978–1982 the relative five-year survival was 83% for those aged less than 70 years, but only 44% among 80-89 years-old, a difference of 39%. In the most recent period, 2008 to 2012, this difference diminished to 10% from 85% to 75%.

Discussion

Management of patients with gynecologic cancer has changed dramatically since 1980. Unorganized mass cervical cancer screening appeared in Denmark in the 1960'ies, initially with an uneven distribution between counties. In the recommendations for the first Danish national screening program from 1986, women aged 23-59 years were offered screening every three years, but the screening program was not implemented on a nationwide basis until 2006. In the guidelines from 2007, women aged 23–49 years are recommended screening every three years, and women aged 50–64 years every five years. Although the screening program has resulted in a significant reduction in the cervical cancer incidence in Denmark [3], the screening effect on the incidence of cervical cancer of the elderly women is probably negligible. The 90+ years-old women were older than the targeted screening population group of 23–59 years in 1986 where the first screening recommendations were published, and hence not invited. Women in the 70–79 and 80–89 age groups, living in counties participating in the screening program, were invited for screening in the 1990s, but the coverage of these women in the program has probably been low. The mortality rate is highest in the older age groups not included in the screening program. The HPV vaccination program was not introduced until 2008 and has not influenced the incidence of cervical cancer in adult women so far.

The backbone of curative intended therapy of stage Ib1 (high risk) to stage IVA cervical cancer is external beam radiation combined with brachytherapy. Although a study by Hata et al [9] concluded that radiotherapy in cervical cancer patients older than 80 years of age is safe and effective, a number of elderly patients will only be offered palliative treatment, because comorbidity prevents them from tolerating the 5–6 weeks course of curative radiotherapy [10].

Besides from refinement of pelvic external beam radiation and brachytherapy, the most important progress in the treatment of women with high risk cervical cancer has been the introduction of concomitant cisplatin. In the late 1990s, a number of studies demonstrated that concomitant chemotherapy, primarily as weekly cisplatin in a dose of 40 mg/m^2 improved progression-free and overall survival, the latter in the order of 11–12% [11,12]. This further explains the higher mortality rates among 70 + years-old, because concomitant cisplatin is not systematically offered to the elderly due to the high risk of toxicity. Women with advanced or recurrent cancer of the cervix benefit from treatment with cisplatin plus paclitaxel or topotecan [13]. The effect of these regimens can be improved by addition of the anti-angiogenetic agent bevacizumab [14]. This will primarily improve the 1-2-year survival rate in the younger population, because the tolerability is low in the elderly.

It is possible that the slight decrease in the incidence rates among 0–69 years-old women with ovarian cancer could be due to changes in pathological criteria for the diagnosis for ovarian carcinomas versus ovarian borderline tumors, and it is possible that the assessment differs among pathologists, however no reference to any temporal shifts in the classification of ovarian tumors have been found [15].

Contrary to cancer of the cervix, no screening method has succeeded in demonstrating a mortality benefit in ovarian cancer [16]. The existing methods including measurement of the tumor marker CA-125 and vaginal and/or abdominal ultrasound have not enabled a definition of precursor lesions with an acceptable sensitivity and specificity. Consequently ovarian cancer is often diagnosed in advanced stage. In a cohort of 961 Danish women with ovarian cancer, 63% of patients aged less than 70 years were diagnosed in stage III-IV compared with 73% of those aged 70 years or more.

Table VII. Average annual number of new corpus uteri cancers in Denmark, 1980–2012.

	0–69 yr		70–74 yr		75–79 yr		80–84 yr		85–89 yr		90 + yr		All ages	
	cases (incidence)		cases (incidence)		cases (incidence)		cases (incidence)		cases (incidence)		cases (incidence)		cases (incidence)	
	N	%	*N*	%	*N*	%	*N*	%	*N*	%	*N*	%	*N*	%
1980	437	69.2	81	12.9	63	9.9	34	5.4	14	2.2	2	0.3	631	100
1990	402	63.2	107	16.8	65	10.2	40	6.3	18	2.9	4	0.6	636	100
2000	350	56.6	97	15.7	88	14.2	54	8.7	22	3.6	7	1.2	618	100
2005	394	59.8	85	12.9	80	12.2	58	8.9	32	4.9	9	1.3	658	100
2010	427	60.1	76	10.7	90	12.7	75	10.5	32	4.5	11	1.5	711	100
2011	454	57.6	119	15.1	101	12.8	71	9.0	27	3.4	16	2.0	788	100
2012	447	57.8	116	15.0	73	9.4	73	9.4	46	6.0	18	2.3	773	100

1980, 1990, 2000, 2005 indicate means for the 5-year period around the year.

Table VIII. Average annual number of deaths from corpus uteri cancer in Denmark, 1980–2012.

	0–69 yr		70–74 yr		75–79 yr		80–84 yr		85–89 yr		90 + yr		All ages	
	cases (mortality)		cases (mortality)		cases (mortality)		cases (mortality)		cases (mortality)		cases (mortality)		cases (mortality)	
	N	%	*N*	%	*N*	%	*N*	%	*N*	%	*N*	%	*N*	%
1980	64	43.5	25	17.2	27	18.2	17	11.6	11	7.6	3	1.9	148	100
1990	55	39.5	26	19.1	22	15.8	18	13.2	13	9.1	5	3.3	138	100
2000	44	33.2	22	16.5	27	20.1	18	13.2	16	11.9	7	5.1	133	100
2005	40	33.1	19	15.6	22	18.0	21	17.1	13	10.8	7	5.5	121	100
2010	30	30.3	20	20.2	16	16.2	18	18.2	11	11.1	4	4.0	99	100
2011	39	40.6	11	11.5	13	13.5	15	15.6	13	13.5	5	5.2	96	100
2012	26	28.3	17	18.5	16	17.4	20	21.7	5	5.4	8	8.7	92	100

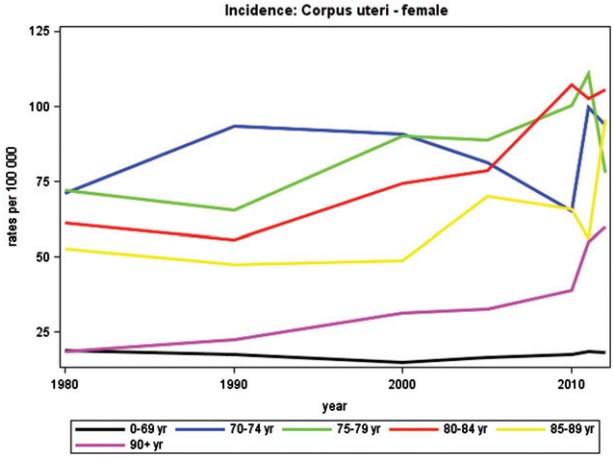

Figure 7. Incidence rates of cancer of the corpus uteri in Denmark, 1980-2012, by age group.

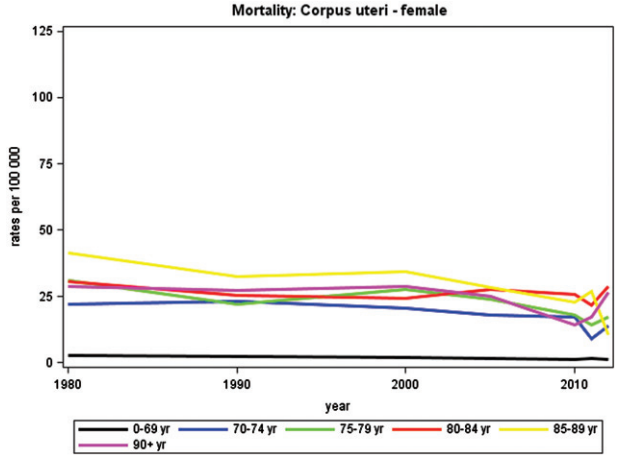

Figure 8. Mortality rates from cancer of the corpus uteri in Denmark, 1980-2012, by age group.

Furthermore, whereas 97% in the younger group underwent primary debulking surgery or interval debulking surgery after neoadjuvant chemotherapy, this was only the case for 85% of patients aged 70 years or more and the proportion of optimally debulked patients (residual tumor <1 cm) was 66% versus 51% respectively [17]. Also the number of patients receiving combination chemotherapy (carboplatin plus paclitaxel) was lower in the group of older cancer patients (77% versus 43%). These findings clearly explain the higher mortality rates and the lower overall and disease-free one- and five-year survival observed in patients aged 70 years or more compared with younger patients. The increase in survival observed for both younger and older patients is more difficult to explain and is probably due to improvement of several factors.

Today, all patients are discussed at multidisciplinary team conferences (MDT) and treatment plans are elaborated on the basis of findings on CT-, MR and/or PET-CT scans with input from specialist in gynecology, clinical oncology, radiology, and pathology. Ovarian cancer surgery has become more extensive with a major effort to remove all tumor tissue macroscopically. In addition to the extensive surgery, a major benefit has undoubtedly been the centralization of ovarian cancer surgery from more than 30 departments performing surgery in advanced ovarian cancer patients in 2003 to only 5 departments in Denmark today [18]. The vast majority of patients are offered combination chemotherapy if they are in good performance status (0-2). The introduction of combination chemotherapy, including paclitaxel in 1996, has further increased the one- and five-year survival [19]. The finding that the second generation platinum, carboplatin, can replace cisplatin without loss of efficacy [20] has increased tolerability,

Table IX. Annual number of persons alive with corpus uteri cancer in Denmark by december 31, 1980–2012.

	0–69 yr		70–74 yr		75–79 yr		80–84 yr		85–89 yr		90 + yr		All ages	
	prev cases		prev cases		prev cases		prev cases		prev cases		prev cases		prev cases	
	N	%	*N*	%	*N*	%	*N*	%	*N*	%	*N*	%	*N*	%
1980	3436	52.7	1154	17.7	919	14.1	656	10.1	291	4.5	60	0.9	6516	100
1990	3537	42.3	1815	21.7	1368	16.3	967	11.6	486	5.8	195	2.3	8368	100
2000	2850	31.4	1574	17.4	1921	21.2	1563	17.2	802	8.8	355	3.9	9065	100
2005	3133	33.6	1295	13.9	1625	17.4	1703	18.2	1124	12.0	458	4.9	9338	100
2010	3539	36.1	1360	13.9	1398	14.3	1511	15.4	1234	12.6	757	7.7	9799	100
2011	3610	36.3	1430	14.4	1420	14.3	1464	14.7	1222	12.3	802	8.1	9948	100
2012	3633	35.8	1556	15.3	1441	14.2	1388	13.7	1253	12.4	867	8.6	10138	100

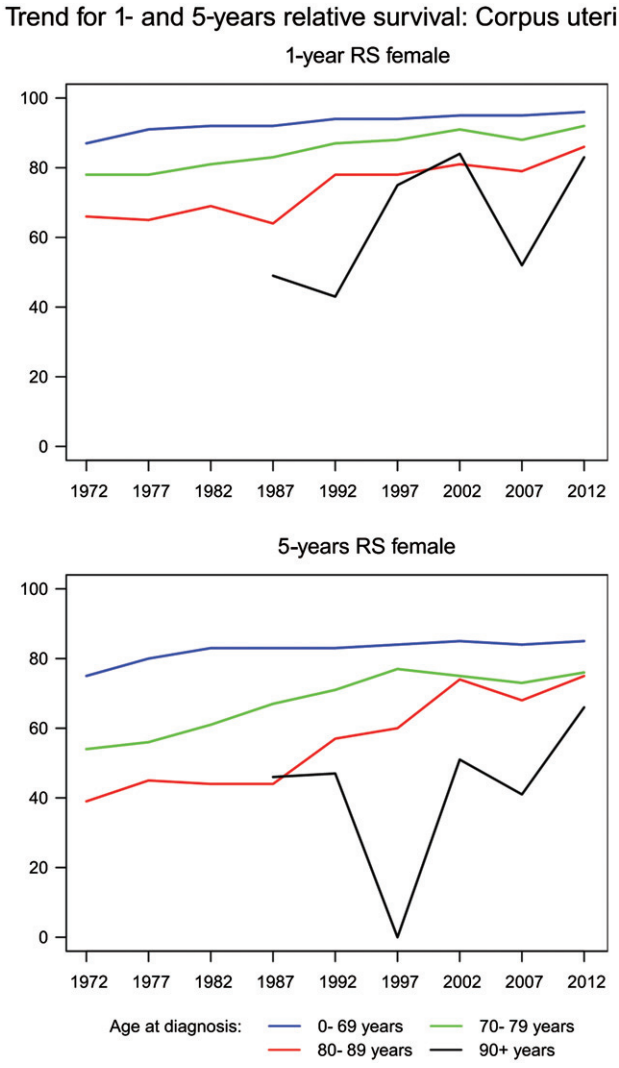

Figure 9. Age-specific relative survival after cancer of the corpus uteri in Denmark.

resulting in the possibility to offer more elderly ovarian cancer patients platinum-based combination chemotherapy.

Endometrial cancer has been the focus of much less research than ovarian cancer, probably due to the much better relative survival. Because of irregular vaginal bleeding, the disease is diagnosed earlier than ovarian cancer and only 20% of patients are diagnosed with stage III-IV disease. Approximately one third of women diagnosed with endometrial cancer will die of the disease and more than 60% of those who die are 70 years or older [21]. The primary treatment is surgery. Radiotherapy reduces the risk of loco-regional recurrence [22], but neither radiotherapy nor chemotherapy has improved survival [22]. In Denmark, radiotherapy is therefore no longer offered as a routine treatment and standard chemotherapy is offered only to stage III-IV patients. Large randomized trials are ongoing to explore the value (if any) of chemotherapy to stage I-II patients with one or more risk factors. The improvement in survival, primarily seen in elderly patients, is therefore probably caused by improvement in surgical techniques and postoperative management. Robotic assisted surgery which has been introduced during the last 5 years is likely to decrease perioperative complications and the improvement in survival among elderly patients is expected to continue.

Conclusion

Cancers of the cervix, corpus uteri, and ovaries represent distinct and different disease entities with respect to incidence (continuing decrease in cervical cancer among younger women and stable incidence rates in the other two cancer diseases), stage of disease at diagnosis (stage III-IV in ovarian and lower stages in the others), treatment options, and survival (poor prognosis in ovarian cancer and a good prognosis of the others). Despite these differences, older women (70 + years) have a 2-3 times higher mortality rate than younger women, and survival is also age-dependent with a significantly shorter survival for the elderly in all three gynecologic cancer diseases. Older gynecologic cancer patients are under-represented in clinical trials [23] and randomized trials focusing on both fit and frail elderly patients are highly warranted in particular in ovarian cancer, due to the poor prognosis in elderly.

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