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Cancer patient survival in Sweden at the beginning of the third millennium – predictions using period analysis

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Abstract

Estimates of cancer patient survival made using traditional, cohort-based, methods can be heavily influenced by the survival experience of patients diagnosed many years in the past and may not be particularly relevant to recently diagnosed patients. Period-based survival analysis has been shown to provide better predictions of survival for recently diagnosed patients and earlier detection of temporal trends in patient survival than cohort analysis. We aim to provide predictions of the long-term survival of recently diagnosed cancer patients using period analysis. The period estimates are compared with the latest available cohort-based estimates. Our results, based on period analysis for the years 2000–2002, suggest an improvement in survival for many forms of cancer during recent years. For all sites combined the 5-, 10-, 15-, and 20-year relative survival ratios were 62%, 53%, 48%, and 47% for males and 67%, 62%, 60%, and 59%, for females. These estimates were 3–14% units higher than those obtained using the latest available cohorts with the respective lengths of follow-up. The interval-specific relative survival stabilised for males at 97% after 8 years of follow-up and for females at 98% after 7 years for both period and cohort analyses.

Introduction

We recently published a comprehensive analysis of the survival of cancer patients diagnosed in Sweden 1960–1998 [1]. The article retrospectively evaluated and discussed changes in survival observed over the last 40 years in relation to available knowledge of factors that may have influenced patient survival.

Although the majority of the excess mortality due to cancer occurs during the first few years subsequent to diagnosis, excess mortality exists up to 20 years following diagnosis and even longer for some forms of cancer. It is therefore necessary to study both short-term and long-term survival in order to gain a complete picture of our progress in reducing cancer mortality. Traditional cohort-based estimates of, for example, 10-year survival are based on patients diagnosed during a period of at least 10 years. Long-term estimates of patient survival made using cohort-based methods can appear irrelevant to clinicians, their patients, and policy makers alike, since estimates are heavily influenced by patients diagnosed many years in the past who may have been treated with methods now considered obsolete. The time-lag between diagnosis and evaluation of survival can be reduced by applying period survival analysis, which was introduced into cancer survival analysis in 1996 [2]. Period analysis has been shown to provide better predictions of survival for recently diagnosed patients and earlier detection of temporal survival trends than cohort-based analysis [3, 4]. Period analysis has previously been used in several countries to derive more up-to-date estimates of survival [5–8].

The aim of this study is to provide predictions of long-term relative survival for cancer patients recently diagnosed in Sweden. The predictions are made by period analysis and the latest observed relative survival for cohorts with 5-, 10-, 15-, and 20-year survival are provided as a comparison.

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Materials and methods

The swedish cancer registry

Since 1958 every clinician, pathologist, and cytologist in Sweden is required by law to notify the Swedish Cancer Registry at the National Board of Health and Welfare of each new cancer diagnosed. The non-reporting rate has been estimated at less than 2% [9]. The Swedish Cancer Registry is population-based and covers today 8.9 million people. From its inception the register has accumulated information on 1.8 million tumours for 1.6 million persons.

Patients

This study was based on cancer cases diagnosed in patients aged less than 90 years between 1980 and 2001. A total of 415, 894 cancers in males and 403, 092 cancers in females were included in the analysis. Ninety-seven percent of the tumours were histologically confirmed and an additional 2% were verified by X-ray, CT, NMR *etc*. Patients diagnosed incidentally at autopsy or without any information regarding follow-up were excluded from the analysis (Table 1). Only the first primary cancer at each site was included in the analyses. Patients with multiple primary cancers diagnosed at different sites were included as independent entities in the analyses although we also performed an analysis restricted to the first primary cancers in each individual and compared the results to test the assumption that multiple primary cancers in the same individual could be analysed independently. Patients with zero survival, but not formally registered as autopsy findings, were included in the analysis. The Cancer Register is linked annually by personal identification numbers to the Cause of Death Register, which is also maintained by the National Board of Health and Welfare, and to the Migration and Population registries at Statistics Sweden, to obtain dates of death or censoring and to confirm continued residency in Sweden. At the time of analysis the follow-up was completed up to and including 31 December 2002. Complete follow-up was available for 99.98% of the recorded cases.

Forty different forms of cancer and all sites combined were analysed. Some histopathological groups were excluded from the analyses due to low incidence and/or survival probabilities that differ from the predominant pattern for that particular site. For cancer of the small intestine, testis, and brain and nervous system,

Table 1. Number of cancers diagnosed 1980–2001 and numbers excluded from the analysis

Year of diagnosis	Number of diagnoses	Autopsy	Multiple cancers at same site	Without follow-up	90 years or older	Included
1980	35 000	2 782	488	12	427	31 291
1981	35 150	2 757	517	14	412	31 450
1982	36 063	2 985	497	7	459	32 115
1983	37 072	2 860	506	6	479	33 221
1984	37 904	2 677	546	8	506	34 167
1985	38 220	2 614	606	10	567	34 423
1986	38 620	2 483	649	5	578	34 905
1987	39 892	2 525	638	4	606	36 119
1988	39 802	2 214	687	4	610	36 287
1989	40 157	1 987	726	8	649	36 787
1990	40 676	1 932	817	4	632	37 291
1991	40 957	1 634	938	2	653	37 730
1992	41 417	1 518	945	10	711	38 233
1993	42 156	1 460	1 062	7	702	38 925
1994	42 914	1 387	1 144	6	744	39 633
1995	42 347	1 261	1 243	5	746	39 092
1996	43 049	1 143	1 364	11	819	39 712
1997	43 015	938	1 345	19	845	39 868
1998	43 938	1 074	1 411	7	914	40 532
1999	45 387	956	1 414	14	944	42 059
2000	45 727	982	1 508	12	945	42 280
2001	46 385	837	1 640	11	1 031	42 866
Total	895 848	41 006	20 691	186	14 979	818 986

Patients diagnosed incidentally at autopsy or without any information regarding follow-up and patients 90 years or older at diagnosis were excluded from the analysis. Patients with zero survival, but not formally registered as autopsy findings, were included in the analysis.

different histopathological groups within the same site were analysed separately. The registry does not include basal cell carcinoma (basalioma) as part of the non-melanoma skin-cancer group. In contrast, all benign and malignant tumours of the endocrine glands are registered and were included in the analyses. A majority of all endocrine tumours are histologically benign and the proportion of benign tumours (among all endocrine tumours) has increased over time. The Swedish Cancer registry did not collect information on clinical stage until 2003 and does not register cases based on death certificates.

Patient survival was estimated for males and females separately as well as for both sexes combined and for different age groups. This article reports only results for males and females, respectively, and for the age group 0–89 years. Detailed results for each site, stratified by age at diagnosis, will for some time be available at our web site www.sos.se/epc.

Statistical analysis

We estimated both cumulative and interval-specific relative survival ratios (RSRs) using period analysis for the years 2000–2002 and cohort-based analysis for patients diagnosed in 1995–1997, 1990–1992, 1985–1987, and 1980–1982. The latter provide observed RSRs for the latest available 5-, 10-, 15-, and 20-year cohorts, respectively. Patients were followed for a maximum of 20 years after diagnosis. Relative survival is defined as the observed survival among the cancer patients divided by the expected survival for a comparable group from the general population with respect to the main factors affecting survival, in this case, sex, age, and calendar year. The RSR provides a measure of the excess mortality experienced by patients diagnosed with cancer, irrespective of whether mortality is directly or indirectly related to the cancer in question.

The calculations were performed with two publicly available SAS macros that can be used for both cohort and period analysis [10]. One macro implements the Hakulinen method [11] and was used to estimate the cumulative RSRs [12]. The other macro implements the Ederer II method [13] and was used to estimate the interval-specific RSRs [14]. The latter macro was adapted to report interval-specific survival and both macros were updated to facilitate the use of annual population survival probabilities.

In period survival analysis only person-time at risk and events (death or censoring) occurring during one particular calendar period are considered. The estimates are obtained by left truncation of all observations at the beginning of the period and right censoring at the end of the period. Whereas cohort estimates represent the survival experience of a well-defined cohort of patients diagnosed during a specified calendar period, period estimates do not represent the survival of any real cohort of patients followed from diagnosis. Period estimates represent the survival that would be observed for a hypothetical cohort of patients who experienced the same interval-specific survival estimates of the patients who were actually at risk during the specified calendar period (2000–2002 in our study). If prognosis improves over time the period estimates are expected to be higher than those obtained by a corresponding cohort analysis. The opposite would be expected if survival was declining and no difference would be seen if survival was constant over time. Empirical studies comparing the two methods using historical data show that period estimates from a given time period in most cases predict, quite well, the long-term survival for cohorts of patients diagnosed during that particular period [3–4].

The cumulative RSR can be interpreted as the proportion of patients alive after a given time of follow-up in the hypothetical situation where the cancer in question is the only possible cause of death. An interval-specific RSR of 100% indicates that, during this particular interval (year of follow-up), mortality in the patient group was equivalent to that of the general population. If this level is maintained during subsequent years of follow-up there is no longer evidence of an excess mortality due to cancer and the patients, as a group, can be considered 'statistically cured'. The approximate ratio and year of stabilisation was determined by visual inspection of the interval-specific RSRs. As such no formal definition was applied, but in most cases this corresponds to when the RSRs first levels off for three consecutive years. However, for some cancers the interval-specific RSRs continue to increase slightly even after the ratio of stabilisation has been said to occur. For cancers with low incidence and/or survival the reported ratio and year of stabilisation should not be taken too literally, but more be seen as an indication of when the excess mortality stabilises after diagnosis. This is illustrated in Figures 1 and 2 for lung cancer and acute myeloid leukemia, respectively (sites chosen for illustrational purpose).

Results

Based on a comparison of period and cohort estimates there is evidence of improvement in relative survival for many forms of cancer during the past two decades. For some sites survival seems to have stabilised at a

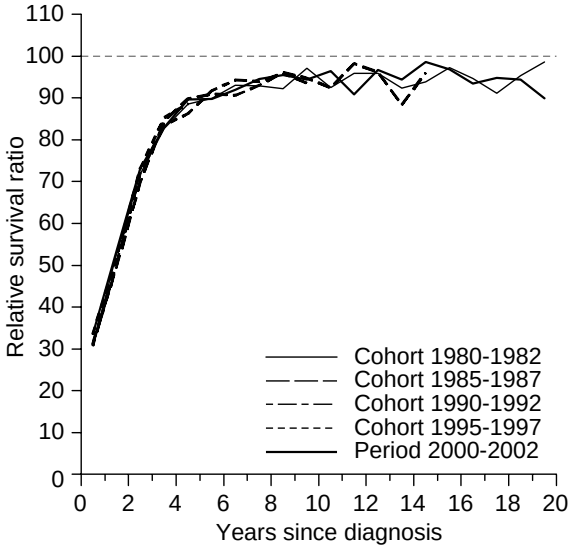

Fig. 1. Cancer of the lung. Interval-specific relative survival curves for period and cohort estimates. Males 0–89 years of age at diagnosis.

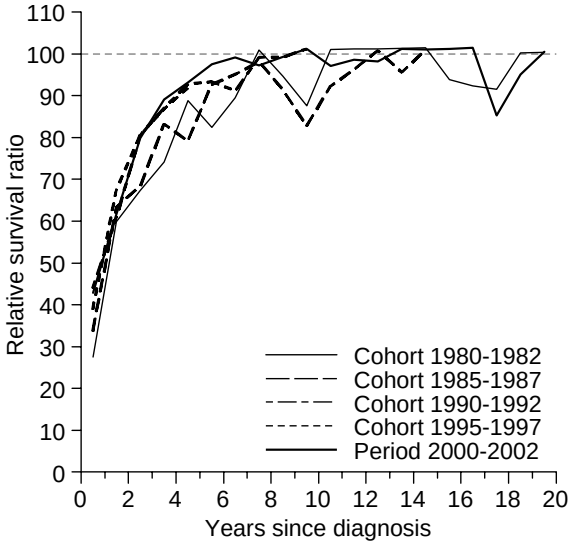

Fig. 2. Acute myeloid leukemia. Interval-specific relative survival curves for period and cohort estimates. Females 0–89 years of age at diagnosis.

relatively high level, whereas other sites show a continued poor survival that has remained essentially unchanged for decades. Females had a better survival than males for all sites combined and for most of the major forms of cancer. The estimates of patient survival are summarised in Tables 2 and 3 for males and females respectively.

For all sites combined the survival experienced by cancer patients during the period 2000–2002 indicates an improvement in long-term survival during the past two decades. The 5-, 10-, 15-, and 20-year period RSRs were 62%, 53%, 48%, and 47% for males and 67%, 62%, 60%, and 59% for females. This is for males some 6%, 10%, 12%, and 14% units higher, and for females some 3%, 5%, 9%, and 11% units higher than experienced by the latest cohorts available with the same lengths of follow-up. In relative terms, this implies an improved survival of between 10% and 43% for males and between 4% and 23% for females compared to the latest cohort estimates. The observed temporal improvements in survival arose primarily due to improvements during the first few years subsequent to diagnosis; differences between the interval-specific RSRs for period and cohort estimates were negligible approximately 6 years following diagnosis for males and approximately 4 years following diagnosis for females. For patients diagnosed 1980–1982, the RSR for the first year of follow-up was 66% for males and 73% for females compared to 80% and 81%, respectively, for patients diagnosed 1999–2001.

By far the most common cancer sites in Sweden are prostate cancer for males and breast cancer for females. They currently constitute approximately 30% of all diagnosed tumours and therefore have a large impact on the survival estimates for all sites combined. Since patients diagnosed with prostate and breast cancer have, on average, better survival than for all sites combined, excluding patients diagnosed with prostate and breast cancer from analyses of survival for all sites combined results in lower survival estimates. The 5- and 10-year period RSRs for males excluding prostate cancer were 53% and 48% and, for females, period RSRs for all cancers other than breast cancer were 57% and 53%. The survival difference between males and females stabilised at six percent units after ten years of follow up if prostate and breast cancers were excluded. For all sites combined the survival difference between the sexes stabilised at 12% units after 15 years of follow up.

The interval-specific RSR stabilised for males at 97% after 8 years of follow-up and for females at 98% after 7 years of follow-up for both period and cohort analysis. This suggests that cancer patients in general have an excess mortality for a considerable length of time after diagnosis. The fact that the interval-specific RSR does not quite reach 100% during the 20 years of follow-up is probably due to the fact that general population mortality underestimates the expected mortality of cancer patients, primarily due to the higher prevalence of smoking among cancer patients compared to the general population.

The interval-specific RSRs for prostate cancer and breast cancer exhibit an unusual pattern (Figures 3 and 4).

Table 2. Cumulative and interval-specific RSR estimated from the period 2000–2002, and observed cumulative RSRs for the last available cohort 5-, 10-, 15-, and 20-year survival (males 0–89 years of age at diagnosis)

Site	Period 2000–2002									Last available cohort[c]			
		Interval-specific[b]		Cumulative RSR						Cumulative RSR			
	Number at risk[a]	RSR	Year	1-year	2-year	5-year	10-year	15-year	20-year	5-year	10-year	15-year	20-year
All sites combined	47 428	97	8	80.6	72.9	62.4	52.8	48.4	46.7	56.6	43.3	36.3	32.6
All sites combined, excluding prostate	30 622	98	8	71.3	62.1	53.3	48.0	46.3	45.8	50.2	42.2	37.1	34.3
Lip	228	99	5	96.5	94.3	89.7	86.1	83.6	70.6	91.1	83.3	82.3	71.8
Oral cavity and mesopharynx	624	98	7	74.9	64.1	53.6	44.7	35.5	33.3	49.7	37.4	27.2	24.7
Oesophagus	601	95	6	36.9	21.3	12.9	9.3	9.1	6.9	11.8	5.1	3.8	2.4
Stomach	1 349	99	8	43.6	27.9	19.2	16.9	15.5	15.0	20.0	16.5	12.5	10.4
Small intestine, adenocarcinoma	78	100	5	49.0	37.0	28.6	32.8	30.5	41.8	21.2	20.9	18.8	23.0
Small intestine, carcinoids	115	97	4	90.8	84.1	74.7	60.0	48.2	42.4	76.4	50.9	43.4	39.9
Colon, adenocarcinoma	3 474	98	7	81.6	71.6	58.1	51.2	47.1	43.8	56.3	44.3	38.6	41.5
Rectum, adenocarcinoma	2 343	99	8	83.2	72.9	57.5	49.3	46.2	40.5	55.0	43.8	33.8	29.7
Liver, primary	418	90	5	24.7	17.3	9.3	5.5	6.1	9.1	6.0	4.4	2.3	0.7
Gall bladder, biliary tract	307	100	9	33.2	21.0	14.0	9.5	11.3	13.8	11.3	7.0	6.7	4.1
Pancreas	860	100	9	14.1	5.7	2.6	2.1	2.2	2.8	2.5	0.8	1.3	2.1
Nose and nasal sinuses	76	100	7	84.4	73.3	54.2	43.3	40.7	28.1	50.7	44.1	45.8	34.3
Larynx	364	96	3	87.1	77.8	67.9	55.7	47.6	45.9	67.2	53.1	42.8	42.3
Lung	3 701	95	8	33.7	18.1	10.1	7.7	6.6	5.4	9.9	6.6	5.2	4.6
Prostate	18 290	95	2	97.1	92.6	79.5	59.3	43.9	31.3	72.5	47.0	32.3	20.4
Testis, seminoma	366	100	1	99.5	99.4	99.3	98.7	96.4	95.8	98.0	96.6	92.5	85.8
Testis, non-seminoma	270	100	3	98.3	97.2	96.9	96.5	94.7	93.2	94.3	94.8	88.3	84.1
Kidney excluding renal pelvis	1 129	97	5	75.6	66.1	56.7	48.7	45.0	41.2	50.4	40.2	33.4	30.1
Urinary bladder and urethra	3 680	99	6	87.8	81.3	73.2	67.8	65.5	63.7	71.5	65.6	59.5	56.5
Malignant melanoma of skin	1 964	99	8	97.0	93.2	85.7	81.3	80.8	80.3	84.3	79.0	70.2	66.2
Malignant skin cancer, excl. melanoma	3 077	98	1	97.4	95.3	88.3	80.0	74.9	74.8	86.5	77.6	72.5	76.7
Eye	138	96	1	96.2	93.1	78.7	62.2	61.4	53.6	76.7	57.2	57.6	57.8
Brain, excl. cranial nerves, meningioma	790	98	6	51.9	35.0	29.8	27.1	26.7	28.1	33.7	27.8	22.5	20.9
Brain, meningioma	182	100	2	93.0	92.6	91.0	82.1	79.1	85.0	88.0	81.7	70.5	68.4
Brain, intracranial nerves neurinoma	123	100	1	100.0	100.8	100.1	94.1	87.7	85.4	99.3	99.6	99.9	115.1
Thyroid gland	179	100	5	85.2	81.0	76.4	74.2	70.6	74.1	77.7	73.0	76.4	70.0
Endocrine glands	472	99	3	93.6	91.7	88.2	83.1	78.9	73.5	87.5	85.4	76.8	73.6
Bone	98	100	8	87.6	78.2	69.5	65.9	65.9	66.1	67.0	62.7	46.2	52.1
Connective tissue, muscle	403	98	6	79.7	71.7	59.2	54.8	57.1	53.1	57.6	55.0	51.5	47.2
Non-Hodgkin lymphoma	1 855	95	6	78.7	69.4	57.5	47.2	42.1	38.9	53.8	42.1	34.5	29.1
Hodgkin's lymphoma	227	98	2	92.9	91.3	86.8	80.0	77.4	73.4	83.0	73.5	65.9	58.1
Multiple myeloma	681	90	9	79.2	65.8	37.9	16.4	11.1	7.4	34.0	13.2	7.5	6.6
Acute lymphocytic leukaemia	131	99	7	85.9	73.7	62.8	61.2	61.2	62.8	67.3	52.7	55.5	36.2
Chronic lymphocytic leukaemia	662	95	6	93.3	89.1	70.6	49.5	33.9	31.9	66.8	37.9	29.7	25.2
Acute myeloid leukaemia	286	100	7	37.8	22.5	16.2	17.0	18.8	23.1	17.5	13.3	11.3	5.2
Chronic myeloid leukemia	127	100	10	89.3	78.2	58.6	38.1	34.0	31.8	53.7	27.3	4.9	3.5

[a] Number at risk during the first year of follow-up in the period 2000–2002.

[b] Approximate interval-specific RSR and year at stabilisation (determined by visual inspection of the interval-specific ratios). For cancers with low incidence and/or survival the reported ratio and year at stabilisation should only be regarded as an indication.

[c] Last available cohort estimate of RSRs. 5-year = Cohort 1995–1997, 10-year = 1990–1992, 15-year = 1985–1987, and 20-year = 1980–1982.

Table 3. Cumulative and interval-specific RSR estimated from the period 2000-2002, and observed cumulative RSRs for the last available cohort 5-, 10-, 15-, and 20-year survival. (females 0–89 years of age at diagnosis)

Site	Period 2000–2002									Last available cohort[c]			
		Interval-specific[b]		Cumulative RSR						Cumulative RSR			
	Number at risk[a]	RSR	Year	1-year	2-year	5-year	10-year	15-year	20-year	5-year	10-year	15-year	20-year
All sites combined	44 158	98	7	81.6	75.1	66.9	61.7	59.6	58.7	64.3	56.6	50.2	47.7
All sites combined, excluding breast	30 682	98	7	74.3	66.1	57.4	53.0	52.1	52.4	55.7	48.6	46.0	45.0
Lip	118	100	3	96.5	93.7	87.5	75.4	69.0	51.7	88.0	87.8	77.3	57.5
Oral cavity and mesopharynx	426	97	6	81.1	70.4	59.9	49.1	46.2	42.2	59.2	42.1	39.7	32.1
Oesophagus	273	99	10	36.7	20.6	13.0	10.3	8.6	9.8	13.6	9.5	9.1	5.5
Stomach	891	100	12	43.1	29.9	21.6	17.0	15.8	14.1	22.7	14.4	17.3	12.4
Small intestine, adenocarcinoma	73	98	6	52.0	40.6	26.3	21.8	18.9	13.2	19.9	29.4	23.8	26.1
Small intestine, carcinoids	101	100	8	88.3	83.4	74.9	60.3	48.6	38.3	66.6	50.7	32.4	24.0
Colon, adenocarcinoma	3 673	99	7	81.1	71.3	59.7	53.6	50.8	46.6	57.1	49.6	46.0	44.3
Rectum, adenocarcinoma	1 722	99	8	83.4	74.2	59.1	53.5	50.6	49.9	60.8	45.7	41.8	37.4
Liver, primary	245	95	8	25.1	16.8	12.1	9.8	7.1		7.1	3.5	3.3	
Gall bladder, biliary tract	503	97	6	26.2	16.2	9.0	7.9	6.5	7.3	8.8	7.3	3.5	4.2
Pancreas	894	90	6	15.6	6.3	2.5	1.3	1.3	1.6	1.9	0.7	1.4	0.7
Nose and nasal sinuses	62	98	4	76.5	66.1	59.7	46.6	40.0	35.8	53.7	59.0	50.5	34.7
Larynx	78	97	4	89.0	79.6	68.9	54.0	51.8	40.3	75.3	60.7	47.2	36.6
Lung	2 713	95	7	39.2	24.0	15.4	11.9	10.2	9.4	16.3	9.4	7.8	7.8
Breast	14 391	98	6	97.8	94.9	87.0	78.8	72.9	68.6	84.9	74.8	60.8	54.3
Cervix uteri	1 066	98	4	87.4	78.2	70.8	66.9	66.9	65.0	70.0	66.9	62.5	59.7
Corpus uteri	3 077	99	6	94.2	89.6	82.8	80.6	79.6	81.8	83.2	76.4	77.8	80.5
Ovary	2 012	99	11	83.0	69.2	46.3	38.0	37.5	37.9	44.5	36.2	38.3	38.3
Kidney excluding renal pelvis	804	97	7	77.2	68.6	58.5	49.3	44.3	40.8	54.0	43.3	32.5	34.3
Urinary bladder and urethra	1 259	98	5	81.7	75.3	68.2	64.1	59.9	58.1	68.3	63.3	60.1	57.7
Malignant melanoma of skin	2 031	99	5	98.1	96.4	91.2	87.7	86.7	86.7	91.9	88.7	83.0	80.2
Malignant skin cancer, excl. melanoma	2 120	99	2	96.6	95.1	90.5	82.9	79.7	73.4	92.2	83.2	83.0	72.7
Eye	141	100	6	97.6	90.0	72.3	62.8	63.4	54.3	72.7	64.3	62.4	57.6
Brain, excl. cranial nerves, meningioma	609	97	6	57.7	43.9	36.0	32.8	32.5	34.1	33.1	30.9	26.0	23.9
Brain, meningioma	493	99	2	97.0	96.4	94.0	88.8	86.7	82.4	91.5	88.9	82.2	68.1
Brain, intracranial nerves neurinoma	117	100	2	98.9	98.8	99.5	103.5	98.6	92.2	100.3	97.5	91.0	87.9
Thyroid gland	490	99	4	88.4	87.0	85.4	84.6	82.6	84.9	88.0	86.3	81.6	82.6
Endocrine glands	1 070	99	1	98.6	98.8	97.3	91.4	88.3	84.0	97.1	87.4	82.3	76.8
Bone	72	95	2	84.2	80.8	75.0	62.4	59.6	54.9	71.0	60.3	65.7	47.7
Connective tissue, muscle	298	97	7	81.3	72.7	57.7	47.7	43.8	45.4	55.4	41.4	50.3	43.8
Non-Hodgkin lymphoma	1 497	96	6	76.5	68.9	58.3	49.2	45.3	41.8	54.8	42.0	34.1	28.9
Hodgkin's lymphoma	187	99	3	94.5	89.9	88.1	84.3	83.5	87.5	83.0	77.5	67.5	49.8
Multiple myeloma	608	88	7	79.1	66.2	34.9	14.7	7.4	3.1	34.2	13.5	8.5	1.5
Acute lymphocytic leukaemia	125	99	6	80.2	72.9	63.9	61.9	62.6	65.3	65.3	57.6	58.3	48.8
Chronic lymphocytic leukaemia	432	95	10	94.8	91.3	76.0	53.5	41.7	44.7	74.3	47.8	33.0	20.1
Acute myeloid leukaemia	267	99	7	43.0	26.9	19.4	21.1	23.8	23.6	18.6	18.1	7.7	6.3
Chronic myeloid leukemia	90	95	9	83.6	72.4	51.8	42.2	33.7	42.4	56.2	23.5	7.9	6.8

[a] Number at risk during the first year of follow-up in the period 2000–2002.

[b] Approximate interval-specific RSR and year at stabilisation (determined by visual inspection of the interval-specific ratios). For cancers with low incidence and/or survival the reported ratio and year at stabilisation should only be regarded as an indication.

[c] Last available cohort estimate of RSRs. 5-year = Cohort 1995–1997, 10-year = 1990–1992, 15-year = 1985–1987, and 20-year = 1980–1982.

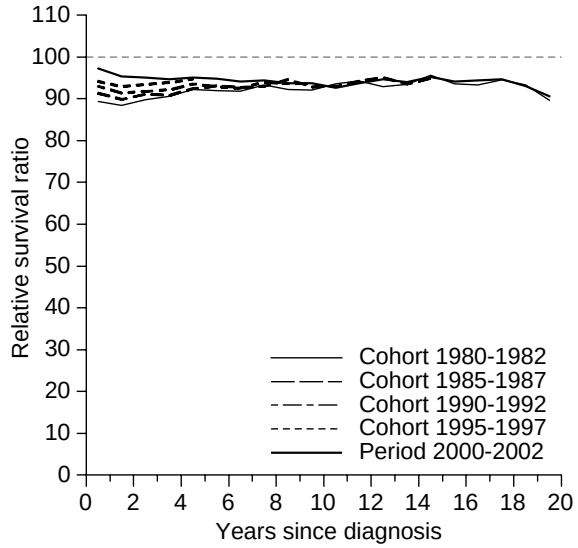

Fig. 3. Cancer of the prostate. Graph illustrating the unusual shape of the interval-specific relative survival curves for period and cohort estimates. Males 0–89 years of age at diagnosis.

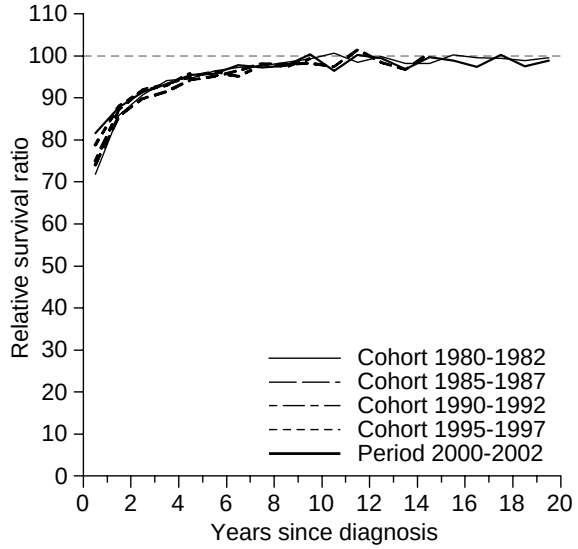

Fig. 5. Cancer of the colon, adenocarcinoma. Interval-specific relative survival curves for period and cohort estimates. Males 0–89 years of age at diagnosis.

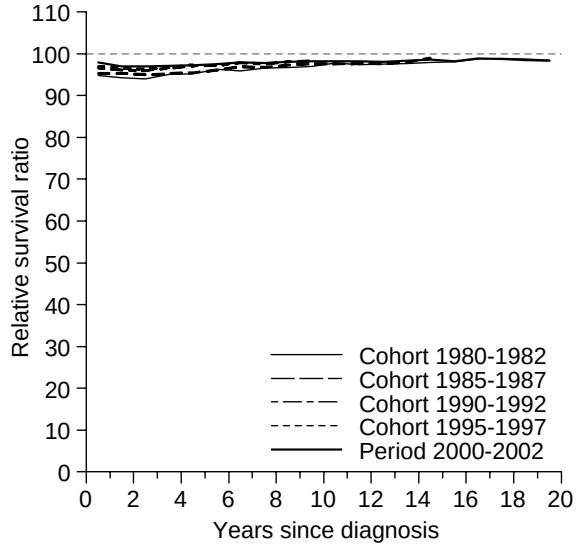

Fig. 4. Cancer of the breast. Graph illustrating the unusual shape of the interval-specific relative survival curves for period and cohort estimates. Females 0–89 years of age at diagnosis.

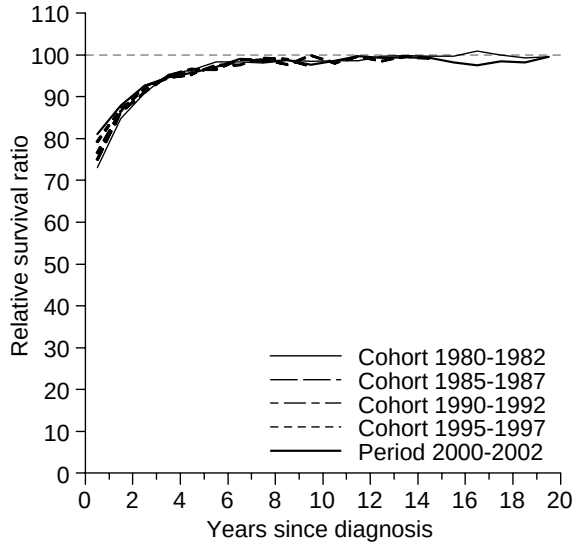

Fig. 6. Cancer of the colon, adenocarcinoma. Interval-specific relative survival curves for period and cohort estimates. Females 0–89 years of age at diagnosis.

Excess mortality for most forms of cancer is usually highest immediately following diagnosis and the level generally decreases with increasing follow-up time until the patients reach the point of statistical cure (where they no longer experience excess mortality). This is illustrated in Figures 5 and 6 for colon cancer (sites chosen for illustrational purpose). Prostate and breast cancer patients, in contrast, experienced an approximately constant excess mortality throughout the first 20 years of follow-up.

Excess mortality for prostate cancer patients was, if anything, slightly lower during the first two years following diagnosis. After seven years the interval-specific RSRs levelled off at 92–94% for the period

and cohorts analysed. Female breast cancer survival exhibited a pattern similar to that of prostate cancer. After six years of follow-up the excess mortality stabilised at 98% for the period estimate.

A comparison of period and cohort estimates suggests that the largest improvements in 10-year survival during the past decade have occurred for cancers of the prostate, kidney, colorectum, and non-Hodgkin lymphoma for males and colorectum, non-Hodgkin lymphoma, corpus uteri, breast, and endocrine glands for females. The increase in 10-year cumulative RSR was between 5% and 12% units for males and 4% and 8% units for females.

Patients diagnosed with some forms of cancer currently have a very favourable prognosis where only a small excess mortality can be seen for the first few years following diagnosis. For seminoma testicular cancer this has been true for many years [1]. For non-seminoma testicular cancer, which for many years had a poor survival compared to seminoma [1], the cumulative RSR is now closer to that for seminoma but still some 2% units lower. The period estimates also indicated an increased 5- and 10-year cumulative survival of approximately 2% units compared to the latest cohort estimates for both seminoma and non-seminoma testicular cancer. Patients diagnosed with neurinoma, a histologically benign tumour in the intracranial nerves of the brain, have had a good survival since the latter part of the 1970s [1] and based on the interval-specific RSRs virtually no survival disadvantage can be seen for recently diagnosed patients. The small observed reduction in cumulative RSR is likely caused by random variation due to low incidence. Other major sites for which the cumulative RSR have levelled off or remained constant, although not at the same high level as for those mentioned above are, for males, stomach, pancreas and, lung and, for females, pancreas, cervix uteri, urinary bladder, and skin cancer. These sites appear to have had a relative constant 10-year RSR during the past decade.

There remain several cancer sites for which patient survival continues to be poor, for example, oesophagus, liver, gall bladder (including biliary tract), pancreas, and lung. Only some long-term improvements can be seen for these sites between the period and cohorts analysed. For liver cancer the period estimates indicate an improved 5-year cumulative RSR of 3% units for males and 5% units for females. For females the period estimates also indicate an improved future 10-year cumulative RSR for liver cancer of 6% units, and for males an improved 10-year cumulative RSR for oesophagus cancer of 4% units. This figure should however be interpreted with caution due to the high fatality of these diseases. Fortunately, these sites also show short-term survival improvements. For patients diagnosed with oesophageal cancer the 1-, and 2-year cumulative RSR increased from 30% and 15% in the early 1990s to 38% and 21% for those diagnosed 1999–2001.

Patients diagnosed with liver cancer experienced an increase in short-term survival of approximately 10% units during the past decade with 1- and 2-year cumulative RSRs of 26% and 18% for those diagnosed 1999–2001. For cancer of the gall bladder (including biliary tract), males had a better survival compared to females although the improvement in survival during the past decade was similar for males and females. The 1- and 2-year cumulative RSRs for patients diagnosed 1999–2001 were 34% and 22% for males and 27% and 17% for females. Survival following a diagnosis of pancreatic cancer was similar for males and females; the 1-year RSR was 18% (compared to 12% for patients diagnosed a decade earlier) and the 2-year RSR was 8% (compared to 4% for patients diagnosed a decade earlier). Females have a better lung cancer survival compared to males. The 1- and 2-year cumulative RSR for males increased from 30% and 15% in the early 1990s to 35% and 19% for men diagnosed 1999–2001. For females the corresponding improvements were from 33% and 18% to 41% and 25%. The long-term excess mortality among lung cancer patients (Figure 1) is probably due to cardiovascular disease and other smoking related mortality. Results were similar when restricted to the first primary tumour in each individual suggesting that there are no serious problems with the assumption that mortality from multiple primary tumours can be considered independent.

Discussion

Using period survival analysis, this study shows that patient survival for many forms of cancer today can be expected to be higher than previously estimated by cohort-based analysis. Improvements in survival may reflect a variety of different factors such as increased and/or earlier diagnosis, a shift towards more favourable histopathological subtypes, or improved treatment. Regardless of the origin of the improvements, empirical evaluations based on historical data suggest that period analysis provides more accurate predictions of survival of recently diagnosed patients [3–4]. Most of the excess mortality experienced by cancer patients occurs during the first few years after diagnosis, on which the long-term cumulative survival is heavily dependent whereas later years of follow-up have a more limited impact on the cumulative estimates. Period estimates of survival

during the years directly following diagnosis are based only on patients diagnosed recently, thereby allowing period analysis to respond quickly to changes in survival.

Period analysis may overestimate long-term survival if the introduction of screening programmes or improvements in methods for early diagnosis introduce a lead-time bias. An example can be seen in this study regarding prostate cancer where PSA-testing has probably caused both lead-time bias and length time bias, *i.e.*, a larger proportion of non-fatal tumours are now reported to the Cancer Registry. Age-standardised incidence of prostate cancer increased by 3.2% and 5.5% annually during the periods 1992–2001 and 1997–2001, respectively despite the fact that incidence levelled of during 2000 and 2001 [15]. There was a six fold increase in PSA-testing in Sweden during the 1990s [16, 17] and the proportion of localised prostate cancers diagnosed among men below 75 years of age increased from 22% in 1997 to 32% in 2001 [18]. During the same period the proportion of localised tumours diagnosed among men 75 years or older decreased by two percent units, the proportion of men diagnosed with metastases at diagnosis decreased from 39% to 27%, the proportion of prostate tumours with unspecified stage increased by three percent units [18], and the mean age at diagnosis decreased from 74 years in 1997 to 72 years in 2001. This is consistent with what would be expected if an organised screening programme was introduced; a shift towards younger patients and earlier stages.

It is likely that lead-time introduced by prostate cancer screening is a contributing factor to why the estimated 10-year cumulative period RSR for all sites combined is as high as 53%. Period estimates for 1997, the year prior to the rapid increase in prostate cancer incidence in the late 1990s [15], show a 10-year cumulative RSR of 46% for all sites combined. For prostate cancer, period estimates of the 10-year cumulative RSR were 49% for the period 1997 and 59% for the period 2000–2002. This suggests that period analysis will overestimate the 10-year cumulative RSR for clinically detected prostate cancers by 20% but for PSA-detected cancers the latest period estimate is likely to be an underestimate of the true survival. The incidence of female breast cancer has increased steadily at 1.8% annually between 1992 and 2001 [15] and there is some evidence that the survival estimates are also influenced by lead time and length time bias although not to the same extent as for prostate cancer.

Predictions of survival for newly diagnosed patients based on period analysis have so far only been published for a few countries and the estimates have all been based on different periods and, in some instances, slightly different combinations of cancers. The Finnish cancer registry published period estimates for the periods 1995–1997 [5] and 1999–2001 [19]. For the United States, period estimates have been published for the period 1998 based on data collected by the Surveillance, Epidemiology, and End Results (SEER) programme of the National Cancer Institute [6]. Estimates for England and Wales were published in 2003 for the period 1990–1995 [8]. These estimates were published for all ages and, with the exception of one report from Finland [19], only for males and females combined. Of the countries for which estimates have been published, patient survival is lowest in England and Wales. Sweden seems to have a slightly better survival than Finland, but the fact that the Swedish estimates are based on a later period has to be taken into account.

The largest survival difference between Sweden and the United States SEER data can be seen for prostate cancer. The 5-, 10-, 15-, and 20-year cumulative RSRs are 20, 36, 43, and 50% units higher in the Unites States compared to Sweden. This huge difference is likely to be due to an earlier or more extensive use of PSA-testing in the United States. Screening for prostate cancer increased in the United States during the early 1990s [20], whereas a large increase in prostate cancer incidence was first seen in Sweden in the late 1990s. The differences between the countries can, apart from the different time periods analysed and that the Swedish analysis does not include patients above 89 years of age or an otherwise heterogeneous age distribution, also be influenced by the possible use of diverging inclusion criteria for cancer sites and patients. For example, we have analysed adenocarcinoma for colon and rectum and are not including cancers based on death certificates in our analysis.

It is important to consider both short- and long-term survival in order to obtain a complete picture of trends in patient survival. There is a risk that short-term improvements will be missed if attention is directed solely, as it often is, at long-term survival at fixed intervals such as 5- and 10-years. Cancer sites with low and constant long-term survival, *e.g.*, lung, pancreas, and liver, should be considered at shorter follow-up intervals than the five years traditionally used. However, for short-term survival it does not matter whether cohort or period analysis is used since, depending on the years included, these estimates are essentially the same.

It remains to be seen if the predictions of the future long-term survival reported in this study will hold for patients diagnosed today. There is no way to tell at the present time, although evaluations of period analysis based on historical data are promising. We will have the answer to this question during the next two decades.

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