Long-term survival rates of cancer patients achieved by the end of the 20th century: a period analysis

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Summary

Background Long-term survival rates for many types of cancer have substantially improved in past decades because of advances in early detection and treatment. However, much of this improvement is only seen many years later with traditional cohort-based methods of survival analysis. I aimed to assess achievements in cancer patients' survival by an alternative method of survival analysis, known as period analysis, which provides more up-to-date estimates of long-term survival rates than do conventional methods.

Methods The 1973–98 database of the Surveillance, Epidemiology, and End Results (SEER) programme of the US National Cancer Institute was analysed by period analysis.

Findings Estimates of 5-year, 10-year, 15-year, and 20-year relative survival rates for all types of cancer were 63%, 57%, 53%, and 51%, respectively, by period analysis. These estimates were 1%, 7%, 11%, and 11% higher, respectively, than corresponding estimates by cohort-based survival analysis. By period analysis, 20-year relative survival rates were close to 90% for thyroid and testis cancer, exceeded 80% for melanomas and prostate cancer, were about 80% for endometrial cancer, and almost 70% for bladder cancer and Hodgkin's disease. A 20-year relative survival rate of 65% was estimated for breast cancer, of 60% for cervical cancer, and of about 50% for colorectal, ovarian, and renal cancer.

Interpretation Timely detection of improvements in long-term survival rates might help to prevent clinicians and their patients from undue discouragement or depression by outdated and often overly pessimistic survival expectations. It also adds to the value of cancer surveillance as a basis for appropriate public-health decisions.

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Introduction

One of the most widely used global measures of achievement in health is life expectancy, which is derived from population life tables. These tables can be regarded as a special type of survival analysis, because they quantify survival of newborn babies. Two main approaches are used to derive such tables. The first quantifies survival of a cohort of newborn babies. Although the conception and interpretation of this approach is very straightforward, its use is limited by the fact that it takes a human lifespan before the life table can be completed and life expectancy can be calculated. The second approach uses period life tables, which are based on mortality of a population within a recent period, such as a recent year. With this approach, survival data for various ages are obtained from cohorts of people born in different years. Although the interpretation of period life tables is slightly less straightforward than that for cohort life tables, they are widely used in health statistics because they provide much more up-to-date estimates of life expectancy than do cohort life tables.

Up to now, long-term cancer survival statistics have almost always been calculated from cohorts of patients diagnosed many years ago,[1,2] and they could therefore be quite out of date when they were derived. The idea to use the period principle to obtain estimates of long-term cancer survival rates was proposed a few years ago.[3,4] Meanwhile, extensive empirical evaluation studies have shown that period analysis provides much more up-to-date estimates of long-term survival of cancer patients than does cohort-based survival analysis.[5–7] Furthermore, period estimates for a particular time quite accurately predict long-term survival rates of patients diagnosed in that period.[6,7]

Up to now, period estimates of long-term survival rates of cancer patients have been reported by only a few European cancer registries, which cover populations that are limited in size[8–10] or age range.[11] In this study, I applied period analysis to obtain up-to-date estimates of long-term survival rates in cancer patients in the USA.

Methods

All data were obtained from the 1973–98 public-use database of the Surveillance, Epidemiology, and End Results (SEER) programme of the US National Cancer Institute.[12] Although the SEER programme is not a true nationwide population-based cancer registry, it is the most comprehensive source of information on cancer incidence and survival in the USA, and it is judged the standard for quality in cancer registries around the world. Quality control has been an integral part of SEER since its beginning. Every year, studies are done to assess quality and completeness of data reported (SEER's standard for case ascertainment is 98%). Here, data included in the 1973–98 SEER database are from population-based cancer registries in Connecticut, New Mexico, Utah, Iowa, Hawaii, Atlanta, Detroit, Seattle-Puget Sound, and San Francisco-Oakland, which together cover a population of about 24 million people. Here, data are presented for all ethnic groups, all ages, and, apart from

	Cohort analysis		Period analysis	
	Diagnosis	Follow-up	Diagnosis	Follow-up
Survival				
5 years	1993	1993–98	1993–98	1998
10 years	1988	1988–98	1988–98	1998
15 years	1983	1983–98	1983–98	1998
20 years	1978	1978–98	1978–98	1998

Table 1: **Periods of diagnosis and follow-up included in most recent estimates of survival obtained by cohort and period analysis**

gynaecological cancers and cancers of the prostate and testis, both sexes combined.

Patients were included with first diagnosis of cancer between 1978 and 1998, who were followed up until the end of 1998. Those with a diagnosis of basal and squamous skin cancer were excluded, because this disease is often under-reported in cancer registries. Also excluded were those with missing information for month or year of diagnosis (15 197, 0·6%), survival time (39 589, 1·5%), or ethnic origin (23 615, 0·9%), or those whose cancer was reported only by death certificate (24 369, 0·9%) or autopsy (15 220, 0·6%), leading to a total number of 1 730 564 patients included in the analysis.

Table 1 shows the difference between conventional (cohort-based) survival analysis and period analysis. In period analysis, only survival during the most recent period for which data are available (in this study, 1998) is included. This calculation is done by left truncation of data at the beginning of that period (ie, at the beginning of 1998) and by right censoring at its end (ie, at the end of 1998). Thus, survival probability in the first year after diagnosis is contributed by patients who were diagnosed in 1997 and 1998, whose first year after diagnosis included some part of 1998. In the same way, conditional survival probability in the second, third, fourth, and fifth year after diagnosis is contributed by those who were diagnosed in 1996 and 1997, 1995 and 1996, 1994 and 1995, and 1993 and 1994, respectively. These probabilities, by year of follow-up for 1998, can then be combined to calculate a period estimate of cumulative 5-year survival, as described elsewhere.[13] Period estimates of 10-year, 15-year, and 20-year survival can be derived accordingly from survival in 1998 of patients diagnosed in 1988–1998, 1983–1998, and 1978–1998, respectively.

Period estimates of 5-year, 10-year, 15-year, and 20-year relative survival rates were calculated for 1998, and these were compared with the most recent cohort-based estimates. All survival rates are relative rather than absolute. Relative survival rates indicate so-called net survival of patients with cancer. They can be interpreted as expected survival rates of cancer patients in the hypothetical situation in which cancer is the only cause of death.[14] Relative survival rates are calculated as the ratio of absolute survival rates of cancer patients divided by expected survival rates for a group of individuals of closely similar age and sex from the general population. Expected survival was estimated with Hakulinen's method.[15] SEs of survival rates were calculated by Greenwood's method.[16] All analyses were done with SAS version 6.12, with an extension of a publicly available macro for both cohort and period analysis, which is described in detail elsewhere.[13]

	Analysis	Relative survival rate, % (SE)			
		5 years	10 years	15 years	20 years
All cancer sites					
Men	Cohort	62·0 (0·3)	44·2 (0·4)	36·1 (0·4)	31·2 (0·5)
	Period	62·8 (0·3)	56·0 (0·4)	51·0 (0·5)	48·6 (0·7)
Women	Cohort	62·7 (0·3)	55·9 (0·3)	47·0 (0·4)	46·6 (0·5)
	Period	63·7 (0·3)	58·0 (0·3)	54·3 (0·4)	51·4 (0·5)
Both	Cohort	62·3 (0·2)	50·4 (0·2)	42·2 (0·3)	40·4 (0·4)
	Period	63·3 (0·2)	57·2 (0·3)	53·2 (0·3)	50·9 (0·4)
All cancer sites apart from lung and bronchus					
Men	Cohort	70·3 (0·3)	52·1 (0·4)	43·5 (0·5)	38·0 (0·6)
	Period	71·2 (0·3)	63·9 (0·4)	58·3 (0·6)	55·2 (0·8)
Women	Cohort	68·6 (0·3)	61·5 (0·4)	51·2 (0·4)	50·0 (0·5)
	Period	69·8 (0·3)	63·9 (0·4)	60·0 (0·4)	56·9 (0·6)
Both	Cohort	69·4 (0·2)	57·2 (0·3)	48·0 (0·3)	45·5 (0·4)
	Period	70·4 (0·2)	64·0 (0·3)	59·5 (0·4)	56·7 (0·5)

Rates derived from SEER 1973–98 database.[12]

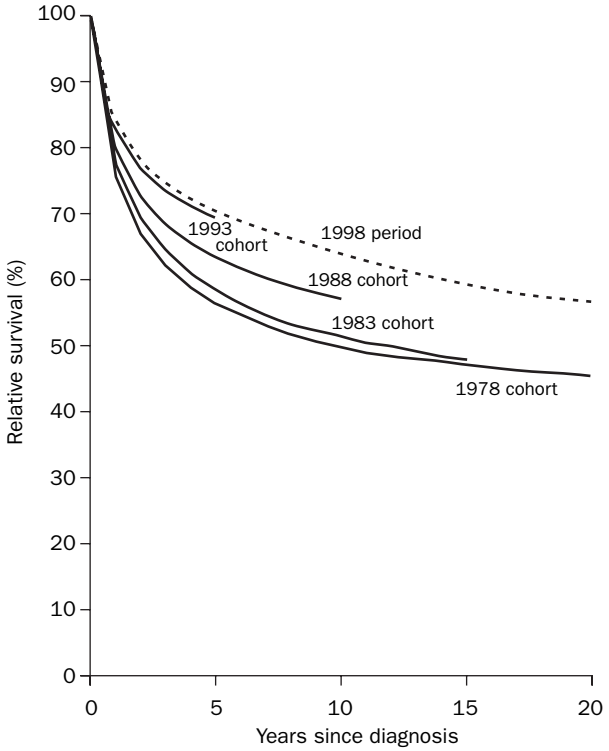
Table 2: **Most recent cohort and period estimates of relative survival rates, by sex**

Results

The most recent 5-year, 10-year, 15-year, and 20-year period estimates of relative survival rates for all invasive cancers combined (all races, both sexes) were about 1%, 7%, 11%, and 11%, respectively, higher than those calculated by cohort-based analysis (table 2). Cohort estimates of long-term survival rates were much lower for men than for women, whereas period estimates for both sexes were closely similar.

One of the reasons why survival rates have in the past been so much lower for men than for women is because of the large proportion of lung cancers (which have a very poor prognosis) in men with cancer. After exclusion of patients with lung and bronchus cancer, survival estimates were higher than those for all invasive cancers (especially for men), differences between survival estimates for men and women diminished, and differences between period and cohort estimates became even larger (table 2).

The figure shows the most recent cohort and period relative survival curves for all invasive cancers, apart from lung and bronchus cancer (all races, both sexes). Cohorts of patients diagnosed many years ago had much lower survival rates throughout follow-up than those diagnosed



20-year period-based and 5-year, 10-year, 15-year, and 20-year cohort-based relative survival curves

Most recent curves derived from SEER 1973–98 database,[12] including all ethnic groups, both sexes, and all cancer sites apart from lung and bronchus.

	Relative survival rate, % (SE)			
	5 years	10 years	15 years	20 years
Cancer site				
Oral cavity and pharynx	54·8 (1·2)	39·3 (1·4)	35·5 (1·6)	32·4 (1·8)
Oesophagus	13·0 (1·3)	6·4 (1·1)	4·1 (1·1)	1·8 (0·9)
Stomach	19·9 (1·1)	18·7 (1·2)	13·7 (1·3)	12·2 (1·5)
Colon	61·4 (0·8)	57·4 (1·0)	49·5 (1·2)	47·2 (1·5)
Rectum	61·5 (1·2)	50·3 (1·4)	39·8 (1·6)	39·3 (2·0)
Liver and intrahepatic bile duct	4·1 (0·8)	3·7 (1·0)	4·2 (1·4)	3·4 (1·6)
Pancreas	3·4 (0·5)	2·4 (0·5)	2·4 (0·5)	0·8 (0·4)
Larynx	62·4 (2·1)	56·3 (2·3)	45·3 (2·6)	39·3 (3·1)
Lung and bronchus	14·9 (0·4)	9·4 (0·3)	8·2 (0·4)	7·2 (0·5)
Melanomas	89·7 (0·9)	84·5 (1·2)	79·3 (1·6)	73·0 (2·1)
Breast	85·9 (0·4)	76·2 (0·6)	58·1 (0·8)	51·8 (0·9)
Cervix uteri	70·7 (1·6)	67·9 (1·7)	61·1 (2·1)	57·0 (2·3)
Corpus uteri and uterus, NOS	84·3 (1·0)	82·2 (1·3)	78·1 (1·6)	83·7 (1·8)
Ovary	48·9 (1·3)	44·5 (1·5)	36·7 (1·7)	34·7 (1·9)
Prostate	97·6 (0·4)	75·6 (1·0)	54·6 (1·5)	43·9 (2·1)
Testis	95·2 (1·0)	93·0 (1·4)	86·4 (2·0)	84·1 (2·8)
Urinary bladder	81·8 (1·0)	76·4 (1·4)	66·5 (1·9)	62·5 (2·5)
Kidney and renal pelvis	62·4 (1·3)	53·3 (1·7)	46·8 (2·1)	41·7 (2·6)
Brain and other nervous system	32·4 (1·4)	26·9 (1·4)	19·5 (1·5)	19·9 (1·7)
Thyroid	95·6 (0·9)	94·9 (1·3)	91·1 (1·8)	96·3 (2·0)
Hodgkin's disease	81·0 (1·7)	73·9 (2·0)	66·2 (2·3)	57·4 (2·7)
Non-Hodgkin lymphomas	53·4 (1·0)	43·4 (1·2)	37·0 (1·5)	30·8 (1·8)
Multiple myeloma	30·7 (1·7)	10·0 (1·3)	7·2 (1·4)	3·7 (1·2)
Leukaemias	45·3 (1·2)	33·4 (1·3)	24·9 (1·4)	20·6 (1·5)

Rates derived from SEER 1973–98 database (both sexes, all ethnic groups).[12]
NOS=not otherwise specified.

Table 3: **Most recent cohort estimates of relative survival rates, by cancer site**

	Relative survival rate, % (SE)			
	5 years	10 years	15 years	20 years
Cancer site				
Oral cavity and pharynx	56·7 (1·3)	44·2 (1·4)	37·5 (1·6)	33·0 (1·8)
Oesophagus	14·2 (1·4)	7·9 (1·3)	7·7 (1·6)	5·4 (2·0)
Stomach	23·8 (1·3)	19·4 (1·4)	19·0 (1·7)	14·9 (1·9)
Colon	61·7 (0·8)	55·4 (1·0)	53·9 (1·2)	52·3 (1·6)
Rectum	62·6 (1·2)	55·2 (1·4)	51·8 (1·8)	49·2 (2·3)
Liver and intrahepatic bile duct	7·5 (1·1)	5·8 (1·2)	6·3 (1·5)	7·6 (2·0)
Pancreas	4·0 (0·5)	3·0 (0·5)	2·7 (0·6)	2·7 (0·8)
Larynx	68·8 (2·1)	56·7 (2·5)	45·8 (2·8)	37·8 (3·1)
Lung and bronchus	15·0 (0·4)	10·6 (0·4)	8·1 (0·4)	6·5 (0·4)
Melanomas	89·0 (0·8)	86·7 (1·1)	83·5 (1·5)	82·8 (1·9)
Breast	86·4 (0·4)	78·3 (0·6)	71·3 (0·7)	65·0 (1·0)
Cervix uteri	70·5 (1·6)	64·1 (1·8)	62·8 (2·1)	60·0 (2·4)
Corpus uteri and uterus, NOS	84·3 (1·0)	83·2 (1·3)	80·8 (1·7)	79·2 (2·0)
Ovary	55·0 (1·3)	49·3 (1·6)	49·9 (1·9)	49·6 (2·4)
Prostate	98·8 (0·4)	95·2 (0·9)	87·1 (1·7)	81·1 (3·0)
Testis	94·7 (1·1)	94·0 (1·3)	91·1 (1·8)	88·2 (2·3)
Urinary bladder	82·1 (1·0)	76·2 (1·4)	70·3 (1·9)	67·9 (2·4)
Kidney and renal pelvis	61·8 (1·3)	54·4 (1·6)	49·8 (2·0)	47·3 (2·6)
Brain and other nervous system	32·0 (1·4)	29·2 (1·5)	27·6 (1·6)	26·1 (1·9)
Thyroid	96·0 (0·8)	95·8 (1·2)	94·0 (1·6)	95·4 (2·1)
Hodgkin's disease	85·1 (1·7)	79·8 (2·0)	73·8 (2·4)	67·1 (2·8)
Non-Hodgkin lymphomas	57·8 (1·0)	46·3 (1·2)	38·3 (1·4)	34·3 (1·7)
Multiple myeloma	29·5 (1·6)	12·7 (1·5)	7·0 (1·3)	4·8 (1·5)
Leukaemias	42·5 (1·2)	32·4 (1·3)	29·7 (1·5)	26·2 (1·7)

Rates derived from SEER 1973–98 database (both sexes, all ethnic groups).[12]
NOS=not otherwise specified.

Table 4: **Most recent period estimates of relative survival rates, by cancer site**

most recently. Period analysis for 1998 suggests that the patients diagnosed with cancer most recently have very favourable long-term survival prospects.

Cohort and period estimates of 5-year, 10-year, 15-year, and 20-year survival rates (with SEs) are shown for 24 frequent cancers in table 3 (cohort) and table 4 (period). Results of period analysis showed that better long-term survival rates for patients with most cancers have been achieved by the end of the 20th century than suggested by cohort estimates. Period estimates are higher than corresponding cohort ones for 16 (67%) of 24 forms of cancer for 5-year relative survival, and for 20 (83%), 22 (92%), and 20 (83%) cancers for 10-year, 15-year, and 20-year survival, respectively. Period estimates of 20-year relative survival exceed corresponding cohort estimates by about 10% or more for patients with rectal, breast and ovarian cancer, melanomas, and Hodgkin's disease, but the most striking difference is seen for patients with prostate cancer (37·2%). A difference of more than 5% is seen for patients with cancers of the colon, bladder, kidney, and the brain and nervous system, and leukaemias. Differences between period and cohort estimates are less pronounced for 5-year and 10-year relative survival rates, but period estimates of 5-year and 10-year survival are substantially higher than corresponding cohort ones for some cancers, such as those of the oral cavity and pharynx, rectum, ovary, prostate, and for Hodgkin's disease.

By period analysis, 20-year relative survival rates are close to 90% for cancers of the thyroid and testis, exceed 80% for melanomas and prostate cancer, are about 80% for endometrial cancer, and almost 70% for bladder cancer and Hodgkin's disease. Breast cancer has a 20-year relative survival rate of 65%, cervical cancer 60%, and colorectal, ovarian, and renal cancer about 50%. By contrast, patients with cancers of the oesophagus, liver, pancreas, and lung, and multiple myeloma continue to have very poor 20-year relative survival rates between 2% and 8%, although period estimates are slightly higher than cohort ones for patients with cancers other than lung cancer.

Discussion

These results show that long-term survival expectations of patients with many types of cancer are substantially better than those suggested by conventional cohort-based estimates, which refer to cohorts of patients diagnosed many years ago. Although survival rates and their changes over time vary strongly by cancer site, period estimates of 10-year, 15-year, and 20-year relative survival are about 7%, 11%, and 11% higher, respectively, than traditional cohort estimates for all cancers.

Differences in traditional estimates of long-term survival in cancer patients from other countries are even greater, in view of the fact that survival rates of patients in the USA have for a long time been higher than those of patients in most other parts of the world, including Europe.[17,18]

Period analysis, which has been widely used in other areas of health statistics such as life tables and life expectancy, was proposed for survival analysis of cancer patients a few years ago.[3,4] Period and cohort analyses have been shown to yield closely similar estimates of long-term survival, as long as survival rates remain constant over time.[3] Such a pattern was noted for lung cancer in this analysis. If survival improves over time, such improvement is more timely captured by period than by cohort estimates of long-term survival rates.[3]

The main reason why long-term survival rates obtained by cohort analysis are so much lower when major improvements in survival arise over time is because they are affected strongly by survival in the first few years after diagnosis. Although the same patients also affect long-term period survival estimates, their contribution to the survival function is restricted to a recent period—ie, many years after diagnosis—when cancer-related deaths

are much less common. By contrast, period estimates of the survival function during the first few years after diagnosis (when most cancer deaths happen) are based exclusively on survival of patients who were diagnosed in recent years.

Fortunately, survival rates have increased for most frequent types of cancer analysed here within the past three decades, and this improvement is reflected in the higher estimates of long-term survival obtained by period analysis. To know the long-term survival expectations of patients newly diagnosed with cancer nowadays would be interesting. However, it will take another 5–20 years until we know definitely their 5-year, 10-year, 15-year, and 20-year survival rates. Still, period estimates of long-term survival have proved quite accurate projections when compared with actual survival rates, which can only be derived many years later.[6,7]

In theory, period analysis could give overoptimistic estimates of long-term survival rates if reductions in early death are offset by increases in late mortality (eg, treatment-related deaths). Extensive empirical evaluation studies have shown, however, that this theoretical concern seems to be of little, if any, relevance in practice. By contrast, even period estimates tend to be too pessimistic in instances of continuing improvement over time, albeit much less so than cohort-based long-term survival estimates.[6,7] This finding accords with others for malignant diseases such as childhood leukaemia, for which an increased risk of late treatment-related death has been seen; this increase seems to be outweighed though by a strong reduction in death from recurrent disease.[19]

Reasons for increases in long-term survival rates in the last decades of the 20th century are probably manifold and vary between cancer sites. For some cancers, such as those of the prostate, early detection has probably made the largest contribution.[20] For other types, such as testicular cancer,[21] Hodgkin's disease,[22] or childhood cancers,[23] improvement is mainly attributable to breakthroughs in treatment. For other cancers, such as those of the breast, early detection and improvements in treatment have probably made major contributions.[24] Detailed analysis, accounting for additional factors such as age and stage at diagnosis, or treatment,[25] which could be done with period analysis in the same way as with cohort-based survival analysis, could help to elucidate the contributions of various factors.

Although period analysis shows major progress in long-term survival rates for many types of cancer, it also identifies those cancers for which progress has not been achieved. For example, period estimates are no better than cohort ones for cancers of the lung and bronchus, showing the absence of major progress in prognosis for these very frequent cancers.

In my analysis, period estimates were restricted to the most recent calendar year included in the database (and cohort estimates were restricted to cohorts diagnosed in 1 calendar year accordingly). Because of the large numbers of patients included in that database, SEs of estimates were reasonably small for most cancers. In other uses, in which sampling error is of concern, precision of period survival estimates could easily be increased, at the expense of some minor loss of their up-to-date attribute, by broadening of the period included in the analysis—eg, to the most recent 2 years included in the database.

A potential drawback of period survival estimates compared with cohort estimates is their slightly less straightforward interpretation, because different parts of the survival function are estimated from patients who were diagnosed in different years, whereas in conventional cohort analysis survival is estimated for cohorts of patients who were diagnosed in defined years. Cohort analysis is the method of choice when survival of such specific cohorts of patients is of primary interest. However, a similar argument would apply to other period measures, such as life expectancy, which nevertheless is one of the most widely used methods to monitor health of populations.

In this report I have focused on comparison of results obtained by period analysis with those gathered by frequently used cohort analysis, in which patients who have been under examination for the entire follow-up only are included.[26,27] Other conventional analyses include patients who have not been seen for the entire follow-up and whose survival time is then censored at the closing date of follow-up (unless they die or are lost to follow-up before that date).[28–30] Although this type of analysis also provides more up-to-date (and precise) long-term survival estimates than conventional cohort analysis, they are still much less up-to-date than estimates from period analysis in instances of continuing improvement in prognosis.[7]

Provision of up-to-date long-term survival rates is not merely an academic exercise—it could help to prevent clinicians and their patients from undue discouragement or depression by outdated and often overly pessimistic survival expectations. Timely detection of improvements in long-term survival rates also adds to the value of cancer surveillance as a basis for appropriate public-health decisions.

Conflict of interest statement
None declared.

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