Cancer Patient Survival—Patterns, Comparisons, Trends

A Population-based Cancer Registry Study in Finland

Lyly Teppo, Paul W. Dickman, Timo Hakulinen, Tapio Luostarinen, Eero Pukkala, Risto Sankila and Bengt Söderman

From the Finnish Cancer Registry, Helsinki, Finland (L. Teppo, T. Hakulinen, T. Luostarinen, E. Pukkala, R. Sankila, B. Söderman), Department of Public Health, University of Helsinki, Helsinki, Finland (T. Hakulinen), and the Cancer Epidemiology Unit, Department of Oncology–Pathology, Karolinska Institutet, Stockholm, Sweden (P.W. Dickman)

Correspondence to: Lyly Teppo MD, Finnish Cancer Registry, Liisankatu 21B, FIN-00170 Helsinki, Finland. Tel: +358 9 135 331. Fax: +358 9 135 5378. E-mail: lyly.teppo@cancer.fi

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The effects of primary site, sex, age, stage and histological type on cancer patient survival were analysed on the basis of the population-based material of the Finnish Cancer Registry from 1985 to 1994. In addition, trends in survival were constructed for the period 1955–1994. Detailed site-specific data are published as Supplement 12 to Vol. 38 of Acta Oncologica. Within a given site, the survival differences by gender were not large. However, because of different site distributions, the average prognosis for female patients, all sites taken together, was superior to that of males: the 5-year relative survival rates (RSR) were 58% and 43%, respectively. In general, older patients had a poorer outcome compared with younger patients (partly because of different stage and histology distributions). Stage was a strong determinant of patient survival. In some cancers with a poor average prognosis the 5-year RSR for localized tumours was reasonable, e.g. 61% for stomach cancer, males, 34% for gallbladder cancer, females, and 29% for lung cancer, males. Most of the survival rates clearly increased over time. In addition to improvements in cancer treatment, changes over time in several other factors affect the trends, such as changes in the stage distribution (early diagnosis as a result of health education, improved diagnostic methods, screening, etc.) and in the composition of the patient material because of changing definitions of cancer (e.g. papilloma versus papillary carcinoma of the bladder, occult carcinoma of the thyroid, and early prostate cancer). The large Cancer Registry material (466000 patients) enabled accurate estimates of the survival rates of cancer patients in Finland. These rates reflect the effectiveness of the healthcare system as a whole and are useful for planning and evaluation purposes. However, the estimated survival rates are based on grouped data, and cannot be directly applied for predicting the prognoses of individual patients, although they can be used as guidelines.

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Population-based survival data based on unselected cancer patient material are indispensable in that they give the real, unbiased, average outcome of the cancer patients in a given area. In addition to the efficacy of surgical, oncological, and other treatment and aftercare of cancer patients, population-based survival rates are influenced by, and reflect, the effectiveness of the whole chain of activities within the healthcare system: success in health education, i.e. in increasing the awareness of the population of cancer symptoms, availability and general acceptance of cancer screening, and the skill of the physicians (not only oncologists) in early diagnosis of cancer. Consequently, the correct way of evaluating advances in cancer care is to analyse trends over time in population-based cancer patient survival using non-selected patient materials derived from cancer registries.

Although in most clinical studies on cancer patient survival the series are more or less selected, they provide, through internal comparisons, valuable information about the relative importance of various clinical, cell biological, and other prognostic factors. In most instances, the survival experience of patients treated in specialized clinics with specific treatment modalities is, owing to selection, superior to that among cancer patients in general. Adequate comparison of the efficacy of different treatment modalities, which are an essential part of clinical cancer research, can only be made through well-planned randomized clinical trials.

The Finnish Cancer Registry has been in operation since 1952. It is population-based and countrywide. It receives information on cancer patients independently from hospitals, pathological, cytological and haematological labora-

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tories, practitioners, private health centres, dentists, and death certificates. The coverage in terms of cancer patients diagnosed in Finland is excellent. It has been estimated that more than 99% of solid cancers are included in the Registry file, while for some haematological malignancies (e.g. chronic leukaemias and multiple myeloma) the registration rates are somewhat lower or reach higher levels after a delay of some years (21).

Another essential feature of the patient material of the Finnish Cancer Registry is the complete follow-up for death and emigration which is readily and correctly effected through computers using the unique person numbers assigned to every Finnish resident. The long tradition in cancer registration and complete follow-up enable survival studies focusing on trends with time in the prognosis of cancer patients along with evaluation of the survival pattern in general.

A large-scale systematic survival analysis was performed at the Finnish Cancer Registry covering patients diagnosed during a 40-year period from 1955 to 1994. Detailed organ-specific results are published as a supplement to Acta Oncologica (7). In this paper we review the results from another perspective, concentrating on general patterns and comparisons. Which cancers have a good or a poor prognosis? How important in relative terms are the age of the patient and the stage of the tumour as prognostic factors? What is the variation in the time trends of cancer patient survival? Examples are also given of the importance of the histology or cell type of the tumour, and its anatomical subsite, as determinants of patient outcome.

Our approach in this paper is intended to be clinician-oriented; in other words, descriptions of sophisticated biostatistical methodology have been avoided. In addition to reporting results, i.e. numerical data on cancer patient survival, we also concentrate on more general survival patterns and discuss the possible factors behind the differences and trends found. We also seek to evaluate what is real in the observed patterns and trends and what could be attributable to technical artefacts.

MATERIAL AND METHODS

The basic material consisted of all tumours registered at the Finnish Cancer Registry in 1955–1994. Each primary site included all malignant tumours irrespective of their histology (e.g. non-Hodgkin's lymphomas were analysed in connection with the primary site in question). However, there were some exceptions: for colon, rectum, cervix uteri and corpus uteri, only carcinomas were considered (and also carcinoids of the colon); for the central nervous system (CNS), only meningiomas and malignant CNS tumours were analysed; in skin cancer, the analyses were made only for melanomas and squamous cell carcinomas; and pleural tumours included only mesotheliomas. Non-Hodgkin's lymphomas not originating in the lymph nodes were also analysed as a separate group, in addition to being included in the sites of origin. Carcinoma in situ lesions and papillomas of the bladder were excluded. Details of the composition of the material can be found in the site-specific presentations of the Finnish cancer patient survival monograph (7).

If the diagnosis was first made at autopsy (zero survival) or if death certificate was the only source of information (uncertainty in the date of diagnosis), the patient was excluded from the material. Autopsy-only patients constituted 2.4% and death certificate-only patients 1.7% of the original material. Multiple primaries in the same individual were analysed as independent cancers. After the exclusions, the material consisted of 466169 patients. The tumour was histologically verified in 90% of the cases.

In this report, the main emphasis was on the material of the years 1985–1994 which was used for comparisons between primary sites, genders, ages, stages, subsites, and histological types. Survival rates were also calculated for individual 10-year periods from 1955–1964 to 1985–1994 in order to study trends over time.

The follow-up started at the time of diagnosis and ended at the time of death or emigration or on December 31, 1995, whichever occurred first. Follow-up for death and emigration was effected through the national population register, and was practically complete.

The measure of survival was the 5-year relative survival rate, defined as the ratio (expressed as a percentage) between the observed 5-year survival rate in the patient group and the expected 5-year survival rate of a comparable group based on nationwide population life tables stratified by age, gender and calendar time (8, 12). The relative survival rate is used to provide a measure in which the effect of causes of death other than the cancer of interest has been eliminated. Thus, the relative survival rate can be interpreted as a measure reflecting the excess mortality resulting from the diagnosis of the cancer in question, i.e. as a survival rate in the situation in which only deaths attributable to the cancer in question (or actually, only the excess deaths in comparison with the general population group) are taken into account. The age standardization of relative survival rates (i.e. calculation of the weighted average of the age-specific rates) enables comparisons of patient survival over time and eliminates or reduces confounding caused by differences in the age distribution of the patients. Age standardization of the rates took place in the trend analyses only, the weights being the site and age-specific numbers of cases (males + females) in the material for the last period considered, i.e. the years 1985–1994. The calculations were conducted using software developed at the Finnish Cancer Registry (13).

COMPARISON OF CANCERS AT DIFFERENT PRIMARY SITES

It is of considerable interest for clinicians, administrators, health care professionals and even for patients and their relatives to know the average outcome of patients with different cancers. However, it must be remembered that the survival rates are meaningful and hold true on a group level only and cannot be applied as such for estimation of the outcome of a given cancer patient.

In Table 1 (males) and 2 (females) all the cancers considered in this survey are arranged in order of decreasing 5-year relative survival rate. All ages are included, and the figures in the columns 'Total' (all stages taken together) thus illustrate the average outcome of the patients with cancer at the given site diagnosed in 1985–1994 in Finland.

The 5-year RSR varied substantially between the sites. The rate was more than 90% in squamous cell carcinomas of the skin, cancer of the lip, and carcinoid tumours of the colon (females). The outcome was favourable (RSR 75–90%) for patients with cancers of the testis, thyroid, corpus uteri (carcinoma), breast (females) and eye, and for those with meningioma, skin melanoma and Hodgkin's disease.

The 5-year RSR was less than 10% in cancers of the pancreas, pleura (mesothelioma), liver, gallbladder and

Table 1

Five-year relative survival rates (%) of MALE patients diagosed with various cancers in Finland in 1985–1994, in decreasing order of the rate, by stage

Primary site	Localized	Regional metastases	Distant metastases	Total
Lip	97	62	14	93
Skin, squamous cell carcinoma	90	64	. .	90
Testis	96	95	60	88
Colon, carcinoid	98	56	16	87
Thyroid	96	96	38	83
Meningioma				83
Eye	82	. .	37	79
Skin melanoma	86	43	13	78
Hodgkin's disease	93	74	62	77
Bladder	89	29	9	72
Sympathetic nervous system	86	72	51	69
Prostate	84	65	25	64
Larynx	75	27	13	62
Salivary glands	87	36	10	60
Bone	73	. .	8	59
Soft tissues	76	30	11	56
NHL, extranodal	65	60	28	55
Acute lymphatic leukaemia				55
Chronic lymphatic leukaemia				53
Kidney	80	29	11	51
Colon, carcinoma	80	57	11	50
Rectum, carcinoma	71	39	10	48
NHL, nodal	77	54	29	47
Oral cavity	58	38	15	47
Tongue	54	49	3	46
Nose, sinuses	67	. .	12	44
ALL SITES	71	31	13	43
Small intestine	74	63	24	43
Brain, malignant				39
Pharynx	50	42	12	36
Multiple myeloma				30
Chronic myeloid leukaemia				27
Stomach	61	19	4	24
Acute myeloid leukaemia				19
Lung	29	13	1	10
Gallbladddder, biliary tract	28	6	1	8
Oesophagus	22	1	1	8
Liver	16	0	1	5
Pleura, mesothelioma	10	. .	0	4
Pancreas	10	6	1	2

. . Owing to the small number of cases, the survival rate is not reliably estimable.

Table 2

Five-year relative survival rates (%) of FEMALE patients diagnosed with various cancers in Finland in 1985–1994, in decreasing order of the rate, by stage

Primary site	Localized	Regional metastases	Distant metastases	Total
Colon, carcinoid	100	113	44	93
Lip	94	. .	. .	92
Skin, squamous cell carcinoma	91	69	32	92
Thyroid	98	93	32	88
Meningioma				87
Skin melanoma	90	40	5	84
Corpus uteri, carcinoma	92	51	37	82
Breast	93	69	22	80
Hodgkin's disease	89	86	64	79
Eye	80	. .	11	76
Salivary glands	85	62	17	74
Sympathetic nervous system	84	. .	40	69
Bladder	76	28	6	63
Bone	75	. .	26	61
Oral cavity	71	45	15	60
Acute lymphatic leukaemia				59
Larynx	69	31	. .	58
ALL SITES	84	61	16	58
Cervix uteri, carcinoma	84	49	28	58
Tongue	75	27	21	58
Soft tissues	73	. .	23	57
NHL, extranodal	65	65	29	55
Chronic lymphatic leukaemia				54
Kidney	70	40	13	54
Colon, carcinoma	83	53	10	50
Pharynx	51	49	20	49
Rectum, carcinoma	71	45	10	48
NHL, nodal	77	52	31	47
Brain, maligant				38
Ovary	84	48	18	37
Nose, sinuses	31	. .	38	36
Chronic myeloid leukaemia				33
Multiple myeloma				28
Stomach	60	25	3	24
Acute myeloid leukaemia				18
Lung	38	16	2	13
Oesophagus	20	9	3	10
Gallbladder, biliary tract	34	7	1	8
Pleura, mesothelioma	10	. .	3	8
Liver	18	0	1	6
Pancreas	13	5	1	3

. . Owing to the small number of cases, the survival rate is not reliably estimable.

oesophagus, and rather unfavourable (RSR 10-25%) for cancers of the lung and stomach and acute myeloid leukaemia.

Many cancers within the favourable prognosis category are located close to the body surface (skin, lip, thyroid, testis, breast, eye), which renders them readily accessible for both diagnostic and therapeutic measures, or they have favourable histological patterns (carcinoid, meningioma). On the other hand, many cancers with poor outcome are located in the internal organs. But the accessibility is by far not the only factor involved. There are subcategories (defined by, for example, histology) with poor prognosis even within cancers with high average survival rates, such as anaplastic carcinoma of the thyroid gland and choriocarcinoma of the testis. Conversely, subcategories (with low proportions though) with a prognosis markedly better than the average can be found among cancers for which the average outcome is poor: e.g. cancers of endocrine origin of the pancreas, MALT lymphoma of the stomach and carcinoid tumour of the lung. Obviously, many mechanisms play a part in determining the growth patterns and potentials of an individual tumour and its response to treatment and, consequently, the aggressiveness of the clinical course of the disease and prognosis of the individual patient.

One of the objectives of clinical cancer research is to improve patient survival across all primary sites. Despite the obvious progress seen in the past 30 years, much remains to be done in this field.

COMPARISON BETWEEN GENDERS

Fig. 1 charts the 5-year relative survival rates of different cancers for males and females diagnosed in 1985–1994. In many cancers, there was no or only a slight difference between the sexes. The rate for males was higher than that for females in cancer of the bladder, and cancer of the nose and sinuses. The opposite was true in cancers of the thyroid, salivary glands, oral cavity, tongue, and pharynx, pleural mesothelioma, and skin melanoma, and also in carcinoids of the colon (Tables 1 and 2), the rate for females exceeding that for males.

Several factors influence the site-specific gender differences in cancer patient survival, such as differences in the age, stage, and subsite distributions between the sexes. Even after controlling for other known prognostic factors, the differences may still remain; e.g. the survival rate for female patients with skin melanoma is higher even after controlling for subsite and stage (16, 22).

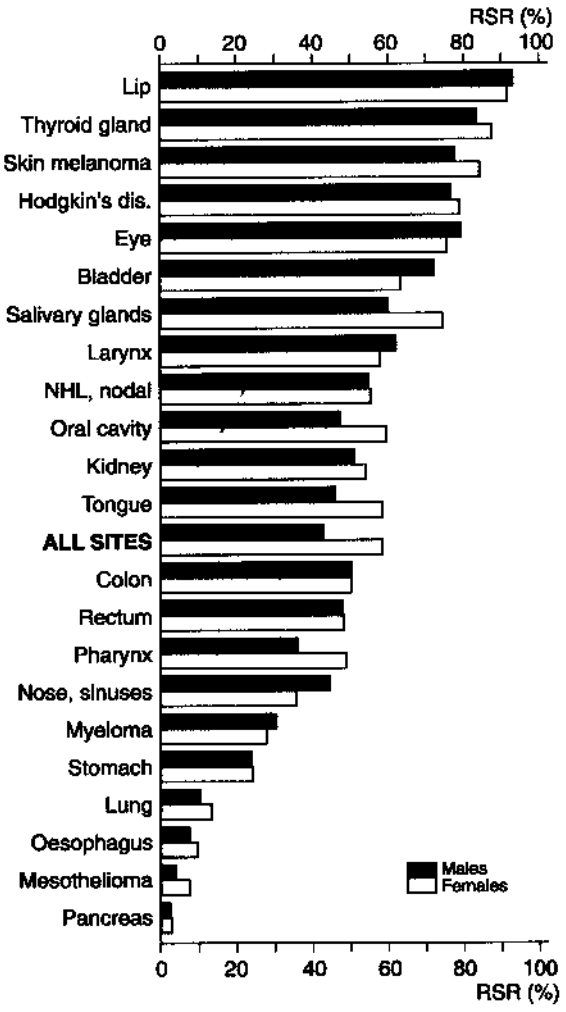

Fig. 1. Five-year relative survival rates (RSR) for selected cancers diagnosed in Finland in 1985–1984, by gender. NHL = non-Hodgkin's lymphomas. The rates for colon and rectum refer to carcinomas only.

Despite the differences between genders in the site-specific survival rates being relatively small—and in opposite directions—the rate for all cancer sites taken together was markedly higher in females than that in males (58% vs. 43%). This is attributable to a clear difference in the site distributions of cancers between males and females. The most common cancers (11) among females have, on average, a better prognosis (5-year RSR 80% for breast cancer, 50% for colorectal carcinoma) than those among males (5-year RSR 64% for prostate cancer, 10% for lung cancer).

COMPARISON BY AGE

Age of the patients is an important determinant of survival (Tables 3 and 4). For most cancers, the 5-year relative survival rate (which corrects for age-dependent differences in general mortality) is highest among young and middle-aged patients. There are several reasons for this pattern. Cancers in children and young adults differ by their histological or cell types from those in adults. In addition to specific childhood cancers, there are the nodular sclerosis type of Hodgkin's disease and papillary carcinoma of the thyroid gland, both having better than average survival rates and both being the predominant type among the young and middle-aged. Many hereditary cancers (e.g. colorectal cancer) occur in younger than average ages (and constitute a substantial proportion of many cancers at those ages) and may have a better than average survival experience (18). These factors contribute to the higher than average survival rates among younger patients.

In leukaemias, the pattern is reversed: acute myeloid leukaemia (with poor outcome) occurs more frequently in young adults and the middle-aged, and chronic lymphatic leukaemia (with a more favourable outcome) in older individuals.

Another explanation for the variation in survival by age is the more unfavourable stage distribution of the tumours among the elderly. For many reasons, their diagnoses are likely to be delayed more often than among the young patients. The elderly also have concomitant diseases and conditions which may interfere with effective and often strenuous treatment. However, in many instances elderly patients have a more unfavourable survival also within a given stage (e.g. in cancers of the colon, lung, breast and prostate). This may be a reflection of various host characteristics among the elderly favouring more aggressive growth patterns and resistance to treatment.

Table 3

Five-year relative survival rates (%) of MALE patients diagnosed with various cancers in 1985–1994 in Finland, by site and age group

Site	Age (years)					
	0–14	15–29	30–44	45–59	60–74	75+
ALL SITES	78	76	63	43	39	40
Tongue			64	39	47	39
Oral cavity			52	49	49	31
Pharynx		70	53	39	31	17
Oesophagus			22	7	8	5
Stomach		60	38	31	22	16
Colon, carcinoma		60	55	50	50	49
Rectum, carcinoma			47	49	49	46
Liver		25	12	6	3	3
Pancreas			7	4	2	1
Larynx			77	63	61	54
Lung			18	13	10	4
Prostate				55	66	64
Testis	100	93	92	86	54	31
Kidney	87	67	68	52	48	40
Bladder		95	92	83	71	63
Skin melanoma		88	81	80	74	67
Eye	100		89	80	74	51
Thyroid		101	96	87	69	36
Bone	69	53	66	65	43	42
Soft tissues	53	66	66	56	51	50
NHL, nodal	82	59	68	54	37	16
NHL, extranodal	78	90	77	61	47	31
Hodgkin's disease	97	89	82	77	51	9
Myeloma			51	49	26	16
Leukaemia	76	45	38	45	34	20
AML	30	43	36	24	9	2
ALL	82	46	16	0	9	

Age groups with less than 10 cases excluded.

COMPARISON OF STAGES

Traditionally, stage has been considered one of the most important prognostic factors in cancer. This is confirmed in the results obtained in the 10-year Finnish cancer patient material when three simple stage categories (localized, regional metastases, distant metastases) are used (see Tables 1 and 2). In these three stage categories, the 5-year RSRs for all sites taken together were 71%, 31% and 13% for males, and 84%, 61% and 16% for females, the rates for females being thus consistently higher than those for males. The large absolute difference in patient survival between the male and female patients in the group of regional metastases (61% vs. 31%) is noteworthy and, to a great extent, attributable to the favourable prognosis of node-positive female breast cancer.

The relative importance of stage as a prognostic factor varies. In many cancers the outcome for patients with localized tumour is good and that for patients with advanced disease poor, resulting in great differences in the 5-year RSR values between the three different stages (localized, regional metastases, distant metastases), e.g. in carcinoma of the colon, males (80%, 57%, 11%), stomach cancer, females (60%, 25%, 3%) and kidney cancer, males (80%, 29%, 11%). In some other cancers even the survival rate of patients with a localized tumour is relatively low (cancers of the liver 17%, pancreas 10% or 13%, and mesothelioma 10%). This of course indicates that undetectable metastases exist in most of these patients at the time of diagnosis, leading to recurrences, and that only a (small) proportion of tumours classified as 'localized' are in fact metastases-free. Hodgkin's disease and testicular cancer present another picture: even patients with advanced disease at the time of diagnosis have a relatively good prognosis (5-year RSR 63% for Hodgkin's disease, 60% for testicular cancer).

The methods used for assessing the stage of cancer have improved markedly with time. Use of endoscopies, new imaging techniques, tumour markers, etc., reveals metastases more often than, say, 20–30 years ago. This means that patients with 'localized' cancer are now more likely than hitherto actually to have a localized disease, because increasing numbers of patients with metastases which previously would have gone undetected have, in recent years, been correctly classified as non-localized. Simultaneously,

the group of non-localized cancers has also changed: in addition to patients with a truly advanced disease (who always have been classified as metastasized), the group now contains patients in whom small metastases can be found with modern techniques and who earlier were likely to have belonged to the localized group. It should be noted that patients with undetectable micrometastases have always been—and still are—classified as localized.

The improvements in methods for assessing and classifying stage have important implications for the interpretation of time trends in patient survival. It would be tempting to construct stage-specific trends in the survival rates, but this exercise is hampered by the fact that the gradual shift in the criteria and methods of assessing the stage results in changes over time in the composition of patient groups defined by stage (so-called stage migration) and thus in incomparability. Even if we could demonstrate improvement in survival among both localized and non-localized cancers, the survival of the total group would not necessarily improve to the same extent (cf. (14), Fig. 183 for female oral cancer).

COMPARISON OF TIME TRENDS

In Fig. 2, the trends with time (four 10-year periods) in the 5-year relative survival rate are given for selected cancers. To improve the site-specific comparability over time, the rates were age-standardized. In general, the rates have increased with time. For all cancers taken together, the increase has been consistent, the rates for females being substantially higher than those for males in each point of time.

In relative terms, the most rapid increases have been for cancers with poor prognosis, such as cancers of the oesophagus, stomach, lung, and gallbladder. However, even after substantial relative increases in the RSR, the average prognosis of patients with these cancers remains unfavourable. The relative improvement in the RSR has been slight, and quite understandably so, in cancers for which the survival rates were already fairly high 30–40 years ago, such as cancers of the lip and skin carcinomas. In absolute terms, substantial increases are observable in cancers for which the 5-year RSR in the 1950s and 1960s

Table 4

Five-year relative survival rates (%) of FEMALE patients diagnosed with various cancers in 1985–1994 in Finland, by site age group

Site	Age (years)					
	0–14	15–29	30–44	45–59	60–74	75+
ALL SITES	82	81	76	71	54	41
Tongue			52	75	63	36
Oral cavity			59	67	70	42
Pharynx			83	57	43	33
Oesophagus				14	15	3
Stomach		32	31	33	27	16
Colon, carcinoma		36	59	55	51	46
Rectum, carcinoma			57	55	51	39
Liver		45	15	10	5	1
Gallbladder, biliary tract			20	11	7	6
Pancreas			14	6	2	2
Lung		59	27	18	14	4
Breast		75	78	84	80	72
Cervix uteri		75	80	67	50	34
Corpus uteri			92	92	81	60
Ovary	72	83	64	45	29	18
Kidney	96	64	76	66	53	36
Bladder			79	80	69	48
Skin melanoma		97	91	87	80	70
Eye	100		93	66	83	48
Thyroid	100	99	99	96	74	43
Bone	66	61	76	71	51	20
Soft tissues	89	63	68	57	52	42
NHL, nodal	76	78	72	61	42	24
NHL, extranodal		88	74	69	52	41
Hodgkin's disease	91	97	90	74	53	32
Myeloma			43	42	33	13
Leukaemia	80	47	42	40	30	21
AML	59	34	36	19	10	4
ALL	84	36	37	28	15	

Age groups with less than 10 cases excluded.

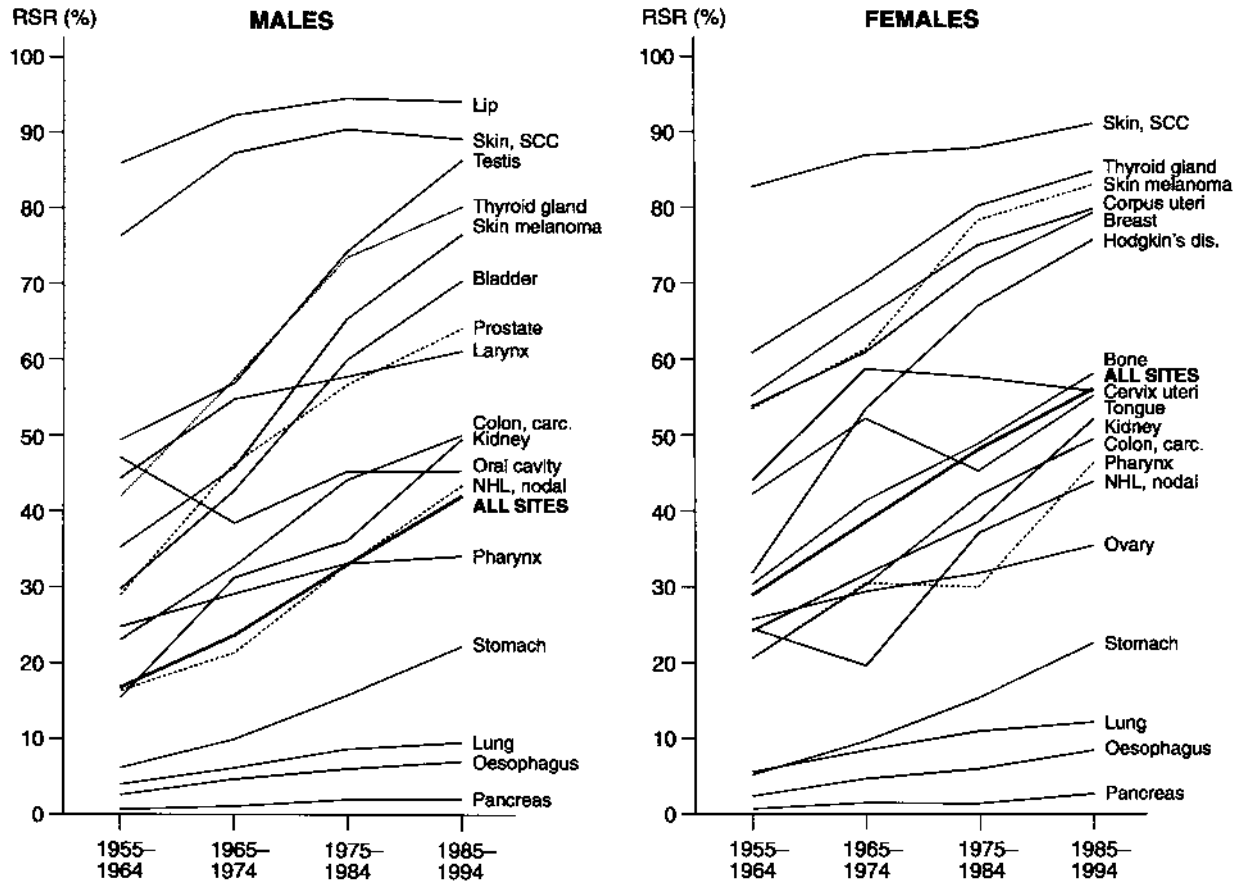

Fig. 2. Trends over time (four 10-year periods) in the 5-year relative survival rate (RSR) for selected cancers, by gender. The rates were standandized for age to the age distribution (males + females) of the material for 1985–1994. SCC = squamous cell carcinoma, NHL = non-Hodgkin's lymphomas.

was some 20–60%. This group includes cancers of the colon, rectum, female breast, corpus uteri, prostate, testis, bladder, thyroid gland, and bone, skin melanoma, Hodgkin's disease, and non-Hodgkin's lymphomas (nodal).

For some cancers, there has only been a modest improvement in survival. The increase in the survival rate of patients with ovarian cancer has been slow, and almost no increase whatsoever can be seen in cancers of the tongue, salivary glands, and oral cavity. For cancer of the cervix uteri, the rate has even started to decrease. This is, of course, not due to less effective treatment but attributable to gradual changes with time in the patient material as a result of the organized population-based screening of cervical cancer in symptomless women which was started in Finland as a nationwide activity in the mid-1960s (19). The proportion of localized tumours among cervical cancers has diminished with time (diagnoses are made at the preclinical stage and the lesions will thus never surface as cancers), indicating that the more rapidly growing tumours in advanced stages at diagnosis (often detected in elderly women) have not been affected to the same extent. In cancer of the pancreas, improvement in the average poor treatment results has been painfully slow. The few patients who do survive for five years or more have had either a malignant tumour of the endocrine elements of the pancreas or a periampullary cancer (or may have had an erroneous diagnosis without histological confirmation).

Many factors have contributed simultaneously to the temporal changes in the survival rates, and it is difficult to assess the exact role of each of them separately. The gradual change in the stage distribution of the tumours towards cancers that, on average, are more treatable than before has certainly had a major impact on the improvement in the survival rates. This, on the other hand, has been the result of several separate factors, such as continuous successful health education and the associated increase in general awareness among the population of early symptoms of cancer, the sharpening of the diagnostic eye of the physicians, general development in diagnostic methodology (e.g. endoscopies, imaging techniques and use of tumour markers), and screening. In addition, new treatment modalities have had an important impact on the time trends of the survival rates of many cancers. A good

example of this is provided by the effect of modern chemotherapy on the survival of patients with Hodgkin's disease, childhood leukaemia, or testicular teratoma.

However, the trends in survival rates do not always reveal the whole truth because several more or less artefactual factors also influence the numerical rate estimates and thus the trends. For example, the morphological criteria of a malignant growth may have changed with time. Many earlier papillomas of the bladder would now be classified as carcinomas grade 1 resulting, on average, in more favourable patient material and higher survival rates. A similar uncertainty (and similar effect on survival) occurs in the differentiation between early colon carcinoma and adenoma with severe dysplasia. Earlier materials of women with in situ carcinoma of the uterine cervix are not comparable with the more recent ones which may consist of all CIN III lesions (and include lesions earlier called severe dysplasias). It is quite probable that the patient materials of cancers of the thyroid gland or prostate have also changed because of the increasing use of the diagnoses occult papillary thyroid carcinoma and early prostate cancer. Consequently, the appropriate interpretation of the trends over time calls for understanding the (in some instances country-specific) changes that have taken place with time in the definition of cancer of the given primary site.

Screening for cancer influences the trends in survival rates. It reveals 'cancers' (of the breast and prostate) that are biologically not too aggressive and which should perhaps not be called cancers at all. This of course results in increasing survival rates. The survival rate estimates also improve through the earlier diagnosis of real invasive cancers at screening (lead time bias).

An ageing population increases the proportion of chronic lymphatic leukaemia, leading to improvement in the average outcome of leukaemia patients. On the other hand, because the outcome of many cancers in older age groups is less favourable than in the younger ones (see the previous section), the effect of the increase in the mean age of the patients is likely to have an opposite effect, i.e. attenuation of the otherwise increasing slope of the trend.

It appears that several factors exist that can have an effect on the trends in cancer patient survival. Some factors are likely to result in changes in the patient material towards, on average, more favourable morphologies or stages and to artefactually improved numerical survival rate estimates without affecting mortality at a population level.

Table 5

Examples of the variation by anatomical subsite in the 5-year relative survival rates (RSR) of patients with selected cancers diagnosed in 1985–1994 in Finland, males and females taken together (95% CI = confidence interval)

Site	5-year RSR (%)	95% CI
Colon		
Caecum/ascending	52	50–55
Transverse	43	40–46
Descending/sigmoid	51	49–54
Skin melanoma		
Head/neck	81	76–86
Trunk	81	78–83
Limbs	85	82–87
Bone		
Short bones	73	40–107
Long bones	57	49–65
Other bones	61	53–70

Table 6

Examples of the variation by histological or cell type in the 5-year relative survival rates (%) of patients with selected cancers diagnosed in 1985–1994 in Finland

	Males	Females
Colon		
Carcinoma	50	50
Carcinoid	87	92
Lung		
Squamous cell carcinoma	16	16
Small-cell carcinoma	3	4
Adenocarcinoma	16	24
Cervix uteri		
Squamous cell carcinoma		58
Adenocarcinoma		62
Testis		
Seminoma	94	
Teratoma	90	
Kidney		
Adenocarcinoma	55	61
Transitional cell carcinoma	60	37
Wilms' tumour	88	92
Eye		
Melanoma	68	65
Retinoblastoma	100	100
Central nervous system		
Meningioma	83	87
Malignant tumours	39	38
No or unknown histology	14	9
Thyroid		
Papillary carcinoma	98	97
Follicular carcinoma	81	80
Bone		
Chondrosarcoma	65	73
Osteosarcoma	57	56
Ewing's sarcoma	34	44
Leukaemia		
ALL	55	59
AML	19	18
CLL	53	54
CML	27	33

COMPARISON OF ANATOMICAL SUBSITES

The anatomical subsite of the tumour is often a prognostic factor (see Table 5 for examples). In carcinoma of the colon, the RSR was lowest in tumours in the transverse colon. Among melanomas, the highest survival rate was found in lesions located in the limbs. The prognosis of sarcomas in the short bones was superior to that of cancers in long bones, although the 95% confidence intervals of the rates overlapped.

The differences in survival by subsite may be due to variation in the accessibility to treatment (e.g. in gliomas). Different stage distributions may explain part of the variation, but the differentials do not totally disappear after allowing for stage (16). One can speculate that tumours at different subsites may also differ in terms of their pathogenesis and various biological characteristics related to clinical behaviour.

COMPARISON OF HISTOLOGICAL OR CELL TYPES

Histology is a well-known prognostic factor in cancer, as has been demonstrated in hundreds of clinico-pathological studies. The analysis of the Finnish countrywide Cancer Registry material (with histologies taken from the notifications, without attempts to review the slides or reclassify the lesions) considered the histology (or cell type) as a prognostic factor for selected cancers in order to demonstrate the magnitude of the observed variation (Table 6).

As might be expected, the variation in survival was substantial and, in general, similar for males and females. Carcinomas of the colon had a poorer prognosis than carcinoids, small-cell carcinoma had by far the worst prognosis among all lung cancer types, and the rates for papillary carcinoma of the thyroid gland were higher than those for follicular carcinoma. Childhood types of cancer, such as Wilms' tumour and retinoblastoma, were associated with an excellent prognosis, much better than that of the other histologies of cancers of the kidney or eye, respectively. The opposite was true for Ewing's sarcoma, in which the survival rates were lower than in the other bone sarcomas. Only a small difference was found between squamous cell carcinoma and adenocarcinoma of the cervix uteri. In the material of the years 1985–1994 the 5-year survival rate of testicular teratoma was almost as high as that of seminoma, which was not the case in earlier decades (when teratoma had a much poorer prognosis).

It is important to note the low survival rates of patients with central nervous system tumours with no or unknown histology. The 'no histology' designation usually means an inaccessible tumour (brain, pancreas), advanced disease at the time of the diagnosis (often coded as a cancer at unknown primary site) or severe concomitant diseases which, from the survival point of view, are more important than the cancer in question. In these instances the outcome is often poor. Fortunately, the 'no histology' group constitutes only a small part of most cancers. But within cancers of many internal organs a separate analysis of the outcome of patients in this category would contribute significantly to the understanding of the general patterns in cancer patient survival.

Histology and cell type should be taken into account more often than has so far been the case in registry-based analyses of cancer patient survival. The examples in Table 6—and many others—indicate that, in order to obtain results that are more relevant to clinical work, different histologies within a given primary site should be considered as different diseases and therefore analysed separately. It is true that due to inconsistencies in the criteria and terminology applied by the pathologists, the quality of data on histology in the cancer registries is not always entirely satisfactory. Even in areas where healthcare is on a high level, there are, on average, some 10% of cancer patients for whom a histological diagnosis of the tumour will never be obtained. Thus, the survival rates calculated for a total group of patients with a given cancer, without taking histologies into consideration, are still useful as general indicators of the efficacy of the cancer care and its improvement with time (14, 20).

DISCUSSION

The survival rate of a group of cancer patients is influenced by a number of factors. In addition to the factors referred to in the previous sections (stage, age, anatomical subsite, and histology) the survival rate can also vary depending on social class and place of residence (1, 5, 6, 17) and, of course, on treatment. In some instances, the outcome of the patient may depend on the experience of the individual physician responsible for treatment. Thus, direct comparison of published survival rates from different areas or countries can be misleading and result in erroneous conclusions unless measures have been undertaken to improve comparability (2). This is seldom achieved, and for an adequate comparison of rates, a separate study is usually needed in which the composition of the materials and the methods of estimating survival rates are made uniform (3, 9, 10). In one such study (EUROCARE), cancer patient survival was compared in areas covered by 30 population-based cancer registries in 11 European countries including Finland (3). In this survey, all survival rates in Finland were among the highest (along with those in one registry in The Netherlands and two registries in Switzerland).

Proper evaluation of the separate effects of individual factors calls for adequate biostatistical methodology. Researchers are too often satisfied with univariate analyses, which are likely to result in well-known associations between different prognostic factors and patient outcome, and in which, for example, the strong intercorrelations of

different prognostic factor are often neglected. The use of proper methodology is of particular importance when various cell biological measurements are being analysed for their prognostic significance (the major clinical determinants of survival must be taken into account).

So what is important and relevant for administrators, clinicians, researchers, etc.? Administrators are generally interested in the average outcome of patients diagnosed with a specific cancer. The survival rates in which age, stage, histology, and so on, have not been taken into account are often the most relevant ones for planning purposes and form the basis of various comparisons and trends. They illustrate the efficacy of the whole chain of activities in the healthcare system. This is one of the most important applications of population-based survival rates.

Clinicians are interested in the prognoses of their individual patients. However, estimated survival rates can only be interpreted as summary measures for patient groups and cannot be applied directly to predict the survival of individual patients; they can, of course, be used as a guideline. Although the patient groups in survival analyses are defined to be as clinically homogeneous as possible (e.g. for age, stage, and histology), substantial differences may nevertheless exist between the individual patients (e.g. general health, performance status and receptiveness to treatment) and tumour characteristics (e.g. resectability, differentiation grade, ploidy and expression of certain genes) within the group, and hence also in their prognoses. Owing to the relatively large basic population covered by the Finnish Cancer Registry, the great number of items collected by the registry (not all population-based cancer registries have access to information on stage and morphology) and the high accuracy of these items, we have been able to estimate the survival for patient groups with relatively narrow definitions in terms of what can usually be achieved in survival analyses, although the definitions are still rather broad in a clinical sense.

For example, the estimated relative survival rates for females aged 45–59, diagnosed with localized colon carcinoma during 1985–1994, are published in the Supplement—as are sex- and stage-specific rates for each cancer site according to 15-year age groups (7). Although this is a rather strict definition, we know that for the individual patients, this group is to some extent heterogeneous. An experienced clinician will be familiar with the range of patients classified in a given group, and will be able to adjust the group-level survival estimate appropriately in order to give a more accurate reflection of the true prognosis of an individual patient.

Scientific research aims at finding factors—clinical, cell biological and others—that determine, in all possible detail, the prognosis of the patients, and at assessing the relative importance of each of them. The findings will gradually be applied in clinical work, i.e. to lead to modifications in the treatment modalities, and, it is hoped, also to improved accuracy in the assessment of the probability of survival of an individual cancer patient. The value of 'artificial neural networks' (4, 15) in improving the accuracy of the survival estimates remains to be demonstrated.

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