

Long-Term Survival in Patients with Cancers

Surveillance, epidemiology and end results-based analysis

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ABSTRACT: Objectives: This study aimed to explore real-world data on the long-term survival of cancer patients using historical records from the Surveillance, Epidemiology, and End Results (SEER) Programme. Long-term survival is an important endpoint in the management of different malignancies. It is rarely assessed due to the unfeasibility of follow-up for a long duration of time. Besides reporting the five-year relative survival, the 10- and 20-year survival rates for different types of cancers were analysed. Additionally, survival trends as a function of time, age and tumour type were reviewed and reported. **Methods:** The study used SEER*Stat (Version 8.3.6.1) for data acquisition from the SEER 9 Regs (November 2019) database. Data from patients diagnosed with cancer between 1975 and 2014 were retrieved and included in the analysis. **Results:** For patients diagnosed with any malignant disease (N = 4,412,024), there was a significant increase in median overall survival over time ($P < 0.001$). The 20-, 10-, and 5-year survival rates were higher in solid tumours compared to haematological malignancies (50.8% versus 38%; 57% versus 47.4%; and 62.2% versus 57.4%, respectively). The highest 20-year relative survival rates were observed in thyroid cancer (95.2%), germ cell and trophoblastic neoplasms (90.3%), melanoma (86.8%), Wilms' tumour (86.2%) and prostate cancer (83.5%). **Conclusion:** Long-term follow-up data were suggestive of high 20-year relative survival rates for most tumour types. Relative survival showed an improving trend over time, especially in solid tumours.

Keywords: Survival; Neoplasms; SEER Program; Prognosis; United States.

ADVANCES IN KNOWLEDGE

- There was a significant increase in long-term survival rates in cancer patients over the period between 1975 and 2014.
- The highest 20-year relative survival rate is seen in thyroid cancer, germ cell and trophoblastic neoplasms, melanoma, Wilms' tumour and prostate cancer.
- 20-year relative survival rates are higher in solid cancers compared to haematological malignancies.

APPLICATIONS TO PATIENT CARE

- Improved cancer diagnostics and therapeutic options have led to a substantial increase in survival rates over time. This necessitates the development of long-term follow-up programmes to accommodate the growing number of cancer survivors.
- The 20-year survival rates for some malignancies are high. Patients diagnosed with those types of tumours should be aware of their probability of survival and be counselled about cancer survivorship.

IN THE USA, NEARLY 609,360 PERSONS WERE projected to die from cancer in 2022. In fact, cancer is currently considered the second most common cause of death in both men and women in the US.¹ The dominance of cancer over the other causes of death is a daunting fact for cancer patients and their families. It remains consistent among different ethnicities and variable age groups.²

Although many researchers have studied cancer-related mortality, cancer survivorship usually remains an underrepresented topic in the literature despite the growing interest in the concept in the past decade. In 2019, more than 16.9 million Americans survived cancer—a number that is projected to reach more than 22.1 million by 2030.³ With recent advances in cancer diagnostics and therapeutics, survival is expected to improve with a further increase in the number of cancer survivors among the overall population.^{4,5}

Cancer survival rates can vary according to tumour type and patients' clinicodemographics.^{4,5} Exploring survival rates can provide valuable insights into the natural history of different cancers. It can also enlighten us about the changes that happened over time because of the introduction of novel treatment options or incorporation of new preventive strategies including screening programmes. Most studies reporting on cancer survival, including clinical trials, have addressed either 5-year or 10-year survival rates.^{6–9} However, looking into survival rates from a more holistic approach that goes beyond 10 years is imperative, though this is usually impractical to address in short-term studies or even in the context of prospective clinical trials.

This study aimed to investigate the long-term survival, including 20-year survival rates, of different cancers in the USA. It also explored possible differences

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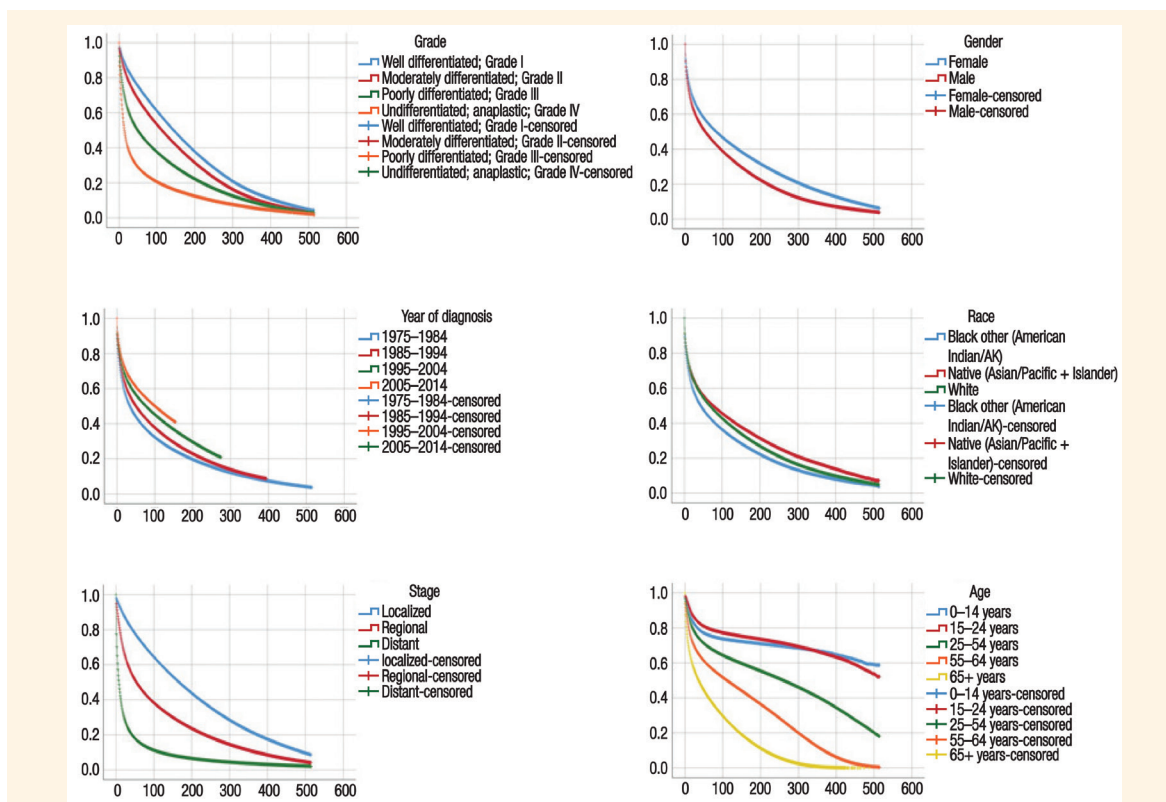


Figure 1: Kaplan-Meier curve for cases diagnosed with cancer between 1975 and 2014 stratified by age group, ethnicities, gender, stage, grade and year of initial diagnosis.

in survival rates across tumour types, their association with different sociodemographic parameters and their trends as a function of time.

Methods

Data were obtained from the Surveillance, Epidemiology, and End Results (SEER) Program.¹⁰ The SEER Program was initiated in the early 1970s by the US National Cancer Institute to collect data from nationwide cancer registries. Its current databases cover 47.9% of the US population and are presumably generalisable to patients with cancer all over the USA. The SEER 9 database (November 2019), which covers 9.4% of the population and includes historic data that go back to 1973, was used as the data source in this study. The study was exempted from institutional review board approval, being a SEER-based study according to the guidance of the National Bureau of Economic Research.¹¹

The case-listing function in SEER*Stat, Version 8.3.6.1 (National Institutes of Health, National Cancer Institute, USA) was used to export data on cancer cases diagnosed between 1975 and 2014. The study included patients of known ages who had cancers with malignant behaviour at the time of initial data entry. The relative survival was calculated in SEER*Stat

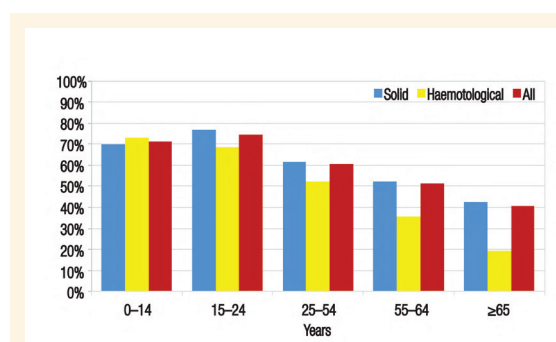


Figure 2: The 20-year survival rates for different age groups stratified according to tumour type. The highest survival rates are observed in the 15–24 age group. Age groups are plotted on the x-axis and survival probability is plotted on the y-axis.

using the Ederer II method. The probability of relative survival compares survival in the patients included in the analysis with the expected survival of the general population obtained from the US 1970–2017 expected survival life tables.¹² For relative survival, cases with a missing cause of death and/or survival time were excluded from the analysis.

The study classified tumours into either solid tumours (8000/3-9581/3) or haematological malignancies (9590/3+) according to the third edition of the International Classification of Diseases for Oncology. Age at diagnosis was categorised into five

Table 1: Patients' characteristics in the included cohort

Characteristic	n (%)
Age group in years	
0–14	31,594 (0.7)
15–24	41,614 (0.9)
25–54	917,720 (20.8)
55–64	968,584 (22.0)
≥65	2,452,512 (55.6)
Gender	
Male	2,262,378 (51.3)
Female	2,149,646 (48.7)
Ethnicity	
White	3,705,309 (84.0)
Black	407,066 (9.2)
Other (American Indian/AK native, Asian/Pacific islander)	281,266 (6.4)
Unknown	18,383 (0.4)
Year of diagnosis	
1975–1984	758,808 (17.2)
1985–1994	1,025,529 (23.2)
1995–2004	1,220,374 (27.7)
2005–2014	1,407,313 (31.9)
Tumour type	
Solid	4,019,427 (91.1)
Haematology	392,597 (8.9)
Diagnosis	
Breast	657,211 (14.9)
Prostate	610,247 (13.8)
Lung and bronchus	592,921 (13.4)
Urinary bladder	196,378 (4.5)
Melanoma of the skin	168,236 (3.8)
Corpus uteri	136,199 (3.1)
NHL-nodal	120,148 (2.7)
Kidney and renal pelvis	114,658 (2.6)
Pancreas	112,114 (2.5)
Other tumours	1,703,912 (39.0)

NHL = non-Hodgkin lymphoma.

main categories (0–14, 15–24, 25–54, 55–64 and ≥65 years). For comparing trends over time, the study stratified years of diagnosis into four groups with a 10-year interval for each group.

Statistical analysis was performed using the Statistical Package for the Social Sciences (SPSS),

Table 2: Survival data of cancers having highest 20-year relative survival

Type of cancer	5-year survival				10-year survival				20-year survival				
	1975–1984	1985–1994	1995–2004	2005–2014	All years	1975–1984	1985–1994	1995–2004	2005–2014	1975–1984	1985–1994	1995–2004	2005–2014
Thyroid carcinoma	92.90%	94.60%	96.60%	98.50%	96.80%	91.40%	93.50%	95.90%	98.50%	90.10%	92.40%	95.10%	N/A
Germ cell and Trophoblastic Neoplasms	85.10%	92.50%	94.40%	95.50%	92.60%	83.80%	91.50%	94.20%	95.20%	80.40%	90.30%	93.30%	N/A
Melanoma	82.00%	87.50%	91.00%	93.10%	89.90%	77.10%	84.40%	89.10%	92.10%	75.00%	83.40%	88.90%	N/A
Wilms' tumour	79.30%	91.10%	90.70%	94.10%	89.00%	77.70%	90.50%	89.10%	93.00%	76.60%	89.00%	86.10%	N/A

N/A = The 20-year survival rates cannot be calculated for this patient population due to short follow up to date.

Table 3: Cox regression analysis for different prognostic factors affecting survival time

Factor	Regression coefficient	HR (95% CI)	P value
Age	0.623	1.865 (1.862–1.867)	<0.001
Year of diagnosis	-0.106	0.899 (0.898–0.900)	<0.001
Stage	0.163	1.177 (1.176–1.178)	<0.001
Grade	0.071	1.073 (1.073–1.074)	<0.001
Cancer type (solid and haematological)	-0.242	0.785 (0.781–0.788)	<0.001
Gender	0.008	1.008 (1.006–1.011)	<0.001
Ethnicity	-0.063	0.939 (0.938–0.940)	<0.001

HR = hazard ratio; CI = confidence interval.

Version 26.0. (IBM Corp, Armonk, New York, USA). Frequencies and percentages were used to describe categorical variables. Survival analysis was performed using the Kaplan-Meier analysis method, where the log-rank test was used to test for statistical differences. Cox regression analysis was performed to adjust for potentially confounding factors. The *P* value of 0.05 was used to determine statistical significance.

Results

In total, 4,412,024 cases diagnosed with cancer between 1975 and 2014 were included in this analysis. The elderly population (≥ 65 years) was the largest age group in the study ($n = 2,452,512$; 55.6%). The majority of the study cohort was male ($n = 2,262,378$; 51.3%) and white ($n = 3,705,309$; 84%). The most commonly encountered diagnosis was breast cancer ($n = 657,211$; 14.9%), with solid tumours constituting 91.1% ($n = 4,019,427$) of the included cohort [Table 1].

The median overall survival for all patients included in the study was 66 months (95% confidence interval [CI]: 65.8–66.2 months) and showed a significant increase over time (35 months, 51 months, 77 months, and 101 months for cases diagnosed between 1975 and 1984, 1985 and 1994, 1995 and 2004 and 2005 and 2014, respectively; $P < 0.001$) [Figure 1]. The highest 20-year relative survival was observed in thyroid cancer (95.2%), germ cell and trophoblastic neoplasms (90.3%), melanoma (86.8%), Wilms' tumour (86.2%) and prostate cancer (83.5%) [Table 2].

Survival was compared across different prognostic factors including age, gender, stage, grade and cancer type. Results revealed that the 15–24 age group had better median overall survival compared to the 25–54, 55–64 and ≥ 65 age groups (363.3 versus 261, 112 and 37 months, respectively; $P < 0.001$) [Figures 1 and 2].

Female patients had longer overall survival compared to male patients (83 versus 54 months; $P < 0.001$) [Figure 1]. Patients of black ethnicity had

lower survival rates compared to (American Indians/Alaska natives, Asians/Pacific islanders) and whites (115.2 versus 152.2 and 134.9 months; $P < 0.001$). In Cox regression analysis, improvement in survival across time remained significant (hazard ratio [HR] = 0.899) and the significance was also maintained across different age groups (HR = 1.865), genders (HR = 1.008), ethnicities (HR = 0.939) and tumour types (HR = 0.781) [Table 3].

Despite consistent increases in survival rates in both tumour types, the 20-, 10-, and 5-year survival rates were higher in solid tumours compared to haematological malignancies (50.8% versus 38%, 57% versus 47.4% and 62.2% versus 57.4%, respectively). Table 4 shows survival rates for commonly diagnosed cancers.¹

Discussion

The progress made in the oncology field substantially improved cancer outcomes, but little is known about how this was translated into a long-term survival benefit in patients with cancer.¹³ To the best of the present authors' knowledge, this is the widest-scale analysis of long-term survival for cancer patients that explored follow-up data for up to 20 years after diagnosis using a tumour-agnostic approach. The data presented in this study are crucial for informing treating physicians about the probability of long-term survival in different malignancies. This information is commonly addressed during doctor-patient conversations, particularly in patients with advanced diseases. Current evidence suggests that the accuracy of oncologists' expectations for survival in end-stage cancer patients is as low as 25%. This inaccuracy can not only lead to a lack of credibility in physicians' disclosed information, but also mislead treatment-related decisions such as the need to refer patients for hospice care or the necessity of continuation of active treatment.^{14–16}

Table 4: Survival data for commonly diagnosed tumours. Cancers listed are those shown to have highest incidence rates according to Siegel *et al.*¹

	5-year survival					10 year survival					20 year survival				
	1975-1984	1985-1994	1995-2004	2005-2014	All Years	1975-1984	1985-1994	1995-2004	2005-2014	All Years	1975-1984	1985-1994	1995-2004	2005-2014	All Years
	Breast	75.50%	84.00%	89.00%	91.10%	86.10%	63.60%	76.10%	83.50%	86.30%	78.80%	53.20%	67.50%	75.70%	N/A
Prostate	70.50%	89.10%	98.60%	99.10%	93.40%	55.70%	81.90%	97.90%	99.10%	89.70%	39.60%	72.40%	94.40%	N/A	81.70%
Lung and bronchus	12.70%	13.40%	15.30%	19.60%	15.40%	8.70%	9.00%	10.20%	13.10%	10.40%	4.80%	4.80%	5.50%	N/A	5.60%
Colon and rectum	52.10%	60.00%	64.00%	66.40%	60.80%	46.50%	53.90%	58.40%	60.10%	54.90%	42.60%	49.50%	52.60%	N/A	50.00%
Corpus and uterus, NOS	83.50%	82.80%	83.60%	83.20%	83.30%	81.60%	80.40%	80.70%	80.30%	80.80%	79.50%	76.80%	76.40%	N/A	77.70%
Urinary bladder	74.60%	78.80%	79.80%	78.70%	78.20%	66.50%	71.50%	73.10%	72.30%	71.00%	55.20%	60.10%	61.50%	N/A	59.70%
Melanoma of the skin	82.90%	88.60%	92.00%	94.00%	90.90%	78.40%	86.00%	90.50%	93.40%	88.90%	76.60%	85.20%	90.40%	N/A	88.40%
Kidney and renal pelvis	51.50%	58.40%	65.50%	75.10%	65.80%	44.50%	50.80%	57.70%	68.80%	58.40%	36.80%	40.90%	47.00%	N/A	47.60%
Non-Hodgkin lymphoma	49.00%	51.30%	63.20%	73.40%	61.70%	37.20%	41.10%	55.70%	66.50%	52.60%	26.80%	31.70%	46.60%	N/A	41.80%
Oral cavity and pharynx	52.50%	55.00%	60.50%	67.40%	59.30%	42.30%	44.40%	51.30%	59.30%	49.40%	29.80%	32.40%	38.40%	N/A	36.10%
Leukaemia	36.20%	44.20%	52.30%	64.50%	50.90%	25.40%	33.90%	44.70%	57.60%	41.60%	17.90%	26.70%	37.00%	N/A	32.90%
Pancreas	2.70%	3.80%	4.90%	9.10%	5.60%	1.80%	2.60%	3.60%	6.50%	3.90%	1.30%	1.80%	2.10%	N/A	2.60%
Thyroid	92.70%	94.40%	96.50%	98.40%	96.60%	91.30%	93.30%	95.80%	98.40%	96.00%	89.90%	92.10%	94.90%	N/A	95.00%

N/A = The 20-year survival rates cannot be calculated for this patient population due to short follow-up to date; NOS = not otherwise specified.

The study demonstrated, based on data from the US cancer registries, that several malignancies have considerable long-term survival rates. The highest 20-year relative survival was observed in thyroid cancer (95.2%), followed by germ cell and trophoblastic neoplasms, melanoma and Wilms' tumour (90.3%, 86.8% and 86.2%, respectively). A potential explanation for high survival rates in these tumours is the early disease-related manifestations, the availability of easy-access diagnostic approaches, and the advances in treatment options with curative intent in those tumour types. Similar data were reported in the UK by Quaresma *et al.*, who have reported the highest 10-year survival in patients with testicular cancer (98.2%).¹⁷

Although some data support the notion that the highest rates of cancer survival are reported in the US and Canada,¹⁸ trends in our survival analysis were consistent with findings from other studies in other parts of the world. Most publications addressing shorter survival intervals have reported improved survival over time, which is usually attributed to the introduction of new treatment options for various tumours.¹⁷⁻¹⁹ This has been consistent with data reported in the present study, which showed a steady increase in 5-, 10- and 20-year survival across almost all tumour types. Interestingly, the survival probability showed an incremental decrease after five years as compared to the anticipated linear increase in the probability of death. For example, breast cancer survival probability fell from 86.4% at the 5-year follow-up to only 70.1% at 20 years. In colorectal cancer, the 20-year survival rate of 50.5% compares to that of 61.4% at five years. This highlights the fact that most death events would occur early in the course of the disease. Therefore, whether to inform patients about the long-term prognosis of their illness should not be based only on short-term survival data, which can sometimes be misleading. The findings of this study were concordant with data from a similar study that was done 20 years ago and reported on the long-term survival of patients diagnosed between 1974 and 1991. In the study by Samet and Bradley, an incremental decrease in survival rates happened after five years in patients with colorectal cancer with a 15-year survival rate reported at 50% compared to a 57% survival rate at five years.²⁰

The findings suggested that solid malignancies have a higher 20-year relative survival than haematological malignancies. This difference in survival was consistent among all age groups and was more prominent in older patients versus patients less than 14 years old, who had better survival with haematological malignancies. Improvements in

the survival rates in haematological malignancies seemed more prominent (73.6% increase) than in solid malignancies (51.2% increase). These data were similar to the data reported in previous studies from different geographic areas.^{7,21,22} The survival difference between different age groups was also reported in a population-based study in the UK, where the net survival in the elderly population remained lower than that in younger patients over a period of 40 years (1971–2011).²⁰ Thus, observing such a discrepancy is not surprising, as both solid and haematological malignancies are heterogeneous groups of different diseases with different natural histories and treatment options. Elderly patients commonly show late manifestations and have multiple comorbidities that can affect both treatment decisions and liability to treatment-induced toxicity.

Improvements in survival, however, do not come without costs. Long-term cancer survivors are more likely to experience treatment-induced long-term side-effects, including organ failure and secondary malignancies. Long-term non-medical effects, including financial toxicity and lifestyle changes, can also add burdens on long-term survivors. Thus, addressing cancer survivorship issues, particularly in patients with potentially high survival rates, and establishing follow-up guidelines that not only go beyond the normal follow-up periods but also address the medical and non-medical needs of cancer survivors, are imperative. An effort to address the cancer survivorship issue was made by the European Society for Medical Oncology (ESMO), which provided expert consensus guidelines for the management of cancer survivorship. The guidelines identified core components that need to be addressed in cancer survivors including physical and psychological effects, social and financial impact, active surveillance for recurring cancers and second primaries and promotion of well-being including improvement of cancer prevention approaches and overall health.²³

This study addressed a huge number of patients with long follow-up durations. Notwithstanding the resulting comprehensiveness of analysis, the study had several limitations. First, the SEER database does not provide detailed data on the treatment options the patients received. The included cohort was diagnosed over a long period, which might have resulted in the heterogeneous availability of treatment options and subsequent differences in clinical outcomes. Second, the 20-year survival data could only be calculated for the SEER 9 database, which includes cancer registries present since the inception of the SEER Program. Major updates were performed in SEER, which currently includes 22 cancer registries covering 47.9% of the total

cancer patient population in the USA. However, the use of long-term data from newly incorporated cancer registries will not be feasible until a couple of years later when the follow-up duration can allow for long-term survival analysis. Third, methods to evaluate survival rates can vary and lead to differences in outcome interpretation.²⁴ For example, slightly higher relative survival rates with the Ederer II method compared to Hakulinen or Ederer I method have been reported, in which the follow-up duration exceeded 10 years. In some cases, as in malignancies diagnosed over a wide range of ages (e.g. thyroid cancer), long-term relative survival for all ages combined may vary depending on the method used to estimate expected survival. This is because Ederer I and Hakulinen methods will provide similar and higher relative survival compared to that calculated by Ederer II.²⁵ Finally, in general, and as with data originating from cancer registries, SEER extracted data must be interpreted with caution given the challenges of unrecorded variables, underreported and incomplete adjuvant treatment data, the disparity in coding and reporting and the migration of patients between SEER registry regions.²⁶

Conclusion

Long-term follow-up data suggested that the 20-year relative survival rates were high for many tumour types. The relative survival rates significantly improved over time. Long-term follow-up programmes for cancer survivors should be incorporated into the clinical management of patients with cancer.

AUTHORS' CONTRIBUTION

MAG conceptualised the study, while RAS, EIZ and MAG designed the methodology. RAS, AAN, EIZ and MAG drafted the original manuscript, and AAN reviewed and edited the manuscript and supervised the work. All authors approved the final version of the manuscript.

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CONFLICT OF INTEREST

The authors declare no conflict of interests.

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