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Conditional Survival in Pediatric Malignancies: Analysis of data from the Childhood Cancer Survivor Study and the Surveillance, Epidemiology and End Results Program

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Abstract

Background—Long-term survivors of pediatric cancer are at risk for life-threatening late effects of their cancer. Previous studies have shown excesses in long-term mortality within high-risk groups defined by demographic and treatment characteristics.

Methods—To investigate conditional survival in a pediatric cancer population, we performed an analysis of conditional survival in the original Childhood Cancer Survivor Study (CCSS) cohort and the Surveillance, Epidemiology and End Results (SEER) database registry. The overall probability of death for patients in 5 years and 10 years after they survived 5, 10, 15, and 20 years since cancer diagnosis, and cause-specific death in 10 years for 5-year survivors were estimated using the cumulative incidence method.

Results—Among CCSS and SEER patients who were alive 5 years post cancer diagnosis, within each diagnosis group at least 92% are alive in the subsequent 5 years, except leukemia patients of whom only 88% of 5-year survivors remain alive in the subsequent 5 years. The probability of all-cause mortality in the next 10 years on patients who survived at least 5 years after diagnosis, was 8.8% in CCSS and 10.6% in SEER, approximately three quarter of which were due to neoplasms as causes of death.

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Conclusion—The risk of death of pediatric cancer survivors in 10 years can vary between diagnosis groups by at most 12% even up to 20 years post diagnosis. This information is clinically important in counseling patients on their conditional survival, particularly when survivors are seen in long-term follow-up.

Keywords

pediatric cancer; survivors; conditional survival; cause-specific mortality; cohort study

Introduction

Improvements in therapy and supportive care for children diagnosed with cancer have increased the overall 5-year survival rate from 45% for patients diagnosed in the mid-1970s to over 80% [1]. Estimates place the number of childhood cancer survivors in the U.S. at 420,000 at the end of 2013 [2]. Moreover, it is estimated that the number of years of life saved by the successful treatment of childhood cancer exceeds all other cancer in the United States (US) [1]. When compared to adults, children have more potential life-years ahead of them, thus the quality of survivorship becomes even more important. Long-term survivors of childhood cancer are at risk for serious, disabling, life-threatening or fatal treatment-related late effects including second malignancies, cardiac and vascular abnormalities, and pulmonary complications [2–7]. Previous studies of childhood cancer survivors have shown excesses in long-term mortality and have characterized high-risk groups defined by demographic and treatment characteristics [8–11].

Conditional survival is the likelihood of continued survival for a specified interval of time after having already survived for a specific time interval after cancer diagnosis [12–16]. This measurement of survival is clinically relevant because the likelihood of survival changes with increasing duration of follow-up from initial cancer diagnosis. As an example, the risk of recurrence and disease-related mortality is higher in the immediate period after diagnosis, whereas the risk of non-cancer related death and treatment-related death often increases with time [13–15]. In this instance, conditional survival is particularly useful for evaluation of childhood malignancies with a relatively high initial rate of cancer-related mortality that diminishes with time [15].

In contrast to the pediatric oncology literature, conditional survival is increasingly being applied in assessment of adult cancers through the use of large population databases such as the National Cancer Institute's Surveillance, Epidemiology and End Results (SEER), as well as selected clinical trials [13–20]. To investigate conditional survival in the pediatric cancer population, we performed an analysis in two large and commonly cited populations of childhood cancer patients, the original Childhood Cancer Survivor Study (CCSS) cohort and the SEER-9 database. The CCSS cohort includes 5-year survivors of selected childhood cancers diagnosed and treated at 26 collaborating academic institutions. SEER collects and publishes cancer incidence and survival data from population-based cancer registries within the US. The objective of this analysis is to estimate conditional survival over time for pediatric cancer survivors starting with 5-year survivors for all causes and cause-specific deaths and determine the effect of primary diagnosis and institution (CCSS)/geographic

location (SEER) on conditional survival. These data will provide a framework by which clinicians can counsel survivors and their families on survival with time.

Methods

CCSS Cohort

The CCSS is a multi-institutional retrospective cohort study of individuals with cancer before the age of 21 and survived for five or more years. Details of the study design, methods, and cohort characteristics have been previously reported [21]. In brief, eligibility criteria for CCSS are: a) diagnosis of leukemia, CNS malignancies (all histologies), Hodgkin lymphoma, non-Hodgkin lymphoma, malignant kidney tumor, neuroblastoma, soft tissue sarcoma, or bone tumor; b) diagnosis and initial treatment at one of the 26 collaborating CCSS institutions; c) diagnosis date between January 1, 1970 and December 31, 1986; d) age less than 21 years at diagnosis; e) survival of five years from diagnosis. The CCSS protocol and contact documents were reviewed and approved by the Human Subjects Committee at each participating institution.

CCSS data include self-report questionnaires and medical record abstraction of detailed treatment data from the treating institution [22, 23]. The initial baseline questionnaire was administered beginning in 1994 and was updated periodically with follow-up questionnaires through 2009. Demographics, including race and ethnicity were obtained on the baseline survey. Characteristics of the original cancer diagnosis were abstracted from the medical records at the treating institution.

Causes of Death in CCSS

Methods for ascertaining and categorizing deaths within the CCCS cohort have been described previously [8, 9]. In brief, to determine vital status of all eligible individuals, as of December 31, 2007, a National Death Index (NDI) search was requested for deaths occurring during the time period 1979–2007. For those who died in the US, cause of death information was provided by the NDI, using the International Classification of Disease (ICD-9 & ICD-10) classification [24]. For deaths occurred in 1975–78 (i.e., the years not covered by the NDI), copies of the death certificates were requested from all states where deaths had occurred. Death certificate data were not available for survivors who were Canadian residents at the time of death, thus they were excluded from the analyses. Within CCSS, there were 2,287 individuals who had been reported to have died by December 31, 2007.

SEER Registry

The SEER Program of the National Cancer Institute (NCI) is a source of information on cancer incidence and survival in the United States [25]. Between 1975 and 1986, the SEER registries were limited to nine regions (SEER-9): Atlanta, Connecticut, Detroit, San Francisco-Oakland, Seattle-Puget Sound, and the entire states of Hawaii, Iowa, New Mexico and Utah. The cancer diagnoses were restricted to those included in the CCSS cohort. Mortality data reported by SEER are provided by the National Center for Health Statistics. For the analyses reported here, the most recent follow-up year for mortality data was 2007.

Data Analysis

To select the same calendar years of diagnosis as SEER, CCSS survivors whose childhood cancer diagnosis occurred between 1975–86 were included. Demographic and clinical characteristics of survivors in the CCSS and the patients in SEER who survived at least 5 years since the original cancer diagnosis were tabulated. Patients with missing demographic or clinical characteristics, except race, were not included in the analysis. We compared demographic and clinical characteristics of the CCSS and SEER 5-year survivors using the Chi-square test. Conditional survival curves were estimated for CCSS and SEER separately with the Kaplan-Meier estimator, conditioned on having survived 5, 10, 15, and 20 years, for all survivors and by cancer diagnoses. Conditional probabilities of cause-specific death in 10 years for 5-year survivors (by 15 years since cancer diagnosis) and their 95% confidence interval were estimated by the cumulative incidence method, treating death due to any other causes as competing risk events. Causes of death were categorized into five groups: neoplastic (ICD-9 codes 140-239 & ICD-10 codes C00-C97, D00-D48); infectious (ICD-9 codes 001-018, 020-037, 039-088, 090-139, 461, 480-487, 541 & ICD-10 codes A00-A08, A15-A33,A40-B99,J09-J18); cardiac/vascular (ICD-9 codes 390-398, 401-404, 410-438, 440-448, 451-453, 456-459 & ICD-10 codes I00-I13, I20-I51, I60-I78,); external (ICD-9 codes 800-999 & ICD-10 codes U01-U03, V00-X59, X60-Y09, Y35, Y85-Y87, Y89); and the others. The permutation test was used to compare CCSS and SEER conditional probabilities of cause-specific death within 15 years of cancer diagnosis.

Five year probability of death conditioned on surviving 5 years, 10 years, 15, years and 20 years since cancer diagnosis and their 95% confidence interval were estimated by the cumulative incidence method, treating death as all cause of death for all survivors and for survivors of specific childhood cancer diagnoses. Graphs were produced using R, version 2.15.2 [26]. All the other statistical analyses were performed using SAS version 9.3 (SAS Institute).

Results

Study population characteristics

A total of 16,602 survivors in the CCSS cohort and 6,576 survivors in SEER registry met the eligibility criteria for this analysis. Demographic and clinical characteristics of survivors are shown in Table 1. The CCSS and SEER survivors were similar with respect to treatment era and sex, but different with respect to cancer diagnosis group, age at diagnosis, and possibly race/ethnicity (a proportion of CCSS survivors did not report their race/ethnicity). The median age at diagnosis among the 5-year survivors was 6.8 years in the CCCS cohort, compared to 11.0 years among the SEER survivors.

Conditional survival in CCSS and SEER

Conditional survival curves are shown in Figure 1 for all patients and by primary diagnosis, conditioned on 5, 10, 15, and 20 years of survival since diagnosis. Among all CCSS patients who were alive at least 5 years up to 20 years since cancer diagnosis, at least 91.6% of them within each diagnosis group were alive in the subsequent 5 years. Similarly, within SEER, at least 91.9% of all patients within each diagnosis group who survived at least 5 years up to

20 years after cancer diagnosis were alive in the subsequent 5 years, except leukemia patients of whom only 88% of 5-year survivors remain alive in the subsequent 5 years.

In both CCSS and SEER cohorts, in survival curves conditioned on 10-, 15-, and 20-year survival were similar and largely independent of their survival time since cancer diagnosis. For kidney tumors, neuroblastoma, and lymphoma patients, survival curves were parallel for 5-, 10-, 15- and 20-year survivors, meaning the chance of being alive for the next period(s) or time(s) was similar regardless of the number of years survived since 5-years after cancer diagnosis.

Probability of death in the next 10 years for 5-year survivors in CCSS and SEER

Tables 2A and Table 2B show the overall and diagnosis-specific probability of all cause and cause-specific death by 15 years. The probability of death by 15 years since diagnosis for patients who have survived 5 years since cancer diagnosis was 8.8% in CCSS and 10.6% in SEER. This probability of death in 10 years varied greatly by diagnosis: in CCSS, 12.9% among CNS survivors was the highest, followed by 10.8% among soft tissue/Ewing sarcoma survivors, 9.9% among leukemia survivors, and 9.5% among osteosarcoma/other bone tumor survivors. Lymphoma (6.9%), neuroblastoma (4.2%), and kidney tumors (2.6%) survivors had substantially lower conditional probabilities of death. In SEER, the highest probability of death was 16.0% among leukemia followed by 11.4% among osteosarcoma/other bone tumor survivors, 10.0% among lymphoma survivors, 9.7% among CNS survivors, and 9.2% among soft tissue/Ewing sarcoma survivors. Neuroblastoma (4.8%) and kidney tumor (2.2%) survivors had substantially lower conditional probabilities of death in the next 10 years for those who survived 5 years since cancer diagnosis. The majority of deaths for 5-year survivors in the next 10 years (5–15 years from diagnosis) were due to “neoplasms”.

Five year mortality of CCSS patients conditioned on surviving 5-, 10- years, 15- and 20-years after cancer diagnosis

Table 3A shows the risk of death in the subsequent 5-years overall and by diagnosis for 5-, 10-, 15- and 20-year survivors of pediatric cancer. For patients with kidney tumors who had survived at least 5 years, the subsequent 5-year mortality was less than 2% for 5- 10-, 15- and 20-year survivors with little change in mortality across time periods. The risk of mortality in next 5 years for 5-year survivors of leukemia was much higher than their risk of mortality having survived 10 years since cancer diagnosis. A similar pattern was seen for patients with a history of neuroblastoma, soft tissue sarcoma, Ewing sarcoma, osteosarcoma, other bone tumors, and CNS tumors. The 5 year risk of death for lymphoma patients was highest in 5-year and 20-year survivors, the differences in risk of death did not vary more than 2% across patients’ years since cancer diagnosis.

Five year mortality of SEER patients conditioned on surviving 5-, 10-, 15-, and 20-years after cancer diagnosis

Table 3B shows the mortality in the next 5 years for each diagnosis group and overall for patients in SEER who survived 5-, 10-, and 15-years since cancer diagnosis. Comparable to the CCSS data, the mortality of kidney tumors patients who survived at least 5 years since

cancer diagnosis was less than 2 % across all time periods of follow up and their change in mortality across all time periods was less than 1%. Also similar to CCSS the 5-year mortality for leukemia, neuroblastoma, soft tissue sarcoma, and Ewing sarcoma patients was much higher for 5-year survivors versus those who had survived 10-years or more. The 5 year mortality of Osteosarcoma patients and Other bone tumors patients were similar when they were five years since cancer diagnosis and when they were 20 years since cancer diagnosis. Unlike other cancer groups, the 5 year mortality of CNS patients and lymphoma patients were the highest after they survived 20 years since cancer diagnosis and the difference in 5 year mortality across years since cancer diagnosis in these two cancer group patients can be more than 5 percent.

Discussion

Investigation of long-term outcomes using conditional survival can provide useful information for pediatric cancer survivors, family members, and healthcare providers. To our knowledge there is very limited data looking at conditional survival in a cohort of pediatric cancer survivors. The CCSS and SEER databases provided us the opportunity to investigate conditional survival in two large cohorts of survivors of childhood cancer. For the overwhelming majority of diagnoses, the current data demonstrate subsequent five year survival to be ≥ 92% when conditioning on having survived 5, 10, 15, and 20 years from initial diagnosis.

The current study allowed for a more detailed analysis of conditional survival than the previous analyses of the CCSS, where overall mortality of 5-year childhood cancer survivors was found to be increased when compared to the general US population. We originally reported on late mortality in 2001 with an update in 2008 [8, 9]. In these earlier analyses of late mortality, there was a decrease in the standardized mortality rate (SMR) with increasing survival time after diagnosis. All-cause 30-year cumulative mortality was 18.1% (95% CI = 17.3 to 18.9) for 5-year survivors, 12.4% (95% CI = 10.3 to 11.6) for 10-year survivors, 9.5% (95% CI = 8.7 to 10.3) for 15-year survivors, and 7.0% (95% CI = 6.3 to 7.8) for 20-year survivors [9]. Within the CCSS cohort, 20-year conditional survival after surviving 5 years is over 90% for all diagnoses except CNS tumors. Of particular interest in our previous mortality analysis, there were several diagnoses (acute lymphoblastic leukemia, neuroblastoma, kidney tumors) whose 20-year conditional survival exceeded 95%, which were comparable to expected survival curves from the US general population [8].

Bleyer *et al*. used the SEER database to determine the conditional survival of 15- to 39-year olds diagnosed with cancer during 1975–2000 compared with younger (< 15 years of age) and older patients (≥ 40 years of age) [27]. It was found that although adolescents and young adults (AYAs 15–39 year olds) had a better prognosis at diagnosis, their probability of survival thereafter did not increase as rapidly as younger and older patients, particularly for relative survival. In fact, AYAs had a lower conditional survival improvement than any other age group, including infants and the elderly. In the SEER data, we found a similar pattern with individuals diagnosed with lymphoma whose 20 year conditional survival rates were the lowest among all diagnoses. The explanation for this is not known, but may be due

to the occurrence of life-threatening late effects (i.e., subsequent cancer, cardiac disease) reported in 20+ year survivors of Hodgkin lymphoma [5, 28].

When looking at the results of this analysis, it is important to highlight differences in the two cohorts, which may account for some of the discordance seen in these analyses. First, the SEER survivor population is older, with 36% of this cohort being between the ages of 15–20 at diagnosis (vs. 17% in CCSS), and only 29% being diagnosed between 0–4 (vs. 40% in CCSS). Second, the frequency of diagnoses differs, with more leukemia survivors seen at CCSS institutions (43% vs. 24% in SEER), and less CNS tumor (14% vs. 23% at SEER sites) and fewer lymphoma patients seen at CCSS (20% vs. 27% at SEER sites). These differences may be indicative of possible policies for pediatric institutions that restrict patients over the age of 18 years or referral patterns by healthcare providers who may be more likely to refer younger patients to a children's hospital, and adolescents to adult facilities, or comfort level within adult facilities to see younger patients. In addition, analysis of CCSS to SEER data may serve as a surrogate comparison of patients likely treated in an academic/pediatric cooperative group setting (i.e., Children's Oncology Group) to patients from a large population-based dataset (SEER) which is more likely to contain information on patients treated at non-academic and adult institutions. Likewise, the CCSS cohort may be more likely to contain patients treated on clinical trials versus the SEER database.

There are several limitations to this analysis. First, a large proportion of SEER patients and CCSS survivors were missing race/ethnicity and we could not adjust for it completely, limiting our ability to look at conditional survival comparisons among these sub-groups. Second, diagnosis staging data was not available on either cohort, limiting our ability to control for this in our analysis. It would be of interest in future analyses to be able to look at other possible risk factors, such as socioeconomic status, to understand the differences seen in these two populations. Lastly, it is possible that there may be misclassification regarding cause of death in both cohorts. However, since both cohorts utilize US vital records, we can assume that the bias would be similar in both cohorts.

Clinicians are often faced with questions from patients and parents about prognosis, including when they can be considered to be cured. The information typically available to clinicians is survival curves created from the cancer diagnosis. This, however, only describes what happens to patients starting from the beginning (diagnosis). The conditional survival data presented here allows clinicians a new way of thinking about long-term follow-up, namely, after having survived certain numbers of years, what will happen. The CCSS itself is an example of conditional survival analysis in that patients were required to have survived 5 years in order to participate in this cohort study. Most reports from the CCSS detail what happens to patients after they have already survived the first 5 years from cancer diagnosis. This current study starts to take the next step towards allowing clinicians to give more individualized prognosis when they see patients in long-term follow-up. At each visit, patients and parents will be able to receive updated information about the future that is based on the time points they have already achieved.

Conclusion

Overall, conditional survival is high in 5-year survivors of pediatric cancer, however there still remains a risk for death in these survivors even up to 20 years post diagnosis. The similarities in the trends seen in both cohorts allow clinicians a new way of thinking about long-term follow-up. In addition, this measurement of survival is clinically relevant because it more accurately reflects future patient outcomes, taking into account a patient's time since initial cancer diagnosis. For healthcare providers, as with survivors and their families, this information is clinically important and warrants continued follow-up and ongoing medical care in these long-term survivors.

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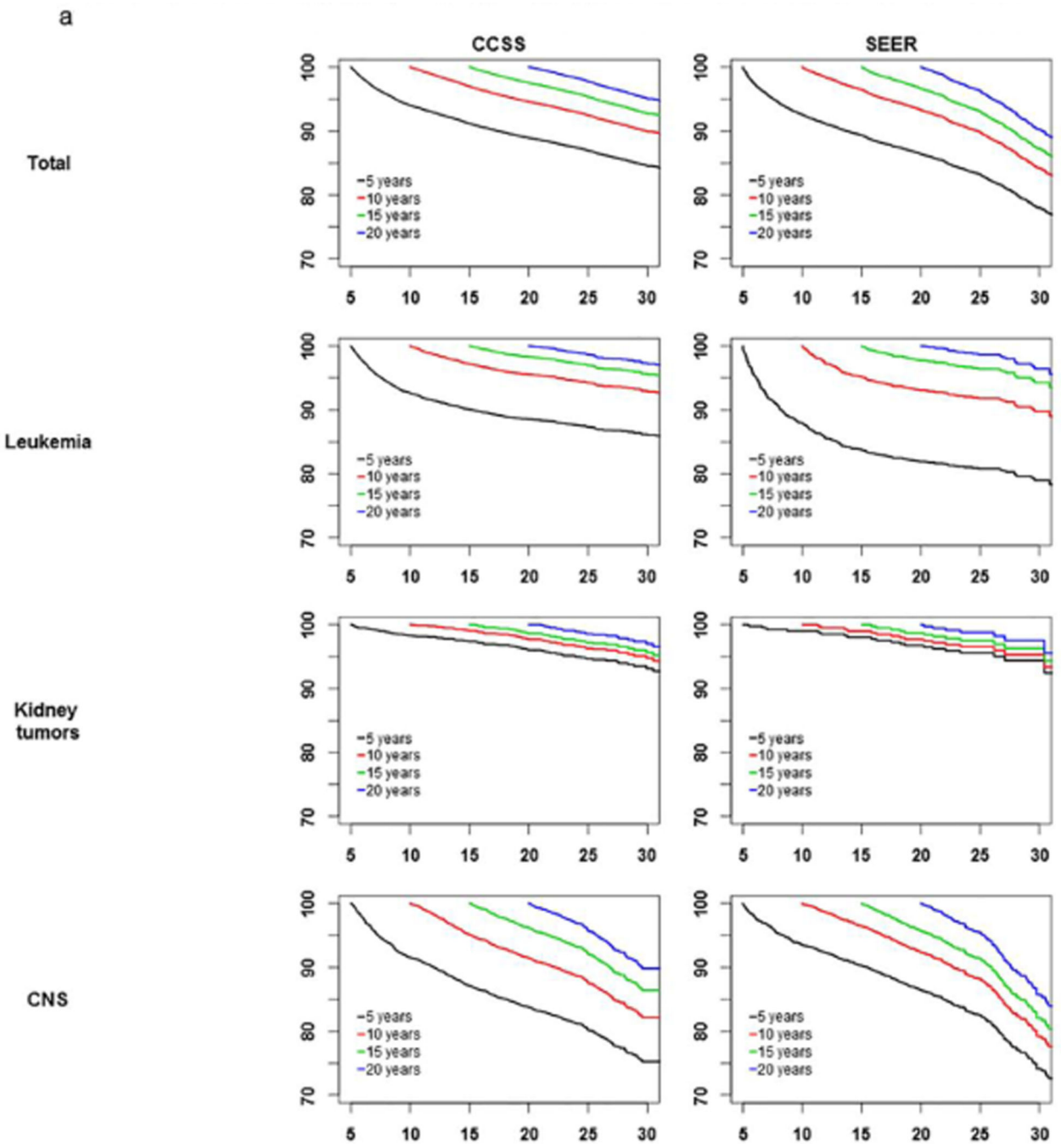

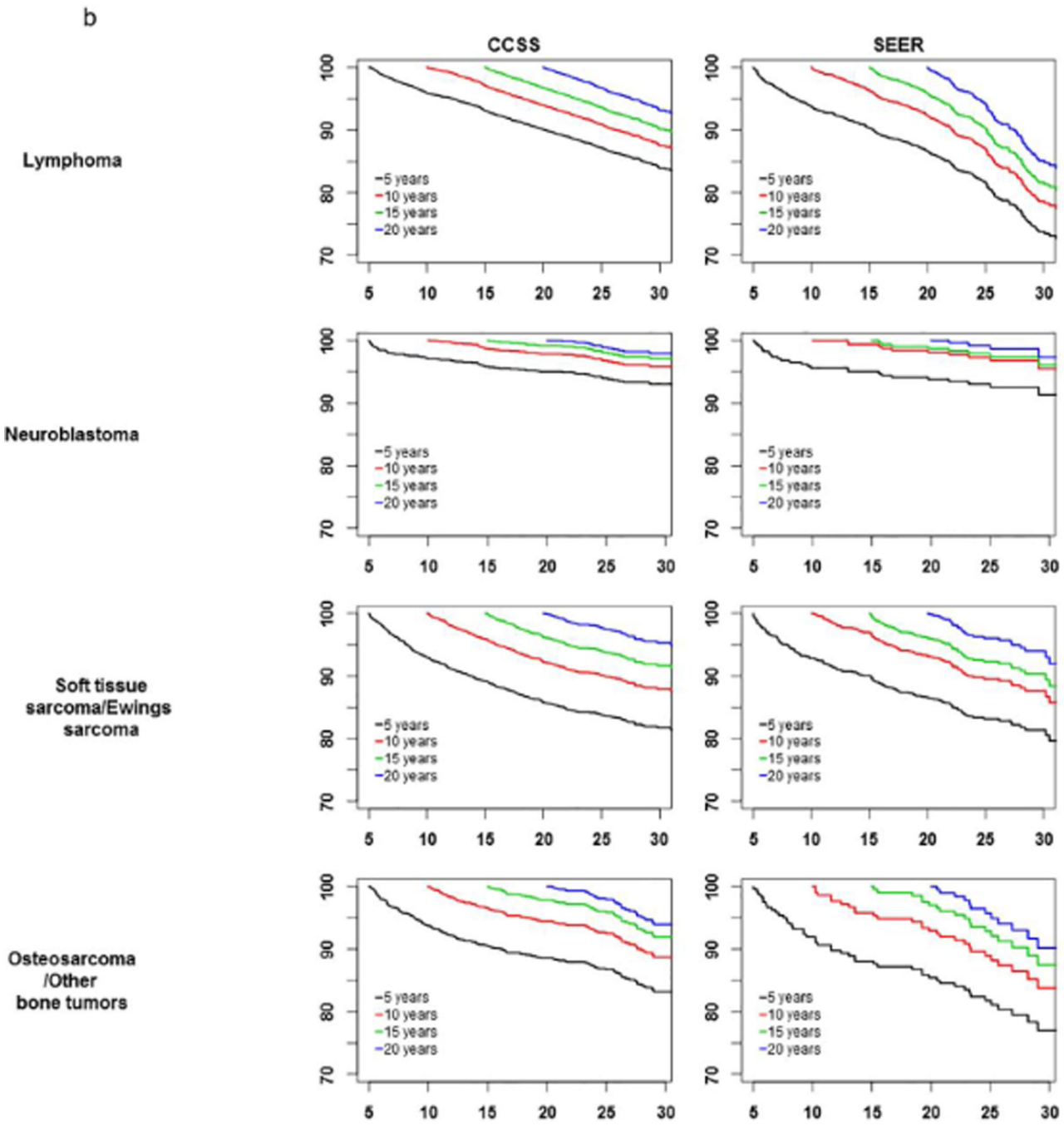

Figure 1.

a-b: Survival curves conditioned on 5-, 10-, 15-, 20-years survival after cancer diagnosis.

Table 1

Characteristics of pediatric cancer patients who survived 5+ years post diagnosis

	CCSS		SEER		p-value
	N	%	N	%	
Total 5-year survivors	**16,602**		**6,576**		
Death status for those with survival/censor time 5+ years					
Alive	14315	5389	5389	82.0	
Dead	2287	1187	1187	18.0	
Sex					**0.01**
Female	7411	3056	3056	46.5	
Male	9191	3520	3520	53.5	
Race/Ethnicity					
White, Non-Hispanic	10094	37	37	0.6	**<0.001**
Black, Non-Hispanic	591	5610	5610	85.3	
Other	1058	553	553	8.4	
missing	4859	376	376	5.7	
Diagnosis group					**<0.001**
Leukemia					
Acute lymphoblastic	4983	1329	1329	20.2	
Acute myeloid leukemia	438	131	131	2.0	
Other leukemia	188	99	99	1.5	
Lymphoma					
Hodgkin lymphoma	1999	1244	1244	18.9	
Non-Hodgkin lymphoma	1273	475	475	7.2	
Bone Tumor					
Ewing sarcoma	484	125	125	1.9	
Osteosarcoma	899	192	192	2.9	

	CCSS		SEER		p-value
	N	%	N	%	
Other bone tumors	82	47	47	0.7	
Central Nervous System					
Astrocytomas	1488	837	837	12.7	
Medulloblastoma, PNET*	481	190	190	2.9	
Other CNS tumors	374	505	505	7.7	
Kidney tumors	1413	408	408	6.2	
Neuroblastoma	1101	345	345	5.3	
Soft tissue sarcoma	1399	649	649	9.9	
Age at diagnosis					**<0.001**
0–4	6714	1902	1902	28.9	
5–9	3715	1189	1189	18.1	
10–14	3318	1157	1157	17.6	
15–20	2855	2328	2328	35.4	
Treatment Era					**<0.001**
1975–1980	7364	3059	3059	46.5	
1981–1986	9238	3517	3517	53.5	

*Primitive Neuroectodermal Tumor

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Table 2

A. The probability of death in the next 10 years of CCSS patients who survived 5 years after cancer diagnosis by cause of death and cancer type

Diagnosis Group	Survival probability		All cause of death		Cause-specific death*			
					Neoplasms		Infectious	
	%	95% CI	%	95% CI	%	95% CI	%	95% CI
Total	91.2	(90.8, 91.6)	8.8	(8.4, 9.2)	6.3	(6.0, 6.7)	0.3	(0.2, 0.4)
Leukemia	90.1	(89.3, 90.9)	9.9	(9.1, 10.7)	7.4	(6.7, 8.1)	0.4	(0.2, 0.5)
Kidney tumors	97.4	(96.5, 98.2)	2.6	(1.8, 3.5)	1.6	(0.9, 3.9)	0	-
CNS	87.1	(85.8, 88.5)	12.9	(11.5, 14.2)	9.5	(8.3, 10.7)	0.3	(0.1, 0.5)
Lymphoma	93.1	(92.3, 94.0)	6.9	(6.0, 7.7)	4.4	(3.7, 5.1)	0.3	(0.1, 0.5)
Neuroblastoma	95.8	(94.6, 97.0)	4.2	(3.0, 5.4)	2.9	(1.9, 3.9)	0.1	(0, 0.3)
Soft tissue sarcoma/ Ewing sarcoma	89.2	(87.8, 90.6)	10.8	(9.4, 12.2)	8.1	(6.8, 9.3)	0.2	(0, 0.3)
Osteosarcoma/Other bone tumors	90.5	(88.7, 92.4)	9.5	(7.6, 11.3)	6.6	(5.1, 8.2)	0.4	(0, 0.8)

Diagnosis Group	Cause-specific death*							
	Cardiac/Vascular		External		Other		Unknown	
	%	95% CI	%	95% CI	%	95% CI	%	95% CI
Total	0.3	(0.2, 0.4)	0.5	(0.4. 0.6)	0.4	(0.3. 0.5)	1.0	(0.9, 1.1)
Leukemia	0.1	(0, 0.2)	0.3	(0.2, 0.5)	0.4	(0.3, 0.6)	1.3	(1.0, 1.6)
Kidney tumors	0.4	(0.1, 0.8)	0.3	(0, 0.6)	0.3	(0, 0.6)	0.1	(0, 0.2)
CNS	0.2	(0,0.3)	0.6	(0.3, 0.9)	0.6	(0.3, 0.9)	1.8	(1.3, 2.3)
Lymphoma	0.7	(0.4, 1.0)	0.6	(0.3, 0.8)	0.4	(0.2, 0.6)	0.6	(0.3, 0.8)
Neuroblastoma	0.2	(0, 0.4)	0.4	(0, 0.7)	0.2	(0, 0.4)	0.5	(0, 0.9)
Soft tissue sarcoma/ Ewing sarcoma	0.5	(0.2, 0.8)	0.5	(0.2, 0.9)	0.5	(0.2, 0.9)	1.1	(0.6, 1.5)
Osteosarcoma/Other bone tumors	0.4	(0, 0.8)	0.8	(0.3, 1.4)	0.3	(0, 0.7)	0.9	(0.3, 1.5)

B. The probability of death in the next 10 years of SEER patients who survived 5 years after cancer diagnosis by cause of death and cancer type

Diagnosis Group	Survival probability		All cause of death		Cause-specific death*			
					Neoplasms		Infectious	
	%	95% CI	%	95% CI	%	95% CI	%	95% CI
Total	89.4	(88.6, 90.3)	10.6	(9.7, 11.4)	8.1	(7.4, 8.7)	0.3	(0.2, 0.4)
Leukemia	83.7	(81.9, 85.6)	16.3	(14.4, 18.1)	13.3	(11.6, 15.0)	0.4	(0.1, 0.8)
Kidney tumors	98.0	(96.7, 99.4)	2.0	(0.6, 3.3)	1.5	(0.3, 2.7)	0	-
CNS	90.3	(88.8, 91.7)	9.7	(8.3, 11.2)	7.6	(6.3, 9.0)	0.2	(0, 0.4)
Lymphoma	90.3	(88.9, 91.7)	9.7	(8.3, 11.1)	6.3	(5.1, 7.4)	0.3	(0.1, 0.6)
Neuroblastoma	95.0	(92.7, 97.3)	5.0	(2.7, 7.3)	3.8	(1.8, 5.8)	0	-
Soft tissue sarcoma/ Ewing sarcoma	90.1	(87.9, 92.2)	9.9	(7.8, 12.1)	7.7	(5.8, 9.6)	0.1	(0, 0.4)
Osteosarcoma/Other bone tumors	88.1	(83.9, 92.2)	11.9	(7.8, 16.1)	9.0	(5.3, 12.6)	1.3	(0, 2.7)

Diagnosis Group	Cause-specific death*							
	Cardiac/Vascular		External		Other		Unknown	
	%	95% CI	%	95% CI	%	95% CI	%	95% CI
Total	0.4	(0.3, 0.6)	0.5	(0.3, 0.7)	0.5	(0.3, 0.6)	0.8	(0.6, 1.0)
Leukemia	0.3	(0, 0.5)	0.5	(0.1, 0.8)	0.7	(0.2, 1.1)	1.2	(0.6, 1.7)
Kidney tumors	0	-	0.3	(0, 0.7)	0	-	0.2	(0, 0.7)
CNS	0.2	(0, 0.4)	0.4	(0.1, 0.7)	0.7	(0.3, 1.2)	0.6	(0.2, 1.0)
Lymphoma	1.0	(0.5, 1.5)	0.9	(0.5, 1.4)	0.3	(0, 0.5)	0.8	(0.4, 1.3)
Neuroblastoma	0.6	(0, 1.4)	0	-	0	-	0.6	(0, 1.4)
Soft tissue sarcoma/ Ewing sarcoma	0.4	(0, 0.8)	0.4	(0, 0.8)	0.4	(0, 0.8)	0.9	(0.2, 1.6)
Osteosarcoma/Other bone tumors	0	-	0.4	(0, 1.2)	0.9	(0, 2.0)	0.4	(0, 1.3)

Table 3

5-year mortality of CCSS and SEER patients when they survived 5 years, 10 years, 15 years and 20 years after cancer diagnosis

Diagnosis Groups	CCSS	SEER
	% Death (95% CI)	% Death (95% CI)
Total Patients		
5–10 years	5.96 (5.92, 6.01)	7.35 (7.22, 7.48)
10–15 years	3.03 (2.96, 3.10)	3.34 (3.12, 3.55)
15–20 years	2.47 (2.39, 2.55)	3.31 (3.08, 3.54)
20+ years	3.04 (2.97, 3.12)	5.97 (5.79, 6.15)
Leukemia		
5–10 years	7.31 (7.19, 7.44)	10.96 (10.58, 11.34)
10–15 years	2.81 (2.59, 3.03)	4.55 (3.85, 5.26)
15–20 years	1.70 (1.41, 2.00)	2.01 (0.86, 3.15)
20+ years	1.67 (1.37, 1.97)	1.94 (0.71, 3.17)
Kidney tumors		
5–10 years	1.70 (0.64, 2.75)	1.25 (0, 6.71)
10–15 years	0.94 (0, 2.39)	1.00 (0, 5.87)
15–20 years	1.38 (0.18, 2.58)	1.28 (0, 5.67)
20+ years	1.77 (0.69, 2.85)	1.88 (0, 5.68)
CNS		
5–10 years	8.41 (8.13, 8.68)	6.40 (5.91 6.89)
10–15 years	4.89 (4.49, 5.30)	3.46 (2.72, 4.19)
15–20 years	3.82 (3.34, 4.30)	4.22 (3.53, 4.91)
20+ years	5.45 (5.03, 5.87)	8.02 (7.49, 8.54)
Lymphoma		
5–10 years	4.10 (3.81, 4.39)	6.17 (5.72, 6.61)
10–15 years	2.90 (2.54, 3.26)	3.64 (3.01, 4.27)
15–20 years	3.25 (2.90, 3.60)	4.09 (3.46, 4.72)
20+ years	4.61 (4.31, 4.92)	9.38 (8.95, 9.80)
Neuroblastoma		
5–10 years	2.91 (1.88, 3.94)	4.34 (1.68, 7.01)
10–15 years	1.31 (0, 2.90)	0.62 (0, 8.33)
15–20 years	0.85 (0, 2.86)	1.27 (0, 6.77)
20+ years	1.43 (0, 2.99)	1.35 (0, 6.99)
Soft tissue sarcoma/Ewing sarcoma		
5–10 years	7.01 (6.63, 7.39)	7.11 (6.19, 8.02)
10–15 years	4.11 (3.57, 4.65)	2.97 (1.39, 4.55)
15–20 years	3.81 (3.23, 4.40)	3.88 (2.42, 5.34)

Diagnosis Groups	CCSS	SEER
	% Death (95% CI)	% Death (95% CI)
20+ years	3.22 (2.55, 3.89)	4.44 (3.00, 5.89)
Osteosarcoma/Other bone tumors		
5–10 years	6.22 (5.44, 6.99)	7.95 (5.16, 10.74)
10–15 years	3.48 (2.36, 4.60)	4.23 (0, 8.61)
15–20 years	2.14 (0.65, 3.63)	2.94 (0, 8.46)
20+ years	3.68 (2.53, 4.84)	6.70 (2.93, 10.47)