Long-Term Survivors of Childhood Cancers in the United States

Angela B. Mariotto,[1] Julia H. Rowland,[1] K. Robin Yabroff,[1] Steve Scoppa,[2] Mark Hachey,[2] Lynn Ries,[1] and Eric J. Feuer[1]

[1]Division of Cancer Control and Population Sciences, National Cancer Institute, Bethesda, Maryland and
[2]Information Management Systems, Inc., Rockville, Maryland

Abstract

Purpose: **To estimate the number of individuals in the United States diagnosed with cancer as children (ages 0-19 years) as of 2005, with a focus on those surviving for >30 years.**
Methods: **To estimate the national prevalence of survivors of childhood cancers, we used data from the Surveillance Epidemiology and End Results program from 1975 to 2004. Long-term childhood cancer survivors, diagnosed before 1975, were estimated using incidence and survival models extrapolated into years before 1975.**
Results: **We estimated that there are a total of 328,652 survivors of childhood cancer in the United States as of January 1, 2005, of these, 24% have survived >30 years since diagnosis. The cancer sites with the largest number of survivors are brain (51,650), acute lymphoblastic leukemia (49,271), germ cell tumors (34,169), and Hodgkin lymphoma (31,598). Sites with higher proportions of survivors diagnosed >30 years ago are germ cell (43%), soft tissue (38%), renal (34%), and bone (26%). Historical trends from Connecticut data show major improvements in survival for all of the childhood cancer sites.**
Conclusion: **The number of survivors of childhood cancers is expected to increase in the future consequent to the lifesaving advances in treatment introduced after 1970, especially for acute lymphoblastic leukemia. Because this population is at increased risk for illness-related morbidity and mortality, appreciating the number of survivors who were treated as children is important both to determining the national cancer burden and planning for the future health care needs of these individuals.** (Cancer Epidemiol Biomarkers Prev 2009;18(4):1033–40)

Introduction

Substantial improvements in treatment effectiveness for malignant disease in childhood have resulted in cure or longer survival for this population. The consequence is that the number of long-term childhood cancer survivors in the United States is rapidly increasing. Many of these survivors are now adults. However, there is growing awareness that the ''cure'' associated with cancer treatment may incur other long-term risks. Short-term and long-term effects of treatment, including increased risk of subsequent cancers, are common (1, 2), and have the potential to adversely affect survivors' future physical, cognitive, and/or psychosocial health (3, 4). Although some problems, such as cognitive deficits after cranial radiotherapy, are apparent within a few years of completion of therapy (2), there are often long latencies before the occurrence of other problems. Recent epidemiologic studies suggest that over 40% of childhood cancer survivors treated in the 1960s to the early 1990s have experienced at least 1 chronic disease, often severe in nature (2, 5, 6). Increasingly, resources are being requested to reduce adverse health-related outcomes and improve quality of life of these young cancer survivors (7). An important challenge to this effort is estimating the number of individuals who may carry this history and be at risk for increased morbidity and mortality secondary to cancer treatment as children or adolescents.

From 1975, the Surveillance Epidemiology and End Results (SEER-9; ref. 8) tumor registry program has collected information about all incident cancer patients from 9 geographic areas. Two monographs have reported on children, adolescents, and young adults diagnosed with cancer in the SEER-9 areas: cancer incidence and survival among children and adolescents diagnosed between 1975 and 1995 (9) and the epidemiology of cancer in older adolescents and young adults ages 15 to 29 years diagnosed between 1975 to 2000 (10). Survivors of childhood cancers diagnosed in 1975 or after would have a maximum of 30 years of follow-up in 2005. This period is still not long enough to estimate the number of survivors of childhood cancer who were older than ages 51 years on January 1, 2005. As far as we know, there are no recent data published on the total number of survivors of childhood cancers in the United States that include this important group of individuals; specifically, those living with a history of childhood cancer diagnosed >30 years earlier. Previous estimates were based on the Historical Connecticut Cancer Registry (CT) that reports cases since 1935 (7). Because SEER-9 covers a much larger population than CT, it provides more accurate and precise prevalence estimates especially for more rare cancer sites, as is the case for

Received 10/17/08; revised 1/9/09; accepted 1/26/09; published OnlineFirst 3/31/09.
Requests for reprints: Angela B. Mariotto, Statistical Research and Applications Branch/Surveillance Research Program, Division of Cancer Control and Population Sciences, National Cancer Institute, Suite 504, MSC 8317, 6116 Executive Boulevard, MSC 7344 Bethesda, MD 20892-7344. Phone: 301-594-1723; Fax: 301-435-3710. E-mail: mariotta@mail.nih.gov

doi:10.1158/1055-9965.EPI-08-0988

some childhood cancers. More recently, statistical methods have been developed to estimate the number of long-term survivors diagnosed before the start of cancer registration, which began in 1975 for the SEER-9 area. The aim of this paper is to provide an estimate of the nature and scale of this potentially at risk population in the United States with particular attention to these long-term survivors, adults diagnosed with cancer as children over 30 years ago, using the SEER-9 data. Although CT may not provide as accurate and precise prevalence estimates as SEER-9, CT nevertheless represents the best longitudinal population-based data against which to validate long-term survivor prevalence estimates.

Materials and Methods

Overview. To estimate the prevalence of survivors of childhood cancers by single sites as well as all cancer sites combined in the United States in 2005, we used incidence and survival data from the SEER registries from 1975 to 2004. We first estimated the prevalence of childhood cancer survivors diagnosed between the years 1975 and 2004 using a method that counts the people alive and adjusts for those lost to follow-up (11). We then fitted models to SEER incidence and survival for each cancer site as well as all cancer sites combined. These models were extrapolated into the past to estimate the prevalence of survivors diagnosed before 1975 (12). We used data from the Historical Connecticut Tumor registry (CT) from 1935 to 1997 to validate estimates of longer term survivors for all cancer sites combined.

Data Sources

SEER Data and Sample Population. In this analysis, we used incidence and follow-up data from cancer diagnosed in individuals ages 19 years and younger from 1975 to 2004 in 9 SEER registries (8), including the states of Connecticut, Hawaii, Iowa, New Mexico, and Utah and the metropolitan areas of Atlanta, Detroit, San Francisco-Oakland, and Seattle/Puget Sound. These registries represent ~10% of the U.S. population. The cancer sites considered were as follows: leukemias (I), acute lymphoblastic leukemia (ALL), acute myeloid leukemia (Ib), lymphomas (II), Hodgkin lymphomas (IIa), non–Hodgkin lymphomas including Burkitt lymphoma (IIb-c), brain and central nervous system tumors (III), neuroblastomas and sympathetic nervous system tumors (IV), retinoblastomas (V), renal tumors (VI), bone tumors (VIII), osteosarcomas (VIIIa), Ewing tumors (VIIIc), soft tissue tumors (IX), germ cell tumors (IX), and all cancer sites combined. We only considered malignant tumors, and all cancer sites combined are modeled as a separate site. We used the International Classification for Childhood Cancer (9), which emphasizes morphology rather than topology codes for all of the cancer sites groupings, with the exception of ALL for which we used the SEER site recode (13). For the major cancer sites considered, the two classifications are very similar, as can be seen from Table 1. The reason for using ALL instead of the International Classification for Childhood Cancer grouping lymphoid leukemia (Ia) is statistical and is related to the different frequencies of leukemia subtypes diagnosed between ages 0 and 19 years and ages 20 and older years. The statistical method used to estimate long-term survivors fits a parametric age and period model to incidence and survival across all ages at diagnosis, including ages 20 years and older. Lymphoid leukemia and ALL are very similar for cancers diagnosed in children, ALL accounts for 99% of all lymphoid leukemias diagnosed between ages 0 and 19 years. However, they differ considerably in adults ages 20 years and older. Only 10% of lymphoid leukemias diagnosed in adults are ALL. Because ALL is

Table 1. Number of cases diagnosed with malignant cancers between ages 0 and 19 y by major cancer sites groupings from International Classification of Childhood Cancer and percent captured by the corresponding SEER site recode grouping, when it applies, SEER-9, 1975 to 2005

ICCC classification		SEER site recode		% of cases captured by SEER site recode
Cancer site	No. cases	Cancer site	No. cases	
Leukemia (I)	8,362	Leukemia	8,361	100%
Lymphoid leukemia (Ia)	6,263	ALL	6,207	99%
Acute myeloid leukemia (Ib)	1,494	Acute myeloid leukemia	1,344	90%
Lymphoma (II)	5,284	Lymphoma	5,147	97%
Hodgkin (IIa)	2,887	Hodgkin	2,887	100%
Non–Hodgkin including Burkitt (IIb-c)	2,090	Non–Hodgkin	2,082	100%
Brain tumor/central nervous system (III)	5,979	Brain and ONS	5,826	97%
Neuroblastoma (IV)	1,893	—	—	—
Retinoblastoma (V)	688	—	—	—
Renal tumors (VI)	1,479	Kidney and renal pelvis	1,474	100%
Hepatic tumors (VII)	389	—	—	—
Bone tumors (VIII)	1,819	Bone	1,797	99%
Osteosarcomas (VIIIa)	988	—	—	—
Ewing tumors (VIIIc)	628	—	—	—
Soft tissue tumor (XI)	2,440	Soft tissue and heart	1,420	58%
Germ cell (X)	2,278	—	—	—
Carcinomas (XI)	3,252	—	—	—
Remaining	232	—	—	—
All cancer sites	34,095	All cancer sites	34,095	100%

NOTE: Only the first tumor per person is included.
Abbreviation: ICCC, International Classification for Childhood Cancer.

less heterogeneous than lymphoid leukemia between adults and children, simpler models were better able to fit the data.

To estimate the number of long-term female survivors for all cancer sites, we have excluded breast cancer from the data of female all cancer sites combined for similar reasons. Breast cancer incidence and survival have changed dramatically in the last 2 decades due in part to mammography screening in women ages 40 years and older. Because breast cancer represents a large proportion of all cancers diagnosed among women older than 40 years, inclusion of breast cancer might have compromised the parametric form of the incidence and survival models at younger ages (0-19 years). However, the elimination of breast cancer from all female childhood cancer does not affect prevalence estimates because female breast cancer is rarely diagnosed during the childhood or adolescent years. In the SEER database, only 39 breast cancers of 14,593 were diagnosed in females under age 20 years, representing only 0.14% of all cancer sites combined. The same reasons could apply for prostate cancer; however, prostate cancer is diagnosed at older ages than breast cancer and prostate cancer incidence did not seem to affect the incidence of all cancer sites at younger ages. Other sites that presented difficulties in modeling and for which we did not include data separately in this study are as follows: hepatic tumors (VI), retinoblastomas (V) and carcinomas, and other epithelial neoplasms (XI). These tumor sites are reflected in the total prevalence estimates, however.

Data from the CT from 1935 through 1997 was used to validate SEER estimates of long-term survivors and to estimate cancer survival trends before 1975. Population estimates from the U.S. Census Bureau, and all-cause mortality from National Center for Health Statistics were obtained from the SEER*Stat software (14).

Analysis. The number of people in the United States alive in 2005 and diagnosed with cancer between ages 0 and 19 years was calculated in 3 steps. We first calculated the proportion of survivors alive in the SEER-9 areas diagnosed with childhood cancer between years 1975 and 2004 and ages 0 and 19 years by cancer site, sex, race (White, Black, other; where unknown race was grouped with White race) and age, using the SEER*Stat software (14) and the counting method (11). To estimate complete U.S. childhood cancer survivor prevalence estimates for the United States, we multiplied the site/sex/race/age-specific SEER cancer prevalence proportions by the respective U.S. sex/race/age-specific populations. To obtain childhood cancer prevalence for all races combined, we summed over all races. The next step consisted of estimating the number of childhood cancer survivors diagnosed before 1975 and is described below.

Complete prevalence of childhood cancer, which includes adults diagnosed with childhood cancer before 1975, is calculated using the CHILDPREV method (12) and implemented in the publicly available COMPREV software (15). Briefly, the method uses age and period parametric cancer site/sex-specific incidence and survival models fitted to SEER data, to estimate the proportion of prevalent childhood cancer survivors diagnosed before 1975. Because survival before 1975 is an important input into the estimation of long-term survivors, a trend before 1975 has been estimated from the CT data and has been incorporated into the survival models. The survival model with the pre-1975 Connecticut trend is described in detail in Simonetti and colleagues (12).

We present childhood cancer survival and incidence trends, for some of the most common childhood cancer sites, to aid in interpretation of the prevalence estimates. Joinpoint models are fitted to age-adjusted incidence rates, using the Joinpoint software (16), as a way to describe significant changes in the observed trends. The estimated annual percent change was calculated by fitting a regression line to the natural logarithm of the rates r using calendar year x as a regressor variable, i.e., $ln(r) = a + b\,x$. The annual percent change is calculated as $100\ (e^{-b}\text{-}1)$ and displayed in the figures.

Validation of Prevalence Estimates using the Historical Connecticut Data. The CT contains incident cases from 1935 to 1997 and allows estimation of 62-year limited duration prevalence at January 1, 1997, which is a good approximation of complete prevalence. The validation consisted of comparing CT 62-year prevalence proportions with SEER complete prevalence proportions. SEER complete prevalence was estimated by calculating 22-year limited duration prevalence using cases diagnosed between 1975 to 1996 at January 1, 1997, and applying the CHILDPREV method as described above. Prevalence statistics were compared as prevalent percents and calculated at January 1, 1997. Comparing prevalence at January 1, 1997, and not January 1, 2005, does not impair the value of the validation. In fact, the validation is strengthened because we are estimating the prevalence of long-term survivors using a shorter series of data.

Results

Using the methodology described above, we estimated that there are a total of 328,652 survivors of childhood cancer in the United States as of January 1, 2005 (Table 2). Of this number, 24% had survived >30 years since their original diagnosis, and would not have been included without the CHILDPREV method. The cancer sites with the largest number of survivors are brain (51,650), ALL (49,271), germ cell tumors (34,169), and Hodgkin lymphoma (31,598). The proportion of log term (30 or more years) survivors varied by cancer site. Germ cell, soft tissue, renal, and bone are the sites with the largest proportions of these long-term survivors, 43%, 38%, 34%, and 26%, respectively. Leukemia is the site with the smallest proportion of long-term survivors, with only 7% surviving >30 years. Childhood cancer survivors age 60 years and older represent 3% of all childhood cancer survivors. The cancer sites with the largest proportion of survivors 60 years and older are germ cell (15%) and soft tissue (12%).

Validation of Prevalence Estimates. Figure 1 compares estimated complete (*light gray area*) and 22-year (diagnosis years, 1975-1996) SEER prevalence percent (*dark gray area*) with observed 62-year (diagnosis years, 1935-1996) CT prevalence percents (*black line*), respectively, for all cancers diagnosed at ages 0 to 19 years for males (*A*) and females (*B*). The prevalence for those age 20 to 42 years on January 1, 1997, is underreported just using SEER data because some portion of them were diagnosed before 1975. Thus, the difference between the dark and light

Table 2. U.S. Childhood Cancer Survivors at January 1, 2005. Number of people previously diagnosed with cancer as children (ages 0-19 y) in the United States alive January 1, 2005, by age group, sex, and site

Site	Sex/age	Complete prevalence counts							Diag. between 1975-2004	Diag. before 1975 (all ages)	
		00-19	20-29	30-39	40-49	50-59	60+	All ages	No.	No.	%
All sites	Both	103,319	81,193	56,588	49,426	25,672	12,454	**328,652**	248,811	79,841	24%
	Males	55,964	41,416	27,417	21,183	10,782	5,854	**162,616**	127,908	34,708	21%
	Females*	47,355	39,777	29,171	28,243	14,890	6,600	**166,036**	120,903	45,133	27%
Leukemia (I)	Both	31,721	16,165	7,790	2,831	566	32	**59,105**	54,826	4,279	7%
	Males	17,289	8,563	3,997	1,420	260	15	**31,544**	29,553	1,991	6%
	Females	14,432	7,602	3,793	1,411	306	17	**27,561**	25,273	2,288	8%
ALL	Both	27,037	13,484	6,980	1,715	55	0	**49,271**	45,975	3,296	7%
	Males	14,831	7,244	3,788	893	33	0	**26,789**	25,051	1,738	6%
	Females	12,206	6,240	3,192	822	22	0	**22,482**	20,924	1,558	7%
Acute myeloid leukemia (Ib)	Both	3,388	1,619	913	394	41	0	**6,355**	5,893	462	7%
	Males	1,772	740	401	219	23	0	**3,155**	2,921	234	7%
	Females	1,616	879	512	175	18	0	**3,200**	2,972	228	7%
Hodgkin lymphomas (IIa)	Both	3,822	9,360	7,967	7,215	2,868	366	**31,598**	25,625	5,973	19%
	Males	2,205	4,498	4,024	3,414	1,465	196	**15,802**	12,608	3,194	20%
	Females	1,617	4,862	3,943	3,801	1,403	170	**15,796**	13,017	2,779	18%
Non–Hodgkin lymphomas (IIb)	Both	5,716	5,522	3,502	2,066	1,214	648	**18,668**	15,133	3,535	19%
	Males	3,890	3,783	2,367	1,146	635	408	**12,229**	10,292	1,937	16%
	Females	1,826	1,739	1,135	920	579	240	**6,439**	4,841	1,598	25%
Brain/central nervous system (III)	Both	19,212	12,401	9,000	7,619	2,837	581	**51,650**	39,673	11,977	23%
	Males	10,837	6,941	4,592	3,537	1,275	267	**27,449**	21,977	5,472	20%
	Females	8,375	5,460	4,408	4,082	1,562	314	**24,201**	17,696	6,505	27%
Neuroblastoma (IV)	Both	8,560	3,098	1,667	1,323	1,128	365	**16,141**	12,316	3,825	24%
	Males	4,479	1,411	596	429	299	92	**7,306**	6,213	1,093	15%
	Females	4,081	1,687	1,071	894	829	273	**8,835**	6,103	2,732	31%
Renal tumors (VI)	Both	7,959	4,310	3,298	3,316	1,259	269	**20,411**	13,465	6,946	34%
	Males	3,899	1,939	1,625	1,757	740	164	**10,124**	6,309	3,815	38%
	Females	4,060	2,371	1,673	1,559	519	105	**10,287**	7,156	3,131	30%
Bone tumors (VIII)	Both	3,399	3,807	2,561	2,636	1,560	309	**14,272**	10,619	3,653	26%
	Males	1,882	2,094	1,346	1,194	756	195	**7,467**	5,768	1,699	23%
	Females	1,517	1,713	1,215	1,442	804	114	**6,805**	4,851	1,954	29%
Osteosarcomas (VIIIa)	Both	1,895	1,953	1,460	1,283	1,016	538	**8,145**	5,767	2,378	29%
	Males	966	1,110	762	553	457	274	**4,122**	3,063	1,059	26%
	Females	929	843	698	730	559	264	**4,023**	2,704	1,319	33%
Ewing (VIIIc)	Both	1,142	1,268	717	523	259	38	**3,947**	3,309	638	16%
	Males	680	656	325	257	102	11	**2,031**	1,777	254	13%
	Females	462	612	392	266	157	27	**1,916**	1,532	384	20%
Soft tissue (IX)	Both	6,624	5,585	4,188	4,618	3,280	3,249	**27,544**	17,036	10,508	38%
	Males	3,725	2,993	2,101	2,123	1,445	1,900	**14,287**	9,188	5,099	36%
	Females	2,899	2,592	2,087	2,495	1,835	1,349	**13,257**	7,848	5,409	41%
Germ cell tumors (X)	Both	4,666	6,708	5,794	6,796	5,182	5,023	**34,169**	19,313	14,856	43%
	Males	2,482	4,261	3,257	3,420	2,573	2,163	**18,156**	11,226	6,930	38%
	Females	2,184	2,447	2,537	3,376	2,609	2,860	**16,013**	8,087	7,926	49%

NOTE: Percent diagnosed before 1975 of all ages complete prevalence counts. Sites are ordered by decreasing prevalence.
Abbreviation: Diag, diagnosis.
*All sites females exclude breast cancer.

gray areas represents the prevalence of children age 0 to 19 years diagnosed before 1975 in SEER, estimated using the CHILDPREV method. Furthermore, the 22-year prevalence is 0 for ages 42 years and older because this group of childhood cancer survivors would have been diagnosed with cancer at age 19 years or younger before 1975. There is good agreement between the SEER estimated complete and the 62-year CT prevalence proportions (*solid line*) for both males and females, indicating that the method estimates the number of long-term survivors very well. Prevalent percents from CT show greater variability than the SEER prevalence percents because of smaller numbers. There were some differences between CT and SEER prevalence percent estimates at ages 20 to 35 years for males and 15 to 30 years and 45 to 55 years for females. Apart from the 45 to 55 years age group, most of the differences between CT and SEER estimated complete prevalence occur at younger age groups when the estimates are based entirely or partially on observed data, rather than modeling assumptions. For the younger age groups, these differences likely represent actual differences in prevalence between CT and SEER or variability of the estimates, rather than differences due to the statistical method used.

Because prevalence is a function of both incidence and survival, we also compared 5-year relative survival in SEER and CT. Figure 2A and B display 5-year relative survival trends from the CT (1940-1997) and SEER (1975-2004) data for selected cancer sites with both sexes combined. Historical trends of 5-year childhood cancer survival varied by cancer site, and this explained most of the variability in the proportion of long-term survivors. For ALL 5-year relative, survival was close to 0 before

1960, which explains the absence of survivors of this disease at age 60 years and over. As improvements in treatment occurred in the 1970s, ALL 5-year relative survival improved such that today, over 80% of children diagnosed can expect to be alive in 5 years. On the other hand, almost 40% of children diagnosed with brain cancer in the 1960s survived 5 years. These differences in historical trends explain why brain survivors are more prevalent than ALL survivors, although ALL is more commonly diagnosed than brain cancer. There was an improvement in 5-year relative survival for all cancer sites, especially for ALL, non-Hodgkin, Hodgkin, and renal and germ cell tumors. For cancers of the brain and soft tissue, and osteosarcoma, the improvement was smaller because these sites had a better prognosis in the 1940s compared with the other sites. Some of the CT survival curves show large variability due to the small numbers in the CT data, especially in the earlier years.

Figure 3A and B show annual percent change and joinpoint models (*lines*) fitted to the SEER age-adjusted incidence rates (*dots*). All cancer sites, ALL, acute myeloid leukemia, non-Hodgkin, neuroblastoma, soft tissue, and germ cell tumors had significant increasing trends in age-adjusted rates, whereas brain/central nervous system and Hodgkin showed a decreasing trend, although not significant. The increasing incidence for childhood cancers overall seems to reflect the increase in ALL incidence, and the reduced pace of this increase after 1985 seems to reflect the stable brain/central nervous system tumor incidence since the mid-1980s.

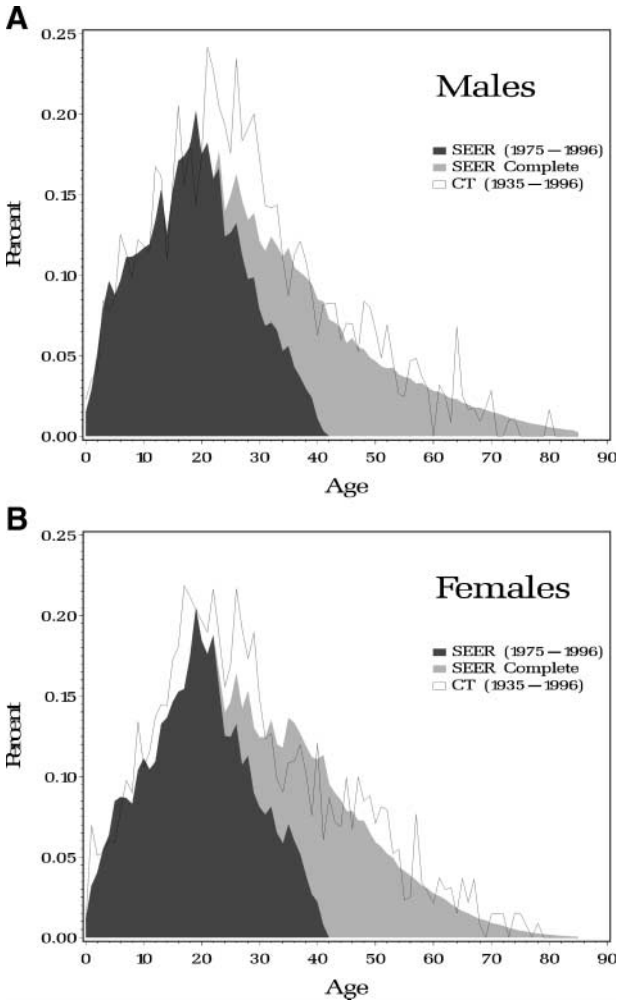

Figure 1. Comparison of estimated childhood cancer prevalence percent for males (**A**) and females (**B**) by age on January 1, 1997. Complete prevalence (estimated from the CHILDPREV method) represents the percent of people alive and ever diagnosed with cancer between ages 0 and 19 y. SEER (1975-1996) and CT (1935-1996) represent prevalence of people alive diagnosed with cancer between ages 0 and 19 in the y indicated inside parenthesis. The difference between the light and dark gray areas represents estimated childhood cancer prevalence diagnosed before 1975.

Discussion

Cancer among children is an important public concern. Each year in the United States, ~12,400 children and adolescents younger than age 20 years are diagnosed with cancer (9). Although childhood cancer is rare, it is the most common cause of disease related mortality for children age 1 to 19 years, with ~2,300 children and adolescents dying of cancer every year in the United States (17). Because both incidence as well as survival rates for childhood cancers have been steadily increasing, the number of childhood cancer survivors is expected to increase in the future.

We estimated that there are 328,652 survivors of childhood cancers in the United States as of January 1, 2005, and of this number, ~27% are age 40 years and older. To our knowledge, this is the only study to estimate complete prevalence for survivors of childhood cancers in the United States. Our application of the CHILDPREV method allowed inclusion of this group of long-term survivors who were diagnosed before routine registration of cancer patients in the SEER areas. The sites with the largest number of long-term adult survivors of childhood cancers are germ cell, soft tissue, renal, and bone. Leukemia is the site with the smallest proportion of long-term survivors. We estimated that ALL survivors are less prevalent than brain cancer survivors, although ALL is more common than brain cancer and for the past 30 years has a better prognosis. This seemingly counterintuitive finding is due to differences in survival before 1970. Before 1970, 5-year relative survival for ALL was practically 0, compared with a 20% to 40% 5-year relative survival for brain cancer, as illustrated in Fig. 2A. Among ALL survivors, 18% are 30 years and older, whereas for brain cancer survivors, 39% are 30 years and older.

Others have reported that adult survivors of childhood cancers have poorer quality of life and more health limitations than similar adults without a cancer history (3). Compared with their siblings without cancer, cancer survivors are also more likely to have lower levels of educational attainment and have poorer employment outcomes (18). Costs of medical care for this group is largely unknown. Because the number of childhood cancer survivors is expected to continue to increase, further evaluation of the long-term health, employment, and economic consequences for childhood cancer survivors will be an important area for additional research.

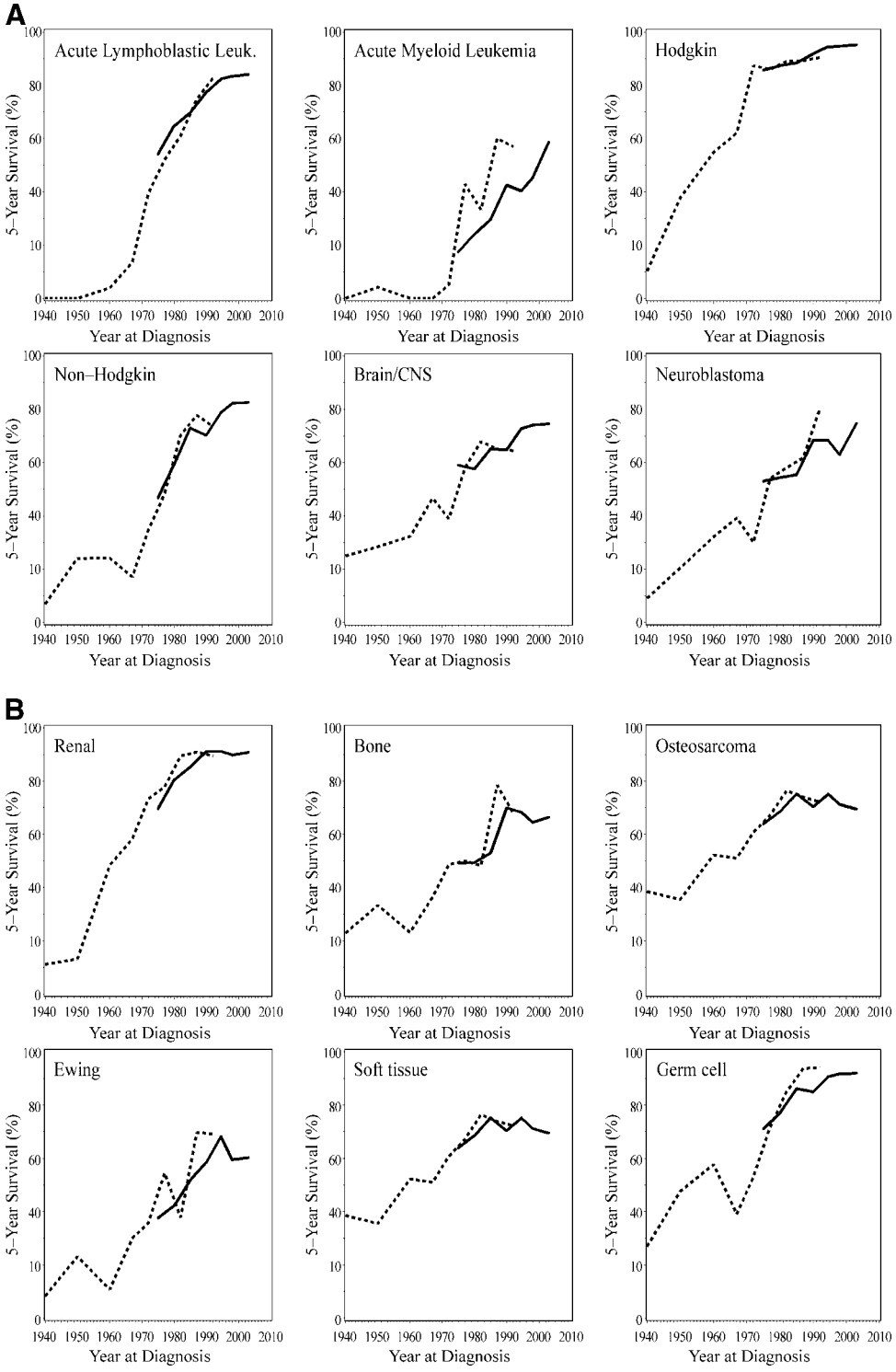

Figure 2. 5-y relative survival trends for children diagnosed with cancer at ages 0 to 19 y in SEER (*solid lines*) and Connecticut (*dashed lines*) areas. Survival trends are shown for both sexes combined and for selected cancer sites: ALL, acute myeloid leukemia, Hodgkin lymphoma, non–Hodgkin lymphoma, brain tumor, neuroblastoma (**A**), renal, bone, osteosarcoma, Ewing, soft tissue, and germ cell tumors (**B**).

Despite the strengths of this study, there are some limitations to the estimates presented here. Estimates of the number of long-term survivors are based on incidence and survival models estimated from SEER data and extrapolated into the past. However, validations for all cancer sites combined for males and females showed that the prevalence proportion of long-term survivors using these models was comparable with observed prevalence proportions from the CT data. There were some differences between the estimated SEER and actual CT prevalence proportions. However, these differences occur at younger age groups and are also evident in the 22-year limited duration prevalence and likely represent actual differences in prevalence between CT and SEER, rather

than differences due to modeling or the estimation method used. Similar validations for some of the major cancer sites have revealed comparable results (data not shown). For the more rare cancer sites, it was not possible to validate findings because of the very small number of cases available from the CT data. Projection of prevalence proportions from SEER to the U.S. population accounts for differences in age, sex, and race distribution in the United States and SEER but not other factors, such as socioeconomic status.

In 2011, the first of the baby boom generation will turn 65 years. Because cancer is principally a disease

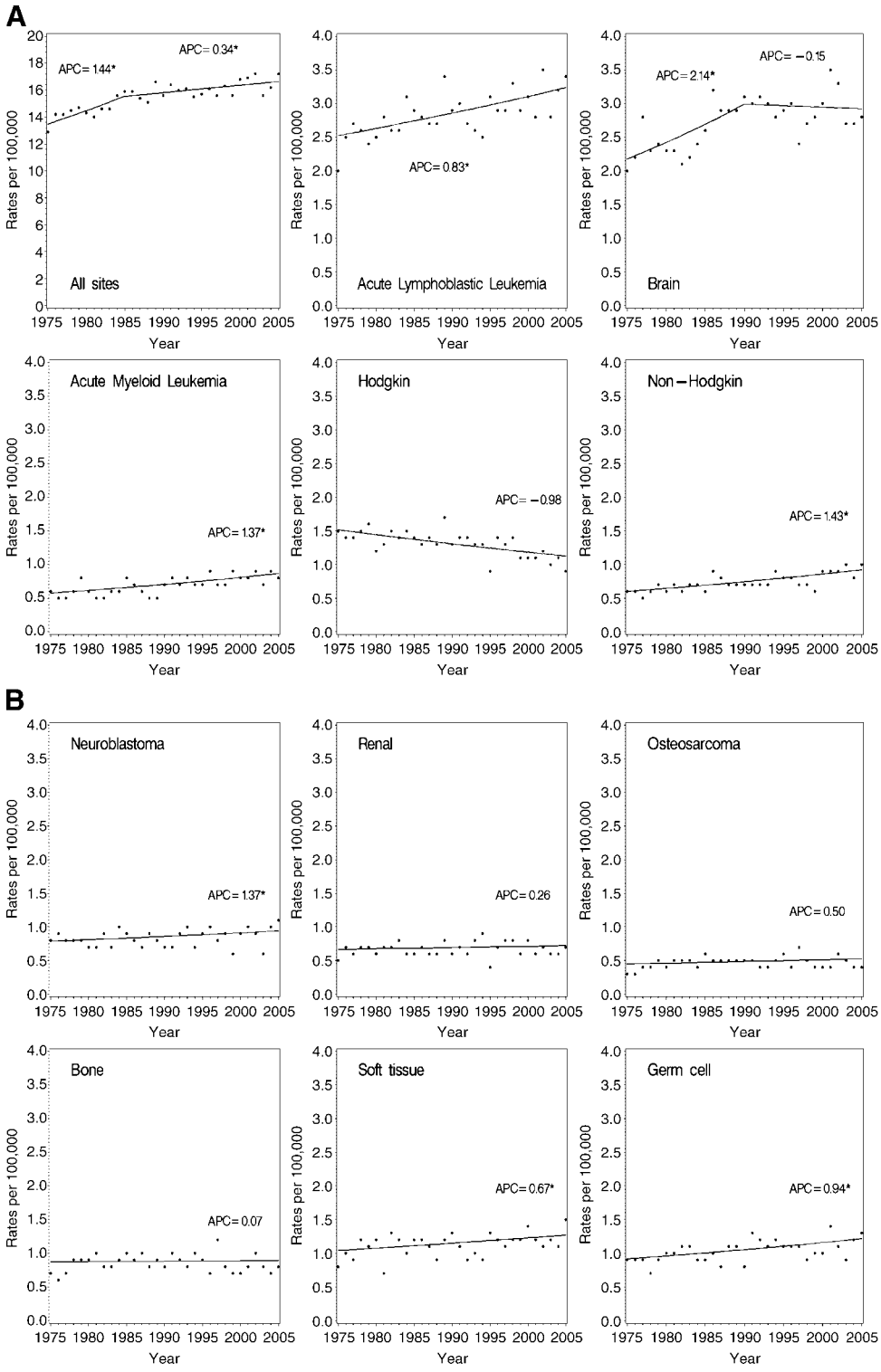

Figure 3. Age-adjusted incidence trends (rates per 100,000) for both sexes combined by selected cancer sites: all sites, ALL, brain tumor, acute myeloid leukemia, Hodgkin lymphoma, and non–Hodgkin lymphoma (**A**), and neuroblastoma, renal, osteosarcoma, bone, soft tissue, and germ cell tumors (**B**). The annual percent change (*APC*) is the annual percent change for the regression line segments. *, annual percent change significantly different from 0 ($P < 0.05$). Rates adjusted to the 2000 U.S. population.

associated with aging, the number of cancer survivors in the United States is expected to increase as a function of the aging of the U.S. population (19, 20). The number of survivors of childhood cancers is also expected to increase, however, for different reasons. This increase will not be due to the growth of the childhood population but rather occur as a function of the dramatic improvements since 1970 in survival for those treated as children or adolescents for most cancer sites but especially for ALL. It will also reflect the slow but continuing increase in incidence of childhood cancers. Thus, the number of older adults who will be survivors of childhood cancer is expected to increase in the future.

To our knowledge, this is the first time that the total number of survivors of childhood cancers in the United States, including long-term survivors, has been presented. Although survivors of pediatric cancers constitute a small percentage of the population (1 of 1,000) and 3% of the total cancer survivor population (17), they represent a special segment of the cancer survivor population. With the expanding prospect of living not just with but through and beyond their cancer treatment, these individuals and their families are living long enough to fully manifest the human costs of cure. This includes increased risk of disease and treatment-related morbidity and mortality, mortality due to other life threatening conditions, and chronic morbidity or functional impairment caused or exacerbated by a cancer treatment history. Attention in particular to the effect of survivors' health behaviors and medical follow-up care on their overall morbidity and mortality is a growing area of clinical and research focus (2, 5). There is a growing need to screen for and, as possible, prevent or mitigate chronic or late occurring problems (e.g., heart disease, thyroid dysfunction, osteoporosis, second malignancy), and to promote health, to maximize the social, psychological, and economic well-being of long-term cancer survivors and their families. It is hoped that by providing estimates of the scale of the problem, researchers and health officials will be galvanized to conduct needed long-term survivorship research among this fast maturing population, and to develop models of follow-up care that will enable us to capitalize on the advances made in treating childhood cancer and eliminate unnecessary suffering and death secondary to this therapy.

Disclosure of Potential Conflicts of Interest

No potential conflicts of interest were disclosed.

Acknowledgments

The costs of publication of this article were defrayed in part by the payment of page charges. This article must therefore be hereby marked *advertisement* in accordance with 18 U.S.C. Section 1734 solely to indicate this fact.

We thank Drs. Malcolm Smith and Nita Seibel from the Cancer Therapy Evaluation Program of the National Cancer Institute for their insightful comments on an earlier version of the article, and the anonymous peer reviewers for their helpful suggestions.

References

1. Henderson TO, Whitton J, Stovall M, et al. Secondary sarcomas in childhood cancer survivors: a report from the Childhood Cancer Survivor Study. J Natl Cancer Inst 2007;99:300–8.
2. Oeffinger KC, Mertens AC, Sklar CA, et al. Chronic health conditions in adult survivors of childhood cancer. N Engl J Med 2006;355:1572–82.
3. Zeltzer LK, Lu Q, Leisenring W, et al. Psychosocial outcomes and health-related quality of life in adult childhood cancer survivors: a report from the Childhood Cancer Survivor Study. Cancer Epidemiol Biomarkers Prev 2008;17:435–46.
4. Hudson MM, Mertens AC, Yasui Y, et al. Health status of adult long-term survivors of childhood cancer: a report from the Childhood Cancer Survivor Study. JAMA 2003;290:1583–92.
5. Oeffinger KC, Robison LL. Childhood cancer survivors, late effects, and a new model for understanding survivorship. JAMA 2007;297:2762–4.
6. Geenen MM, Cardous-Ubbink MC, Kremer LC, et al. Medical assessment of adverse health outcomes in long-term survivors of childhood cancer. JAMA 2007;297:2705–15.
7. Hewitt M, Weiner SL, Simone JV, editors. Childhood Cancer Survivorship: Improving Care and Quality of Life. Washington (DC): The National Academies Press; 2003.
8. Surveillance, Epidemiology, and End Results (SEER) Program - SEER 9 Registries (1975–2005), released April 2008, based on the November 2007 submission. National Cancer Institute. Available from: http://www.seer.cancer.gov/.
9. Ries LAG, Smith MA, Gurney JG, editors. Cancer Incidence and Survival among Children and Adolescents: United States SEER Program 1975–1995, National Cancer Institute, NIH Pub. No. 99–4649; 1999.
10. Bleyer A, O'Leary M, Barr R, Ries LAG, editors. Cancer Epidemiology in Older Adolescents and Young Adults 15 to 29 years of Age, Including SEER Incidence and Survival: 1975–2000. National cancer Institute, NIH Pub. No. 06–5767; 2006.
11. Feldman AR, Kessler L, Myers MH, Naughton MD. The prevalence of cancer: estimates based on the Connecticut Tumor Registry. N Engl J Med 1986;315:1394–7.
12. Simonetti A, Gigli A, Capocaccia R, Mariotto A. Estimating complete prevalence of cancers diagnosed in childhood. Stat Med 2008;27:990–1007.
13. SEER site recode definition. Available from: http://seer.cancer.gov/siterecode/iccc/iccc3.html.
14. Surveillance Research Program, National Cancer Institute SEER*Stat software version 6.3.5 (2007). Available from: http://www.seer.cancer.gov/seerstat.
15. ComPrev: Complete Prevalence Software, Version 1.0 (2005). Statistical Research and Applications Branch, National Cancer Institute. Available from: http://srab.cancer.gov/comprev.
16. Joinpoint: Joinpoint Regression Program Version 3.3 (2008). Statistical Research and Applications Branch, National Cancer Institute. Available from: http://srab.cancer.gov/joinpoint/.
17. Ries LAG, Melbert D, Krapcho M, et al. SEER Cancer Statistics Review, 1975–2005. National Cancer Institute; April 2008. Available from: http://seer.cancer.gov/csr/1975_2005.
18. Pang JWY. Employment status among adult survivors in the Childhood Cancer Survivor Study. Pediat Blood Cancer 2008;50:104–10.
19. Mariotto AB, Yabroff KR, Feuer EJ, De Angelis R, Brown M. Projecting the number of patients with colorectal carcinoma by phases of care in the US: 2000–2020. Cancer Causes Control 2006;17:1215–26.
20. Rowland JH, Bellizzi KM. Cancer survivors and survivorship research: a reflection on today's successes and tomorrow's challenges. Hematol Oncol Clin North Am 2008;22:181–200.