SEER PEDIATRIC MONOGRAPH

Cancer Incidence and Survival among Children and Adolescents: United States SEER Program 1975-1995

This publication was prepared by:

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Suggested citation for the monograph:

Ries LAG, Smith MA, Gurney JG, Linet M, Tamra T, Young JL, Bunin GR (eds). *Cancer Incidence and Survival among Children and Adolescents: United States SEER Program 1975-1995*, National Cancer Institute, SEER Program. NIH Pub. No. 99-4649. Bethesda, MD, 1999.

Citation for a chapter should also include the chapter authors and chapter title.

This publication and additional data available on the SEER web site:
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Cancer Incidence and Survival among Children and Adolescents: United States SEER Program 1975-1995

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FOREWORD

Cancer among children is a substantial public concern. Each year in the United States, approximately 12,400 children and adolescents younger than 20 years of age are diagnosed with cancer. Approximately 2,300 children and adolescents die of cancer each year, which makes cancer the most common cause of disease-related mortality for children 1-19 years of age. This monograph assembles under one cover the most detailed information available on the incidence of childhood cancer in the United States. These population-based data will be extremely important in furthering our understanding of the variations in childhood cancer by histologic type and primary site and the variations in incidence of these cancers over time. The monograph provides information about childhood cancer incidence and mortality rates that can enhance the level of public discourse, and it can be used in planning research that will help us to better understand these cancers and their causes.

Unlike adult cancers that are usually tabulated by primary site, the childhood cancers are more meaningfully grouped by histologic type and primary site based on the recently developed International Classification of Childhood Cancer (ICCC). The monograph details incidence for 1975-1995 and survival by ICCC group and by patient demographic characteristics. For each of the major ICCC groups, information on known risk factors is also presented.

The monograph emphasizes not only ICCC group but also age as important factors in childhood cancer incidence. The cancers discussed include those occurring in children younger than 15 years of age as well as those occurring in adolescents up to age 19 years. Some cancers such as neuroblastoma and hepatoblastoma have highest rates among infants and young children, while others such as Hodgkin's disease, germ cell tumors (e.g., testicular cancer) and bone cancers have higher rates among adolescents. It is important that different distributions of cancer types by age be considered when research programs are developed to improve outcomes for children and adolescents with cancer.

I would like to thank and congratulate the scientists at the National Cancer Institute (NCI) and at the various universities and institutions across the United States who collaborated to make this monograph possible including the Epidemiology and Cancer Control Strategy Group of the NCI-supported Children's Cancer Group, which provided the review of risk factors. I would also like to thank all of the individuals who make the SEER Program a reality: staff members of the SEER population-based registries, Information Management Services, Inc., and NCI. It is through their diligence that these data have been collected, analyzed, and interpreted. The monograph highlights the importance of the SEER Program as a national resource. I believe that this document will prove to be a seminal reference work on childhood cancer for scientists, policy makers and the public. All of us look forward to the extensive use of this information and the stimulation of scientific thought that it will engender and ultimately, the reduction of cancer incidence and mortality in children.

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Acknowledgments: Risk Factor Tables

The individuals listed below from the Epidemiology and Cancer Control Strategy Group, of the NCI-supported Children's Cancer Group, provided the review of risk factors for selected cancers. Dr. Greta R. Bunin provided editorial oversight of this effort.

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Acknowledgments: SEER

The editors wish to thank the Principal Investigators and the staffs of the contract organizations who provided the cancer incidence data for this report. These organizations, funded through National Cancer Institute (NCI) contracts, include:

Contracting Organization	*Principal Investigator*
Northern California Cancer Center	Dr. Dee W. West
Connecticut State Department of Health	Dr. Anthony P. Polednak Mr. Daniel Savino
Emory University	Dr. John L. Young. Jr. Dr. J. William Eley Dr. Jonathan M. Liff
University of Hawaii	Dr. Laurence N. Kolonel Dr. Marc T. Goodman
The Fred Hutchinson Cancer Research Center	Dr. David B. Thomas Dr. Beth Mueller
University of Iowa	Dr. Charles F. Lynch Dr. Charles E. Platz
Wayne State University	Dr. Linda Weiss Dr. G. Marie Swanson
University of New Mexico	Dr. Charles R. Key
University of Southern California	Dr. Ronald K. Ross Dr. Dennis Deapen Dr. Leslie Bernstein
University of Utah	Dr. Joseph Simone

The production of this report would not have been possible without the efforts of the NCI staff who ensure the quality and completeness of the SEER data: Benjamin Hankey, Limin Clegg, April Fritz, Carol Johnson, Carol Kosary, Barry Miller, Constance Percy, Barbara Ravas, Lynn Ries, Gopal Singh, Thea Tamra (visiting scientist) and Elliott Ware of the Cancer Statistics Branch and Brenda Edwards of the Cancer Surveillance Research Program.

Computer support services were provided by Information Management Services (IMS), Inc.

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INTRODUCTION

Nearly 30 percent of the United States (US) population is younger than 20 years of age. Although cancer is rare among those younger than 20 years of age, it is estimated that approximately 12,400 children younger than 20 years of age were diagnosed with cancer in 1998 and 2,500 died of cancer in 1998 [1]. As a cause of death, cancer varies in its relative importance over the age range from newborn to age 19. Based on data for 1995, in infants younger than one year of age, there were fewer than one hundred cancer deaths (representing only 0.2% of infant deaths), making it a minor cause of death in comparison to other events during the perinatal period. For children between one and nineteen, cancer ranked fourth as a cause of death behind unintentional injuries (12,447), homicides (4,306), and suicides (2,227). The probability of developing cancer prior to age 20 varies slightly by sex. A newborn male has 0.32 percent probability of developing cancer by age 20, (i.e., a 1 in 300 chance). Similarly a newborn female has a 0.30 percent probability of developing cancer by age 20, (i.e., a 1 in 333 chance) [2].

Childhood cancer is not one disease entity, but rather is a spectrum of different malignancies. Childhood cancers vary by type of histology, site of disease origin, race, sex, and age. To explain some of these variations, this monograph presents detailed cancer incidence and survival data for 1975-95, based on nearly 30,000 newly diagnosed cancers arising in children during this 21-year interval in the United States (US). Cancer mortality data collected for the entire US are also shown for the same time period.

MATERIALS AND METHODS (for definitions and additional details, see the technical appendix at end of chapter):

Sources of data

The population-based data used in this monograph for incidence and survival are from the Surveillance, Epidemiology and End Results (SEER) Program of the National Cancer Institute (NCI) [2]. Information from five states (Connecticut, Utah, New Mexico, Iowa, and Hawaii) and five metropolitan areas (Detroit, Michigan; Atlanta, Georgia; Seattle-Puget Sound, Washington; San Francisco-Oakland, California; and Los Angeles, California) comprising about 14% of the United States' population are used in this monograph. While Los Angeles did not officially become a SEER area until 1992, the long standing cancer registry in Los Angeles provided a special childhood data file for this study which included population-based cancer incidence data back to 1975. This monograph includes 29,659 cancers diagnosed between 1975 and 1995 in persons younger than 20 years of age who resided in the SEER areas listed above: 19,845 cases for those younger than 15 years of age and 9,814 cases for adolescents aged 15-19 years.

The mortality data are for the same time period but cover all cancer deaths among children in the total United States. Data based on underlying cause of death were provided by the National Center for Health Statistics (NCHS).

Table 1: Percent distribution of childhood cancers by ICCC category and age group, all races, both sexes, SEER, 1975-95

	Age					
	<5	5-9	10-14	15-19	<15	<20
All Sites - Number of cases	9,402	5,024	5,419	9,814	19,845	29,659
	%	%	%	%	%	%
All Sites	100.0	100.0	100.0	100.0	100.0	100.0
I(total) - Leukemia	36.1	33.4	21.8	12.4	31.5	25.2
Ia - Lymphoid Leukemia	29.2	27.2	14.7	6.5	24.7	18.7
Ia - excl. Acute Lymphoid	0.2	0.3	0.2	0.1	0.2	0.2
Acute Lymphoid	29.0	27.0	14.5	6.4	24.5	18.5
Ib - Acute Leukemia	4.6	4.1	5.4	4.1	4.7	4.5
Ib - excl. Acute Myeloid	1.9	0.9	1.6	0.9	1.5	1.3
Acute Myeloid	2.8	3.2	3.8	3.2	3.2	3.2
Ic - Chronic myeloid leukemia	0.6	0.7	0.9	1.2	0.7	0.9
Id - Other specified leukemias	0.2	0.2	0.1	0.1	0.2	0.2
Ie - Unspecified leukemias	1.4	1.2	0.8	0.5	1.2	1.0
II(total) - Lymphomas and reticuloendothelial neoplasms	3.9	12.9	20.6	25.1	10.7	15.5
IIa - Hodgkins' disease	0.4	4.5	11.4	17.7	4.4	8.8
IIb - Non-Hodgkins' Lymphoma	2.0	5.2	6.1	6.0	4.0	4.6
IIc - Burkitt's lymphoma	0.8	2.4	1.9	0.6	1.5	1.2
IId - Miscellaneous lymphoreticular neoplasms	0.4	0.2	0.3	0.2	0.3	0.3
IIe - Unspecified lymphomas	0.3	0.7	0.9	0.7	0.6	0.6
III(total) - CNS and miscellaneous intracranial and intraspinal neoplasms	16.6	27.7	19.6	9.5	20.2	16.7
IIIa - Ependymoma	2.6	1.3	1.1	0.5	1.9	1.4
IIIb - Astrocytoma	6.7	14.2	11.8	6.0	10.0	8.7
IIIc - Primitive neuroectodermal tumors	4.3	6.3	3.1	1.0	4.5	3.3
IIId - Other gliomas	2.2	5.0	2.9	1.5	3.1	2.6
IIIe - Miscellaneous intracranial and intraspinal neoplasms	0.2	0.3	0.3	0.3	0.3	0.3
IIIf - Unspecified intracranial and intraspinal neoplasms	0.5	0.6	0.4	0.2	0.5	0.4
IV(total) - Sympathetic nervous system	14.3	2.7	1.2	0.5	7.8	5.4
IVa - Neuroblastoma and ganglioneuroblastoma	14.0	2.6	0.8	0.3	7.5	5.1
IVb - Other sympathetic nervous system tumors	0.3	0.1	0.3	0.1	0.3	0.2
V(total) - Retinoblastoma	6.3	0.5	0.1	0.0	3.1	2.1
VI(total) - Renal tumours	9.7	5.4	1.1	0.6	6.3	4.4
VIa - Wilms' tumor, rhabdoid and clear cell sarcoma	9.7	5.2	0.7	0.2	6.1	4.2
VIb - Renal carcinoma	0.1	0.1	0.4	0.4	0.2	0.2
VIc - Unspecified malignant renal tumors	0.0	0.0	0.0	0.0	0.0	0.0

Table 1 (cont'd): Percent distribution of childhood cancers by ICCC category and age group, all races, both sexes, SEER, 1975-95

	Age					
	<5	5-9	10-14	15-19	<15	<20
All Sites - Number of cases	9,402	5,024	5,419	9,814	19,845	29,659
	%	%	%	%	%	%
VII(total) - Hepatic tumors	2.2	0.4	0.6	0.6	1.3	1.1
VIIa - Hepatoblastoma	2.1	0.2	0.1	0.0	1.0	0.7
VIIb - Hepatic carcinoma	0.1	0.3	0.5	0.5	0.3	0.3
VIIc - Unspecified malignant hepatic tumors	0.0	0.0	0.0	0.0	0.0	0.0
VIII(total) - Malignant bone tumors	0.6	4.6	11.3	7.7	4.5	5.6
VIIIa - Osteosarcoma	0.2	2.2	6.6	4.4	2.4	3.1
VIIIb - Chondrosarcoma	0.0	0.1	0.6	0.6	0.2	0.3
VIIIc - Ewing's sarcoma	0.3	2.1	3.7	2.3	1.7	1.9
VIIId - Other specified malignant bone tumors	0.1	0.1	0.3	0.3	0.2	0.2
VIIIe - Unspecified malignant bone tumors	0.0	0.1	0.1	0.1	0.1	0.1
IX(total) - Soft-tissue sarcomas	5.6	7.5	9.1	8.0	7.0	7.4
IXa - Rhabdomyosarcoma and embryonal sarcoma	3.4	4.2	2.8	1.9	3.4	2.9
IXb - Fibrosarcoma, neurofibrosarcoma and other fibromatous neoplasms	1.0	1.4	3.1	3.1	1.7	2.1
IXc - Kaposi's sarcoma	0.0	0.1	0.0	0.1	0.0	0.1
IXd - Other specifed soft-tissue sarcomas	0.7	1.2	2.2	2.1	1.3	1.5
IXe - Unspecifed soft-tissue sarcomas	0.4	0.7	1.0	0.9	0.6	0.7
X(total) - Germ-cell, trophoblastic and other gonadal tumors	3.3	2.0	5.3	13.9	3.5	7.0
Xa - Intracranial and intraspinal germ-cell tumors	0.2	0.8	1.3	0.9	0.7	0.7
Xb - Other and unspecified non-gonadal germ-cell tumors	1.7	0.1	0.5	1.4	1.0	1.1
Xc - Gonadal germ-cell tumors	1.4	1.1	3.0	9.4	1.7	4.2
Xd - Gonadal carcinomas	0.0	0.0	0.4	1.9	0.1	0.7
Xe - Other and unspecified malignant gonadal tumors	0.0	0.1	0.1	0.3	0.1	0.1
XI(total) - Carcinomas and other malignant epithelial neoplasms	0.9	2.5	8.9	20.9	3.5	9.2
XIa - Adrenocortical carcinoma	0.2	0.1	0.1	0.1	0.1	0.1
XIb - Thyroid carcinoma	0.1	1.0	3.5	7.4	1.2	3.3
XIc - Nasopharyngeal carcinoma	0.0	0.1	0.7	0.8	0.2	0.4
XId - Malignant melanoma	0.4	0.7	2.0	6.8	0.9	2.9
XIe - Skin carcinoma	0.0	0.0	0.1	0.1	0.0	0.0
XIf - Other and unspecified carcinomas	0.2	0.7	2.5	5.7	1.0	2.5
XII(total) - Other and unspecified malignant neoplasms	0.5	0.3	0.6	0.8	0.5	0.6
XIIa - Other specified malignant tumors	0.1	0.1	0.1	0.3	0.1	0.1
XIIb - Other unspecified malignant tumors	0.4	0.3	0.5	0.5	0.4	0.4

In order to calculate rates, population estimates were obtained from the Bureau of the Census. In 1990 there were 7,179,865 children residing in the SEER areas younger than 15 years of age and 9,436,324 younger than 20 years of age. In the 1990 census, there were about 72 million children younger than 20 years of age in the whole United States. Twenty-two percent of the US population is younger than 15 years of age and an additional 7% are 15-19 years of age. Annual population estimates include estimates by 5-year age groups (<5,5-9,10-14,15-19). Enumeration of the population at risk by single years of age was available only for the census years 1980 and 1990. The US Bureau of the Census provides intercensal population estimates by 5-year age groups, but not by single years of age. Therefore, the population estimates for 1980 were used in rate calculations for cases diagnosed from 1976-84 and the 1990 estimates were used for cases diagnosed from 1986-94. Whenever rates by single year of age are shown, the rates are centered around a decennial census year, namely, 1976-84 and 1986-94 or the two sets of years combined.

Calculation of rates (see technical appendix)

The incidence and mortality rates are the annual rates per million person years. For simplicity, these are labeled as rates per million. Rates representing more than 5-years of age are age-adjusted to the 1970 US standard million population. Survival rates are expressed as percents.

Classification of site and histologic type

The SEER program classifies all cases by cancer site and histologic type using the *International Classification of Diseases for Oncology, Second Edition* (ICD-O-2) [3]. In contrast to most cancer groupings, which are usually categorized by the site of the cancer, the pediatric classification is determined mostly by histologic type. The SEER data have been grouped according to the International Classification of Childhood Cancers (ICCC) specifications [4] with a couple of exceptions for brain cancer. Please refer to Table 1 for the distribution by ICCC groupings and age group.

Histologic confirmation

In the SEER program most of the pediatric cancers (95%) are histologically confirmed. This is important because most childhood cancer classifications are based on histologic types: leukemia, lymphoma, retinoblastoma, neuroblastoma, etc. The percentage of histologically confirmed cases, however, does vary by ICCC category ranging from a low of 90 percent for the central nervous system (CNS) (ICCC group III) to a high of 99 percent for leukemia (ICCC group I).

OVERVIEW OF CHILDHOOD CANCER PATTERNS

All sites combined

While grouping all cancer sites together may be helpful to understanding the overall cancer burden in young Americans, it masks the contributions of each primary site/histology. Therefore, most of the emphasis of this monograph is on individual primary site or histologic groupings; a separate chapter is shown for each of the ICCC groupings except group XII which has few cases.

Overall trends

While the incidence rates for some forms of childhood cancer have increased since the mid-1970s, death rates have declined dramatically for most childhood cancers and survival rates have improved markedly since the 1970's. Each year approximately 150 children out of every million children younger than 20 years of age will be diagnosed with cancer. The

overall cancer incidence rate increased from the mid-1970's, but rates in the past decade have been fairly stable (Figure 1). During the last time period, 1990-95, there is an indication of a leveling off or slight decline in the overall incidence rates for each of the 5-year age groups (data not shown). The overall childhood cancer mortality rates have consistently declined throughout the 1975-95 time period (Figure 1). Note that the data are plotted at the mid-year point throughout this monograph.

Sex

For all sites combined, cancer incidence was generally higher for males than females during the 21-year period (Figure 2). Yet again, an all-sites-combined-rate masks the sites/histologies for which there is a female predominance. For some sites/histologies, there are other factors such as age where there are differences by sex. For example, males have somewhat higher rates of Hodgkin's disease for children younger than 15 years of age, but females have higher rates for adolescents, 15-19 years of age.

Figure 1: Trends in age-adjusted* SEER incidence & U.S. mortality rates for all childhood cancers age<20, all races, both sexes, 1975-95

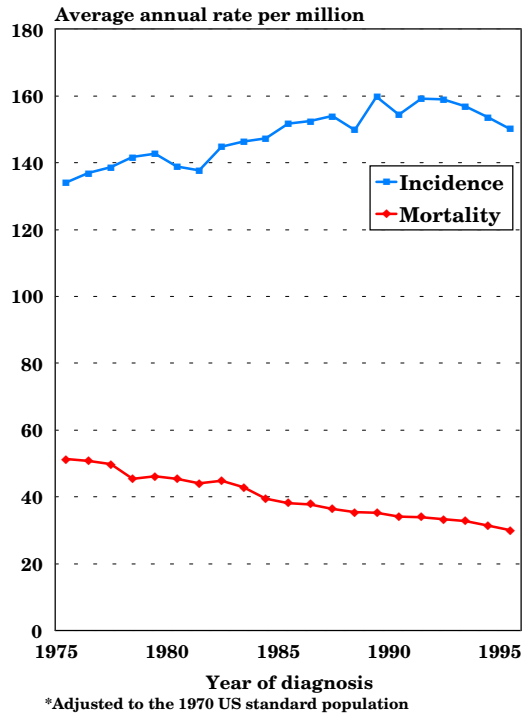
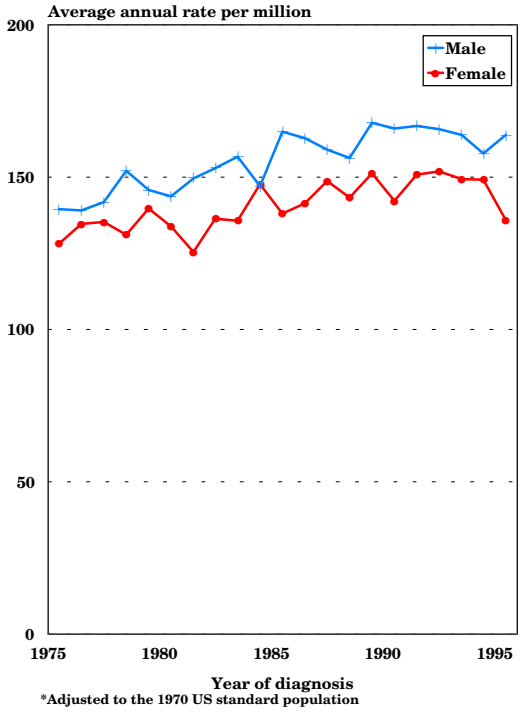


Figure 2: Trends in age-adjusted* incidence rates for all childhood cancers by sex, age <20 all races combined, SEER, 1975-95



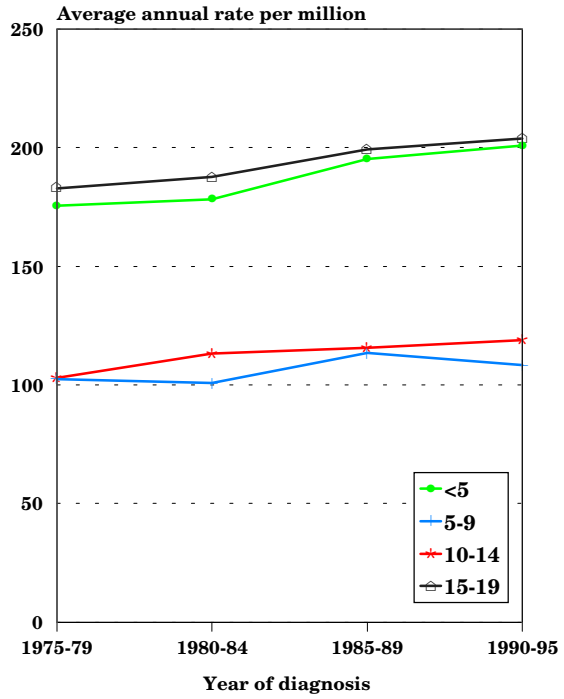
Age (5-year age groups)

The average age-specific incidence rates for each of the four calendar periods of observation show similar and much higher cancer rates for the youngest (younger than 5 years of age) and oldest (15-19 years of age) age groups than the two intermediary age groups (Figure 3). Even though those aged 15-19 years and those younger than 5 years of age have similar incidence rates, they have different mixtures of sites and histologies. The cancer incidence rates for 5 to 9 year olds are similar to those seen among 10-14 year olds.

Age and ICCC group

Fifty-seven percent of the cancers found among children younger than 20

Figure 3: Trends in age-specific incidence rates for all childhood cancers by age, all races both sexes, SEER, 1975-95



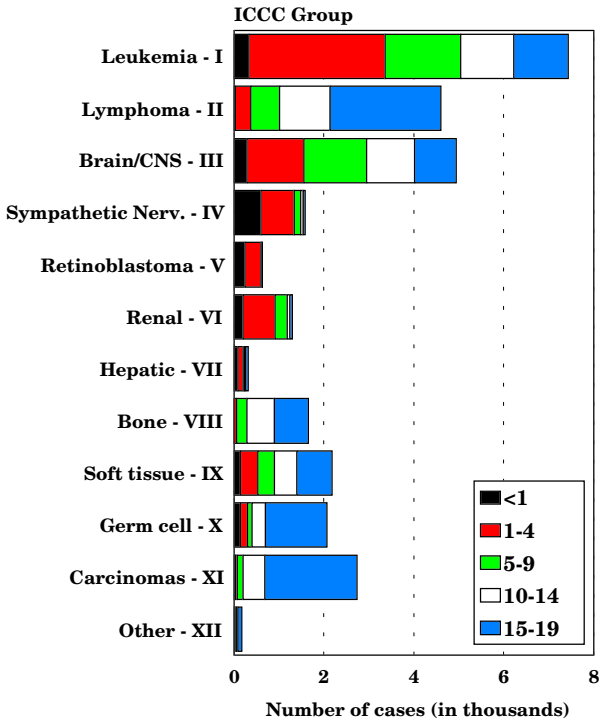
years of age were leukemia, malignant tumors of the central nervous system (CNS) or lymphoma. The relative percentage, however, varied by age group (Table 1). Leukemia was the most common diagnosis for those younger than 5, 5-9, and 10-14 years of age but the relative proportion of it decreased as age increased, from 36 percent for those younger than 5 years of age to only 12 percent for adolescents 15-19 years of age. For 15-19 year olds, lymphomas were the most common diagnosis, comprising one-fourth of the cases. The second most common type of cancer was malignant tumors of the central nervous system for younger than 5 and 5-9 years of age, and lymphoma for 10-14 and leukemia for 15-19 year olds (Table 1).

Figure 4 shows the numbers of cases used in this study by ICCC group and age. Leukemia (group I) had the largest number of cases. Note that these numbers are over the period 1975 to 1995 for the SEER areas and do not represent the total number of childhood cancers in the US in one year. These numbers indicate the reliability in the incidence and survival rates, i.e. large numbers imply stable rates and small numbers imply unstable rates. Even though ICCC groups I-III have most of the cases, there are differences by age group: group I has more 1-4 year olds, group II has more 15-19 year olds and group III has nearly equal numbers for each age group. There are less than 1,000 cases each in groups V, VII and XII. Groups VIII-XI tend to have fewer children younger than 10 years of age compared to 10-19 years of age.

Incidence by ICCC group

Figure 5 shows the incidence rates per million children for each of the ICCC groups. The highest rates are for groups I (leukemia), II (lymphoma), and III (CNS).

Figure 4: Number of cases of all childhood cancers by ICCC and age group, all races both sexes, SEER, 1975-95

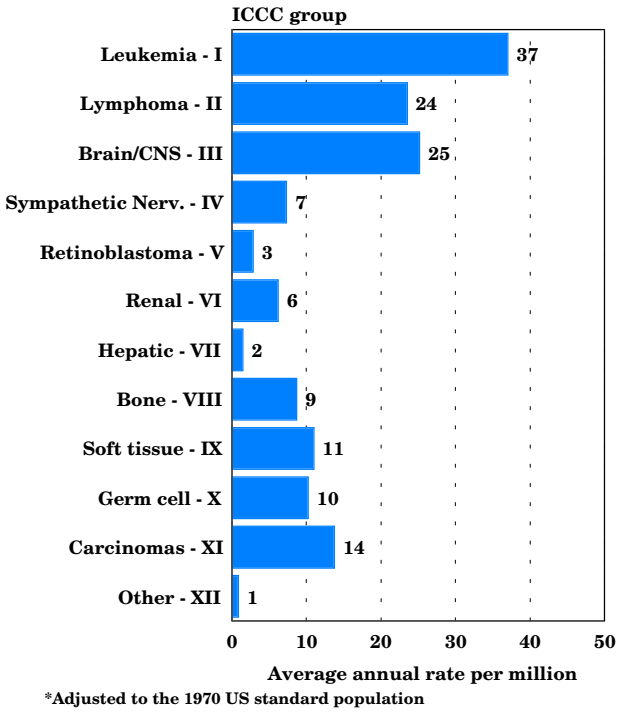


While the ICCC major groupings indicate which broad groups of sites/histologies are important, the sub-groups under each are necessary to really delineate which histologies are driving these rates. More detailed information on the ICCC groups and subgroups are contained in other chapters.

Race / ethnicity

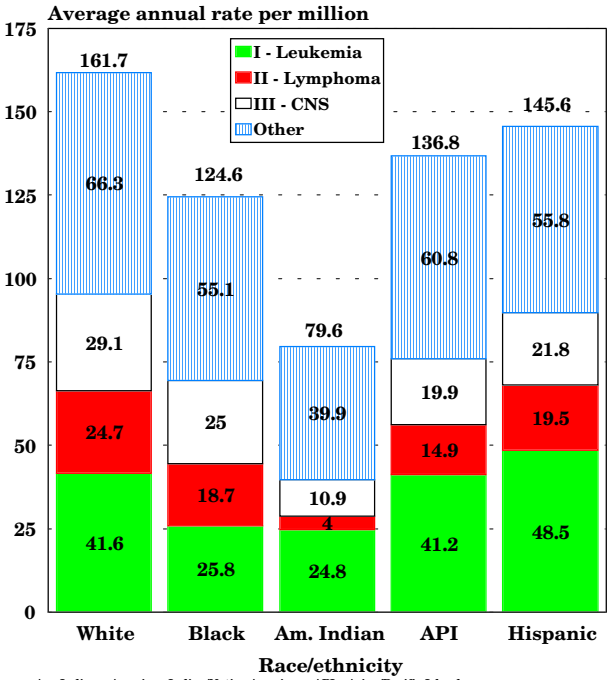
For many adult cancers, blacks have higher incidence rates than whites. For children, however, black children had lower incidence rates in 1990-95 than white children overall and for many of the specific sites (Figure 6). The time period, 1990-95, was used for racial/ethnic comparisons because it was the only time period except for the decennial census years (1980 and 1990) for which the Census Bureau provided population estimates for racial groups other than white and black. The largest racial difference was for leukemia (ICCC I) where the rate for whites (41.6 per million)

Figure 5: Age-adjusted* incidence rates for childhood cancer by ICCC group, age <20, all races both sexes, SEER, 1975-95



*Adjusted to the 1970 US standard population

Figure 6: Age-adjusted* incidence rates for childhood cancer by ICCC group and race/ethnicity age <20, both sexes, SEER, 1990-95



Am. Indian = American Indian/Native American; API = Asian/Pacific Islander
Hispanic = Hispanic of any race and overlaps other categories

*Adjusted to the 1970 US standard population

was much higher than that for blacks (25.8 per million). Cancer incidence rates for Hispanic children and Asian/Pacific Islander children were intermediate to those for whites and blacks. The rates for Asian/Pacific Islanders were similar to whites for leukemia but lower than whites for CNS and lymphomas. The incidence rates for American Indians were much lower than any other group.

Single year of age

For all sites combined, incidence varied by age with the highest rates in infants. The incidence rates declined as age increased until age 9 and then the incidence rates increased as age increased after age 9. The pattern, however, varied widely by ICCC group and single year of age. For example, high rates were seen among the very young for retinoblastoma (ICCC group V) and among adolescents for lymphoma