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ARTICLE

Cancer Incidence Among Children and Adolescents in the United States, 2001–2003

Jun Li, MD, PhD, MPH[a,b], Trevor D. Thompson, BS[a], Jacqueline W. Miller, MD[a], Lori A. Pollack, MD, MPH[a], Sherri L. Stewart, PhD[a]

[a]Division of Cancer Prevention and Control, National Center for Chronic Disease Prevention and Health Promotion, Centers for Disease Control and Prevention, Atlanta, Georgia; [b]Epidemic Intelligence Service, Office of Workforce and Career Development, Atlanta, Georgia

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What's Known on This Subject

Cancer is the leading disease-related cause of death among children in the United States. Studies have described incidence in other countries; however, the incidence of childhood cancer in the majority of the United States, especially its geographic variation, has not been well described.

What This Study Adds

Using data from the vast majority of the US population, our study is the first to demonstrate distinct differences in cancer incidence between the 4 US census regions and provide data for myelodysplastic syndromes. We also confirm some historic findings of childhood cancer incidence according to age, gender, race, and ethnicity.

ABSTRACT

OBJECTIVE. Our goal was to describe current childhood cancer incidence in the United States and identify demographic and geographic variation among children and adolescents with cancer.

METHODS. We examined data from 39 National Program of Cancer Registries and 5 Surveillance, Epidemiology, and End Results statewide registries (representing >90% of the US population) to identify cancers diagnosed among persons aged 0 to 19 from 2001–2003. Diagnosed cancers were grouped by the third version of the International Childhood Cancer Classification. Analyses were stratified according to gender, age, race, ethnicity, and US census region. A multivariable negative binomial regression model was used to evaluate demographic and geographic differences in incidence for all cancers combined.

RESULTS. We identified 36 446 cases of childhood cancer with an age-adjusted incidence rate of 165.92 per million. Stratified analyses showed that, for all cancers combined, boys had a significantly higher rate than girls; children (aged 0–14 years) had a significantly lower rate than adolescents (aged 15–19 years); and white children had the highest incidence rate among all races. Young people living in the Northeast had the highest incidence rate among all US census regions, which may be partially attributed to significantly higher incidence rates for central nervous system neoplasms and lymphomas in this region compared with other US census regions. Negative binomial regression analysis demonstrated that the childhood cancer-incidence rate varied significantly according to gender, age, race, ethnicity, and geography.

CONCLUSIONS. This study is the first to demonstrate substantial regional differences in the incidence of childhood cancer. It also shows that incidence varies according to gender, age, race, and ethnicity. Our research findings are useful for prioritizing future childhood cancer research needs. *Pediatrics* 2008;121:e1470–e1477

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The findings and conclusions in this report are those of the authors and do not necessarily represent the views of the Centers for Disease Control and Prevention.

Key Words
neoplasms, child, adolescent, pediatrics, SEER program

Abbreviations
NPCR—National Program of Cancer Registries
CDC—Centers for Disease Control and Prevention
SEER—Surveillance, Epidemiology, and End Results
ICCC—International Classification of Childhood Cancer
ICD-O—*International Classification of Disease for Oncology*
CNS—central nervous system
A/PI—Asian/Pacific Islander
AI/AN—American Indian/Alaska Native
CI—confidence interval
RR—rate ratio

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Address correspondence to Sherri L. Stewart, PhD, Centers for Disease Control and Prevention, Division of Cancer Prevention and Control, 4770 Buford Hwy, K-53, Atlanta, GA 30341. E-mail: sstewart2@cdc.gov

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CANCER IS THE leading disease-related cause of death among children in the United States.[1] With advances in treatment, prognoses have improved dramatically for many childhood cancers[2,3]; thus, death rates do not adequately depict the current picture for this group of diseases. A recent European study characterized childhood cancer incidence using data from 63 population-based registries[4]; however, the incidence of childhood cancer in the United States, especially its geographic variation, has not been well described. The objective of this study was to describe the current incidence of childhood cancer and determine geographic and demographic variation among children and adolescents with cancer in the United States.

Because childhood cancer is rare, it is difficult to describe its incidence accurately without having access to nationwide cancer data.[5–7] The National Program of Cancer Registries (NPCR), administered by the Centers for Disease Control and Prevention (CDC), funds statewide cancer-registry programs in 41 states and the District of Columbia. The Surveillance, Epidemiology, and End Results (SEER) program, administered by the National Cancer

Institute, funds 5 state and 6 metropolitan cancer registries; 4 additional state cancer registries are funded dually by the NPCR and the SEER program. Combined data from these 2 programs provide the best source of information on population-based cancer incidence for the nation.[8] For this study we used a data set that combines information from statewide cancer registries affiliated with these programs; this data set is used to publish the official federal statistics on cancer in the United States.[8]

Unlike adult cancers, which are usually coded according to primary site, childhood cancers are more meaningfully grouped according to histologic type and primary site using the International Classification of Childhood Cancer (ICCC), which was derived from the *International Classification of Disease for Oncology* (ICD-O). To incorporate newly improved diagnostic methods, the third edition of the ICD-O (ICD-O-3) was issued in 2000, and it became effective with 2001 diagnoses.[9] The ICD-O-3 necessitated a revision of the ICCC, ICCC version 3 (ICCC-3), to introduce the major changes in coding and classifying cancers. The ICCC-3 is structured into 3 levels of hierarchical classifications: 12 main diagnostic groups, 47 diagnostic subgroups, and 2 to 11 divisions of selected subgroups.[10] Grouping cancers by using the ICCC-3 allows researchers to characterize homogenous collections of tumors at the cytogenetic or molecular level.[10] To our knowledge, we are the first to characterize the incidence of childhood cancer by using the new ICCC-3 coding scheme in a population representing >90% of the United States.

METHODS

Data Source

New cases of cancer (incident cases) were collected by population-based cancer registries affiliated with the NPCR or SEER programs using medical charts as the source of information for tumor and demographic characteristics.[11,12] Both NPCR and SEER data were collected and reported by using standard data items, uniform codes, and procedures as documented by the North American Association of Central Cancer Registries.[12] Cancer-registry data for cases diagnosed from 2001 to 2003 (the most current data available for analysis from both programs) collected by NPCR registries were reported to the CDC as of January 31, 2006, whereas SEER data were reported to the National Cancer Institute as of November 1, 2005, and made available through the SEER program's public-use data file released in April 2006. Data from 4 states that are supported by both the NPCR and the SEER program are presented as reported to CDC as of January 31, 2006. Incidence data for diagnoses occurring from 2001 to 2003 were evaluated according to high-quality data criteria that measure registry-specific data completeness and accuracy.[8] Data from 39 NPCR and 5 SEER cancer registries that met these criteria for all study years were included in these analyses; the data covered 90.3% of the US population. Data from North Dakota, Maryland, Virginia, Mississippi, Tennessee, Arizona, and Wyoming were excluded.

Case Definition

Cases were restricted to children (aged 0–14 years) and adolescents (aged 15–19 years) who were diagnosed with a primary malignant neoplasm in the United States from 2001 to 2003. Diagnoses were grouped according to the ICCC-3, which applied the rules, nomenclature, and topographic, morphologic, and behavioral codes of the ICD-O-3.[9]

We abbreviated some major diagnostic groups as follows: "leukemias" indicates leukemias, myeloproliferative and myelodysplastic diseases; "lymphomas," lymphomas and reticuloendothelial neoplasms; and "CNS neoplasms," central nervous system (CNS) and miscellaneous intracranial and intraspinal neoplasms. Each heading of a major diagnostic group is preceded by a Roman numeral in all the tables and figures. We also abbreviated "neuroblastoma and ganglioneuroblastoma" as just "neuroblastomas."

Analyses

We stratified the cases in the 12 ICCC-3 groups according to gender and age (0–19, 0–14, and 15–19 years). For some tumors with a relatively large number of cases (lymphoid leukemias, acute myeloid leukemias, Hodgkin's lymphomas, astrocytomas, neuroblastoma, retinoblastoma, nephroblastoma, and rhabdomyosarcomas), we also stratified according to 5 age groups (<1, 1–4, 5–9, 10–14, and 15–19 years). We stratified the 3 cancer groups with the highest rates (leukemias, lymphomas, and CNS neoplasms) according to race (white, black, Asian/Pacific Islander [A/PI], and American Indian/Alaska Native [AI/AN]), ethnicity (Hispanic and non-Hispanic origin), and US census region (Northeast, Midwest, South, and West). US census regions were defined according to US Census Bureau definitions.[8]

We used annual population estimates, obtained from the SEER program, as denominators to calculate age-adjusted incidence rates.[8] We suppressed rates when fewer than 16 cases were reported in a specific category to maintain confidentiality and avoid presenting unstable data.[8] All rates are listed per million persons and were age-adjusted to the 2000 US standard population by the direct method using age groups of <1, 1 to 4, 5 to 9, 10 to 14, and 15 to 19 years.[8] Age-adjusted rates and the corresponding 95% confidence intervals (CIs) were estimated by using SEER*Stat 6.2.4 (www.seer.cancer.gov/seerstat).[13] We estimated incidence rate ratios (RRs), the corresponding 95% CIs defined as F intervals,[14] and their *P* values to assess significant variation according to demographics and regions. *P* values of <.05 were used to determine statistical significance, except for racial and regional analyses. In racial and regional analyses, we set white race and the Northeast region as reference groups, respectively. Because of multiple comparisons, the Bonferroni correction was applied, and significance was determined by *P* values of <.0167.

A multivariable negative binomial regression model was used to examine the adjusted effects of age, gender, race, ethnicity, census region, and year of diagnosis on childhood cancer-incidence rates. Because of overdispersion of nonzero counts relative to the Poisson distribu-

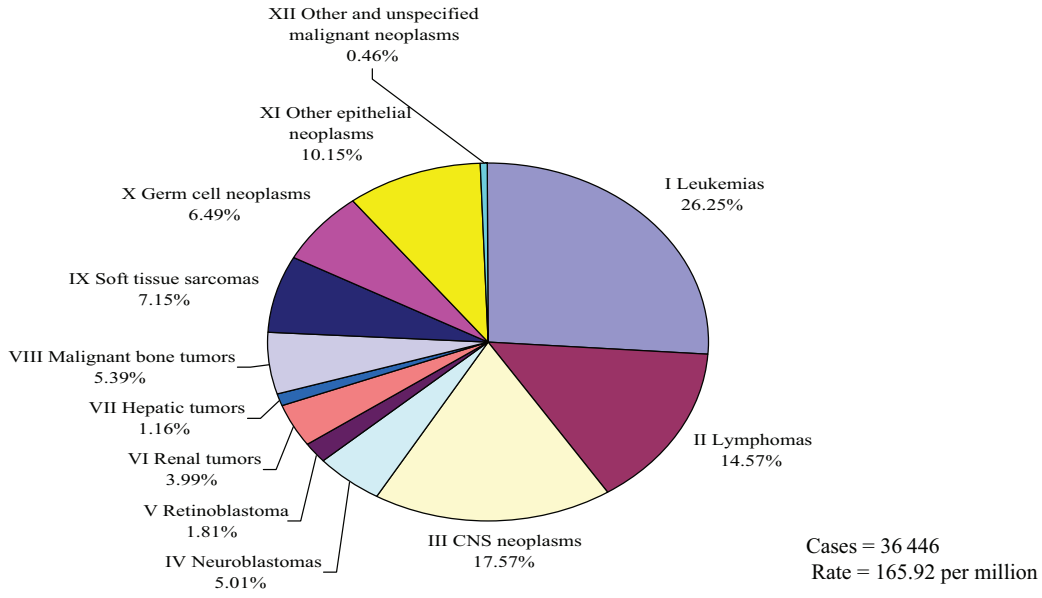

FIGURE 1
Childhood cancer incidence in those aged 0 to 19 years: United States, 2001–2003. Rates are per million and were age adjusted to the 2000 US standard population. Data are from population-based cancer registries that participate in the NPCR or the SEER program. These data include malignant tumors only and cover 90.3% of the US population.

tion, a negative binomial model was used.[15] Statistical testing in the negative binomial model was performed by using the likelihood-ratio test.

RESULTS

A total of 36 446 childhood cancer cases were diagnosed in the United States from 2001 to 2003, for an age-adjusted incidence rate of 165.92 per million (Fig 1). Overall, leukemias were the most common cancer (26.25%), with lymphoid leukemia being the most common type (Table 1); CNS neoplasms were the second most common (17.57%), and lymphomas were the third most common (14.57%). These 3 diseases accounted for almost 60% of childhood cancers.

We compared childhood cancer-incidence rates according to ICCC-3 group and subgroup and gender (Table 1). For all childhood cancers combined, age-adjusted incidence rates were 174.28 per million for boys and 157.14 for girls; overall, boys were more likely to be diagnosed with cancer than girls (RR: 1.11 [95% CI: 1.09–1.13]). Cancers occurring more often in boys included lymphoid leukemia, non-Hodgkin's lymphoma, Burkitt lymphoma, hepatoblastoma, osteosarcomas, Ewing tumor, rhabdomyosarcomas, intracranial and intraspinal germ-cell tumors, and malignant gonadal germ-cell tumors ($P < .05$). Cancers occurring more frequently in girls were nephroblastoma and other nonepithelial renal tumors, extracranial and extragonadal germ-cell tumors, thyroid carcinomas, and malignant melanomas ($P < .05$).

We also compared incidence rates according to ICCC-3 group and age (Fig 2). For all cancers combined, age-adjusted incidence rates were 150.97 per million for children aged 0 to 14 years and 210.42 for adolescents aged 15 to 19 years; the incidence rate was significantly lower for children than adolescents (RR: 0.72 [95% CI: 0.70–0.73]). Adolescents had a significantly higher incidence rate of lymphomas, malignant bone tumors, soft tissue sarcomas, germ-cell neoplasms, other epithelial neoplasms, and other unspecified malignant neoplasms ($P < .05$), whereas children had significantly higher rates of leukemias, CNS neoplasms, neuroblastomas, retinoblastoma, renal tumors, and hepatic tumors ($P < .05$). Age patterns of certain cancers are further depicted in Fig 3. The highest incidence rates for acute myeloid leukemias (16.39 per million), neuroblastomas (57.83 per million), and retinoblastomas (25.05 per million) were observed during infancy. The peak incidence rates for lymphoid leukemias (71.52 per million), astrocytomas (18.10 per million), nephroblastomas (18.32 per million), and rhabdomyosarcomas (8.60 per million) occurred among children aged 1 to 4 years. The highest incidence rate of Hodgkin's lymphoma (32.14 per million) occurred among young people aged 15 to 19 years.

Comparisons of incidence rates of all cancers combined and the top 3 cancers (leukemias, CNS neoplasms, and lymphomas) according to race, ethnicity, and US census region are shown in Table 2. For all cancers combined, the age-adjusted incidence rate for white children (173.21 per million) was significantly higher than the rate for black (117.87 per million), A/PI (131.43 per million), and AI/AN (97.32 per million) children ($P < .0167$). White children also had the highest incidence rates for lymphomas (25.08 per million) and CNS neoplasms (30.78 per million) compared with those of other races ($P < .0167$). For all cancers combined, the incidence rate in the Northeast (179.12 per million) was significantly higher than the rates in the Midwest (165.50 per million), the South (158.65 per million), and the West (165.26 per million) ($P < .0167$). In addi-

TABLE 1 **Gender-Specific Childhood Cancer-Incidence Rates for Those Aged 0 to 19 Years According to ICCC-3 Group and Subgroup: United States, 2001–2003**

ICCC Group	Male		Female		Male/Female RR (95% CI)	*P*
	Cases, *n*	Rate	Cases, *n*	Rate		
All ICCC groups combined	19 617	174.28	16 829	157.14	1.11 (1.09–1.13)	.00
I Leukemias	5297	47.22	4269	39.96	1.18 (1.13–1.23)	.00
I(a) Lymphoid leukemias	3842	34.33	2977	27.92	1.23 (1.17–1.29)	.00
I(b) Acute myeloid leukemias	930	8.24	805	7.50	1.10 (1.00–1.21)	.05
I(c) Chronic myeloproliferative diseases	209	1.85	222	2.07	0.89 (0.74–1.08)	.26
I(d) Myelodysplastic syndrome and other myeloproliferative	175	1.55	147	1.37	1.13 (0.90–1.42)	.30
I(e) Unspecified and other specified leukemias	141	1.25	118	1.10	1.14 (0.89–1.47)	.33
II Lymphomas	3139	27.84	2170	20.25	1.37 (1.30–1.45)	.00
II(a) Hodgkin's lymphomas	1432	12.67	1274	11.89	1.07 (0.99–1.15)	.10
II(b) Non-Hodgkin's lymphomas (except Burkitt lymphoma)	1151	10.22	687	6.41	1.59 (1.45–1.75)	.00
II(c) Burkitt lymphoma	436	3.89	108	1.01	3.84 (3.10–4.79)	.00
II(d) Miscellaneous lymphoreticular neoplasms	84	0.74	69	0.64	1.16 (0.83–1.62)	.40
II(e) Unspecified lymphomas	36	0.32	32	0.30	1.07 (0.65–1.79)	.87
III CNS neoplasms	3474	30.96	2928	27.40	1.13 (1.08–1.19)	.00
III(a) Ependymomas and choroid plexus tumor	292	2.60	258	2.41	1.08 (0.91–1.28)	.39
III(b) Astrocytomas	1667	14.85	1476	13.81	1.08 (1.00–1.15)	.04
III(c) Intracranial and intraspinal embryonal tumors	839	7.49	546	5.11	1.47 (1.32–1.64)	.00
III(d) Other gliomas	558	4.97	536	5.02	0.99 (0.88–1.12)	.88
III(e) Other specified intracranial/intraspinal neoplasms	71	0.63	74	0.69	0.91 (0.65–1.28)	.65
III(f) Unspecified intracranial and intraspinal neoplasms	47	0.42	38	0.35	1.18 (0.75–1.86)	.53
IV Neuroblastomas	947	8.39	879	8.16	1.03 (0.94–1.13)	.57
IV(a) Neuroblastoma and ganglioneuroblastoma	928	8.22	863	8.01	1.03 (0.93–1.13)	.60
IV(b) Other peripheral nervous cell tumors	19	0.17	16	0.15	1.13 (0.55–2.35)	.86
V Retinoblastoma	360	3.19	301	2.78	1.14 (0.98–1.34)	.09
VI Renal tumors	691	6.17	762	7.14	0.86 (0.78–0.96)	.01
VI(a) Nephroblastoma and other nonepithelial renal tumors	632	5.65	709	6.64	0.85 (0.76–0.95)	.00
VI(b) Renal carcinomas	55	0.49	50	0.47	1.04 (0.70–1.56)	.91
VI(c) Unspecified malignant renal tumors	—	—	—	—	—	—
VII Hepatic tumors	243	2.15	181	1.68	1.28 (1.05–1.56)	.01
VII(a) Hepatoblastoma	177	1.57	118	1.09	1.44 (1.13–1.83	.00
VII(b) Hepatic carcinomas	64	0.57	61	0.57	1.00 (0.69–1.44)	1.00
VII(c) Unspecified malignant hepatic tumors	—	—	—	—	—	—
VIII Malignant bone tumors	1128	9.97	837	7.79	1.28 (1.17–1.40)	.00
VIII(a) Osteosarcomas	653	5.77	466	4.33	1.33 (1.18–1.50)	.00
VIII(b) Chondrosarcomas	43	0.38	34	0.32	1.20 (0.74–1.93)	.51
VIII(c) Ewing tumor and related sarcomas of bone	365	3.23	286	2.67	1.21 (1.03–1.42)	.02
VIII(d) Other specified malignant bone tumors	46	0.41	38	0.36	1.15 (0.73–1.82)	.60
VIII(e) Unspecified malignant bone tumors	21	0.19	—	—	—	—
IX Soft tissue sarcomas	1454	12.89	1152	10.75	1.20 (1.11–1.30)	.00
IX(a) Rhabdomyosarcomas	643	5.73	446	4.17	1.37 (1.22–1.55)	.00
IX(b) Fibrosarcomas, peripheral nerve and other fibrous	157	1.39	126	1.17	1.18 (0.93–1.50)	.18
IX(c) Kaposi sarcoma	—	—	—	—	—	—
IX(d) Other specified soft tissue sarcomas	509	4.50	468	4.36	1.03 (0.91–1.17)	.65
IX(e) Unspecified soft tissue sarcomas	141	1.24	110	1.02	1.21 (0.94–1.57)	.14
X Germ-cell neoplasms	1492	13.19	873	8.12	1.63 (1.49–1.77)	.00
X(a) Intracranial and intraspinal germ-cell tumors	249	2.20	90	0.84	2.62 (2.05–3.38)	.00
X(b) Extracranial and extragonadal germ-cell tumors	150	1.32	201	1.86	0.71 (0.57–0.88)	.00
X(c) Malignant gonadal germ-cell tumors	1074	9.50	454	4.23	2.25 (2.01–2.51)	.00
X(d) Gonadal carcinomas	—	—	70	0.65	—	—
X(e) Other and unspecified malignant gonadal tumors	—	—	58	0.54	—	—
XI Other epithelial neoplasms	1329	11.75	2372	22.14	0.53 (0.50–0.57)	.00
XI(a) Adrenocortical carcinomas	—	—	35	0.33	—	—
XI(b) Thyroid carcinomas	256	2.26	1019	9.51	0.24 (0.21–0.27)	.00
XI(c) Nasopharyngeal carcinomas	82	0.72	56	0.52	1.39 (0.98–1.99)	.07
XI(d) Malignant melanomas	583	5.15	728	6.80	0.76 (0.68–0.85)	.00
XI(e) Skin carcinomas	—	—	—	—	—	—
XI(f) Other and unspecified carcinomas	382	3.38	525	4.90	0.69 (0.60–0.79)	.00
XII Other and unspecified malignant neoplasms	63	0.56	105	0.98	0.57 (0.41–0.79)	.00
XII(a) Other specified malignant tumors	28	0.25	65	0.61	0.41 (0.25–0.65)	.00
XII(b) Other unspecified malignant tumors	35	0.31	40	0.37	0.83 (0.51–1.34)	.49

Rates are per million and were age adjusted to the 2000 US standard population. Data include malignant tumors only and cover 90.3% of the US population. — indicates that the statistic is not displayed because there were fewer than 16 cases.

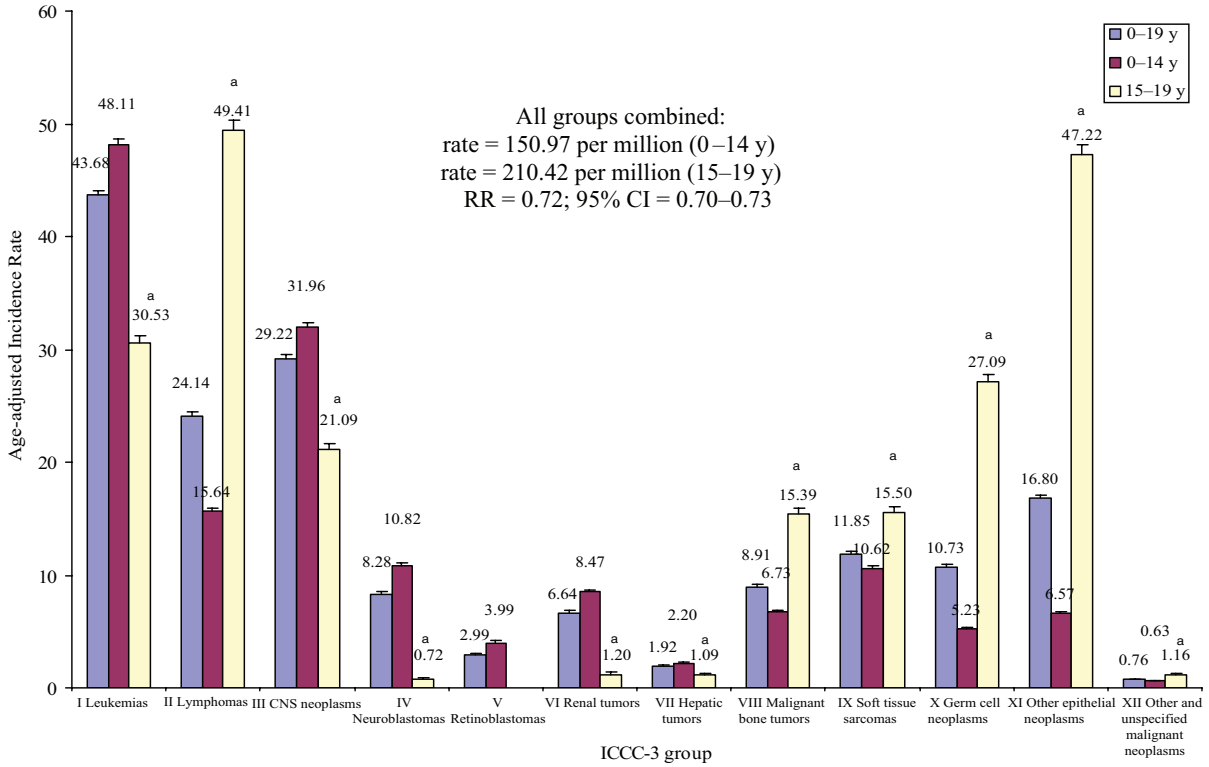

FIGURE 2

Age-specific childhood cancer-incidence rates according to ICCC-3 group: United States, 2001–2003. [a] Significant difference between children (aged 0–14 years) and adolescents (aged 15–19 years). Retinoblastomas are not shown for those aged 15 to 19 years because there were fewer than 16 cases in this category.

tion, young people living in the Northeast had the highest incidence rate for lymphomas (27.58 per million) and CNS neoplasms (32.64 per million) ($P < .0167$) compared with those in other census regions. The rate of leukemias for Hispanic children (53.71 per million) was significantly higher than that for non-Hispanic children (41.37 per million), whereas the rate of CNS neoplasms for Hispanic children (25.01 per million) was significantly lower than that for non-Hispanic children (30.31 per million) ($P < .05$).

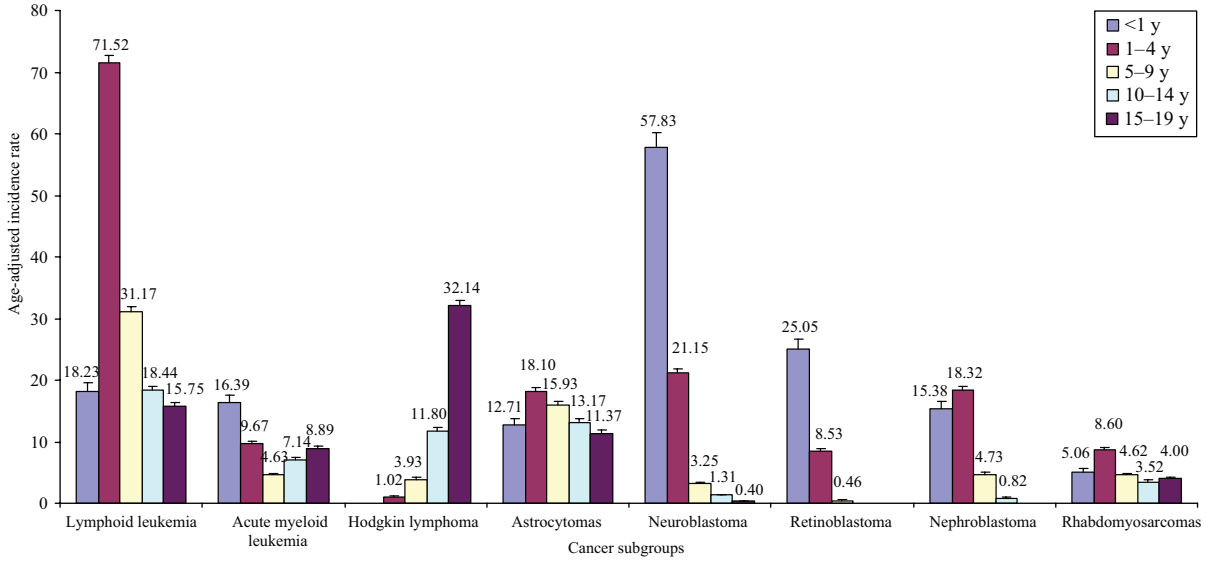

FIGURE 3

Age-specific childhood cancer-incidence rates according to certain cancer subgroups: United States, 2001–2003. Because there were fewer than 16 cases in these categories, data are not shown: Hodgkin's lymphoma for those aged <1 year, retinoblastoma for those aged 10 to 14 and 15 to 19 years; and nephroblastoma for those aged 15 to 19 years.

TABLE 2 **US Childhood Cancer-Incidence Rates According to ICCC-3 Group, Race, Ethnicity, and Census Region: United States, 2001–2003**

	All ICCC Groups		I Leukemias		II Lymphomas		III CNS neoplasms	
	Cases, *n*	Rate (95% CI)	Cases, *n*	Rate (95% CI)	Cases, *n*	Rate (95% CI)	Cases, *n*	Rate (95% CI)
Total	36 446	165.92 (164.22–167.64)	9566	43.68 (42.81–44.57)	5309	24.14 (23.49–24.79)	6402	29.22 (28.51–29.95)
White[a]	29 934	173.21 (171.25–175.18)[b]	7940	46.16 (45.15–47.18)	4347	25.08 (24.34–25.83)[b]	5297	30.78 (29.96–31.62)[b]
Black[a]	4004	117.87 (114.24–121.58)	885	25.99 (24.30–27.76)	636	18.85 (17.42–20.38)	712	20.90 (19.39–22.49)
A/PI[a]	1328	131.43 (124.45–138.70)	431	42.54 (38.62–46.76)	191	19.10 (16.49–22.02)	194	19.26 (16.65–22.18)
AI/AN[a]	273	97.32 (86.06–109.76)	90	32.40 (26.02–39.99)	31	10.62 (7.21–15.26)	36	13.01 (9.09–18.18)
Hispanic[c]	6729	163.79 (159.88–167.78)	2262	53.71 (51.51–55.99)[b]	869	22.22 (20.76–23.76)	1045	25.01 (23.51–26.59)[b]
Non-Hispanic	29 717	166.32 (164.43–168.22)	7304	41.37 (40.42–42.33)	4440	24.44 (23.73–25.17)	5357	30.31 (29.40–31.03)
Northeast	7676	179.12 (175.14–183.18)[b]	1895	44.57 (42.59–46.63)	1196	27.58 (26.04–29.20)[b]	1394	32.64 (30.95–34.40)[b]
Midwest	9011	165.50 (162.09–168.95)	2310	42.85 (41.12–44.63)	1303	23.65 (22.38–24.97)	1559	28.79 (27.39–30.27)
South	11 082	158.65 (155.71–161.63)	2900	41.46 (39.97–43.00)	1609	23.21 (22.09–24.38)	1954	28.06 (26.83–29.34)
West	8677	165.26 (161.80–168.78)	2461	46.80 (44.97–48.69)	1201	22.98 (21.70–24.32)	1495	28.42 (27.00–29.90)

Rates are per million and were age-adjusted to the 2000 US standard population. Data include malignant tumors only and cover 90.3% of the US population. Regional population coverage was 100% for the Northeast, 99% for the Midwest, 79% for the South, and 91% for the West.

[a] Unknown race and race groups other than white, black, A/PI, and AI/AN are not listed but are included in the total case count.

[b] The reference group is significantly different from any other group in racial/ethnical or regional comparison.

[c] Hispanic origin is not mutually exclusive from race categories (white, black, A/PI, and AI/AN).

Negative binomial regression analysis (Table 3) showed that the incidence rate of all childhood cancers varied significantly according to gender, age, race, ethnicity, and geographic census region. Older age, male gender, white race, and non-Hispanic ethnicity were all associated with increased incidence. The Northeast had a significantly higher incidence compared with that in the Midwest and South. Differences between the Northeast and West were no longer significant after adjusting for demographics and year of diagnosis. There was a borderline nonsignificant linear trend toward lower incidence with increasing diagnosis year (incidence RR for 1-year increase: 0.98 [95% CI: 0.96–1.00]; $P = .0546$).

DISCUSSION

With this study we have summarized childhood cancer incidence in the United States and addressed variation in incidence according to age, gender, race, ethnicity, and geography. Consistent with results of previous studies, leukemias were the most common childhood cancer; boys were more likely to be diagnosed with cancer than girls; adolescents were diagnosed more frequently than children; white children had the highest incidence of any race; and non-Hispanic children had a higher incidence rate than that of Hispanic children.[16–20] Age patterns for lymphoid leukemias, acute myeloid leukemias, Hodgkin's lymphomas, astrocytomas, neuroblastomas, retinoblastomas, nephroblastomas, and rhabdomyosarcomas were similar to what has been reported previously.[20]

This study also resulted in several important novel findings. We found that young people living in the Northeast had the highest incidence rate of all cancers combined. This finding may be partially attributed to the

TABLE 3 **Negative Binomial Modeling Assessing the Variation of Childhood Cancer-Incidence Rates According to Demographic and Geographic Factors: United States, 2001–2003**

Characteristic	Likelihood Ratio χ^2	*df*	*P*	Incidence RR	95% Likelihood Ratio CI
Age	149.20	1	<.0001	—	—
15–19 vs 0–14 y	—	—	—	1.35	1.31–1.40
Gender	34.86	1	<.0001	—	—
Male vs female	—	—	—	1.11	1.07–1.14
Race	289.91	3	<.0001	—	—
Black vs white	—	—	—	0.66	0.63–0.69
API vs white	—	—	—	0.73	0.69–0.78
AI/AN vs white	—	—	—	0.55	0.48–0.61
Ethnicity	27.99	1	<.0001	—	—
Hispanic vs Non-Hispanic[a]	—	—	—	0.90	0.86–0.94
Region	8.30	3	.0403	—	—
Midwest vs Northeast	—	—	—	0.93	0.89–0.98
South vs Northeast	—	—	—	0.95	0.91–1.00
West vs Northeast	—	—	—	0.96	0.92–1.01
Year	3.69	1	.0546	—	—
1-y increase	—	—	—	0.98	0.96–1.00

Rates are per million and were age adjusted to the 2000 US standard population. Data include malignant tumors only and cover 90.3% of the U.S. population. Regional population coverage is 100% for the Northeast, 99% for the Midwest, 79% for the South, and 91% for the West. *df* indicates degree of freedom.

[a] Hispanic origin is not mutually exclusive from race categories (white, black, A/PI, and AI/AN).

highest rate of lymphomas and CNS neoplasms in this region compared with that of other US census regions. The higher rate of leukemias among children in the West region as compared with those in the Northeast region may be a reflection of increased diagnoses of childhood leukemias that were under investigation as a potential cancer cluster in Fallon, Nevada.[21,22] Although overall childhood cancer-incidence rates were found to be highest in the Northeast, childhood cancer death rates are the lowest in this region of the United States and have been decreasing since 1990.[23] Regional differences in incidence and survival patterns for childhood cancers have also been documented in European populations.[4] Similar to European populations,[4] genetic, environmental, and lifestyle factors and differences in access to and quality of health care may be related to childhood cancer incidence and mortality in the United States.

With this study we have also described the burden of myelodysplastic syndrome and other myeloproliferative diseases for the first time in the United States; these diseases are considered to be malignant in the ICD-O-3 but not in the ICD-O-2. These diseases are classified in the leukemia group; therefore, their addition resulted in an increased overall leukemia rate compared with previously published leukemia rates.[8] Myelodysplastic syndromes run an aggressive course in childhood and can arise in a previously healthy child or can be a result of chemotherapy or radiation therapy received for other cancers.[24,25] The inclusion of incidence data in this report provides a baseline measure for tracking incidence trends of these syndromes over time in the United States.

We found distinct variation in cancer-incidence patterns among children aged 0 to 14 years compared with adolescents aged 15 to 19 years for all ICCC-3 cancer groups presented. Cancer-incidence patterns among children aged 0 to 14 years were significantly different compared with those of adolescents aged 15 to 19 years for all 12 ICCC-3 groups presented. For instance, the incidence rate of retinoblastoma was 3.99 per million for children in the United States between 2001 and 2003 but almost zero for adolescents.

Childhood cancer is uncommon, and the rarity of this group of diseases might lead to imprecise and biased findings in research studies because of small case counts and poor representation of the targeted population.[26] The combined data from the NPCR and the SEER program provides the most geographically comprehensive source of data on cancer incidence. We used only high-quality registry data, which mitigated the influence of misclassification of gender, age, and race/ethnicity and other pitfalls in the estimation of cancer incidence.[8,27] Moreover, because the ICD-O-3 was first implemented in 2001, we limited our data source to 2001 and onward to achieve consistency in the data set. With an increase in using genetic and pathologic methodologies in the diagnosis of cancer, numerous morphology codes (particularly for leukemias and lymphomas) have been generated; the ICD-O-3 was published to introduce these major changes in coding and classifying neoplasms. Codes in the third edition reflect the concept of eliminating the largely artificial distinction between lymphoid leukemias and lymphomas by sharing nomenclature between these disorders.[10] Last, we documented regional variations in cancer incidence by using definitions of the US Census Bureau; at present, few publications provide information on cancer incidence according to US census region. Our findings may lay the groundwork for generating research hypotheses regarding differences in exposures and behaviors between populations living in different regions. To our knowledge, this is the first study to show regional variations in the incidence of childhood cancer. Regional incidence of childhood cancer could not be characterized previously because cancer-registry data were limited to the states and metropolitan-area registries included in the SEER program. The addition of NPCR data allows the ability to study geographic variation, adding data that are integral in assessing potential relationships regarding environmental and lifestyle factors that may be associated with incidence rates in particular regions.

Some limitations in the data sources and the methods used may influence these research findings. First, although the overall quality of race and ethnicity data that were included in this study is very good, the data quality for individual races may vary. A study comparing SEER registry data to that of self-reported data obtained from the US Census Bureau has shown that there was overall excellent agreement for race and ethnicity between these 2 sources for white, black, and A/PI populations.[28] The AI/AN population was found to be substantially underclassified in registry data.[28] The Hispanic population was also found to be slightly underclassified.[28] Second, although these data are the most geographically comprehensive data available, data were not included from all US states, which resulted in a range of coverage by US census region (79% in the South to 100% in the Northeast); therefore, some populations might not be well represented. Third, because of the rarity of childhood cancer, characterization at local levels (state or county) is difficult.

CONCLUSIONS

We have presented data representing the vast majority of the US population to describe the burden of childhood cancer in the United States. Our study demonstrates distinct differences in cancer incidence between the 4 US census regions. We have also confirmed some historic findings from other researchers that indicated significant variations in cancer incidence according to age, gender, race, and ethnicity. Our research findings may be useful for prioritizing childhood cancer research and control needs in terms of these demographic and geographic variations. Moreover, the recent availability of high-quality national cancer data on the occurrence of childhood cancers provides unprecedented opportunities for better understanding and tracking the incidence of a variety of childhood cancers. These data can be used to support additional research regarding avoidable or modifiable risk factors for childhood cancers.

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REFERENCES

1. Jemal A, Siegel R, Ward E, et al. Cancer statistics, 2006. *CA Cancer J Clin.* 2006;56(2):106–130
2. Pastore G, Peris-Bonet R, Carli M, Martinez-Garcia C, Sanchez de Toledo J, Steliarova-Foucher E. Childhood soft tissue sarcomas incidence and survival in European children (1978–1997): report from the Automated Childhood Cancer Information System project. *Eur J Cancer.* 2006;42(13):2136–2149
3. Linet MS, Ries LA, Smith MA, Tarone RE, Devesa SS. Cancer surveillance series: recent trends in childhood cancer incidence and mortality in the United States. *J Natl Cancer Inst.* 1999; 91(12):1051–1058
4. Steliarova-Foucher E, Stiller C, Kaatsch P, et al. Geographical patterns and time trends of cancer incidence and survival among children and adolescents in Europe since the 1970s (the ACCIS project): an epidemiological study. *Lancet.* 2004; 364(9451):2097–2105
5. Wenceslao S, Gotay CC, Cheung LW, White K. Patterns of childhood cancer in Hawaii between 1975 and 2000. *Hawaii Med J.* 2006;65(8):221–225
6. Pallapies D. Trends in childhood disease. *Mutat Res.* 2006; 608(2):100–111
7. Linet MS, Wacholder S, Zahm SH. Interpreting epidemiologic research: lessons from studies of childhood cancer. *Pediatrics.* 2003;112(2):218–232
8. US Cancer Statistics Working Group. *United States Cancer Statistics: 2003 Incidence and Mortality*. Atlanta, GA: US Department of Health and Human Services, Centers for Disease Control and Prevention, and National Cancer Institute; 2006
9. Fritz A, Percy C, Jack A, et al. *International Classification of Disease for Oncology*. 3rd ed. Geneva, Switzerland: World Health Organization; 2000
10. Steliarova-Foucher E, Stiller C, Lacour B, Kaatsch P. International Classification of Childhood Cancer, third edition. *Cancer.* 2005;103(7):1457–1467
11. Hankey BF, Ries LA, Edwards BK. The surveillance, epidemiology, and end results program: a national resource. *Cancer Epidemiol Biomarkers Prev.* 1999;8(12):1117–1121
12. Wingo PA, Jamison PM, Hiatt RA, et al. Building the infrastructure for nationwide cancer surveillance and control: a comparison between the National Program of Cancer Registries (NPCR) and the Surveillance, Epidemiology, and End Results (SEER) Program (United States). *Cancer Causes Control.* 2003; 14(2):175–193
13. National Cancer Institute. *SEER*Stat* [computer program]. Version 6.2.4. Bethesda, MD: National Cancer Institute; 2006
14. Fay MP, Tiwari RC, Feuer EJ, Zou Z. Estimating average annual percent change for disease rates without assuming constant change. *Biometrics.* 2006;62(3):847–854
15. Byers AL, Allore H, Gill TM, Peduzzi PN. Application of negative binomial modeling for discrete outcomes: a case study in aging research. *J Clin Epidemiol.* 2003;56(6):559–564
16. Desandes E, Clavel J, Berger C, et al. Cancer incidence among children in France, 1990–1999. *Pediatr Blood Cancer.* 2004; 43(7):749–745
17. Chen VW, Schmidt BA, Wu XC, et al. Childhood cancer in Louisiana 1988–1996. *J La State Med Soc.* 2002;154(2):91–99
18. Ries LAG, Smith A, Gurney JG, et al. *Cancer Incidence and Survival Among Children and Adolescents: United States SEER Program 1975–1995*. Bethesda, MD: National Cancer Institute, SEER Program; 1999. NIH publication 99–4649
19. McNamara C, Bayakly AR, Young JL, Horan J. *Georgia Childhood Cancer Report, 2005*. Atlanta, GA: Georgia Department of Human Resources, Division of Public Health, Chronic Disease, Injury, and Environmental Epidemiology Section; 2005. Publication DPH06/075HW
20. American Cancer Society. *Cancer Facts and Figures 2000* Atlanta, GA: American Cancer Society; 2000
21. Steinmaus C, Lu M, Todd RL, Smith AH. Probability estimates for the unique childhood leukemia cluster in Fallon, Nevada, and risks near other U.S. Military aviation facilities. *Environ Health Perspect.* 2004;112(6):766–771
22. Sheppard PR, Speakman RJ, Ridenour G, Witten ML. Temporal variability of tungsten and cobalt in Fallon, Nevada. *Environ Health Perspect.* 2007;115(5):715–719
23. Centers for Disease Control and Prevention. Trends in childhood cancer mortality: United States, 1990–2004. *MMWR Morb Mortal Wkly Rep.* 2007;56(48):1257–1261
24. Locatelli F, Zecca M, Pession A, Masserati E, De Stefano P, Severi F. Myelodysplastic syndromes: the pediatric point of view. *Haematologica.* 1995;80(3):268–279
25. Hasle H. Myelodysplastic and myeloproliferative disorders in children. *Curr Opin Pediatr.* 2007;19(1):1–8
26. Kaatsch P, Haaf G, Michaelis J. Childhood malignancies in Germany: methods and results of a nationwide registry. *Eur J Cancer.* 1995;31A(6):993–999
27. Izquierdo JN, Schoenbach VJ. The potential and limitations of data from population-based state cancer registries. *Am J Public Health.* 2000;90(5):695–698
28. Clegg LX, Reichman ME, Hankey BF, et al. Quality of race, Hispanic ethnicity, and immigrant status in population-based cancer registry data: implications for health disparity studies. *Cancer Causes Control.* 2007;18(2):177–187

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Jun Li, Trevor D. Thompson, Jacqueline W. Miller, Lori A. Pollack and Sherri L. Stewart

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