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Childhood and Adolescent Cancer Survival in the U.S. by Race and Ethnicity (Diagnostic Period 1975–1999)

Amy M. Linabery, M.S., M.P.H.¹ and Julie A. Ross, Ph.D.^{1,2}

¹ Division of Pediatric Epidemiology and Clinical Research, Department of Pediatrics, University of Minnesota, Minneapolis, Minnesota

² University of Minnesota Cancer Center, Minneapolis, Minnesota

Abstract

Background—Survival trends provide a measure of improvement in detection and treatment over time. We present updated childhood and adolescent cancer survival statistics overall and among demographic subgroups, including Hispanics, for whom national rates have not been previously reported. These results extend those provided by the National Cancer Institute’s Surveillance, Epidemiology, and End Results (SEER) program in their detail and interpretation.

Methods—Survival trends of primary cancers in children and adolescents (0–19 years) were evaluated using the SEER 9 data. Five- and 10-year relative survival rates across 5-year (1975–1979, 1985–1989, 1995–1999) and 10-year (1975–1984, 1985–1994) cohorts were compared via Z-tests. Annual percent change (APC) in survival was computed via weighted least squares regression. Rates in Hispanic children and adolescents were compared to those in non-Hispanic whites and blacks (SEER 13, 1995–1999).

Results—Five-year survival rates increased significantly overall (1975–1979: 63% vs. 1995–1999: 79%, $p<0.0001$) and for nearly all histologic types examined; increases were greatest for ependymoma (+37%, $p<0.0001$) and non-Hodgkin lymphoma (+34%, $p<0.0001$). Hispanic children and adolescents had somewhat poorer 5-year rates than non-Hispanic whites overall (74% vs. 81%, $p<0.0001$) and for Ewing sarcoma, leukemia, CNS tumors, and melanoma. Ten-year rates also increased significantly overall (1975–1984: 61% vs. 1985–1994: 72%, $p<0.0001$) and for a majority of cancer types. The largest improvements were noted for acute lymphoblastic leukemia (+19%, $p<0.0001$) and non-Hodgkin lymphoma (+19%, $p<0.0001$).

Conclusions—Observed trends reinforce the need for resources devoted to advancing treatment modalities, reducing disparities among racial/ethnic groups and adolescents, and providing long-term care of survivors.

Keywords

epidemiology; childhood cancer; adolescents; survival; trends

Cancers constitute the leading cause of disease-related mortality among children and adolescents in the United States;¹ ~1,545 children and adolescents aged 0–14 years were predicted to die of a malignant neoplasm in 2007.² The last comprehensive reports on childhood cancer survival³ and mortality trends⁴ included data through 1995. We provide an updated analysis of childhood and adolescent cancer survival, including rates among

Corresponding author: Julie A. Ross, Ph.D., Department of Pediatrics, University of Minnesota, 420 Delaware Street SE, MMC 422, Minneapolis, MN 55455; Telephone: 612–626–2902, Fax: 612–626–4842, Email: rossx014@umn.edu.

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Hispanics, for whom national rates have not been previously reported. These findings extend those furnished by the Surveillance, Epidemiology, and End Results (SEER) program by providing greater detail and interpretation of results.

METHODS

SEER program data were analyzed to evaluate childhood and adolescent cancer survival trends.⁵ Since 1973, SEER has actively collected data on all cancer cases (excluding nonmelanoma skin cancers) in Connecticut, Hawaii, Iowa, New Mexico, Utah, Detroit, and San Francisco-Oakland. Seattle-Puget Sound was added in 1974 and Atlanta in 1975.⁶ These nine registries represent approximately 9% of the U.S. population.⁶ In 1992, SEER added Los Angeles, San Jose-Monterey, rural Georgia, and the Alaskan Native Tumor Registry, permitting the calculation of 5-year relative rates among Hispanic children and adolescents.⁶ This expanded SEER 13 dataset⁵ encompasses 14% of the population (while the full SEER 17 dataset covers 26% of the U.S. population).⁶ With an estimated case ascertainment rate of 98%,⁷ SEER captures information on demographics, tumor site and morphology, stage at diagnosis, and treatment. SEER performs active ascertainment of vital status, with ~14% of pediatric and adolescent patients lost to follow-up.³

We included first malignancies diagnosed during three 5-year periods (1975–1979, 1985–1989, 1995–1999) and two 10-year periods (1975–1984, 1985–1994) among those aged ≤19 years in the SEER 9 registries and first malignancies diagnosed during the period 1995–1999 among children and adolescents in the SEER 13 dataset. Fifteen common cancers and eight subtypes were grouped according to International Classification of Diseases for Oncology, Third Edition (ICD-O-3)⁸ histology and topography codes (Supplementary Table 1). Approximately 95% of diagnoses were confirmed by histology.

Statistical Analysis

Five- and 10-year relative survival rates were calculated via the life tables method in SEER*STAT.⁹ Ten-year survival has not been traditionally reported, but may be a more relevant measure of survival in children and adolescents, given advancements in survival duration and greater potential for years of life lost. Relative rates, presented as percentages, are ratios of observed-to-expected survival. Observed rates included all individuals diagnosed with a malignancy actively followed through 2004; expected rates were based on National Center for Health Statistics data. Expected rates account for differing distributions of age, sex, race and year of diagnosis. Adjustments were made for relative rates >1.0, increasing rates, and heterogeneity in withdrawal (exact method).

Standard errors⁹ and 95% confidence intervals (CIs) were calculated and Z-tests employed to compare the relative survival functions across the three diagnostic cohorts in the SEER 9 populations.¹⁰ Similarly, 5-year survival functions among Hispanic children/adolescents were compared to those among non-Hispanic whites and blacks (data not shown) in the SEER 13 registries.¹⁰ Survival differences corresponding to a p-value of ≤0.05 were considered statistically significant. To examine 5-year trends across the 25-year period, average annual percent change (APC) and the corresponding 95% confidence interval (CI) were computed via weighted least squares regression using Joinpoint software,¹¹ where the independent variable was calendar year and the dependent variable was the natural logarithm of the relative rate. Rates across strata of sex (male, female), race (white, black) and age group (<1, 1–4, 5–9, 10–14, 15–19 years) were also evaluated (Supplementary Tables 2–3). Other races (American Indian/Alaskan Native, Asian/Pacific Islander) were not included due to small numbers.

This study was approved by the University of Minnesota Institutional Review Board.

RESULTS

Overall

Five-year survival rates increased significantly for all histologic types combined, from 63% for those diagnosed in 1975–1979 to 79% for 1995–1999, or by 1.1% annually during the period 1975–1999 (Table 1). Significant increases were observed for most cancer types examined (Figure 1). The greatest increases were observed for ependymoma (+37%) and non-Hodgkin lymphoma (NHL, +34%); the smallest increases were observed in Hodgkin lymphoma (HL, +9%) and melanoma (+10%). Five-year rates were >90% for six cancers in 1995–1999; children/adolescents with HL (96%), retinoblastoma (97%) and thyroid carcinoma (98%) had the highest rates. Acute myeloid leukemia (AML) patients had the lowest 5-year rates (45%), although they experienced the greatest annual increase over the 25-year period ($APC=3.7\%$). Annual observed and expected 5-year rates, as determined by joinpoint regression, are shown in Figure 1.

Five-year rates were higher in females than males in the three periods examined, although the increase observed from 1975–1979 to 1995–1999 was greater in males (+20%, $APC=1.4\%$ vs. +13%, $APC=0.9\%$ in females). White children/adolescents had higher 5-year rates than black children/adolescents in each period and experienced a greater increase (+17% vs. +13%); however, the rates of change were equivalent ($APC=1.1\%$). Adolescents diagnosed at 15–19 years in 1995–1999 had the highest 5-year rates (81%), while infants had the lowest (76%); significant improvements were observed in all age categories ($APC_{<1}=0.9\%$, $APC_{1-4}=1.3\%$, $APC_{5-9}=1.2\%$, $APC_{10-14}=1.4\%$, $APC_{15-19}=0.8\%$).

Ten-year survival increased 11% across the two diagnostic cohorts (1975–1984: 61% vs. 1985–1994: 72%; Table 2). Significant increases were observed for nearly all cancers; 10-year rates improved the most for acute lymphoblastic leukemia (ALL) and NHL (+19%, respectively), AML (+18%), and ependymoma (+17%) and improved the least for HL and melanoma (+8%, respectively). For those diagnosed in 1985–1994, 10-year rates were =90% for melanoma ($\geq 90\%$), Wilms tumor (91%), retinoblastoma (93%) and thyroid carcinoma (99%); AML patients experienced the poorest survival (37%). The patterns described above for sex, race and age categories were also observed for 10-year survival, although 10-year rates and increases were smaller in magnitude.

Five-year rates, 95% CIs, and Z-test results for all subgroups are shown in Supplementary Tables 2–3; notable trends are discussed below.

Leukemias

Significant 5-year rate increases were observed in all demographic subgroups for any leukemia and ALL, and in most subgroups for AML, except black children/adolescents, infants, and those aged 5–9 years. ALL patients experienced notably higher survival than AML patients. ALL rates were greater for females than males in the first period; however, males experienced a greater increase from 1975–1979 to 1995–1999 (+31% vs. +22% in females), such that the rates were similar by 1995–1999 (83% vs. 86%). For AML, the increase also occurred earlier in females and the 5-year rates were similar by 1995–1999 (47% females vs. 43% males). Survival among black children/adolescents with ALL lagged behind 5-year rates in whites in each time period (1995–1999: 75% vs. 85%), while AML survival among black children/adolescents was more comparable across the three cohorts. By the 1990s, peak ALL rates were observed among those aged 1–4 (92%) and 5–9 years (84%) and were lowest among older adolescents (59%) and infants (57%); little difference was observed among AML patients across age groups by 1995–1999.

Ten-year rates improved significantly in all subgroups for leukemia overall (+16–21%), for ALL in all subgroups except infants, and for AML in both sexes, white children/adolescents, and children/adolescents aged 10–19 years. Ten-year rates in females exceeded those in males in both cohorts for ALL (1985–1994: 77% vs. 71%) and AML (43% vs. 32%). Ten-year rates in white children/adolescents were greater than those in black children/adolescents for ALL (1985–1994: 74% vs. 62%), but were equivalent for AML (39%). Infants experienced the poorest survival for ALL (1985–1994: 37%), while 10-year rates peaked among children aged 1–4 (82%). AML 10-year rates ranged from 34–43% among all age groups.

Lymphomas

For HL, similar 5-year rates were observed in males and females (1995–1999: 96%), among white children/adolescents (97%), and in those aged 10–19 years at diagnosis (96%). Black children/adolescents had lower 5-year rates in 1985–1989, but by 1995–1999 had approached the rates of whites (91%). Ten-year survival rates of $\geq 88\%$ were observed for those diagnosed in 1985–1994 for both sexes, white children/adolescents, and children/adolescents aged 5–19 years. Ten-year rates in black children/adolescents were slightly lower (83%).

For NHL, 5-year survival in females was greater than in males diagnosed in 1975–1979 (57% vs. 42%), but was equivalent in subsequent years (1995–1999: 81%). Substantial improvements in five-year rates were found in whites, blacks, and among those diagnosed at ≥ 1 year. For the 1995–1999 cohort, 5-year rates were $\sim 80\%$ across racial groups and peak survival rates were observed among those diagnosed at 10–14 (87%) and 5–9 years (85%). Improvements in 10-year survival were similar to those in 5-year rates. For those diagnosed in 1985–1994, 10-year rates were $\geq 70\%$ for all subgroups except infants (60%) and adolescents (68%); children aged 1–4 years achieved the highest 10-year rate (78%).

CNS malignancies

Five-year rates of CNS tumors increased significantly in all subgroups except infants. Five-year rates were slightly higher in females than males (1995–1999: 77% vs. 73%) and were higher in whites compared to blacks (77% vs. 64%) across the three diagnostic periods. Children/adolescents diagnosed at >9 years had greater 5-year rates (1995–1999: 80%) compared with those diagnosed at younger ages (<1 year: 56%, 1–4 years: 71%, 5–9 years: 73%). Ten-year rates increased among males, white children/adolescents, and those aged 5–19 years. Similar patterns to the 5-year rates were observed by sex and race. Ten-year survival for those diagnosed in 1985–1994 increased monotonically with age to reach a maximum among those aged 15–19 years (infants: 46%; 15–19 years: 71%).

For astrocytoma, 5-year rates in males and females were comparable in the first two periods, while rates among females were somewhat greater in the 1990s (89% vs. 83% in males). Whites had consistently higher 5-year survival rates compared with blacks (1995–1999: 87% vs. 75%). Children aged 1–4 had the highest 5-year survival rates (1995–1999: 90%), while infants and adolescents aged 15–19 had the lowest rates (80% and 81%, respectively). Substantial increases in 10-year rates were observed for males, females, whites, infants, and those aged 10–19 at diagnosis. Males and females had similar 10-year rates in both cohorts (1985–1994: 76% vs. 73%), while 10-year rates were lower in black children/adolescents compared with whites (68% vs. 75%, respectively). Children aged 1–4 years at diagnosis fared the best (1985–1994: 80%), while 10-year rates among other age groups were $>70\%$ in 1985–1994.

For PNET, a significant 25% increase in 5-year survival was observed for males between 1975–1979 and 1995–1999, such that rates in males and females were equivalent in 1995–1999 (65% vs. 64%). Five-year rates were comparable in white and black children/adolescents in the three time periods (1995–1999: 67% vs. 63%); a substantial increase was seen among whites during the period of observation (+20%). Children/adolescents aged 10–14 years had the highest 5-year survival rates (1995–1999: 81%) and infants had the lowest (28%); significant improvements were observed between 1975–1979 and 1995–1999 for children/adolescents aged 5–14 years. Further analysis revealed a significant improvement in 5-year survival for medulloblastoma over the 25-year period among those aged 0–19 (1975–1979: 47% vs. 1995–1999: 68%). Ten-year rates increased among males (1975–1984: 40%; 1985–1994: 54%) and those aged 5–9 years at diagnosis (1975–1984: 44%; 1985–1994: 63%).

Neuroblastoma

Significant increases in 5-year survival were observed across the 25-year period for males (+16%), females (+9%), white children/adolescents (+14%), infants (+7%) and those aged 1–4 years at diagnosis (+24%). For those diagnosed in 1995–1999, 5-year rates were similar among males (68%) and females (66%) and across the two racial groups examined (67–68%). Five-year rates in infants were appreciably higher than rates in children diagnosed at 1–4 years across all three cohorts (1995–1999: 93% vs. 55%); few cases were diagnosed at older ages. Ten-year survival increased in the groups listed above, with the exception of infants, who experienced the greatest rates in both diagnostic cohorts (83%).

Wilms tumor

Increases in 5-year survival occurred primarily between the 1975–1979 and 1985–1989 cohorts and were observed in males (+16%), females (+18%), whites (+16%), and blacks (+28%). Five-year rates were ≥90% for each of these subgroups by the 1990s. Significant increases were also observed over the entire period of observation among children aged 0–9 years (+15–17%); the highest 5-year rates were observed in infants (1995–1999: 98%). Similarly, males (+13%), females (+10%), whites (+12%), and children aged 1–4 years (+12%) experienced significant increases in 10-year rates; rates reached or exceeded 90% in these subgroups.

Osteosarcoma

Noteworthy increases in 5-year survival were observed in males between 1975–1979 and 1995–1999 (+28%); rates among males and females were comparable in the 1990s (66% vs. 63%). Significant 5-year rate increases were observed for white children/adolescents (+24%), and children and adolescents diagnosed at 10–14 years (+23%). Ten-year survival improved significantly in males (+14%), females (+15%), white children/adolescents (+16%) and adolescents aged 15–19 years (+17%). Ten-year rates in females were substantially greater than those in males in both cohorts (1985–1994: 65% vs. 55%, respectively).

Ewing sarcoma

Five-year rates were disparate between males (36%) and females (54%) diagnosed in 1975–1979; this gap closed in the intervening time (1995–1999: 68% and 65%, respectively). White children/adolescents (1975–1979: 42% vs. 1995–1999: 65%), children/adolescents aged 10–14 years (47% vs. 74%), and adolescents aged 15–19 years (28% vs. 53%) also experienced substantial increases. Ten-year rates increased significantly in males, white children/adolescents, and adolescents (1985–1994: 44%, 51%, and 44%, respectively). All rates are based on few cases and should be interpreted cautiously.

Rhabdomyosarcoma

Five-year increases were principally observed between 1975–1979 and 1985–1989 and were found in males (+18%), whites (+13%), and 15–19 year-olds (+29%). A substantial increase in 5-year survival was also seen between 1975–1979 and 1995–1999 for those diagnosed at 10–14 years (+21%). Ten-year rates improved for males (+13%), whites (+10%) and children aged 1–4 years (+25%); males (1985–1994: 66%), whites (65%) and children aged 1–4 and 5–9 years (86% and 66%, respectively) experienced the highest 10-year survival.

Germ cell tumors

For those diagnosed in 1975–1979, the 5-year rate in females (78%) was greater than that of males (66%), but by 1995–1999, rates were nearly equivalent (93% vs. 91%, respectively). Substantial improvements were observed in white children/adolescents (+23%) and among those aged 1–4 (+27%), 10–14 (+15%) and 15–19 years (+22%), such that 5-year rates in the 1995–1999 cohort were ≥90% in white children/adolescents and in those aged 1–19 years; 5-year rates were 88% in blacks and 86% in infants. Ten-year rates were ≥80% for those diagnosed in 1985–1994 for most demographic groups; infants (73%) and children aged 5–9 years (77%) experienced lower rates.

Melanoma

Improvements in 5-year survival were observed in males between 1975–1979 and 1995–1999 (+16%), such that equal rates in males and females were reached in 1995–1999 (93–94%). Increases were also observed in whites (+11%) and in those aged 5–9 (+43%) and 15–19 years (+13%); few cases were seen among black children/adolescents and those <10 years old. These improvements were mainly attributable to the interval between 1975–1979 and 1985–1989. Significant improvements in 10-year survival were observed for females (+9%), whites (+9%), and those aged 15–19 years (+12%). The 10-year rate for males diagnosed in 1985–1994 (83%) lagged behind that of females (94%) considerably.

Hispanics

Five-year survival among Hispanic children/adolescents diagnosed in 1995–1999 was lower than that of non-Hispanic white children/adolescents (74% vs. 81%, respectively; Table 3). The greatest difference occurred for Ewing sarcoma (Hispanics: 27% vs. non-Hispanic whites: 64%). Five-year rates were also significantly lower among Hispanic children/adolescents for leukemias overall (−9%), ALL (−9%), CNS tumors overall (−11%), astrocytoma (−12%), other gliomas (−25%), and melanoma (−16%). There were no statistically significant differences observed between Hispanic and non-Hispanic black children/adolescents, likely due to insufficient numbers of black cases.

DISCUSSION

Substantial increases in 5- and 10-year survival rates have been observed in the U.S. for pediatric and adolescent cancers overall and for the majority of cancer types and demographic subgroups examined. Similarly, survival data collected on >100,000 children and adolescents aged 0–19 years via population-based registries throughout Europe showed a 73% 5-year rate for those diagnosed in the 1990s and improved survival across all ICCC categories compared with those diagnosed in the 1970s and 1980s.¹²

Progress in the treatment of pediatric and adolescent cancers includes improved understanding of the molecular basis of childhood cancers, customized therapies based on patient prognostic characteristics and tumor biology, and multimodal and combination therapies.^{12,16,17} A prime example is the improved ALL survival due to the introduction of risk-based therapies, which account for leukemic subtype and individual patient

characteristics.^{17,18} The development and application of similar methods is predicted to have a dramatic impact on AML outcomes.¹⁹ Improvements in CNS cancer survival are attributable to better diagnosis via enhanced imaging techniques, and advancements in neurosurgery and therapeutic radiation, in combination with conventional chemotherapy.²⁰ Advances have also been made in rare tumors.²¹

Observed increases can be attributed in large part to advances in therapeutic interventions developed by cooperative clinical trials groups, such as the Children's Oncology Group (COG).¹³ More than 200 COG institutions treat an estimated 71–94% of cancer patients aged 0–14 years in North America.^{14, 15} The Phase III randomized trials conducted by COG and other cooperative networks allows the safety and efficacy of novel therapeutic modalities to be investigated in reference to standard treatments on a larger scale than would otherwise be feasible. Oversight of these studies permits gatekeeping, such that successful therapies are retained and those deemed ineffective or harmful are abandoned, ultimately leading to better outcomes for affected patient populations.¹⁶

Differential survival was observed in infants compared to other age groups with respect to ALL, CNS tumors, neuroblastoma, Wilms' tumor, and hepatoblastoma; significant increases were detected in each of these, with the exception of CNS tumors. Factors impacting disease severity and prognosis are distributed differently in infants, including the higher prevalence of *MLL* rearrangements associated with reduced survival among infant leukemia cases¹⁷ and higher prevalence of hyperdiploidy, and lower prevalence of *MYCN* amplification, loss of heterozygosity at 1p, and trisomy of 17q associated with higher survival of infant neuroblastoma.¹⁸ Infants' tolerance of and sensitivity to therapeutic agents differs from that of older children, and infants are at increased risk for treatment-related morbidity and mortality.¹⁹ For example, infant ALL cases have demonstrated a poor response to conventional chemotherapeutic agents, leading to the investigation of alternate therapies, such as cytarabine and FLT-3 inhibitors.¹⁹ Further, there is a strong aversion to the use of radiation therapy in treating infant CNS tumors due to concerns about adverse neuropsychological effects.²⁰

Although adolescents aged 15–19 years experienced the greatest overall survival compared to their younger counterparts, they had notably lower 5-year rates for ALL, NHL, Ewing sarcoma, and rhabdomyosarcoma. Importantly, increases were observed in each of these cancers between 1975–1979 and 1995–1999, except for rhabdomyosarcoma. At least three factors contribute to lower adolescent rates. The principle factor is that adolescent malignancies differ from those in younger cases on important biological prognostic factors. For example, favorable attributes of ALL, such as hyperdiploidy and *TEL-AML1* translocations, occur primarily in children diagnosed at ages 1–9 years,³ while unfavorable characteristics, such as L2 morphology, pro-T-cell immunophenotype, and the *BCR-ABL* translocation, are more common among adolescents.²¹ For NHL, adolescents are more likely to be diagnosed with diffuse large B-cell lymphomas, including primary mediastinal B-cell lymphomas, and other rare histologies than younger cases,^{3,22} which have lower survival rates.²² Similarly, the proportion of cases with alveolar rhabdomyosarcoma, associated with poorer survival compared with embryonal rhabdomyosarcoma, is greater among adolescents.²³ Second, there is a delay in cancer detection among this group due to psychological, social and economic factors.²⁴ Third, adolescents with cancers commonly found in younger children have better outcomes when treated on pediatric therapeutic protocols;²⁴ however, a minority of adolescent patients have historically participated in pediatric or adult cooperative group trials, irrespective of race or ethnicity.^{15, 25} Initiatives are currently underway to address this inequity.²⁴

Sizable discrepancies in 5-year survival between males and females diagnosed in the 1970s largely disappeared by the 1990s, except possibly in astrocytoma, while sex differences in 10-year survival overall and for ALL, AML, PNET, osteosarcoma, Ewing sarcoma, rhabdomyosarcoma, and melanoma were observed in the 1985–1994 cohort. These 10-year rates should be monitored to ensure the gaps narrow.

Differences between white and black children/adolescents were noted overall and for ALL, CNS tumors (astrocytoma), and osteosarcoma. Disparities across racial groups must be interpreted with caution, since there were relatively few cases in black children/adolescents, particularly rare tumors. Racial and ethnic differences in survival may reflect differential access to healthcare along socio-economic boundaries; however, this assumption should be investigated further. The registration rates reported within COG are fairly consistent across white and black racial groups (58–59%).¹⁵ Nevertheless, several ALL studies have reported poorer outcomes for black children with standard risk and fewer studies showed evidence of poorer survival among Hispanics with high-risk characteristics.²⁶ With respect to other cancers, a single-center study reported no difference in 10-year survival rates for black versus white children overall and for most cancer types, with the exception of osteosarcoma, in the modern treatment era.²⁷ Other possible explanations for disparities include racial/ethnic differences in protocol adherence or drug metabolism,²⁶ delayed detection, or less favorable tumor characteristics.

There were significant differences in survival among Hispanic children/adolescents compared to non-Hispanic whites. The large disparity in Ewing sarcoma survival, while statistically significant, was based on few Hispanic cases; survival rates should be monitored to see whether this pattern continues. Greater leukemia incidence rates have been observed in Hispanics compared to non-Hispanic whites,²⁸ poorer survival for ALL has been reported among Hispanics with high-risk characteristics,²⁶ and a recent cytogenetics study of childhood ALL revealed fewer *TEL-AML1* translocations among Hispanic children.²⁹ This evidence suggests a different etiology, and perhaps severity, of leukemia. We speculate 5-year survival rates may be lower among Hispanic children/adolescents for astrocytomas and other gliomas due to a lag in access to improved diagnostic methods, such as magnetic resonance imaging and computerized topography technologies, analogous to the period before 1984 in other sects of the population.³⁰ Detection of melanomas among Hispanic children/adolescents may be delayed due to a lack of perceived susceptibility.³¹ Of note, Hispanic children/adolescents are registered with COG at a rate slightly below that of non-Hispanic white and black children/adolescents (54%).¹⁵ These results underscore a need for attention to this growing subset of the U.S. population.

The present analysis provides a comprehensive update of U.S. pediatric cancer survival statistics. The chief strength in utilizing SEER data is the high rate of case ascertainment from a large portion of the U.S. However, SEER is not a national registry, and important demographic and/or etiologic differences between the 9% and 14% of the population monitored by the SEER 9 and 13 registries, respectively, and the 91% and 86% not under surveillance could occur by chance.³² Follow-up for vital status on pediatric and adolescent patients is more difficult than for adult cancer patients, as children eventually leave their parents' homes and some change their names, resulting in ~14% lost to follow-up.³ SEER race classification has shown excellent agreement with self-report, however, SEER tends to slightly over-classify individuals as Hispanic.³³ Such misclassification may underestimate differences in survival between Hispanics and non-Hispanics. Further, molecular classification may be more informative for evaluating rates in rare subgroups (e.g., *MLL* rearrangements), yet this information is not available in SEER. Minor changes in classification³⁴ or detection may have influenced survival trends. Additionally, our trend analysis did not allow for joinpoints (i.e., points where the slope of the regression line

changes in magnitude or direction). Allowing joinpoints may reveal changes in trends, such as plateaus in rates in the 1990s that can be inferred from visual inspection of Figure 1. This is addressed in part by the comparison of rates between 1985–1989 and 1995–1999 shown in Table 1, wherein statistically significant differences were observed for the most prevalent cancers. Finally, minor random fluctuations may erroneously demonstrate noteworthy trends.

Our results confirm that survival rates for many pediatric and adolescent cancers have increased over time. Enhancements in survival have produced an expanding population of survivors at risk for adverse physical/psychosocial effects and in need of long-term care.³⁵ Future efforts should focus on therapeutic advances, elimination of disparities among minorities and adolescents, and care of survivors.

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Figure 1. Observed (data points) and expected (joinpoint regression lines) 5-year relative survival rates from SEER 9 registries for children and adolescents 0–19 years diagnosed in 1975–1999 with: A) leukemias; B) CNS tumors; C) neuroblastoma, Wilms tumor, rhabdomyosarcoma (RMS), and non-rhabdomyosarcoma soft tissue sarcomas (NRSTS); D) lymphomas, osteosarcoma, Ewing sarcoma, and germ cell tumors.

5-year relative survival rates of childhood and adolescent cancers in SEER 9 registries for diagnosis years 1975–1979, 1985–1989, and 1995–1999 and annual percent change (APC, 1975–1999).

Table 1

Cancer	1975–1979			1985–1989			1995–1999			1975–1999		
	N (%)	5-year Survival Rate (%) [*]	95% CI [†]	N (%)	5-year Survival Rate (%) [*]	95% CI [†]	N (%)	5-year Survival Rate (%) [*]	95% CI [†]	APC (95% CI)		
Total [‡]	4,908 (100.0%)	62.9	(61.6–64.3)	5,196 (100.0%)	72.8//	(71.6–74.0)	5,750 (100.0%)	79.3//¶	(78.2–80.3)	1.1 (1.0–1.2)		
Leukemias	1,136 (23.1%)	48.1	(45.2–51.0)	1,284 (24.7%)	66.2//	(63.6–68.8)	1,464 (25.5%)	76.1//¶	(73.9–78.4)	2.0 (1.6–2.4)		
Acute lymphoblastic leukemia (ALL)	784 (16.0%)	56.8	(53.3–60.3)	979 (18.8%)	74.9//	(72.2–77.6)	1,135 (19.7%)	83.8//¶	(81.7–86.0)	1.6 (1.2–2.0)		
Acute myeloid leukemia (AML)	210 (4.3%)	21.0	(15.4–26.5)	203 (3.9%)	36.0//	(29.3–42.7)	267 (4.6%)	44.8//	(38.8–50.8)	3.7 (2.6–4.9)		
Other/unspecified leukemias	142 (2.9%)	40.0	(31.8–48.1)	102 (2.0%)	41.7	(32.1–51.4)	62 (1.1%)	70.9//¶	(59.5–82.4)	§		
Hodgkin lymphoma	564 (11.5%)	87.0	(84.2–89.9)	466 (9.0%)	90.0	(87.3–92.8)	440 (7.7%)	96.0//¶	(94.1–97.9)	0.5 (0.4–0.7)		
Non-Hodgkin lymphoma	319 (6.5%)	46.9	(41.4–52.4)	328 (6.3%)	68.6//	(63.5–73.7)	371 (6.5%)	81.0//¶	(76.9–85.0)	2.1 (1.5–2.6)		
Central Nervous System (CNS) tumors	801 (16.3%)	58.6	(55.2–62.1)	962 (18.5%)	64.8//	(61.8–67.9)	1022 (17.8%)	74.4//¶	(71.7–77.1)	1.2 (0.9–1.5)		
Ependymoma	60 (1.2%)	36.4	(24.1–48.7)	88 (1.7%)	57.8//	(47.4–68.2)	88 (1.5%)	73.4//¶	(64.1–82.8)	3.1 (2.0–4.1)		
Astrocytoma	390 (7.9%)	68.8	(64.2–73.5)	495 (9.5%)	72.6	(68.7–76.6)	480 (8.3%)	85.4//¶	(82.2–88.6)	1.2 (0.9–1.5)		
Primitive neuroectodermal tumors (PNET)	152 (3.1%)	47.5	(39.5–55.5)	190 (3.7%)	54.5	(47.3–61.6)	256 (4.5%)	64.9//¶	(59.0–70.8)	1.2 (0.4–2.1)		
Other gliomas	168 (3.4%)	53.9	(46.3–61.5)	155 (3.0%)	58.7	(50.9–66.5)	174 (3.0%)	59.9	(52.6–67.2)	0.1 (–1.0–1.1)		
Other/unspecified CNS tumors	31 (0.6%)	54.1	(36.2–72.0)	34 (0.7%)	54.8	(37.7–71.8)	24 (0.4%)	64.6	(44.6–84.6)	§		
Neuroblastoma	242 (4.9%)	54.3	(48.0–60.7)	270 (5.2%)	58.2	(52.2–64.2)	297 (5.2%)	67.0//¶	(61.5–72.5)	1.4 (0.7–2.2)		
Retinoblastoma	88 (1.8%)	92.5	(86.8–98.2)	106 (2.0%)	92.0	(86.5–97.4)	111 (1.9%)	96.5	(92.8–100 ^{**})	§		
Wilms tumor	185 (3.8%)	75.0	(68.7–81.3)	207 (4.0%)	92.0//	(88.3–95.8)	223 (3.9%)	91.5//	(87.8–95.2)	0.5 (0.1–0.9)		
Hepatoblastoma	25 (0.5%)	44.3	(24.7–64.0)	38 (0.7%)	60.7	(45.0–76.4)	59 (1.0%)	60.3	(47.5–73.0)	§		
Osteosarcoma	137 (2.8%)	45.4	(37.0–53.8)	155 (3.0%)	62.8//	(55.2–70.5)	174 (3.0%)	65.1//	(58.0–72.2)	1.5 (0.6–2.5)		
Ewing sarcoma	94 (1.9%)	42.4	(32.4–52.5)	94 (1.8%)	57.3//	(47.2–67.4)	84 (1.5%)	66.8//	(56.7–76.9)	3.0 (1.6–4.4)		
Rhabdomyosarcoma	140 (2.9%)	49.2	(40.8–57.5)	157 (3.0%)	60.0//	(52.3–67.7)	167 (2.9%)	62.8//	(55.4–70.1)	0.7 (–0.3–1.7)		
Non-rhabdomyosarcoma soft tissue sarcomas	215 (4.4%)	76.1	(70.4–81.9)	206 (4.0%)	78.6	(72.9–84.3)	260 (4.5%)	78.7	(73.7–83.8)	0.1 (–0.3–0.5)		
Germ cell tumors	319 (6.5%)	71.8	(66.8–76.7)	332 (6.4%)	86.2//	(82.4–89.9)	378 (6.6%)	92.0//¶	(89.2–94.9)	0.9 (0.6–1.3)		

Cancer	1975–1979		1985–1989		1995–1999		1975–1999	
	N (%)	5-year Survival Rate (%) [*]	95% CI [†]	N (%)	5-year Survival Rate (%) [*]	95% CI [†]	N (%)	5-year Survival Rate (%) [*]
Thyroid carcinoma	174 (3.5%)	99.5	(98.3–100 ^{**})	169 (3.3%)	98.5	(96.5–100 ^{**})	203 (3.5%)	98.2
Melanoma	155 (3.2%)	82.8	(76.8–88.8)	162 (3.1%)	90.3	(85.6–95.0)	173 (3.0%)	93.3 ^{//}

^{*} 5-year relative survival rate calculated via actuarial method.

[†] 95% CI: 95% confidence interval

[‡] The frequencies and percentages in a column will not sum to those found in the “Total” row, as only the most common cancers are reported.

[§] The statistic could not be calculated.

^{//} Survival curve is significantly different from 1975–1979 curve (p<0.05).

[¶] Survival curve is significantly different from 1985–1989 curve (p<0.05).

^{**} Upper confidence level truncated at 100% and/or lower confidence level truncated at 0%.

Table 2

10-year relative survival rates of childhood and adolescent cancers in SEER 9 registries for diagnosis years 1975–1984 and 1985–1994.

Cancer	1975–1984			1985–1994		
	N (%)	10-year Survival Rate (%) [*]	95% CI [†]	N (%)	10-year Survival Rate (%) [*]	95% CI [†]
Total [‡]	9,817 (100.0%)	61.1	(60.2–62.1)	10,662 (100.0%)	71.8//	(70.9–72.7)
Leukemias	2,329 (23.7%)	45.7	(43.6–47.7)	2,616 (24.5%)	64.5//	(62.7–66.4)
ALL	1,671 (17.0%)	54.2	(51.8–56.6)	1,953 (18.3%)	73.1//	(71.1–75.1)
AML	404 (4.1%)	19.6	(15.7–23.5)	456 (4.3%)	37.3//	(32.9–41.8)
Other/unspecified leukemias	254 (2.6%)	30.5	(24.7–36.2)	207 (1.9%)	43.4//	(36.6–50.3)
Hodgkin lymphoma	1,051 (10.7%)	81.1	(78.6–83.5)	896 (8.4%)	89.0//	(86.8–91.1)
Non-Hodgkin lymphoma	649 (6.6%)	52.8	(48.9–56.7)	674 (6.3%)	71.4//	(67.9–74.9)
CNS tumors	1,553 (15.8%)	54.7	(52.2–57.2)	2,006 (18.8%)	63.4//	(61.2–65.5)
Ependymoma	113 (1.2%)	32.5	(23.7–41.2)	162 (1.5%)	49.1//	(41.3–56.9)
Astrocytoma	781 (8.0%)	64.8	(61.4–68.2)	1,032 (9.7%)	74.3//	(71.6–77.1)
PNET	302 (3.1%)	46.3	(40.6–51.9)	407 (3.8%)	51.6	(46.7–56.5)
Other gliomas	296 (3.0%)	47.0	(41.3–52.8)	345 (3.2%)	54.4	(49.1–59.7)
Other/unspecified CNS tumors	61 (0.6%)	45.6	(32.9–58.3)	60 (0.6%)	46.1	(33.3–58.8)
Neuroblastoma	500 (5.1%)	51.7	(47.2–56.1)	570 (5.3%)	62.8//	(58.8–66.9)
Retinoblastoma	184 (1.9%)	91.9	(87.7–96.1)	243 (2.3%)	92.9	(89.5–96.4)
Wilms tumor	400 (4.1%)	79.9	(75.9–83.9)	440 (4.1%)	91.2//	(88.5–93.9)
Hepatoblastoma	56 (0.6%)	48.3	(35.1–61.6)	85 (0.8%)	61.3	(50.9–71.8)
Osteosarcoma	292 (3.0%)	45.1	(39.3–50.9)	313 (2.9%)	59.3//	(53.8–64.9)
Ewing sarcoma	214 (2.2%)	39.4	(32.8–46.1)	198 (1.9%)	51.2//	(44.1–58.2)
Rhabdomyosarcoma	276 (2.8%)	53.8	(47.8–59.7)	317 (3.0%)	64.5//	(59.2–69.8)
Non-rhabdomyosarcoma soft tissue sarcomas	434 (4.4%)	73.7	(69.4–77.9)	401 (3.8%)	73.0	(68.6–77.5)
Germ cell tumors	671 (6.8%)	75.9	(72.6–79.3)	696 (6.5%)	85.2//	(82.5–88.0)
Thyroid carcinoma	344 (3.5%)	98.3	(96.7–99.9)	328 (3.1%)	98.6	(97.2–100 ^{***})
Melanoma	283 (2.9%)	81.6	(76.9–86.3)	330 (3.1%)	90.0//	(86.6–93.4)

† The frequencies and percentages in a column will not sum to those found in the "Total" row, as only the most common cancers are reported.

‡ The statistic could not be calculated.

§ Survival curve is significantly different from 1975–1984 curve ($p < 0.05$).

** Upper confidence level truncated at 100% and/or lower confidence level truncated at 0%.

Table 3

5-year relative survival rates of cancer among Hispanic children and adolescents in SEER 13 registries in 1995–1999.

Cancer	N (%)	5-year Survival Rate (%) [*]	95% CI [†]
Total [‡]	1,999 (100.0%)	73.9 [§]	(72.0–75.9)
Leukemias	736 (36.8%)	70.5 [§]	(67.2–73.8)
ALL	597 (29.9%)	77.2 [§]	(73.8–80.6)
AML	110 (5.5%)	38.2	(29.0–47.3)
Other/unspecified leukemias	29 (1.5%)	55.3	(37.1–73.4)
Hodgkin lymphoma	127 (6.4%)	94.6	(90.5–98.6)
Non-Hodgkin lymphoma	104 (5.2%)	79.6	(71.8–87.5)
CNS tumors	291 (14.6%)	65.9 [§]	(60.4–71.5)
Ependymoma	19 (1.0%)	71.4	(50.0–92.8)
Astrocytoma	122 (6.1%)	75.4 [§]	(67.7–83.1)
PNET	87 (4.4%)	67.7	(57.8–77.6)
Other gliomas	49 (2.5%)	42.9 [§]	(29.0–56.8)
Other/unspecified CNS tumors	14 (0.7%)	46.6	(19.4–73.8)
Neuroblastoma	76 (3.8%)	69.0	(58.3–79.6)
Retinoblastoma	48 (2.4%)	98.0	(93.9–100//)
Wilms tumor	74 (3.7%)	90.4	(83.6–97.3)
Hepatoblastoma	18 (0.9%)	61.3	(38.7–83.9)
Osteosarcoma	51 (2.6%)	57.0	(43.3–70.6)
Ewing sarcoma	20 (1.0%)	27.0 [§]	(6.9–47.1)
Rhabdomyosarcoma	44 (2.2%)	51.3	(36.3–66.2)
Non-rhabdomyosarcoma soft tissue sarcomas	77 (3.9%)	72.7	(62.6–82.7)
Germ cell tumors	160 (8.0%)	88.8	(83.8–93.9)
Thyroid carcinoma	59 (3.0%)	98.3	(95.0–100//)
Melanoma	13 (0.7%)	76.9 [§]	(54.0–99.9)

^{*} 5-year relative survival rate calculated via actuarial method.

[†] 95% CI: 95% confidence interval

[‡] The frequencies and percentages in a column will not sum to those found in the “Total” row, as only the most common cancers are reported.

[§] Survival curve is significantly different from curve in non-Hispanic whites ($p < 0.05$). No significant differences were observed compared to rates in non-Hispanic black children and adolescents.

// Upper confidence level truncated at 100%.