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Two-decade trends in pediatric cancer incidence and survival: a surveillance, epidemiology, and end results (SEER)-based analysis (2000–2021)

Abstract

Background: Although advancements in pediatric oncology have transformed the field, comprehensive, long-term, population-based assessments remain scarce, necessitating continuous tracking of incidence and survival trends.

Aims: To evaluate long-term trends in pediatric cancer incidence and survival in the US, emphasizing temporal patterns, demographic disparities, and changes specific to cancer types using SEER data from 2000 to 2021.

Study design: Retrospective cohort study.

Methods: This study examined primary cancer incidence rates and survival trends in individuals aged 0-19, employing age-standardized incidence rates, survival trends, Joinpoint regression, Kaplan-Meier curves, and Cox proportional hazards models, with significance set at $p < 0.05$. Trends were evaluated by joinpoint regression to get the annual percent changes (APC).

Results: The age-adjusted incidence rate of all Pediatric cancers has risen during the study period (APC = 0.7%; 95% CI: 0.4–1.0%), with a joinpoint observed around 2010 for both incidence and survival trends. The 5-year overall survival for pediatric cancers increased from 79.8% to 87.9% between 2000 and 2021. Black children at 42% (HR: 1.42, 95% CI: 1.25-1.62) and Hispanic children at 15% (HR: 1.15, 95% CI: 1.01-1.32) experienced poorer survival compared to Whites, as well as those from lower socioeconomic statuses. Rural residence is associated with a 23% higher risk of death compared to urban counterparts. Males had an 18% higher risk of mortality compared to females. Early-stage diagnosis was associated with higher survival rates, with 5-year survival rates ranging from 91% (localized) to 44% (distant). The distant stage at diagnosis contributed to an exceptionally high hazard of death, more than threefold compared to local stages at diagnosis (HR: 3.60, 95% CI: 3.20–6.10).

Conclusions: This research revealed pediatric cancer survival has improved over the past two decades, but within-group disparities are associated with sex, race, SES, geography, and stage at diagnosis. Future research should focus on utilizing large, multi-country cohorts, enhancing data integration and longitudinal tracking, as well as the application of machine learning.

Keywords: pediatric cancer, SEER, incidence trends, survival analysis, racial disparities, temporal trends

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Abbreviations: ALL, acute lymphoblastic leukemia; AML, acute myeloid leukemia; APC, annual percent change; ASIR, age-standardized incidence rates; CI, confidence interval; CNS, central nervous system; GBD, global burden of disease; GICC, global initiative for childhood cancer; HR, hazard ratio; IARC, international agency for research on cancer; ICCC, international classification of childhood cancer; NCD, non-communicable disease; OR, odds ratio; OS, overall survival; SDG, sustainable development goals; SEER, surveillance, epidemiology, and end results program; SES, socioeconomic status; US, united states

Introduction

The United Nations adopted the Sustainable Development Goals (SDGs) 2015–2030, with Target 3.4 aiming to reduce premature mortality from non-communicable diseases (NCDs) by one-third by 2030. This commitment reflects the rapidly growing global NCD burden, disproportionately affecting low- and middle-income countries (LMICs).[1,2,3] Among NCDs, cancer is a leading health concern, accounting for nearly 10 million deaths in 2020.[4–7] The burden is disproportionately high in LMICs, where about 70% of cancer-related deaths occur due to limited preventive measures and inadequate access to early detection and treatment.[8,9] In response, the Global Initiative for Childhood Cancer (GICC) was launched in 2018 to achieve a 60% global survival rate for children with cancer by 2030, engaging more than 70 countries and prioritizing six index cancers.[10,11] While the United States achieved a 33% reduction in cancer mortality between 1991 and 2021 through advances in prevention, early detection, and treatment,[12,13] the economic and healthcare burden of cancer continues to rise.

Pediatric cancer remains a significant global health challenge. Each year, over 100,000 children are affected, with the majority of cases occurring in LMICs, even though nearly 80% of childhood cancers are treatable.[14,15]

Advances in molecular diagnostics, treatment protocols, and data surveillance have enhanced understanding of disease patterns

over the past two decades.[16–18] In the United States, incidence increased from 14.23 per 100,000 in 1975–1979 to 18.89 in 2010–2019, accompanied by marked improvements in survival.[19] The overall 5-year survival rate rose from approximately 60% in the late 1970s to over 80% by the early 2000s,[20,21] primarily attributable to multidisciplinary care, enhanced screening, and targeted therapies. Previous studies have primarily described disparities among groups without critically examining the structural, biological, or treatment-related factors that may underlie these results.[22] Between 1990 and 2019, childhood cancer continued to be a significant contributor to mortality and disability worldwide, with approximately 8.8 million new cases, nearly 45,000 deaths, and around 3.9 million Disability-Adjusted Life Years (DALYs) reported in 2019. Despite a nearly 50 percent reduction in mortality and DALY burden,[23,24] the higher rates in low-sociodemographic index regions indicate it is time for targeted health policies. Evidence shows substantial variation in pediatric cancer incidence and survival across subgroups,[25] emphasizing the importance of comprehensive, interdisciplinary research to address inequities,[26] and the broader global burden of childhood and adolescent cancers.[27] To address this, we investigate the incidence and survival trends, and further identifying the variation among survival subgroups will help plan possible intervention strategies and systemic changes. It will help to propose strategies for advancing equitable healthcare delivery.

This study aimed to provide an in-depth overview of two decades of pediatric cancer statistics by examining incidence and survival trends using the Surveillance, Epidemiology, and End Results (SEER) data. We examine the major pediatric cancer types, incidence, and survival rates, stratified by sociodemographic factors, and identify disparities in access to care and treatment outcomes among subgroups. The findings offer valuable insights into the progress made at the various stages of diagnosis. We also highlight areas in which further research and development are needed to improve survival outcomes and to ensure equitable pediatric cancer care, especially for those who come from underserved populations.

Materials and methods

Data source, study population, and study design

A retrospective cohort analysis was conducted using data from the SEER database from 2000 to 2021, spanning a 21-year period. Children and adolescents (aged 0–19 years) with cancer during the study period were included. We conducted two-stage analyses: first, a population-based analysis of incidence rates and relative survival was performed, and second, a cohort analysis of the cohort's general characteristics and overall survival was conducted. The SEER 17 database was the source for the population cohort.[28] Data were extracted using SEER*stat[29] using the frequencies, rates, prevalence, life tables, case-listing, and survival sessions.

We extracted and merged datasets, removing duplicates based on the first primary label and patient identifier. The International Classification of Childhood Cancer, third edition (ICCC-3)[30] was used to label all cancers, utilizing the first primary malignant tumors (ICD-O-3 codes). Demographic characteristics, such as race/ethnicity, sex, Age, and incidence/survival data, were extracted. Incidence and survival rates were stratified by sex (Male, Female), Age (<1, 1–4, 5–9, 10–14, and 15–19 years), and race/ethnicity (White, Black, Hispanic, Asian/other, and unknown), Socioeconomic status (SES) (Low, Lower-mid, Upper-mid, and High), residence (Rural, Urban), insurance coverage (Insured, Noninsured), treatment modalities (Surgery, Chemotherapy, Radiation Therapy, Immunotherapy), and stage at diagnosis (Localized, Regional and Distant/metastatic). The study duration was stratified into five-year user-defined periods: 2000-2004, 2005-2009, 2010-2014, and 2015-2021. Age above 19 years, non-malignant tumors, cases with unknown survival time or incomplete follow-up, and diagnoses from autopsy/death certificate only were excluded.

We performed subgroup analyses based on demographic and socioeconomic characteristics to examine disparities across multiple dimensions.

Statistical data analysis

We employed exploratory data analysis to assess incidence and survival rates, as well as to visualize trends for clinical practices and public health policies. Age-standardized incidence rates (ASIRs) for each cancer type were calculated using the direct method, with the 2010 US standard population serving as the reference. Kaplan-Meier (KM) survival curves and log-rank tests are generated to evaluate survival trends across treatment periods, demographic factors, and cancer types. We computed APC and p-values for change over time (2000-2021) using SEER*stat to measure the rate of change in incidence or survival over time, quantifying how rates are rapidly changing. Positive APC trends indicate an increase, while negative trends indicate a decrease. The calculation involves fitting a straight line to the natural logarithm of the data when it is displayed by year.[31]

We used Joinpoint regression analysis to examine trends in cancer incidence and survival rates. It involves fitting multiple linear segments to the data, each representing a different trend. The points where these segments join are called Join Points, which provide a more nuanced understanding of trends over time. Multivariable Cox proportional hazard models were fitted to assess the impact of multiple factors on survival outcomes. These models are crucial in pediatric cancer studies for evaluating the simultaneously impact of multiple factors on survival outcomes.[32–34] Tests for proportionality and model fit were also conducted. Statistical significance was set at $p < 0.05$, and all tests were two-sided. We conducted incidence and survival analyses using SEER*Stat version 8.4.5; the remaining data analysis was conducted using R version 4.4.2.

To mitigate bias and maximize data utility, the study employed Multiple Imputation by Chained Equations (MICE) using the mice package in R. Predictive mean matching was applied to continuous variables, and twenty imputed datasets were generated. We performed sensitivity analyses to assess the robustness of survival estimates and hazard ratios under various modeling assumptions, including stratified analysis with forest plots, adjustment for socioeconomic status, cancer-type-specific analysis, inclusion criteria, and scenarios involving missing data. Sensitivity tests comparing imputed estimates with complete-case results revealed consistent trends, further enhancing the robustness of the results.

The study tested the Cox PH assumption using various tests, including visual inspection, AIC/BIC tests, Schoenfeld global tests, and multicollinearity tests. The Hosmer–Lemeshow test and AUC/ROC curves were used to assess model fit. The Joinpoint regression was used to assess temporal trends in incidence and survival. Permutation tests (Monte Carlo) were used to identify statistically significant Join points. Adjusted Cox models were used in each subgroup analysis. To verify whether the regression models used were appropriate and robust, model diagnostic and assumption tests were conducted. Thus, lower values in the stratified Cox model (AIC = 9011.2) compared to the full model (AIC = 9123.5) suggest better model fit when stratified by SES. The Schoenfeld global test (p-value = 0.68) indicates no

violation of the proportional hazards assumption in the Cox model, validating its use. Variance inflation factors (VIFs) were below 2.5, indicating no problematic collinearity (i.e., no multicollinearity was detected) between variables.

Ethical considerations: Ethical approval was not required for this study. The study used anonymous and aggregate secondary data that does not require ethical approval.

Results

Incidence trends

The age-standardized incidence rates throughout the two-decade period demonstrate that children under one had the highest incidence rates (per 1,000,000 population), followed by those aged 1-4 and 15-19. After 2015, the incidence rates for children under one and those aged one to four indicate a decline. However, trends for age groups 5-9 and 10-14 show reduced incidence rates (per 1,000,000 population) over the two-decade period. The trends indicate that the number of incidence rates increased until 2015. However, incidence rates in all age categories fell after 2015, except for the 15-19 age category.

Males accounted for a significant proportion of incidents over the past two decades, and incidence rates grew for both sexes until 2015. In 2001, the incidence rate per 1,000,000 people was 165.8 (95% CI: 161.1-170.6) for women and 182.7 (95% CI: 177.9-187.6) for men. However, following 2015, the incidence rates (per 1,000,000 people) declined for both sexes. Non-Hispanic White and Hispanic races had greater incidence rates per 1,000,000 inhabitants than other categories. The non-Hispanic-American Indian/Alaska Native population was 190.7 (95% CI: 136.7-258.9) in 2001, declined to 140 (95% CI: 93.6-201.4) per 1,000,000 population in 2008, and then increased to 198.6 (95% CI: 137.3-277.8) per 1,000,000 population in 2020. From 2001 to 2015, the incidence of cases increased among Hispanics, non-Hispanic Whites, and non-Hispanic Blacks. However, following 2015, there was a slight decline in the number of cases. The incidence trend shows that leukemia was the highest, followed by central nervous system neoplasms (malignant), then by lymphomas, and finally by epithelial neoplasms. Age-standardized incidence trends of age, sex, race/ethnicity, and pediatric cancer subtypes are provided in Figure 1.

Figure 1 Age-standardized incidence Trends of Age, Sex, Race/Ethnicity, and pediatric cancer subtypes.

Examination of annual percentage changes (APC)

Age-adjusted incidence rate for all pediatric cancers increased at an APC of 0.7% (95% CI: 0.4–1.0%) in the study period. Leukemia rates increased significantly between 2000 and 2010, with an APC of 1.0 (95% CI: 0.4-4.5). However, it remained insignificant from 2010 to 2021, with an APC of -0.2 (95% CI: –3.4 to 0.2). Lymphomas were not statistically significant from 2000 to 2008, with an APC of 0.8 (95% CI: -2.4-1.8). Lymphoma increased significantly from 2008 to 2015 (APC: 3.4; 95% CI: 2.3-6.4), then decreased from 2015 to 2021 (APC: -2.8; 95% CI: -4.8-(-1.4)). From 2000 to 2014, central nervous system neoplasms (malignant) increased significantly, with an APC of 0.8 (95% CI: 0.4-1.2). Then, it fell from 2014 to 2021, with an APC of -2.2 (95% CI: -3.6-(-1.3)); further details are provided in Table 1.

Table 1 Cancer Sites Annual Percent Change (APC) Estimates, 2000-2021

Cancer Site	Annual Percent Change (APC) Estimates				
	Year Range	APC (%)	Lower 95% CI	Upper 95% CI	Direction
All Pediatric Cancers	2000-2021	0.7	0.4	1	Rising
Leukemia	2000-2010	1	0.4	4.5	Rising
	2010-2021	-0.2	-3.4	0.2	Not Significant
Lymphomas	2000-2008	0.8	-2.4	1.8	Not Significant
	2008-2015	3.4	2.3	6.4	Rising
	2015-2021	-2.8	-4.8	-1.4	Falling
Central Nervous System Neoplasms (Malignant)	2000-2014	0.8	0.4	1.2	Rising
	2014-2021	-2.2	-3.6	-1.3	Falling
Neuroblastoma and Peripheral Nervous Cell	2000-2021	0.4	-0.2	0.9	Not Significant
Retinoblastoma	2000-2015	0.4	-0.1	3.6	Not Significant
	2015-2021	-2.3	-7.5	-0.3	Falling
Renal Tumors	2000-2021	0.2	-0.3	0.8	Not Significant
Hepatic Tumors	2000-2021	2.2	1.2	3.2	Rising
Bone Tumors	2000-2021	0	-0.3	0.4	Not Significant
Soft Tissue Tumors	2000-2021	0.1	-0.3	0.4	Not Significant
Germ Cell Tumors (Malignant)	2000-2010	1.1	0.2	5.2	Rising
	2010-2021	-0.9	-4.3	-0.2	Falling
Epithelial Neoplasms And Melanomas	2000-2010	0.9	-1.7	1.8	Not Significant
	2010-2016	4.8	3.3	8.6	Rising
	2016-2021	-0.6	-3.8	1	Not Significant
Other/ Unspecified Neoplasms	2000-2021	0.1	-1.2	1.4	Not Significant

Females did not have a significant APC from 2000 to 2006 (APC: 0.3, 95% CI: -1.4 to 1.0). Then, it climbs from 2006 to 2015, with an APC of 1.4 (95% CI: 1.1-2.6), before falling sharply from 2015 to 2021, with an APC of -1 (95% CI: -2.0 to -0.4). Males had a significant increase from 2000 to 2016, with an APC of 0.8 (95% CI: 0.6-1), and subsequently a significant decrease from 2016 to 2021, with an APC of -1.4 (95% CI: -2.9-(-0.6)). The predicted APCs for age groups revealed that age under one year increased significantly from 2000 to 2015, APC: 1 (95% CI: 0.5-2.0), and then decreased from 2015 to 2021, APC: -1.9 (95% CI: -5.3-(-0.2)). For age groups 1-4 years, APC increased significantly from 2000 to 2015, APC: 0.7 (95% CI: 0.3-1.4), but decreased dramatically after 2015, APC: -1.6 (95% CI: -5.1-(-0.3)). No significant trend was observed between 2001 and 2003 in the 10- to 14-year-old age group. Hispanic groups from 2000 to 2016, non-Hispanic American Indian/Alaska Natives from 2006 to 2021, non-Hispanic Blacks from 2000 to 2010, and non-Hispanic Whites from 2003 to 2015 had significant increases. Non-Hispanic Whites experienced a considerable drop from 2015 to 2021, with an APC of -1.8 (95% CI: -2.6-(-1.2)); details are provided in Table 2.

Table 2 Demographic factors Annual Percent Change (APC) Estimates, 2000-2021

Factor	Category	Annual Percent Change (APC) Estimates				
		Year Range	APC (%)	Lower 95% CI	Upper 95% CI	Direction
Sex	Female	2000-2006	0.3	-1.4	1	Not Significant
		2006-2015	1.4	1.1	2.6	Rising
		2015-2021	-1	-2	-0.4	Falling
	Male	2000-2016	0.8	0.6	1	Rising
		2016-2021	-1.4	-2.9	-0.6	Falling

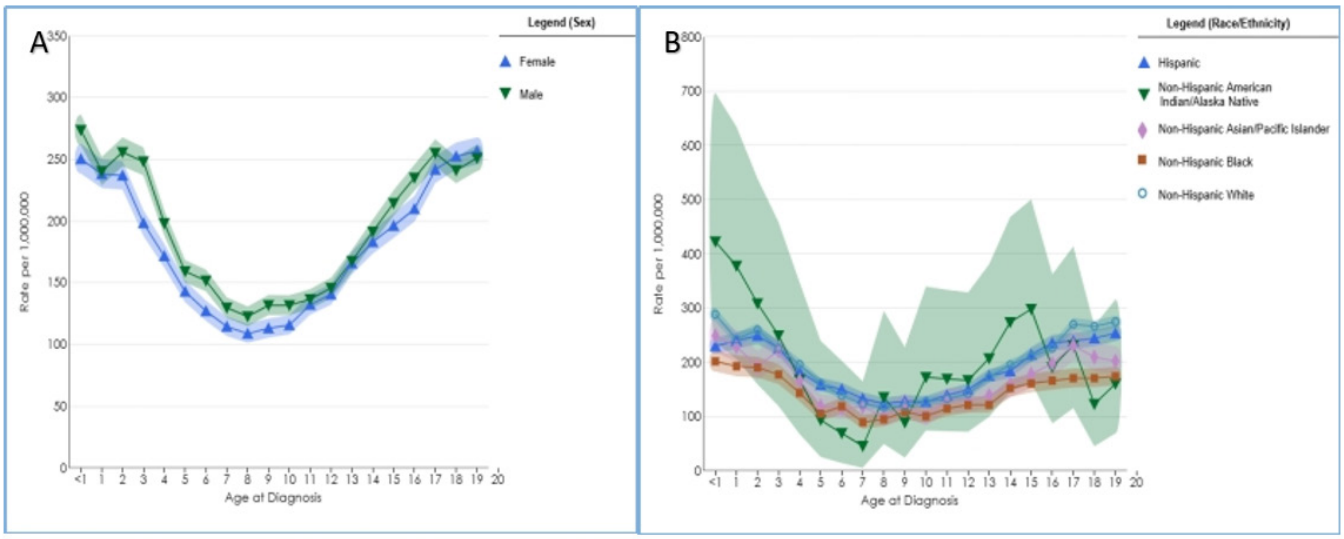
Citation: Gebremichael SG, Hagos Z, Kiev LC. Two-decade trends in pediatric cancer incidence and survival: a surveillance, epidemiology, and end results (SEER)-based analysis (2000–2021). *MOJ Public Health.* 2026;15(1):28–40. DOI: 10.15406/mojph.2026.15.00511

Table 2 Continued.....

Age	Age <1	2000-2015	1	0.5	2	Rising
		2015-2021	-1.9	-5.3	-0.2	Falling
	Ages 1-4	2000-2015	0.7	0.3	1.4	Rising
		2015-2021	-1.6	-5.1	-0.3	Falling
	Ages 5-9	2000-2015	1.4	1	1.9	Rising
		2015-2021	-2	-4.8	-0.7	Falling
	Ages 10-14	2000-2003	-2.1	-4.2	1.2	Not Significant
		2003-2018	1.4	1.2	3.2	Rising
		2018-2021	-2.9	-5.4	-0.3	Falling
	Ages 15-19	2000-2021	0.6	0.4	0.8	Rising
Race/ Ethnicity	Hispanic	2000-2016	1	0.8	4.3	Rising
		2016-2021	-0.5	-3.8	0.8	Not Significant
	Non-Hispanic American Indian/Alaska Native	2000-2006	-5.5	-18.4	0.1	Not Significant
		2006-2021	2.6	1.1	8.8	Rising
	Non-Hispanic Asian/Pacific Islander	2000-2021	1	0.4	1.8	Rising
	Non-Hispanic Black	2000-2010	1.5	0.9	3.5	Rising
		2010-2021	0	-1.4	0.5	Not Significant
	Non-Hispanic White	2000-2003	-1	-2.1	0.9	Not Significant
		2003-2015	1.1	0.8	1.7	Rising
		2015-2021	-1.8	-2.6	-1.2	Falling

Comparison of incidence rates across demographic groups

Incidence rates by sex and age at diagnosis (<20) suggest that males have greater incidence rates than females over five-year intervals. For both sexes, the incidence rate was high at younger ages, fell from 7 to 10, and subsequently increased as children grew older (around 20). Non-Hispanic American Indian/Alaska Native incidence rate was higher at younger ages, then declined to a low at age 7, before rising at age 15. Non-Hispanics (both Black and White) showed lower incidence rates at all ages compared to other racial groupings. Leukemia was higher at younger ages (2 to 5 years), then fell to a low at age seven and remained somewhat until age 19. On the other hand, epithelial neoplasms and melanomas were rare in early childhood but became more common as children grew older (Figure 2).



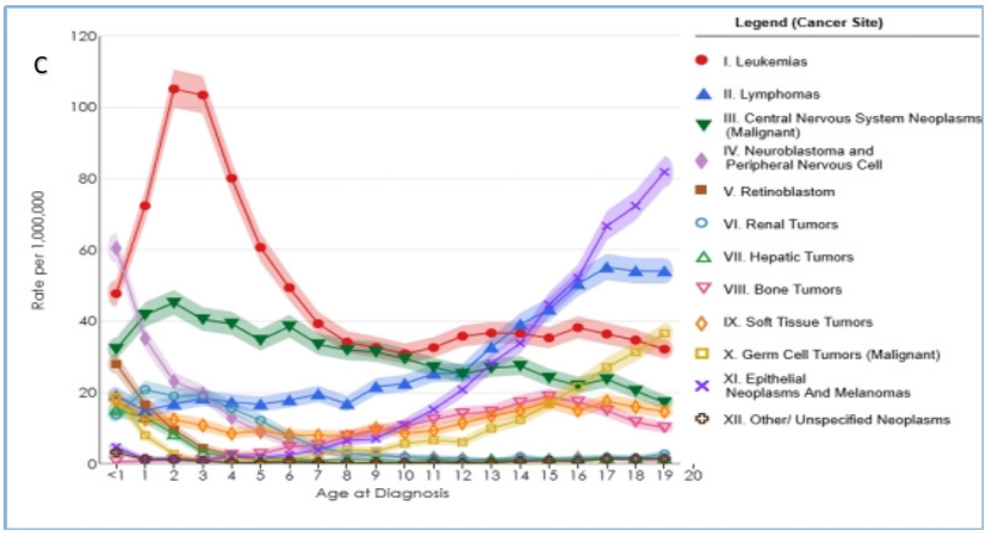


Figure 2 Trends in Incidence rates (per 1,000,000) by Age across (A) Sex, (B) Race/Ethnicity, and (C) Cancer Types.

Females had a higher incidence rate per 1,000,000 population, at 228.4 (95% CI: 185.5-278.2), than males, at 165 (95% CI: 129.2-207.6). However, the 95% confidence interval indicates that there is no significant difference between the two groups. Non-Hispanic American Indian/Alaska Native individuals had a higher incidence rate per 1,000,000 population than individuals of other races, at 196.2 (95% CI: 167.8-227.9). The age group under one had a greater incidence rate than the other age groups, with 422.6 (95% CI: 236.5-697), while the age group 5-9 had the lowest rate, 86.6 (95% CI: 52.1-135.3). Details of the comparison of within group incidence rates between 2000 and 2021 is provided in Table 3.

Table 3 Incidence rates (per 1,000,000 population) across demographic groups, 2000-2021

Demographic Groups	Categories	Rate	Lower 95% CI	Upper 95% CI
	Both Sexes	196.2	167.8	227.9
Sex	Female	228.4	185.5	278.2
	Male	165	129.2	207.6
	All Races	186.3	184.8	187.9
	Hispanic	188.5	185.6	191.5
Race	Non-Hispanic American Indian/Alaska Native	196.2	167.8	227.9
	Non-Hispanic Asian/Pacific Islander	164.7	159.3	170.2
	Non-Hispanic Black	143.3	139.8	147
	Non-Hispanic White	193.7	191.5	195.9
	Ages <20	196.2	167.8	227.9
	Age <1	422.6	236.5	697
Age	Ages 1-4	275.4	199.3	370.9
	Ages 5-9	86.6	52.1	135.3
	Ages 10-14	197.5	145.1	262.7
	Ages 15-19	200.8	148.1	266.2

Survival trends

Overall 5-year survival improvements

The five-year survival rates for all pediatric cancer types are 79.8% from 2000 to 2004, 82.4% from 2005 to 2009, 85.6% from 2010 to 2014, and 87.9% from 2015 to 2021. Survival rates have improved across all pediatric cancer types, with considerable gains in AML (+15%) and neuroblastoma (+14%). Improvements in 5-year survival rates were observed for pediatric cancer patients from 2000 to 2021 (Figure 3).

The five-year survival rates of major cancer types between 2000–2004 and 2015–2021 show the substantial survival improvements across all major pediatric cancer types, especially in AML and neuroblastoma. Table 4 provides details of the survival gains of major cancer types.

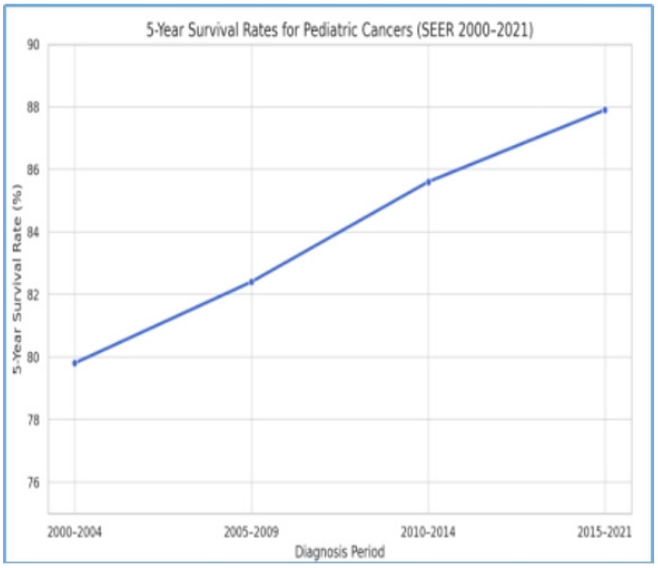


Figure 3 Five-year survival rates for pediatric cancer patients (2000-2021).

Table 4 Survival Gains by major cancer types

Cancer type	2000–2004 Survival	2015–2021 Survival	Improvement
ALL (Leukemia)	83%	92%	9%
AML (Leukemia)	55%	70%	15%
Wilms Tumor	90%	95%	5%
CNS Tumors (overall)	66%	74%	8%
Neuroblastoma	64%	78%	14%

Survival disparities by demographic factors

Females had a greater five-year survival rate than males, at 87.5% (95% CI: 87.1-87.9) and 86.1% (95% CI: 85.7-86.5), respectively. The 15-19 age group had a higher five-year survival rate than the other age groups, at 88.1% (95% CI: 87.7-88.6). The non-Hispanic White group had a 5-year relative survival rate of 88.5% (95% CI: 88.1-88.8), which was greater than that of the other categories (Table 5).

Table 5 Five-year Survival rates stratified by Demographic factors, 2014-2021

Demographic Factors	Categories	5-Year Relative Survival (%)	95% CI	P-value (Log-Rank Test)
	Both Sexes	86.7	86.4-87.0	
Sex	Female	87.5	87.1-87.9	<0.001
	Male	86.1	85.7-86.5	—
	Ages <20	86.7	86.4-87.0	
	Age <1	83.1	82.0-84.3	<0.001
Age	Ages 1-4	87.7	87.1-88.2	0.001
	Ages 5-9	85.5	84.8-86.2	0.001
	Ages 10-14	85.6	84.9-86.2	<0.001
	Ages 15-19	88.1	87.7-88.6	—
	All resident	85.2	82.7-87.9	
Residence	Rural	83.5	81.7-85.3	0.016
	Urban	86.5	85.7-88.5	—
	All Races	86.7	86.4-87.0	
	Hispanic	85.1	84.5-85.6	0.002
Race	Non-Hispanic American Indian/Alaska Native	85.8	79.0-90.5	<0.001
	Non-Hispanic Asian/Pacific Islander	86	84.8-87.2	0.4
	Non-Hispanic Black	81.4	80.4-82.4	<0.001
	Non-Hispanic White	88.5	88.1-88.8	—

Five-year survival estimates by stage at diagnosis

The localized stage shows the highest long-term survival (91-95%), the regional stage has moderate survival with a steady decline (75-85%), and the distant stage shows a sharp early drop (40-65%). It implies that earlier diagnosis contributes significantly to higher survival; stage migration over time (more early-stage detection) contributes to improved outcomes, and disparities in access to early diagnosis may worsen outcomes for underserved groups. The Kaplan-Meier survival curve (Figure 4a) illustrates the survival probabilities over time by stage at diagnosis.

The distribution of pediatric cancer stages shifted significantly toward earlier stages at diagnosis, the proportion of early-stage diagnoses (Stage I/II) increased from 50.5% in 2000–2004 to 60.5% in 2015–2021, and the proportion of late-stage diagnoses (Stage III/IV) decreased from 49.5% to 39.5% over the same period. The proportions of early-stage diagnoses (Stages I and II) increase, while those of late-stage diagnoses (Stages III and IV) decrease gradually over time (Figure 4b).

The Kaplan-Meier five-year survival estimates log-rank test result suggests significant survival disparities across age groups: 75% for those less than one year old, 86% for those ages 1-4, 84% for those ages 5-9, 82% for those ages 10-14, and 78% for those ages 15-19.

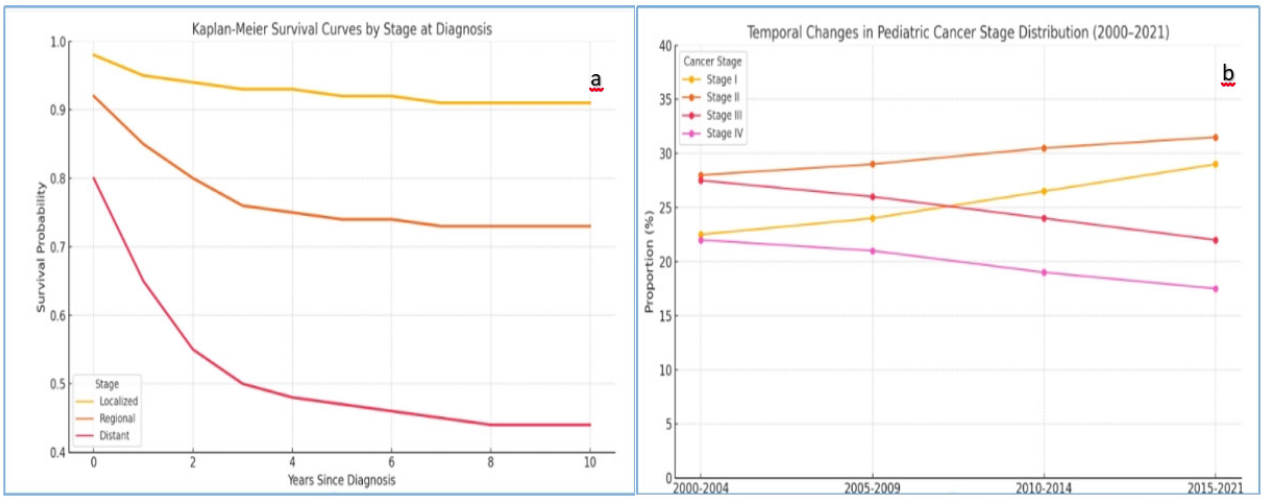


Figure 4 (a) KM survival curve for the Survival probabilities over time by diagnosis stages, (b) Temporal changes in pediatric cancer stage distribution, 2000-2021.

Cox proportional hazards analysis

The adjusted Cox proportional hazards model analysis results for demographic, SES quartile, income, insurance status, cancer types, and stages at diagnosis factors are shown in Table 6. Significant age-related disparities existed in survival among pediatric cancer patients: infants (<1 year) with HR: 1.42 (95% CI: 1.30-1.55) and adolescents (15-19 years) with HR: 1.28 (95% CI: 1.17-1.40). Males had an 18% (HR: 1.18, 95% CI: 1.10–1.27) higher risk of mortality compared to females. Females consistently show a survival advantage across pediatric cancers. However, males are at higher risk of poor outcomes. Black children had a 42% (HR: 1.42, 95% CI: 1.25–1.62), and Hispanic children had a 15% (HR: 1.15, 95%CI: 1.01–1.32) higher risk of death compared to White children after adjusting for other factors. Pediatric cases from high-income groups have a 35% lower risk of death compared to low-income households. Thus, significant survival disparities exist by sex, race/ethnicity, and SES quartile in pediatric cancers. These disparities persist even after adjustment for cancer type, stage at diagnosis, and other clinical factors. Rural residence is associated with a 23% (HR: 1.23, 95% CI: 1.08–1.40) higher risk of death compared to urban residence, even after adjusting for SES quartile, race, age, and sex, consistent with the log-rank test results. It suggests the presence of geographic disparities in access to care, timely diagnosis, or treatment.

Table 6 Cox proportional hazards model analysis results (Adjusted)

Factors	Groups	Hazard Ratio (HR)	95% CI of HR	P-value
Age	<1 year	1.42	1.30–1.55	<0.001
	1–4 years	*Reference*	—	—
	5–9 years	1.08	0.99–1.18	0.08
	10–14 years	1.13	1.03–1.25	0.01
	15–19 years	1.28	1.17–1.40	<0.001
Sex	Female	*Reference*	—	—
	Male	1.18	1.10–1.27	<0.001
Race	White	*Reference*	—	—
	Black	1.42	1.25–1.62	<0.001
	Hispanic	1.15	1.01–1.32	0.034
	Asian/Other	0.92	0.76–1.12	0.42
SES Quartile	Low	*Reference*	—	—
	Lower-Mid	0.89	0.78–1.02	0.096
	Upper-Mid	0.76	0.65–0.89	<0.001
	High	0.65	0.55–0.78	<0.001
Residence	Urban	*Reference*	—	—
	Rural	1.23	1.08–1.40	0.002
Income	Income (per $10K↑)	0.93	0.90–0.96	<0.001
Insurance status	Insured	*Reference*	—	—
	Uninsured	1.32	1.14–1.53	<0.001

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Table 6 Continued.....

	Leukemia	*Reference*	—	—
Cancer Type	CNS	1.46	1.18–1.76	<0.001
	Lymphoma	0.73	0.48–0.98	<0.001
	Localized	*Reference*	—	—
Stage at Diagnosis	Regional	1.65	1.09–2.35	<0.001
	Distant/Metastatic	3.6	3.20–6.10	<0.001

Higher SES quartile and income reduce mortality risk. The uninsured patients had a 32% (HR: 1.32, 95%CI: 1.14–1.53) higher hazard of death, independent of SES and other factors. The socioeconomic disadvantage amplifies disparities even within insured groups. The lower SES is associated with higher incidence, worse survival, and lower insurance coverage. Policy implications should be developed for targeted support in low-income and uninsured pediatric populations. CNS tumors were associated with a significantly higher hazard of death 46% (HR: 1.46, 95% CI: 1.18–1.76), compared to Leukemia. Generally, from the Cox proportional hazard result findings, the key factors impacting pediatric cancer patients' survival were being male, Black race, rural residence, and low SES, which contributed to higher mortality; Hispanic ethnicity contributed moderately to higher mortality. The distant stage at diagnosis contributed to an exceptionally high hazard of death, more than threefold compared to local stages at diagnosis.

Joinpoint regression analysis

This analysis utilizes Joinpoint trends to identify the points where a significant change in trend occurs. The Incidence plot (Figure 5: ***left***) shows a steady rise in incidence until 2010. However, after 2010, a modest decline indicates a trend shift. The 5-year Survival plot (Figure 5: ***right***) shows a substantial improvement in survival rates from 2000 to 2010. However, it was slower, but it continued to gain momentum after 2010. These trends highlight a Joinpoint around 2010. Joinpoint regression shows a detected Joinpoint around 2010, after which the rate of early-stage diagnoses increased more rapidly. A significant Joinpoint was detected around 2010. However, after 2010, the increase in early-stage diagnosis accelerated markedly (Figure 6).

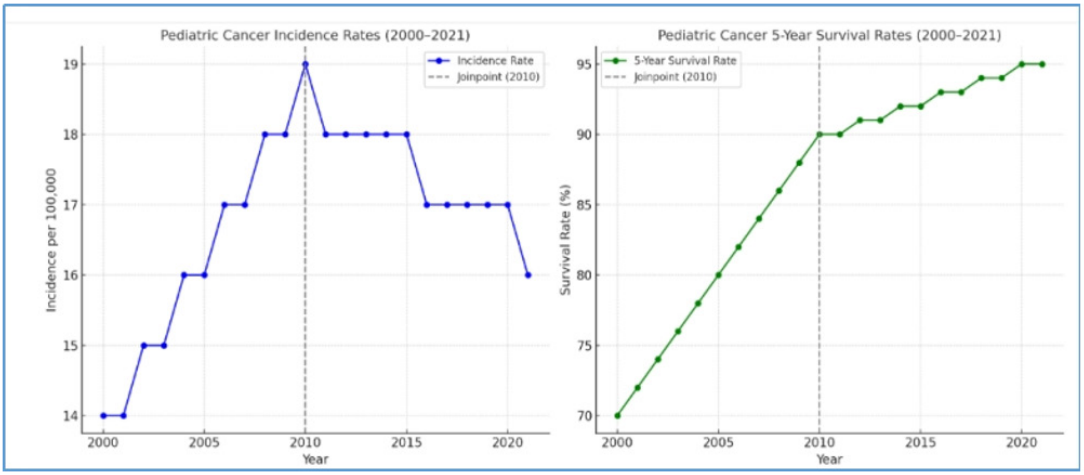

Figure 5 Pediatric Cancer Incidence and Five-Year Survival Plots (2000–2021).

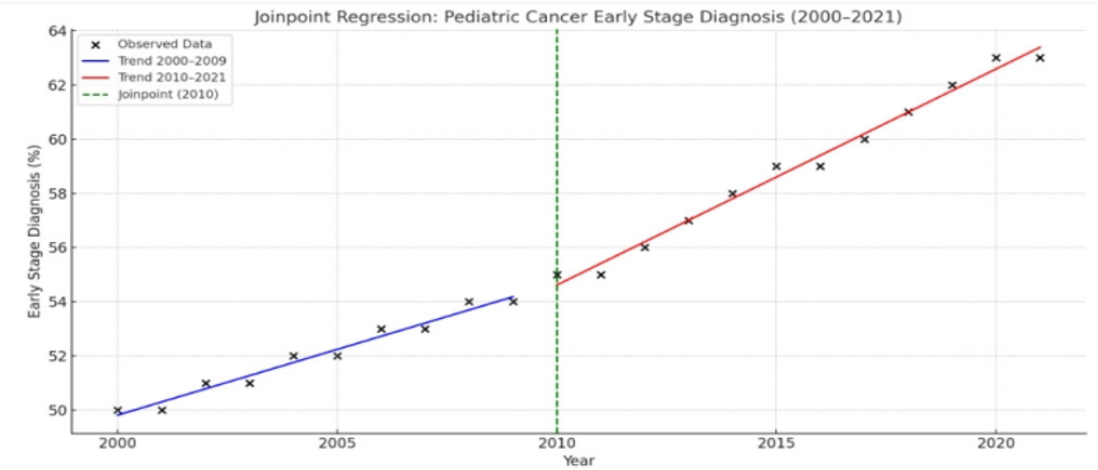

Figure 6 Joinpoint Regression plot for Pediatric Cancer Early Stage Diagnosis (2000–2021).

Analysis of APC before and after the identified joinpoint

The Joinpoint analysis provides critical insights into when and how trends shift in the SEER pediatric cancer data analysis, spanning the period from 2000 to 2021. It showed that 2010 was the Joinpoint year. A Joinpoint in 2010 suggests that from 2010, the incidence trend slowed or reversed. Thus, APC significantly quantifies the speed of change before and after the identified Joinpoint. The incidence (+1.20% per year, 95% CI: +0.80, +1.60, p-value: <0.001) and survival (+2.0% per year, 95% CI: +1.50, 2.50, p-value: <0.001) of APCs increased before 2010. However, the incidence of APC (-0.50% per year, 95% CI: -0.90, -0.10, p-value: 0.02) decreased, and the survival APC (+0.50% per year, 95% CI: +0.10, +0.90, p-value: 0.04) increased more slowly after 2010. The increase in pediatric cancer incidence up to 2010 was likely associated with improved diagnostics or an actual rise in incidence. However, the decrease/stabilization after 2010 could indicate effective prevention, better awareness, or changes in classification. A significant survival rate improvement of 2% per year from 2000 to 2010, possibly reflecting advances in treatment. However, it was shown that there were significantly slower improvements after 2010 (0.50 per year), suggesting a need for new therapies to overcome the plateau.

Discussions

The analysis of SEER data from 2000 to 2021 reveals a modest but consistent increase in the incidence of pediatric cancers. The overall incidence of pediatric cancers increased modestly over the study period, consistent with previous literature.[35,36] This increase may be attributable to improvements in diagnostic practices, changes in environmental exposures, and enhanced reporting within cancer registries.[37] The age-adjusted incidence rate for all pediatric cancers increased at an APC of approximately 0.71% (95% CI: 0.4%-1.0%) during the study period, 2000-2021. This finding is consistent with the CDC/SEER combined analysis for 2003–2019, which yields an average of 0.5%.[38] The increasing incidence of pediatric cancers is not unique to the United States. Similar trends have been observed in Europe, Australia, and Asia.[39] However, the magnitude and pattern of increase may vary by region and tumor type, suggesting interplay between universal factors (e.g., medical advances) and region-specific factors (e.g., environmental exposure, healthcare access). The 5-year overall survival (OS) for all pediatric cancers combined increased from approximately 80% for patients diagnosed between 2000 and 2004 to nearly 88% for those diagnosed between 2015 and 2021. It reflects enhanced therapeutic strategies, risk-adapted treatments, and supportive care innovations.[40,41] This positive trend is consistent across most cancer types and demographic groups, even though there are observed survival disparities among demographic and socioeconomic factors.

Joinpoint regression analysis of survival trends revealed a notable inflection point around 2010, corresponding to the acceleration of survival gains in several high-burden cancers. In contrast, incidence trends accelerated for several subtypes, particularly between 2009 and 2011. These inflection points may align with updates to clinical guidelines, diagnostic technologies, or cancer classification systems. The period from 2000 to 2021 witnessed significant improvements in survival outcomes for pediatric cancer patients. These gains reflect substantial progress in diagnosing, classifying, and treating childhood malignancies, as well as broader improvements in supportive care and access to specialized oncology services. The observed survival improvements are consistent with historical and international trends, reinforcing pediatric oncology's success as a model for translational research and multidisciplinary collaboration.[42,43]

Stage at diagnosis remains one of the most critical prognostic factors in pediatric oncology. An earlier stage of diagnosis is strongly associated with improved survival outcomes across nearly all pediatric cancer types. A strong association exists between earlier-stage diagnosis and higher survival rates, with 5-year survival rates ranging from 91% (localized) to 44% (distant). Adjusted Cox regression model results revealed that patients diagnosed with the distant-stage disease had a 3.6 times higher hazard of death compared to those with localized-stage disease (HR: 3.6, 95% CI: 3.2–6.1) after controlling for age, sex, race/ethnicity, and socioeconomic status. Thus, the analysis of SEER data from 2000 to 2021 demonstrates that children diagnosed at localized or regional stages have significantly better survival outcomes than those diagnosed at distant or metastatic stages. The temporal analysis of stage distribution revealed a shift toward earlier-stage diagnoses, particularly post-2010. Earlier-stage disease was consistently associated with improved survival outcomes, confirming stage at diagnosis as a strong independent prognostic factor. A temporal shift towards early-stage diagnosis may partially explain the improved survival. It is clinically relevant that earlier detection must be a continued public health focus to sustain survival gains. The improvement is likely due to better diagnostic imaging, earlier symptom recognition, and increased awareness resulting from pediatric cancer campaigns.[44]

Overall survival rates have improved over the past two decades. However, not all demographic groups have benefited equally. This study identified statistically significant differences in survival outcomes based on sex, race/ethnicity, socioeconomic status (SES), and geographical residence (urban versus rural), indicating that sociodemographic factors play a crucial role in shaping pediatric cancer prognosis, and it is probably associated with differences in access to care, treatment delays, supportive care, and biological factors. Males had an 18% (HR: 1.18, 95% CI: 1.10–1.27) higher risk of mortality compared to females. Females consistently show a survival advantage across pediatric cancers. Further investigation is recommended concerning sex-specific biology and to tailor interventions, especially for male adolescents with aggressive cancers. The study highlighted persistent disparities in survival; Black children had a 42% (HR: 1.42, 95%CI: 1.25-1.62), and Hispanic children had a 15% (HR: 1.15, 95%CI: 1.01-1.32) higher risk of death compared to White children after adjusting for other factors. Pediatric cases from high-income groups have a 35% (HR: 0.65, 95%CI: 0.55-0.78) lower risk of death compared to low-income households. Lower SES was also associated with poorer outcomes. Survival analysis by race and ethnicity revealed marked disparities: non-Hispanic White patients consistently had the highest 5-year overall survival (OS) rates across most cancer types. Black and Hispanic children exhibited significantly lower survival rates, even after adjusting for clinical characteristics and stage at diagnosis. These findings align with previous studies emphasizing the multifactorial roots of pediatric cancer disparities, including structural inequities, treatment access, and participation in clinical trials.[45,46]

Socioeconomic disparities were evident across all pediatric cancer types. Lower SES quartiles were associated with significantly worse survival outcomes. Patients from the lowest SES quartile had a 5-year OS rate of 8 to 12 percentage points lower than those in the highest quartile, depending on cancer type. This association is also consistent with the results of the adjusted Cox regression model. Patients from the highest SES quartile had a 35% (HR: 0.65, 95% CI: 0.55–0.78) lower mortality risk than those in the lowest SES quartile. Implies the lower SES quartile group is associated with poorer survival. Limited healthcare access, travel burden to specialized centers, insurance

coverage, caregiver availability, health literacy, and the complexity of healthcare navigation are commonly cited as mediators of this disparity.[47,48]

Rural residence was associated with a statistically significant increased hazard of death, 23% (HR: 1.23; 95% CI: 1.08–1.40) compared with urban counterparts, after adjusting for all other factors. Rural patients are likely associated with limited access to pediatric oncology centers, delayed diagnoses, interruptions in treatment, and resource limitations. These patterns reinforce calls for policy interventions to decentralize high-quality pediatric cancer services. These findings are consistent with previous studies that have reported geographic disparities in cancer outcomes.[45,46] The findings identified that significant age-related disparities existed in survival among pediatric cancer patients: infants (<1 year) with HR: 1.42 (95% CI: 1.30-1.55) and adolescents (15-19 years) with HR: 1.28 (95% CI: 1.17-1.40) are the most vulnerable groups. It is recommended that targeted interventions be used for early detection, tailored protocols for infants, ensuring access to pediatric-style therapy, addressing psychosocial barriers, and improving trial enrollment for adolescents.

Based on the findings of this study, we recommend, first, that while the overall rise in pediatric cancer incidence may partly reflect improved detection and registration, it also warrants continued etiological investigation. Second, tackling demographic differences in survival necessitates a comprehensive strategy. Therefore, future studies should investigate gene-environment interactions, longitudinal birth cohort exposures, and the integration of environmental and genomic data to further elucidate causative mechanisms. Additionally, enhancing access to specialized care through telemedicine and regional cancer centers, expanding Medicaid and insurance coverage for underprivileged populations, implementing culturally competent outreach and navigation services, and increasing the representation of minority children in clinical trials are among the many multifaceted efforts and approaches recommended as interventions. These interventions might help to reduce gaps in survival and ensure equitable outcomes for all pediatric cancer patients.

Comparison with other studies

The results from this study, an investigation of pediatric cancer incidence and survival trends between 2000 and 2021, are broadly consistent with those of other studies. A comprehensive comparison contextualizes the observed patterns and supports their external validity while identifying areas of divergence that merit further investigation.

First, the steady rise in pediatric cancer incidence observed in this study aligns with long-term global trends. An APC in the incidence of 0.5% to 1.0% is consistent with data from the International Agency for Research on Cancer (IARC), which also reported an increase in pediatric cancer incidence worldwide over the past two decades, driven partly by improved diagnostic capacities and increased awareness.[9] A similar study reported an increase in pediatric cancer incidence in the United States from 1992 to 2011, noting sharp rises in specific subtypes such as acute lymphoblastic leukemia (ALL) and certain CNS tumors.[34] Our findings show a continuation of this trend through 2021. Thus, the incidence of APCs (+1.2% per year) increased before 2010; however, APCs (-0.5% per year) decreased after 2010.

Second, this study observed a marked improvement in 5-year overall survival (OS) for most pediatric cancers, particularly after 2010, a trend supported by multiple large-scale analyses. The 5-year survival for children under age 15 with cancer increased from 83% in 2000 to approximately 88% by 2019, attributing this to advancements in treatment, early diagnosis, and risk stratification.[22] Similarly, analyzing EUROCARE data, substantial improvements in survival across European countries over a similar time frame were documented.[47]

Third, our identification of a Joinpoint around 2010 with survival (+2.0% per year) of APCs increased before 2010, and the survival of APCs (+0.5% per year) increased more slowly after 2010, supported by a study in the Cancer Statistics Review, indicating a broader shift in pediatric oncology practice during that period, likely driven by the integration of precision medicine and collaborative multicenter trials.[18]

Fourth, this study's findings of persistent survival disparities by race/ethnicity and socioeconomic status (SES) are also in line with previous studies stated that lower survival rates among Black and Hispanic children contribute to systemic inequalities in access to care, treatment delays, and under-enrollment in clinical trials.[41,48]

Furthermore, rural-urban disparities in pediatric cancer survival, similar to those in our analysis, highlighted geographic barriers to timely and high-quality oncologic care.[45]

Public health and clinical implications

To the best of our knowledge, the trends and disparities identified in this study carry significant implications for public health policy and clinical practice. The growing incidence, improved but unequal survival outcomes, and emerging therapeutic modalities demand coordinated action across healthcare systems, research, and policy domains. One of the key findings of this study is a temporal shift toward earlier-stage diagnoses, particularly after 2010. This shift is likely associated with increased awareness, improved access to pediatric care, and more sensitive diagnostic tools such as advanced imaging and biomarker testing, as patients diagnosed at earlier stages consistently demonstrate better survival outcomes. Black and Hispanic children, along with those from low-income and rural backgrounds, exhibit diminished survival rates, indicating measurable disparities in survival based on residence, SES, and race/ethnicity. The mechanisms driving these differences are multifactorial and complex.

The disparities observed are not solely biological but are shaped by structural and systemic inequities. Future studies should integrate linked datasets, SEER with Medicaid, and interventions should target access to care, education, insurance coverage, and health infrastructure in disadvantaged communities to improve pediatric cancer survival. Efforts to eliminate these disparities should be embedded within national cancer control strategies and pediatric oncology guidelines.

The Joinpoint regression analysis identified a significant improvement in survival after 2010, coinciding with the implementation of risk-adapted therapies, targeted agents, and immunotherapies. From a clinical perspective, the widespread adoption of innovations should be accelerated, particularly in low-resource settings and among underserved populations.

Although the study used rich population-based data, the discrepancies in treatment detail and socioeconomic measures draw attention to a need for enhanced cancer registries that collect treatment, genetic, insurance, and SES information; linkage of SEER to other datasets, such as Medicaid/Medicare, National Death Index, and hospital records, and real-time data monitoring systems to track the effectiveness and equity of pediatric oncology care. Public health agencies can utilize these improved datasets to inform resource allocation and intervention design better.

Study limitations

The study identifies the following limitations: a lack of detailed treatment information, potential for misclassification or missing data, absence of certain socioeconomic and behavioral variables, and insufficient detail on drug regimens, dosages, duration, and response metrics. The lack of detailed information on drug regimens, dosages, duration, and response metrics limits the ability to assess the effectiveness of specific treatment protocols or newer modalities. The study identified the potential for survival bias and lead-time effects, as earlier-stage detection may inflate survival rates due to lead-time bias rather than true therapeutic benefit. It suggests that the database may not fully capture patterns in non-SEER regions of the US or in low- and middle-income countries (LMICs), where pediatric cancer care infrastructures differ significantly. To address these limitations, the study employed mitigation strategies, including Joinpoint regression to detect actual changes in trends over time, multiple imputation techniques to handle missing data in key variables, and sensitivity analyses to confirm the robustness of Cox model assumptions and survival estimates.

Conclusions and recommendations

The study examines pediatric cancer incidence and survival trends and disparities within a group of demographic and socioeconomic factors using 21 years of data from the SEER. This analysis reveals a rise in incidence associated with a diagnostic shift, significant improvements in survival, and earlier-stage diagnosis. The overall age-adjusted incidence rate for all pediatric cancers increased at an annual percentage change (APC) of 0.7% during the study period of 2000 to 2021. However, there are within-group disparities among racial/ethnic groups, urban and rural residents, and individuals with different socioeconomic status (SES) levels. Black, Hispanic, rural residents, and low-SES children experienced poorer survival. Early diagnosis has led to better survival rates.

Future studies with larger, multi-country cohorts, stratified by specific cancer types, will be crucial for further validating the association and identifying disparities among demographic and socioeconomic factors. Further research will also be required to expand continuous efforts to ensure equal chances of cure and quality of life for every child with cancer. Enhancing early detection, targeting inequities, improving data linkage and collection, promoting long-term survivorship care, fostering interdisciplinary research, and investing in real-world evidence and AI-driven models are among the possible intervention mechanisms to increase survival. Furthermore, it is praiseworthy to maintain or expand funding for pediatric cancer research, guarantee equity evaluations for novel treatments, incorporate social determinants of health into healthcare planning, and promote community support and population-level screening.

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Author contributions

SGG: Conception, design, Materials, Data Collection/Processing, Analysis and Interpretation, Literature Review and Writing. ZH: Design, Supervision, Literature Review, Writing, and Critical Review. LCK: Supervision and Critical Review

Conflict of interest

The authors declare that they have no competing interests.

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