Racial/Ethnic Disparities in Childhood Cancer Survival in the United States

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ABSTRACT

Background: Non-white patients with childhood cancer have worse survival than Non-Hispanic (NH) White patients for many childhood cancers in the United States. We examined the contribution of socioeconomic status (SES) and health insurance on racial/ethnic disparities in childhood cancer survival.

Methods: We used the National Cancer Database to identify NH White, NH Black, Hispanic, and children of other race/ethnicities (<18 years) diagnosed with cancer between 2004 and 2015. SES was measured by the area-level social deprivation index (SDI) at patient residence and categorized into tertiles. Health insurance coverage at diagnosis was categorized as private, Medicaid, and uninsured. Cox proportional hazard models were used to compare survival by race/ethnicity. We examined the contribution of health insurance and SES by sequentially adjusting for demographic and clinical characteristics (age group, sex, region, metropolitan statistical area, year of diagnosis, and number of conditions other than cancer), health insurance, and SDI.

Results: Compared with NH Whites, NH Blacks and Hispanics had worse survival for all cancers combined, leukemias and lymphomas, brain tumors, and solid tumors (all $P < 0.05$). Survival differences were attenuated after adjusting for health insurance and SDI separately; and further attenuated after adjusting for insurance and SDI together.

Conclusions: Both SES and health insurance contributed to racial/ethnic disparities in childhood cancer survival.

Impact: Improving health insurance coverage and access to care for children, especially those with low SES, may mitigate racial/ethnic survival disparities.

Introduction

Childhood cancer survival has improved dramatically since the 1970s, due in part to widespread participation in clinical trials, improved supportive care, and development of new therapies (1). Improvements in survival have not been experienced equally in all groups, however, and disparities by race/ethnicity among patients with childhood cancer are common in the United States (2–4). Non-Hispanic (NH) Black and Hispanic children have worse survival than their NH White counterparts for many treatable cancer types, including leukemias (5–7), lymphomas (7, 8), and brain tumors (7, 9). Exploring the role of potentially modifiable factors associated with racial/ethnic survival differences can help efforts to mitigate these disparities.

Non-white children are frequently of low socioeconomic status (SES) and underinsured or uninsured (10, 11), potentially reducing their access to high-quality primary and cancer care. A prior study using population-based cancer registry data from limited geographic regions represented in the Surveillance, Epidemiology, and End Results (SEER) registries reported that SES accounted for up to 49% of the Black and White childhood cancer survival disparities, and up to 73% of the disparities in Hispanic and White survival (2). However, several states in the South and West with large NH Black and Hispanic populations are not included in SEER (12, 13). Relatively small sample sizes have limited the evaluation of some less common cancer types. In this study, we used a large and geographically representative (14) national cohort of children newly diagnosed with cancer to assess both the contribution of SES, indirectly measured by area-level social deprivation index (SDI; ref. 15), and health insurance coverage on survival disparities.

Patients and Methods

Data and patients

Children newly diagnosed with cancer were identified from the National Cancer Database (NCDB), a hospital-based cancer registry database jointly sponsored by the American Cancer Society and the American College of Surgeons. The NCDB includes over 70% of all newly diagnosed cancer cases in the United States from more than 1,500 facilities accredited by the American College of Surgeons' Commission on Cancer (CoC). Nearly 70% of all patients with childhood cancer in all the states of the United States were included in the NCDB (14). The NCDB contains standardized data elements required by the CoC's Facility Oncology Registry Data Standards and the North American Association of Central Cancer Registries, including patient demographic characteristics, tumor characteristics, health insurance coverage, receipt of treatment, and follow-up information for vital status (14, 16, 17). The NCDB follows rigorous quality monitoring and validity review procedures. Case records that cannot meet a standardized set of requirements are identified and returned to the reporting facility; data are further examined and verified before release (18).

Thirteen common childhood cancer sites were identified for this study according to the third edition of the International Classification of Childhood Cancer based on ICD-O-3 histology and site code (19), as

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Table 1. Patient with childhood cancer characteristics by race/ethnicity.

	Total (N = 78,784)	NH White (n = 51,029)	NH Black (n = 9,901)	Hispanic (n = 13,216)	NH other (n = 4,638)
Age					
0–4	37.4	37.5	34.5	38.4	40.0
5–9	21.0	20.6	21.5	22.2	21.5
10–14	22.1	21.6	24.8	22.4	21.3
15–17.9	19.4	20.3	19.2	17.0	17.3
Sex					
Female	44.5	44.3	46.7	43.9	44.7
Male	55.5	55.7	53.3	56.1	55.3
Insurance					
Private	63.9	73.9	44.9	39.7	62.4
Medicaid/CHIP	33.6	24.3	52.2	55.5	34.9
Uninsured	2.5	1.8	2.9	4.8	2.7
SDI, area-level[a]					
1%–33%	33.9	43.4	13.1	13.0	34.1
34%–66%	33.0	36.6	24.6	26.1	31.2
67%–100%	33.1	20.0	62.3	61.0	34.8
Region					
Northeast	18.1	18.4	16.8	16.5	21.8
Midwest	25.7	30.5	20.6	13.5	19.2
South	37.1	34.7	55.9	36.8	24.7
West	19.1	16.5	6.6	33.2	34.3
MSA					
Metro areas with population of ≥1,000,000	50.1	43.7	59.3	64.1	62.2
Metro areas with population <1,000,000	31.9	34.2	30.0	26.8	25.9
Nonmetro area	13.7	17.0	8.5	7.1	7.7
Unknown or missing	4.2	5.2	2.3	2.0	4.1
Cancer site					
1. Leukemia and Lymphoma	41.2	40.5	36.2	46.7	43.1
1a. Lymphoid leukemia	23.0	22.6	15.3	29.6	24.9
1b. Myeloid leukemia	4.5	4.1	5.1	5.0	5.6
1c. Hodgkin's lymphoma	7.3	7.5	8.0	6.5	5.4
1d. Non-Hodgkin's lymphoma	6.5	6.3	7.9	5.6	7.2
2. Brain tumors	23.1	23.8	23.0	20.3	22.9
3. Solid tumors	35.8	35.7	40.8	33.0	34.0
3a. Neuroblastoma and other peripheral nervous cell tumors	6.9	7.4	6.5	5.0	6.6
3b. Malignant bone tumors	6.3	6.4	6.2	5.7	6.0
3c. Renal tumors	5.6	5.4	8.4	4.6	3.9
3d. Extraosseous sarcomas	4.9	4.8	6.3	4.5	4.3
3e. Malignant extracranial and extragonadal germ cell tumors	4.5	4.3	4.1	5.4	4.6
3f. Rhabdomyosarcomas	4.1	4.0	5.1	3.9	3.8
3g. Retinoblastoma	2.0	1.7	2.6	2.2	2.7
3h. Hepatic tumors	1.6	1.5	1.6	1.8	2.2
Number of conditions other than cancer					
0	94.2	94.8	90.8	94.2	94.6
1+	5.8	5.2	9.2	5.8	5.4
Facility type[b]					
Community cancer program	1.0	0.8	0.6	0.7	3.9
Comprehensive community cancer program	12.5	12.6	8.5	15.3	12.9
Teaching/research	30.3	29.5	33.9	30.7	30.1
NCI program/network	28.2	29.0	26.1	25.1	33.3
Pediatric cancer program	6.5	6.9	6.8	5.9	3.4
Other and unknown	21.5	21.3	24.1	22.4	16.3

Note: Children ages <18 years at the time of cancer diagnosis between 2004 and 2015 were included in the sample, after exclusion.
Compared with NH Whites, the distributions of all the characteristics were statistically significant for all other race/ethnicities.
[a]Area-level SDI was incorporated into the analyses by linking to residence postal code of cancer diagnosis. SDI is a composite measure of area-level deprivation based on seven characteristics, including income, education, employment, housing, household characteristics, transportation, and demographics. Higher rank indicates more disadvantaged area.
[b]All facility type categories listed in **Table 1** are mutually exclusive (55).

shown in **Table 1**. We further categorized the selected 13 cancer sites into three groups, leukemias and lymphomas, brain tumors, and other solid tumors, to obtain larger sample sizes and more stable estimates.

We selected patients ages <18 years at the time of diagnosis between 2004 and 2015, which allowed at least 2 years of follow-up, through December 31, 2017. The age range was consistent with earlier studies (20). Of the 87,507 patients with a diagnosis of any of the thirteen cancer types, 24 patients with noninvasive cancer were excluded according to the ICD-O tumor behavior code. We further excluded patients with unknown race/ethnicity, with sex other than male or female, and with unknown region of residence. We also excluded 1,301 patients without follow-up time (missing information on date of diagnosis and/or last contact), 580 patients with unknown SDI because of missing data on residence postal code or for constructing SDI, and 3,795 patients with health insurance other than private, Medicaid, or uninsured or with missing information on health insurance. Children covered by Children's Health Insurance Plus (CHIP) were included in the group with Medicaid coverage. We excluded children enrolled in Medicare or dual-enrolled in Medicare and Medicaid due to the small sample size and because eligibility for Medicare in this age group is only from serious health conditions that will affect survival outcomes. The final analytic sample included 78,784 patients with newly diagnosed childhood cancer. The exclusion percentages were 6.1%, 7.5%, 13.3%, and 13.4% for NH White, NH Black, Hispanic, and NH other, respectively. More specifically, the percentage of patients lost follow-up were 3.4%, 4.5%, 8.0%, and 4.7% for NH White, NH Black, Hispanic, and NH other, respectively. Detailed inclusion/exclusion criteria are listed in Supplementary Fig. S1.

Measures

Race/ethnicity was grouped into NH White, NH Black, Hispanic, and NH other. Health insurance coverage was grouped into Medicaid (Medicaid and Medicaid administered through a managed care plan), private (managed care, health maintenance organization, preferred provider organization, TRICARE, military care, and insurance not otherwise specified), and uninsured (not insured or self-pay).

SES was indirectly measured by area-level SDI, which is a composite measure of area-level deprivation based on seven characteristics, including income, education, employment, housing, household characteristics, transportation, and demographics (15). SDI has commonly served as an area-level composite measures of SES in other studies of health and health outcomes (21, 22). Larger SDI ranks indicate more disadvantaged areas. The SDI measure was created by linking patient five-digit residence postal code from the NCDB to the SDI file from the Robert Graham Center (available at: https://www.graham-center.org/rgc/maps-data-tools/sdi/social-deprivation-index.html). SDI was then categorized into tertiles [1%–33% (high SES), 34%–66% (intermediate SES), and 67%–100% (low SES)] based on the sample distribution and the relatively small sample size for some subtypes of patients with childhood cancer.

Overall survival was calculated by the number of months between date of diagnosis and the date of death, the date of last contact, 60 months, or December 31, 2017 (end of study), whichever occurred first.

Statistical analyses

Descriptive statistics were used to characterize the sample. Multivariable Cox proportional hazard models were used to compare survival probabilities by race/ethnicity (NH White vs. NH Black, Hispanic, and NH other) and to assess the contribution of health insurance and area-level SES, measured by the area-level SDI, after confirming that all the variables satisfied the proportional hazards assumption using log[−log(survival)] curves. Specifically, we first adjusted by age group, sex, region, metropolitan statistical area (MSA), year of diagnosis, and number of conditions other than cancer; and then added health insurance and area-level SDI to the models. We compared results from these sequential analyses to examine the contribution of health insurance and area-level SDI. We also used adjusted survival curves to separately compare survival by race/ethnicity and SDI, and by race/ethnicity and health insurance. The groups with sample size <350 were not shown in the figures to avoid unstable curves. SAS 9.4 were used for analyses. Statistical tests were two-sided, and results were considered significant if $P < 0.05$.

Sensitivity analyses

We also conducted sensitivity analyses using a path-specific mediation analyses based on a counterfactual approach (23–27), which allowed for separate evaluation of the mediation effects of SDI and health insurance on the association of race/ethnicity and survival. Details of the path-specific mediation analyses are provided in the Supplementary Materials and Methods. Briefly, we evaluated the area-level SDI mediation of the association of race/ethnicity and survival through two pathways (Supplementary Fig. S2): (i) race/ethnicity→SDI→survival, and (ii) race/ethnicity→SDI→health insurance→survival. We also evaluated independent mediation by health insurance through another pathway: (iii) race/ethnicity→health insurance→survival. The total mediation effects of SDI and health insurance, considering their correlations, were calculated by adding the effects of pathways (i), (ii), and (iii), as have been done elsewhere (23, 24). Because our study spanned the implementation of many provisions of the Affordable Care Act in 2014, we also conducted sensitivity analyses to determine if associations varied before and after 2014.

Results

Among the 78,784 patients with childhood cancer ages <18 years, lymphoid leukemia (23.0%) and brain tumors (23.1%) were the most commonly diagnosed cancers, followed by Hodgkin lymphoma (7.3%), neuroblastoma, and other peripheral nervous cell tumors (6.8%), and non-Hodgkin lymphoma (6.5%). The sample was mostly NH White (64.7%), followed by Hispanic (16.9%), NH Black (12.6%), and NH other (5.8%). Non-white childhood cancer patients were more likely to be covered by Medicaid or uninsured and live in an area with a substantially higher SDI than NH white patients (all $P < 0.05$; **Table 1**). We also compared the racial/ethnic distribution between children newly diagnosed with cancer during 2004 to 2015 from the NCDB and the SEER 18 and found that the SEER had a lower proportion of NH White patient and higher proportion of Hispanic patient (Supplementary Fig. S3), which is consistent with percent of race/ethnicity coverage of SEER (14).

Overall 5-year survival for patients with childhood cancer was lower for NH Blacks (76.4%; 95% CI, 75.4%–77.3%) and Hispanics (80.3%; 95% CI, 79.6%–81.1%) than for NH Whites (82.7%; 95% CI, 82.3%–83.0%; **Table 2**). High SDI score or without private health insurance coverage were associated with lower 5-year survival rate within each race/ethnicity group. Significantly worse survival was observed for non-white patients with childhood cancer for leukemia and lymphoma, brain tumors, and solid tumors when adjusting for demographic and clinical characteristics (age group, sex, region, MSA, year of diagnosis, and number of conditions other than cancer) other than area-level SDI or health insurance (all

Table 2. Five-year survival rate by race/ethnicity, health insurance, and SDI.

	All cancers combined		Leukemia and lymphoma		Brain tumors		Solid tumors	
	Survival rate, %	95% CI	Survival rate, %	95% CI	Survival rate, %	95% CI	Survival rate, %	95% CI
By race/ethnicity								
NH White	82.7	82.3–83.0	89.5	89.0–89.9	74.8	74.0–75.6	80	79.3–80.6
NH Black	76.4	75.4–77.3	83.4	82.1–84.7	65.9	63.8–68.0	75.7	74.2–77.1
Hispanic	80.3	79.6–81.1	86.2	85.3–87.1	69.1	67.1–70.9	78.6	77.2–79.9
NH others	80.6	79.3–81.8	87.7	86.0–89.2	69.7	66.6–72.7	78.4	76.0–80.6
By race/ethnicity and SDI								
NH White								
1%–33%	83.7	83.2–84.2	90.4	89.7–91.0	75.4	74.1–76.6	81.2	80.2–82.1
34%–66%	81.9	81.3–82.5	89.1	88.3–89.8	74.9	73.5–76.2	78.3	77.2–79.4
67%–100%	81.9	81.1–82.7	88.1	87.0–89.1	73.3	71.4–75.1	80.4	79.0–81.8
NH Black								
1%–33%	80.1	77.5–82.4	86.9	83.2–89.9	71.3	64.9–76.8	77.8	73.6–81.5
34%–66%	76.6	74.7–78.4	83.8	81.1–86.2	64.5	59.9–68.7	76.0	72.8–78.9
67%–100%	75.4	74.2–76.6	82.3	80.6–84.0	65.3	62.6–67.9	75.0	73.1–76.8
Hispanic								
1%–33%	81.6	79.5–83.5	87.0	84.1–89.4	70.8	65.1–75.7	80.0	76.2–83.3
34%–66%	81.4	79.9–82.8	87.4	85.5–89.0	70.2	66.4–73.6	79.1	76.3–81.7
67%–100%	79.6	78.6–80.5	85.5	84.2–86.6	67.9	65.4–70.4	77.9	76.1–79.6
NH others								
1%–33%	82.3	80.1–84.2	89.9	87.3–92.1	72.6	66.9–77.5	77.0	72.6–80.9
34%–66%	79.2	76.8–81.3	86.7	83.4–89.4	67.2	61.6–72.1	77.4	73.0–81.2
67%–100%	80.0	77.8–82.1	85.6	82.4–88.3	67.8	62.0–72.9	79.9	75.8–83.3
By race/ethnicity and health insurance								
NH White								
Private	83.6	83.2–84.0	90.4	89.9–90.9	75.8	74.9–76.8	80.8	80.1–81.5
Medicaid	79.9	79.1–80.7	86.7	85.6–87.7	72.2	70.4–73.9	77.3	75.9–78.6
Uninsured	80.1	77.1–82.7	86.3	82.2–89.6	65.3	57.0–72.4	80.8	75.2–85.2
NH Black								
Private	78.4	77.1–79.7	86.0	84.1–87.6	68.6	65.4–71.6	76.4	74.2–78.5
Medicaid	74.7	73.4–76.0	81.0	79.0–82.9	63.7	60.7–66.6	75.4	73.3–77.4
Uninsured	71.8	65.7–77.0	65.9	29.5–86.7	60.2	46.9–71.1	67.3	56.2–76.2
Hispanic								
Private	81.8	80.6–82.9	88.0	86.6–89.4	70.5	67.5–73.3	79.7	77.5–81.7
Medicaid	79.3	78.2–80.3	84.7	83.4–86.0	67.7	65.0–70.2	78.0	76.0–79.8
Uninsured	80.2	76.6–83.3	86.8	82.0–90.4	68.5	58.0–76.9	75.0	68.0–80.7
NH others								
Private	81.1	79.5–82.6	88.2	86.1–90.0	71.7	67.8–75.2	77.8	74.7–80.6
Medicaid	80.0	77.8–82.1	86.9	83.9–89.3	65.8	59.8–71.0	79.2	75.1–82.8
Uninsured	71.0	57.3–81.0	70.1	39.9–87.1	66.6	47.3–80.1	77.5	59.7–88.1

$P < 0.05$; **Table 3**). Survival differences were attenuated after adjusting for health insurance and area-level SDI separately; and further attenuated after adjusting for insurance and SDI together, suggesting the contribution of both health insurance and area-level SDI on racial/ethnic disparities in childhood cancer survival. For all cancers combined, the HR for mortality for NH Black patients was 1.36 (95% CI, 1.30–1.43) compared with NH White patients, when adjusting for demographic and clinical characteristics. The HR attenuated to 1.28 (95% CI, 1.22–1.34) with additional adjustment for health insurance and 1.29 (95% CI, 1.22–1.36) with additional adjustment for SDI, and further attenuated to 1.24 (95% CI, 1.18–1.31) with additional adjustment for both health insurance and SDI together. Similarly, compared with NH White patients, the HR for mortality for Hispanic patients was 1.16 (95% CI, 1.11–1.21) when adjusting for demographic and clinical characteristics, 1.10 (95% CI, 1.05–1.16) with additional adjustment for health insurance, 1.12 (95% CI, 1.07–1.18) with additional adjustment for SDI, and 1.07 (95% CI, 1.02–1.13) with additional adjustment for health insurance and SDI together. These patterns were consistent after stratifying the analysis by pre- and post-ACA diagnosis years (Supplementary Table S1).

As shown in **Fig. 1**, survival rates were highest for NH Whites with private insurance, followed by the other three race/ethnicity groups with private insurance, NH Whites with Medicaid, and other three groups with Medicaid for all cancers combined, leukemia and lymphoma, and solid tumors. A different pattern was observed in brain tumors, for which other races/ethnicity with private insurance had poorer survival than NH Whites with Medicaid.

Sensitivity analysis

Results from pathway-specific mediation analysis confirmed that both SDI and health insurance significantly mediated racial/ethnic disparities in childhood cancer survival. For example, for all cancers combined, SDI could explain 13.1% (95% CI, 7.2%–20.1%) of the survival disparity between NH Blacks and NH

Table 3. Survival disparity by race/ethnicity.

	Unadjusted estimates HR of mortality	Multivariable model adjusted for age group, sex, region, MSA, year of diagnosis, and number of conditions other than cancer HR of mortality	Multivariable model with additional adjustment for health insurance HR of mortality	Multivariable model with additional adjustment for SDI HR of mortality	Multivariable model with additional adjustment for health insurance, and SDI HR of mortality
NH Black vs. NH White					
All cancers combined	**1.39 (1.33–1.46)**	**1.36 (1.30–1.43)**	**1.28 (1.22–1.34)**	**1.29 (1.22–1.36)**	**1.24 (1.18–1.31)**
Leukemia and lymphoma	**1.57 (1.43–1.72)**	**1.48 (1.35–1.63)**	**1.38 (1.25–1.52)**	**1.38 (1.25–1.53)**	**1.30 (1.17–1.44)**
Brain tumors	**1.41 (1.30–1.52)**	**1.36 (1.25–1.48)**	**1.30 (1.19–1.41)**	**1.32 (1.2–1.44)**	**1.27 (1.16–1.39)**
Solid tumors	**1.23 (1.14–1.32)**	**1.23 (1.14–1.32)**	**1.18 (1.09–1.27)**	**1.19 (1.10–1.29)**	**1.16 (1.06–1.25)**
Hispanic vs. NH White					
All cancers combined	**1.16 (1.11–1.21)**	**1.16 (1.11–1.21)**	**1.10 (1.05–1.16)**	**1.12 (1.07–1.18)**	**1.07 (1.02–1.13)**
Leukemia and lymphoma	**1.29 (1.19–1.40)**	**1.35 (1.24–1.47)**	**1.22 (1.12–1.34)**	**1.25 (1.14–1.37)**	**1.16 (1.05–1.27)**
Brain tumors	**1.29 (1.20–1.40)**	**1.25 (1.15–1.36)**	**1.19 (1.1–1.3)**	**1.21 (1.11–1.32)**	**1.18 (1.08–1.28)**
Solid tumors	**1.10 (1.02–1.19)**	**1.12 (1.04–1.21)**	**1.05 (0.97–1.14)**	**1.08 (1.00–1.18)**	1.04 (0.95–1.13)
NH other vs. NH White					
All cancers combined	**1.13 (1.05–1.21)**	**1.15 (1.07–1.24)**	**1.13 (1.05–1.21)**	**1.14 (1.06–1.23)**	**1.12 (1.04–1.20)**
Leukemia and lymphoma	**1.13 (0.98–1.29)**	**1.21 (1.05–1.39)**	**1.15 (1.00–1.32)**	**1.17 (1.02–1.35)**	1.13 (0.98–1.30)
Brain tumors	**1.23 (1.10–1.39)**	**1.18 (1.04–1.33)**	**1.17 (1.04–1.32)**	**1.19 (1.05–1.34)**	**1.17 (1.03–1.32)**
Solid tumors	**1.12 (0.99–1.25)**	**1.18 (1.05–1.32)**	**1.14 (1.01–1.28)**	**1.16 (1.03–1.30)**	**1.14 (1.01–1.28)**

Note: NH White was the reference group. Bold indicates statistically significant ($P < 0.05$).

Whites, and health insurance could explain an additional 12.1% (95% CI, 8.7%–16.3%), resulting in a total mediation effect of 25.2% (95% CI, 18.0%–34.4%). Similarly, 27.7% (95% CI, 13.8%–50.3%) of the survival disparity between Hispanics and NH Whites could be explained by SDI, and another 34.4% (95% CI, 22.5%–56.3%) of the survival disparity could be explained by health insurance (Supplementary Tables S2–S5, Supplementary Materials and Methods).

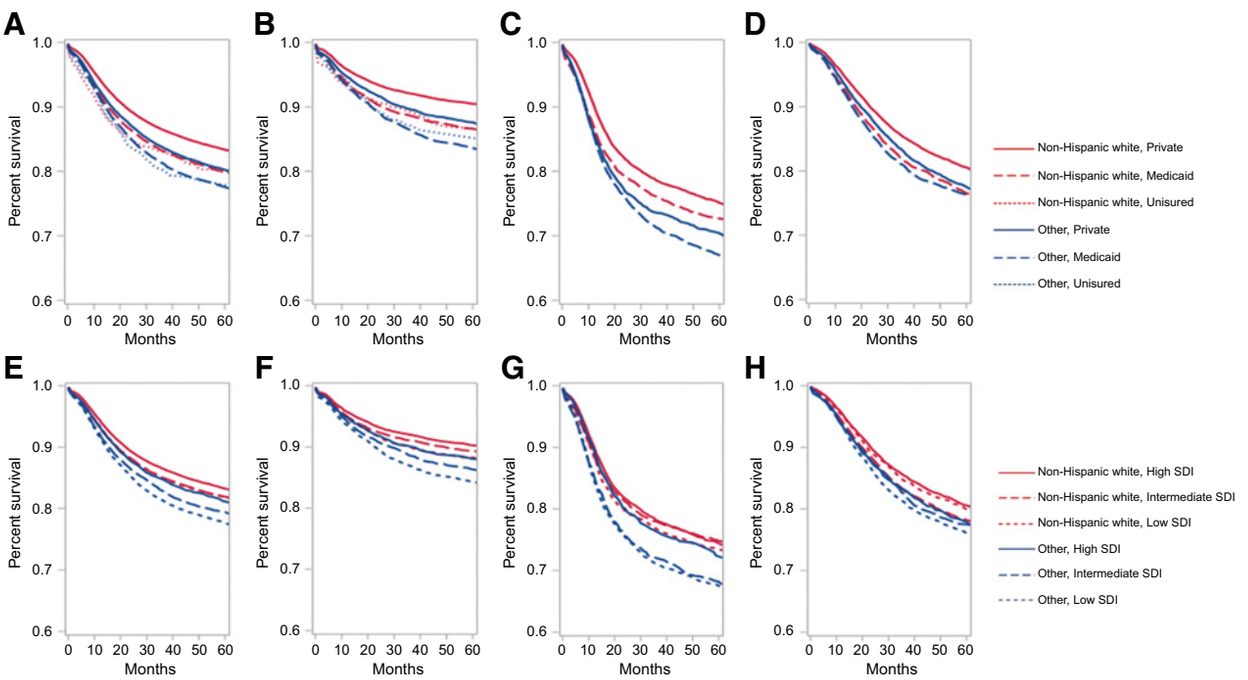

Figure 1.

Childhood cancer 5-year survival by race/ethnicity and health insurance (**A–D**) and by race/ethnicity and socioeconomic status (**E–H**). **A** and **E,** all cancers combined; **B** and **F,** leukemia and lymphoma; **C** and **G,** brain tumors; **D** and **H,** solid tumors. The 'other' group represented NH Blacks, Hispanics, and NH others. The uninsured group was not presented for brain tumors and solid tumors because of the sparse data ($n < 350$).

Discussion

In this study, we used a large national cohort to evaluate modifiable factors that contribute to racial/ethnic disparities in childhood cancer survival in the United States. Compared with NH White patients, NH Black patients, Hispanic patients, and patients of other race/ethnicities had worse survival for all cancers combined, leukemias and lymphomas, brain tumors, and solid tumors, even after adjusting for demographic and clinical characteristics other than SES or health insurance. We found that both health insurance and are-level SES contributed to racial/ethnic disparities in childhood cancer survival. These racial/ethnic disparities in childhood cancer survival are striking and have persisted for many decades (1). This continued inequity in health outcomes among children warrants concerted, multifaceted approaches to address and minimize these disparities in the future. Our findings suggest that increasing health insurance coverage and improving access to high-quality care for childhood cancer patients with low SES might be important for reducing racial/ethnic disparities.

In this study, we found contribution of SES on childhood cancer survival disparities. Non-white patients with childhood cancer were overrepresented in the lower SES stratum, which is associated with problems with health care access and affordability potentially due to a complex interplay of their parents' financial status, employment, health literacy, and transportation (28–30), as well as other systemic factors, including structural racism. Prior studies showed that lower SES was associated with worse childhood cancer survival (31, 32). The mediation mechanism of SES can be complicated. It can be an interplay of patients' and their families' financial status, health and health insurance literacy, health insurance coverage, and other factors such as social environment and experiences of discrimination (33). For example, the high cost of cancer care could be one barrier. The average cost per hospital stay was $40,400 for patients with childhood cancer in 2009 (34). Parents' employment status, which is strongly associated with family income and health insurance coverage, may also affect survival. SES may also affect adherence to treatment. For example, compared with NH Whites, non-white cancer patients have been reported to be less likely to be adherent to oral 6-mercaptopurine, a medication for acute lymphoblastic leukemia which requires 2-year maintenance (35). This could be explained by financial barriers, the parents' lower health literacy, as well as linguistic and contextual barriers, including provider cultural competence, which can result in communication difficulties with healthcare provider teams. The results that Non-white patients had worse survival compared with NH White even after adjusting for demographic and clinical characteristics, health insurance, and SDI indicated that racial/ethnic disparities were also in part due to other factors, including overt and structural racism. There have been increasing concerns that structural racism might be associated with worse access and health outcomes among adults (36, 37). Few studies have focused on the structural racism among patients with childhood cancer. With the increasing attention of this issue in today's social and political climate, futures studies to understand the role of structural racism on childhood cancer survival will be important. Our finding among children with brain tumors, that non-white patients with private insurance had poorer survival than NH Whites with Medicaid suggests additional research is needed to better disentangle the complex role of other factors, such as social determinants of health and structural racism.

Disparities in childhood cancer survival have received increasing attention (38, 39). However, understanding of childhood cancer survival disparities is still limited and few interventions have been developed to reduce these disparities. Widespread participation in clinical trials (nearly 60%) played a large role in improving the 5-year survival of childhood cancer to 80%. However, trial participation rates have been low for minority children with cancer (40), which could be partially explained by barriers resulting from lower SES and being uninsured (41). Increasing access to and funding for clinical trials of childhood cancer, especially programs targeting non-white children, may help reduce the disparities. Programs such as providing financial assistance to childhood cancer patients with low SES may improve their access to treatment. For example, St. Jude Children Research Hospital provides free treatments and reimburses expenses from housing, transportation, and food during treatment to patients with childhood cancer (42). Other programs such as culturally sensitive patient navigation (43), which have been used mainly for adult cancer patients, could be adapted and benefit patients with childhood cancer and their families.

We found that health insurance also contributed to the racial/ethnic childhood cancer survival disparities, suggesting that improving health insurance coverage may help reduce racial/ethnic survival disparities. Health insurance coverage, a strong indicator of access to high-quality care, could contribute to the survival disparities by race/ethnicity through care access. In addition, being uninsured or without adequate coverage may expose patients' family to high out-of-pocket costs and financial burden, requiring them to balance their families' need for housing and food with medical care, which may cause delays in receiving timely care and completing care. compared with NH Whites, non-white childhood cancer patients were substantially less likely to have private insurance and more likely to be covered by Medicaid. We found that children with Medicaid coverage had inferior survival than the privately insured. Earlier studies have shown that children covered by Medicaid were likely to have worse healthcare utilization and health outcomes compared with the privately insured (44), which could potentially be explained by low family income, coverage disruption, and limited access to care due to some providers not accepting patients with Medicaid coverage. More specifically, cancer registries only include health insurance coverage at a single time, and changes in coverage are common, especially among low income populations and those with Medicaid coverage (45). Some newly diagnosed childhood cancer patients gain Medicaid coverage only at the point of their cancer diagnosis and may not have had access to primary care to evaluate signs and symptoms of cancer prior to diagnosis. Of note, some earlier studies reported inconsistent findings and suggested that children covered by Medicaid have care access comparable to that of children with private health insurance (46, 47). Thus, future studies with a large national sample and longitudinal health insurance information are warranted to better understand this issue.

We also found that compared with NH Whites, NH Black and Hispanic patients with childhood cancer were more likely to be uninsured (48). An earlier study showed that the 5-year survival rate was lower for uninsured patients with childhood cancer than those with private insurance (46). Several national and state programs have been developed to increase health insurance coverage for low income populations. For example, about 700,000 low-income children gained coverage through their parents' Medicaid plan after Medicaid expansion under the ACA (49). The CHIP provides low-cost health insurance coverage for children in families that earn too much money to qualify for Medicaid (50). Despite our estimate of an overall uninsured rate of less than 5%, it represents many newly diagnosed patients with childhood cancer nationally each year (51). Programs to simplify the health insurance enrollment process and to provide enrollment in financial assistance to children and families with low SES may further reduce the uninsured rate.

Our study had several limitations. First, we used hospital-based instead of population-based cancer registry data; and misclassification of Hispanic patients as NH white patients in this sample has been reported previously (14). Second, due to lack of individual-level SES, we were only able to evaluate the contribution of area-level SES factors on survival disparities, which might be less accurate and reflect a different concept more relevant to area resources. Third, changes in health insurance status after diagnosis are not available in registry-based data. Multiple measures of health insurance coverage will be important for future data collection efforts. Fourth, the survival rates might be overestimated for Hispanics and NH other because of their higher loss to follow-up (52). The survival information was collected by patient contact, contact with hospitals or related institutions, death certificate, and other sources (53). Historically, Hispanics have less accurate death certificate information than NH Whites, which might lead to underestimation of survival disparities (54) and understated contribution of health insurance and SES on survival disparities. In addition, we used all-cause mortality data because cancer-specific mortality data were unavailable. We were also not able to measure other important potential mediators, such as clinical trial enrollment and transportation difficulties, and parents' sociodemographic information, such as family structure, parents' employment, linguistic barriers, and experiences of discrimination. Stage at diagnosis was not included in this study because it was not available for leukemias and the relatively high missing rates for other cancers. In addition, race/ethnicity, health insurance, and SES, as well as other covariates such as rural or urban are highly correlated. Future studies should explore their inter-relationship and effects on cancer survival using individual-level measures at multiple time-points, especially as more advanced statistical methods are developed. Despite these limitations, we used a large national cohort to evaluate the racial/ethnic childhood cancer survival disparities and quantify the contribution of SES and health insurance on these disparities.

Conclusion

In summary, this study highlighted the substantial racial/ethnic childhood cancer survival disparities and the contribution of area-level SES and health insurance on these disparities in the United States. Programs to expand health insurance coverage may help reduce the survival disparities associated with race/ethnicity.

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Authors' Contributions

J. Zhao: Conceptualization, formal analysis, visualization, methodology, writing–original draft, writing–review and editing. **X. Han:** Conceptualization, methodology, writing–original draft, writing–review and editing. **Z. Zheng:** Conceptualization, methodology, writing–original draft, writing–review and editing. **L. Nogueira:** Conceptualization, methodology, writing–original draft, writing–review and editing. **A.D. Lu:** Conceptualization, methodology, writing–original draft, writing–review and editing. **P.C. Nathan:** Conceptualization, methodology, writing–original draft, writing–review and editing. **K.R. Yabroff:** Conceptualization, supervision, methodology, writing–original draft, writing–review and editing.

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