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Survival disparities for childhood cancers exist when defined by race/ethnicity and sex

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ABSTRACT

Background: There are documented racial/ethnic and sex differences in pediatric cancer survival; however, it is unknown whether pediatric cancer survival disparities exist when race/ethnicity and sex are considered jointly.
Methods: Using SEER data (2000–2017), we estimated survival differences by race/ethnicity within sexes and by sex within race/ethnicity (White, Black, Hispanic, and Asian/Pacific Islander [API]) for 17 cancers in children aged (0–19 years). Kaplan-Meier curves (Log-Rank p-values) were assessed. Cox regression was used to estimate hazards ratios (HRs) and 95 % confidence intervals (95 % CIs) between race/ethnicity/sex and cancer.
Results: We included 51,759 cases (53.6 % male, 51.9 % White). There were statistically significant differences in 18-year survival by race/ethnicity-sex for 12/17 cancers. Within sexes, minorities had an increased risk of death compared to Whites for various cancers including acute lymphoblastic leukemia (ALL) (females: HispanicHR: 1.78, 95 % CI: 1.52, 2.10; BlackHR: 1.70, 95 % CI: 1.29, 2.24; APIHR: 1.42, 95 % CI: 1.07–1.89; males ALL: HispanicHR: 1.58, 95 % CI: 1.39,1.79; BlackHR: 1.57, 95 % CI: 1.26,1,95; API-HR: 1.39, 95 % CI: 1.11, 1.75) and astrocytoma (females: HispanicHR: 1.49, 95 % CI: 1.19, 1.85; BlackHR: 1.67, 95 % CI: 1.29, 2.17; API-HR: 1.51, 95 % CI: 1.05, 2.15; males: HispanicHR:1.27, 95 % CI: 1.04, 1.56; BlackHR: 1.69, 95 % CI: 1.32, 2.17; API-HR: 1.92, 95 % CI: 1.43, 2.58). Sex differences in survival within racial/ethnic groups were observed for White (ALL, osteosarcoma), Hispanic (medulloblastoma), and API (Primitive Neuro-Ectodermal Tumor [PNET]) children.
Conclusions: There are disparities in survival by both race/ethnicity and sex highlighting the societal and biologic influences these features have on survival in children with cancer.

1. Introduction

Racial/ethnic differences in pediatric cancer survival have been reported. There are racial/ethnic disparities in acute lymphoblastic leukemia (ALL) survival such that Black children, who have half the rate of ALL incidence of White children, [1] experience worse outcomes than White children [2] and have a higher frequency of high-risk disease features including a higher white blood cell count, a higher proportion of somatic structural chromosomal anomalies, less high hyperdiploidy, and more central nervous system involvement [3–6]. A higher risk of death has also been reported in Hispanic and American Indian/Alaska Native children with ALL [7]. For brain tumors, the most common solid tumor in children, [8] minority children have an increased risk of death compared to White children [9,10] even after adjustment for age, socioeconomic status, stage of disease and treatment [11]. Minority children fare worse than White for pediatric sarcomas [12]. Survival differences have been observed for Black and Hispanic children compared to White with acute myeloid leukemia (AML), neuroblastoma

Abbreviations: SEER, Surveillance Epidemiology and End Results; API, Asian/Pacific Islander; HR, hazards ratios; 95 % CIs, 95 % confidence intervals; ALL, Acute lymphoblastic leukemia; PNET, Peripheral Neuroectodermal Tumor; AML, acute myeloid leukemia; SES, socioeconomic status; ICCC, International Classification of Childhood Cancer.

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and lymphomas [13]. Often times, racial/ethnic survival disparities are linked to existing differences in socioeconomic status [14]. However, in a mediation analysis examining the role of socioeconomic status (SES) between race/ethnicity and survival from childhood cancers [13] strong direct effects of race/ethnicity were observed suggesting genomics, treatment receipt or response differences may underlie the observed disparities.

We recently reported on sex differences in survival where males had worse overall survival for ALL, ependymoma, neuroblastoma, osteosarcoma, thyroid carcinoma, and malignant melanoma [15]. The observed sex differences in survival could be due to sexually dimorphic tumor profiles as we reported for osteosarcoma, [16] response to treatment, [17] delay in diagnosis [18] or delay in treatment. Given the existing racial/ethnic and sex differences in childhood cancer survival, we conducted stratified analyses by race/ethnicity and sex jointly to better understand the biologic underpinnings of the existing outcome disparities using SEER data for 17 pediatric malignancies. Further, rather than adjust for race/ethnicity in sex-stratified analyses or vice versa, our analytic approach allows us to identify groups that are at an increased risk of death following a childhood cancer diagnosis. Whereas past analyses treated race/ethnicity or sex as an adjustment variable, which may mask effect measure modification of the association between these factors and death after a childhood cancer diagnosis, we are considering both factors for a clearer picture of survival disparities in children with cancer.

2. Methods

Study population. Children aged 0–19 years diagnosed with microscopically confirmed first primary tumors were identified in SEER 18 [19] (2000–2017). We included individuals with a first primary diagnosis classified as one of the main International Classification of Childhood Cancer (ICCC, 3rd edition [20]) types, described below. Cancers with $>$ 500 cases total and $>$ 5 cases in each race/ethnicity-sex stratum were included. As this is publicly available data, it was exempt from review by the University of Minnesota Institutional Review Board.

Cancer type. The ICCC categories included were Ia Acute lymphoid leukemia, Ib Acute myeloid leukemia, IIa Hodgkin lymphoma, IIb non-Hodgkin lymphoma, IIc Burkitt lymphoma, IIIa Ependymoma, IIIb Astrocytoma, IIIc.1 Medulloblastoma, IIIc.2 Peripheral Neuroectodermal Tumor (PNET), IVa Neuroblastoma, V Retinoblastoma, VIa Nephroblastoma, VIIa Hepatoblastoma, VIIIa Osteosarcoma, VIIIc Ewing sarcoma, IXa Rhabdomyosarcoma, and XIb Thyroid carcinoma. Germ cell tumors were excluded as we have characterized racial/ethnic/sex survival differences elsewhere [21].

Variables of interest. The following variables were obtained from SEER: race/ethnicity (non-Hispanic, White [White]; non-Hispanic, Black [Black]; Asian/Pacific Islander [API]; Hispanic), sex (male, female), age at diagnosis (<1, 1–4, 5–9, 10–14, 15–19 years), year of diagnosis (2000–2004, 2005–2009, 2010–2014, 2015–2017), stage of disease (stage was harmonized over the years of SEER data available using the SEER Summary stage 2000_1998 variable for cases diagnosed in 2000–2003 and the SEER summary stage 2000200 for cases diagnosed 2004–2017 and categorized as: local, regional, distant; not available for I Leukemias), years of survival (SEER-defined using the date of diagnosis and date of death from any cause or last contact by 12/31/2017), and vital status (dead, alive; determined through linkages to state registries or the National Death Index). Analyses were conducted within race/ethnicity by sex (female=referent) and within sex by race/ethnicity (White=referent). Additional exploratory analyses were done using race/ethnicity-sex categories defined as White-female (referent), White-male, Hispanic-female, Hispanic-male, Black-female, Black-male, API-female, API-male.

Statistical analysis. Five-year overall survival percentages and 95 % confidence intervals (95 % CI) stratified by race/ethnicity-sex categories for each cancer were estimated using the nonparametric maximum likelihood estimate of the survivor function. Kaplan-Meier survival curves and Log-Rank p-values for overall survival at 18 years post-diagnosis were generated. Cox proportional hazards models were used to estimate hazard ratios (HR) and 95 % CI for the association between race/ethnicity and sex groupings (White and female referent for each relevant analysis) and death for each cancer. For the following analyses, we considered 18-year survival as long-term survival is especially important for children as they survive into young adulthood, where follow-up care is critical for improved quality of life. In sensitivity analyses, we examined HRs at 5, 10, and 15 years and observed largely consistent trends in associations for most cancers (Supplemental Table 1).

Confounders included age, year of diagnosis, and stage of disease for solid tumors and were selected based on availability in SEER and their role in the association between race/ethnicity and death from childhood cancer. There was no violation of the proportional hazards assumption when entering interaction terms for race/ethnicity and time, sex and time, or a race/ethnicity-sex interaction term (White-female, White-male, Black-female, Black-male, etc.) with time in the adjusted model for each cancer (all $p > 0.05$). Further, examination of the Schoenfeld residuals confirmed the lack of violation of the proportional hazards assumption. Adjustment of stage of disease, which is a mediator, has allowed us to estimate the direct effects of race/ethnicity and sex on death. To examine the statistical interaction between sex and race/ethnicity, a sex*race/ethnicity term was entered into the models and the likelihood ratio test p-value was evaluated ($p < 0.05$ was indicative of statistical interaction between race/ethnicity and sex). Analyses were done using SAS v9.4 (SAS Institute, Cary, NC). Figures were generated in GraphPad Prism v9 (La Jolla, CA) and R. Statistical significance was determined using two-sided hypothesis tests (alpha = 0.05). No adjustment for multiple comparisons was made due to the observational nature of this research.[22].

3. Results

3.1. Survival differences

There were 51,759 cases included (53.6 % male) (Table 1). Counts by race/ethnicity-sex were 14,377 (27.8 %) White-male, 12,478 (24.1 %) White-female, 8340 (16.1 %) Hispanic-male, 7118 (13.8 %) Hispanic-female, 2919 (5.6 %) Black-male, 2526 (4.9 %) Black-female, 2131 (4.1 %) API-male, and 2131 (4.1 %) API-female.

When considering 5-year survival (Table 2), 11 out of 17 cancers displayed $>$ 10 % difference in 5-year survival when comparing the groups with the highest and lowest survival percentages. White males and females accounted for 10 of the highest survival percentages while Black males and females had the lowest survival percentage for 10 cancers. Cancers with $>$ 20 % differences in the percent survival were ependymomas (24.4 % difference, White-female 85.9 %, Black-male 61.5 %), PNET (51.9 % difference, Hispanic-female 67.1 %, API-male 15.2 %), hepatoblastoma (36.5 % difference, API-female 86.7 %, Black-female 50.2 %), and Ewing sarcoma (21.8 % difference, Black-male 75.2 %, Black-female 53.4 %).

In Kaplan-Meier analyses of racial/ethnic survival differences within sexes (Fig. 1, non-significant curves, Supplemental Figure 1), there were racial/ethnic differences in survival among males for ALL, non-Hodgkin lymphoma, ependymoma, astrocytoma, PNET, neuroblastoma, nephroblastoma, and Ewing sarcoma. In females, racial/ethnic differences in survival existed for ALL, AML, Hodgkin lymphoma, ependymoma, astrocytoma, PNET, neuroblastoma, retinoblastoma, hepatoblastoma, and thyroid carcinoma. By sex within race/ethnicity, there were few cancers with statistically significant sex differences in 18-year survival and females never had worse survival than males (Fig. 2, non-significant curves Supplemental Fig. 2). Among Whites, males had worse survival than females for ALL, neuroblastoma, and osteosarcoma. For Hispanics, males had worse survival for ALL. Within APIs, males had worse survival

Table 1
Case demographic and clinical characteristic distributions by race/ethnicity and sex for each childhood cancer, SEER 2000–2017. Case counts less than 10 have been suppressed (denoted with "-").

		Cases	Stage of disease				Vital status*		Age in years				Year of diagnosis			
		N (%)	Local	Regional	Distant	Missing	Alive	Dead	0–4	5–9	10–14	15–19	2000–2004	2005–2009	2010–2014	2015–2017
ALL (N = 14,431)																
Females	**White**	2852 (19.8)	n/a	n/a	n/a	n/a	2603 (91.3)	249 (8.7)	1501 (52.6)	696 (24.4)	414 (14.5)	241 (8.5)	797 (28.0)	807 (28.3)	788 (27.6)	460 (16.1)
	Black	427 (3.0)	n/a	n/a	n/a	n/a	363 (85.0)	64 (15.0)	193 (45.2)	109 (25.5)	78 (18.3)	47 (11.0)	128 (30.0)	99 (23.2)	123 (28.8)	77 (18.0)
	Hispanic	2478 (17.2)	n/a	n/a	n/a	n/a	2114 (85.3)	364 (14.7)	1138 (45.9)	650 (26.2)	420 (17.0)	270 (10.9)	581 (23.5)	695 (28.1)	757 (30.6)	445 (18.0)
	API	518 (3.6)	n/a	n/a	n/a	n/a	459 (88.6)	59 (11.4)	280 (54.1)	125 (24.1)	68 (13.1)	45 (8.7)	136 (26.3)	126 (24.3)	151 (29.2)	105 (20.3)
Males	**White**	3727 (25.8)	n/a	n/a	n/a	n/a	3294 (88.4)	433 (11.6)	1713 (46.0)	940 (25.2)	525 (14.1)	549 (14.7)	1131 (30.4)	1035 (27.8)	972 (26.1)	589 (15.8)
	Black	567 (3.9)	n/a	n/a	n/a	n/a	465 (82.0)	102 (18.0)	216 (38.1)	129 (22.8)	139 (24.5)	83 (14.6)	125 (22.1)	192 (33.9)	160 (28.2)	90 (15.9)
	Hispanic	3234 (22.4)	n/a	n/a	n/a	n/a	2689 (83.2)	545 (16.9)	1347 (41.7)	765 (23.7)	553 (17.1)	569 (17.6)	760 (23.5)	907 (28.1)	947 (29.3)	620 (19.2)
	API	628 (4.4)	n/a	n/a	n/a	n/a	538 (85.7)	90 (14.3)	216 (38.1)	129 (22.8)	139 (24.5)	83 (14.6)	149 (23.7)	185 (29.5)	180 (28.7)	114 (18.2)
AML (N = 3242)																
Females	**White**	703 (21.7)	n/a	n/a	n/a	n/a	473 (67.3)	230 (32.7)	261 (37.1)	75 (10.7)	128 (18.2)	239 (34.0)	197 (28.0)	193 (27.5)	213 (30.3)	100 (14.2)
	Black	194 (6.0)	n/a	n/a	n/a	n/a	110 (56.7)	84 (43.3)	78 (40.2)	19 (9.8)	46 (23.7)	51 (26.3)	45 (23.2)	67 (34.5)	44 (22.7)	38 (29.6)
	Hispanic	491 (15.1)	n/a	n/a	n/a	n/a	317 (64.6)	174 (35.4)	194 (39.5)	65 (13.2)	109 (22.2)	123 (25.1)	131 (26.7)	135 (27.5)	134 (27.3)	91 (18.5)
	API	153 (4.7)	n/a	n/a	n/a	n/a	98 (64.1)	55 (36.0)	45 (29.4)	32 (20.9)	27 (17.7)	49 (32.0)	34 (22.2)	40 (26.1)	50 (32.7)	29 (19.0)
Males	**White**	780 (24.1)	n/a	n/a	n/a	n/a	514 (65.9)	266 (34.1)	268 (34.4)	102 (13.1)	173 (22.2)	237 (30.4)	246 (31.5)	226 (29.0)	201 (25.8)	107 (13.7)
	Black	222 (6.9)	n/a	n/a	n/a	n/a	128 (57.7)	94 (42.3)	79 (35.6)	30 (13.5)	62 (27.9)	51 (23.0)	69 (31.1)	62 (27.9)	51 (23.0)	40 (18.0)
	Hispanic	531 (16.4)	n/a	n/a	n/a	n/a	338 (63.7)	193 (36.4)	201 (37.9)	72 (13.6)	120 (22.6)	138 (26.0)	121 (22.8)	154 (29.0)	168 (31.6)	88 (16.6)
	API	168 (5.2)	n/a	n/a	n/a	n/a	114 (67.9)	54 (32.1)	64 (38.1)	25 (14.9)	48 (28.6)	31 (18.5)	41 (24.4)	38 (22.6)	55 (32.7)	34 (20.2)
Hodgkin lymphoma (N = 4965)																
Females	**White**	1382 (27.8)	143 (10.7)	800 (59.6)	400 (29.8)	39	1313 (95.0)	69 (5.0)	7 (0.5)	54 (3.9)	287 (20.8)	1034 (74.8)	405 (29.3)	417 (30.2)	350 (25.3)	210 (15.2)
	Black	280 (5.6)	32 (11.7)	123 (44.9)	119 (43.4)	6	249 (88.9)	31 (11.1)	2 (0.7)	21 (7.5)	82 (29.3)	175 (62.5)	69 (24.6)	94 (22.6)	69 (24.6)	48 (17.1)
	Hispanic	509 (10.3)	53 (10.6)	246 (49.3)	200 (40.1)	10	488 (95.9)	21 (4.1)	11 (2.2)	41 (8.1)	146 (28.7)	311 (61.1)	112 (22.0)	142 (27.9)	157 (30.8)	98 (19.3)
	API	124 (2.5)	13 (10.7)	57 (46.7)	52 (42.6)	2	113 (91.1)	11 (8.9)	3 (2.4)	5 (4.0)	26 (21.0)	90 (72.6)	27 (21.8)	39 (31.5)	32 (25.8)	26 (21.0)
Males	**White**	1495 (30.1)	248 (17.1)	679 (46.9)	520 (35.9)	48	1424 (95.3)	71 (4.8)	18 (1.2)	121 (8.1)	373 (25.0)	983 (65.8)	406 (27.2)	461 (30.8)	296 (26.5)	232 (15.5)
	Black	329 (6.6)	64 (20.3)	104 (33.0)	147 (46.7)	14	308 (93.6)	21 (6.4)	8 (2.4)	51 (15.5)	87 (26.4)	183 (55.6)	73 (22.2)	95 (28.9)	100 (30.4)	61 (18.5)
	Hispanic	662 (13.3)	98 (15.3)	258 (40.4)	283 (44.3)	23	619 (93.5)	43 (6.5)	26 (3.9)	124 (18.7)	184 (27.8)	328 (49.6)	166 (25.1)	194 (29.3)	209 (31.6)	93 (14.1)
	API	182 (3.7)	19 (10.4)	83 (45.6)	80 (44.0)	2	174 (94.6)	10 (5.4)	6 (3.3)	26 (14.1)	49 (26.6)	103 (56.0)	40 (21.7)	54 (29.4)	60 (32.6)	30 (16.3)

(*continued on next page*)

Table 1 (*continued*)

		Cases	Stage of disease				Vital status*		Age in years				Year of diagnosis			
		N (%)	Local	Regional	Distant	Missing	Alive	Dead	0–4	5–9	10–14	15–19	2000–2004	2005–2009	2010–2014	2015–2017
Non-Hodgkin lymphoma (N = 3758)																
Females	**White**	659 (17.5)	201 (32.3)	128 (20.6)	294 (47.2)	36	569 (86.3)	90 (13.7)	65 (9.9)	108 (16.4)	196 (29.7)	290 (44.0)	195 (29.6)	165 (25.0)	192 (29.1)	107 (16.2)
	Black	212 (5.6)	60 (29.6)	41 (20.2)	102 (50.3)	9	169 (79.7)	43 (20.3)	26 (12.3)	38 (17.9)	55 (25.9)	93 (43.9)	58 (27.4)	65 (30.7)	63 (29.7)	26 (12.3)
	Hispanic	362 (9.6)	122 (36.3)	68 (20.2)	146 (43.5)	26	302 (83.4)	60 (16.6)	53 (14.6)	63 (17.4)	105 (29.0)	141 (39.0)	66 (18.2)	103 (28.5)	109 (30.1)	84 (23.2)
	API	132 (3.5)	52 (41.6)	25 (20.0)	48 (38.4)	7	113 (85.6)	19 (14.4)	11 (8.3)	26 (19.7)	33 (35.0)	62 (47.0)	32 (24.2)	31 (23.5)	52 (29.4)	17 (12.9)
Males	**White**	1234 (32.8)	371 (32.0)	211 (18.2)	579 (49.9)	73	1077 (87.3)	157 (12.7)	138 (11.2)	210 (17.0)	313 (25.4)	573 (46.4)	328 (26.6)	334 (27.1)	346 (28.0)	226 (18.3)
	Black	337 (9.0)	109 (33.8)	58 (18.0)	156 (48.3)	14	273 (81.0)	64 (19.0)	21 (6.2)	64 (19.0)	100 (29.7)	152 (45.1)	77 (22.9)	97 (28.8)	107 (31.8)	56 (16.6)
	Hispanic	613 (16.3)	186 (31.9)	109 (18.7)	289 (49.5)	29	518 (84.5)	95 (15.5)	60 (9.8)	152 (24.8)	173 (28.2)	228 (37.2)	149 (24.3)	149 (24.3)	199 (32.5)	116 (18.9)
	API	209 (5.6)	68 (33.8)	40 (19.9)	93 (46.3)	8	181 (86.6)	28 (13.4)	29 (13.9)	39 (18.7)	58 (27.8)	83 (39.7)	42 (20.1)	47 (22.5)	75 (35.9)	45 (21.5)
Burkitt lymphoma (N = 1034)																
Females	**White**	109 (10.5)	26 (24.1)	17 (15.7)	65 (60.2)	1	97 (89.0)	12 (11.0)	18 (16.5)	30 (27.5)	28 (25.7)	33 (30.3)	31 (28.4)	30 (27.5)	26 (23.9)	22 (20.2)
	Black	28 (2.7)	8 (29.6)	5 (18.5)	14 (51.9)	1	24 (85.7)	4 (14.3)	5 (17.9)	10 (35.7)	8 (28.6)	5 (17.9)	5 (17.9)	12 (42.9)	5 (17.9)	6 (21.4)
	Hispanic	53 (5.1)	15 (29.4)	8 (15.7)	28 (54.9)	2	51 (96.2)	2 (3.8)	8 (15.1)	19 (35.9)	11 (20.8)	15 (28.3)	11 (20.8)	13 (24.5)	18 (34.0)	11 (20.8)
	API	13 (1.3)	6 (50.0)	2 (16.7)	4 (33.3)	1	12 (92.3)	1 (7.7)	0 (0.0)	5 (28.5)	5 (28.5)	3 (23.1)	4 (30.8)	4 (30.8)	1 (7.7)	4 (30.8)
Males	**White**	534 (51.6)	137 (26.1)	121 (23.1)	267 (50.9)	9	479 (89.7)	55 (10.3)	64 (12.0)	189 (35.4)	157 (29.4)	124 (23.2)	145 (27.2)	158 (29.6)	149 (27.9)	82 (15.4)
	Black	72 (7.0)	15 (21.7)	17 (24.6)	37 (53.6)	3	60 (83.3)	12 (16.7)	13 (18.1)	21 (29.2)	16 (22.2)	22 (30.6)	18 (25.0)	23 (31.9)	18 (25.0)	13 (18.1)
	Hispanic	156 (15.1)	39 (25.3)	42 (27.3)	73 (47.4)	2	141 (90.4)	15 (9.6)	34 (21.8)	44 (28.2)	38 (24.4)	40 (25.6)	48 (30.8)	30 (19.2)	44 (28.2)	34 (21.8)
	API	69 (6.7)	14 (20.6)	15 (22.1)	39 (57.4)	1	62 (89.9)	7 (10.1)	9 (13.0)	21 (30.4)	20 (29.0)	19 (27.5)	22 (31.9)	17 (24.6)	19 (27.5)	11 (15.9)
Ependymoma (N = 1076)																
Females	**White**	250 (23.2)	187 (77.3)	38 (15.7)	17 (7.0)	8	204 (81.6)	46 (18.4)	125 (50.0)	43 (17.2)	41 (16.4)	41 (16.4)	62 (24.8)	72 (28.8)	67 (26.8)	49 (19.6)
	Black	59 (5.5)	39 (70.9)	9 (16.4)	7 (12.7)	4	39 (66.1)	20 (33.9)	29 (49.2)	15 (25.4)	9 (15.3)	6 (10.2)	23 (39.0)	9 (15.3)	18 (30.5)	9 (15.3)
	Hispanic	156 (14.5)	105 (69.5)	36 (23.8)	10 (6.6)	5	109 (69.9)	47 (30.1)	82 (52.6)	38 (24.4)	21 (13.5)	15 (9.6)	44 (28.2)	43 (27.6)	47 (30.1)	22 (14.1)
	API	31 (2.9)	26 (86.7)	3 (10.0)	1 (3.3)	1	25 (80.7)	6 (19.4)	11 (35.5)	11 (35.5)	3 (9.7)	6 (19.4)	9 (29.0)	8 (25.8)	10 (32.3)	4 (12.9)
Males	**White**	290 (27.0)	221 (80.4)	35 (12.7)	19 (6.9)	15	218 (75.2)	72 (24.8)	143 (49.3)	41 (14.1)	56 (19.3)	50 (17.2)	84 (29.0)	82 (28.3)	81 (27.9)	43 (14.8)
	Black	70 (6.5)	57 (82.6)	10 (14.5)	2 (2.9)	1	43 (61.4)	27 (38.6)	33 (47.1)	18 (25.7)	8 (11.4)	11 (15.7)	17 (24.3)	14 (20.0)	25 (35.7)	14 (20.0)
	Hispanic	174 (16.2)	123 (75.0)	34 (20.7)	7 (4.3)	10	124 (71.3)	50 (28.7)	85 (48.9)	39 (22.4)	30 (17.2)	20 (11.5)	48 (27.6)	49 (28.2)	47 (27.0)	30 (17.2)
	API	46 (4.3)	36 (78.3)	8 (17.4)	2 (4.4)	0	36 (78.3)	10 (21.7)	22 (47.8)	12 (26.1)	5 (10.9)	7 (15.2)	6 (13.0)	12 (26.1)	16 (34.8)	12 (26.1)
Astrocytoma (N = 5271)																

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Table 1 (*continued*)

		Cases	Stage of disease				Vital status*		Age in years				Year of diagnosis			
		N (%)	Local	Regional	Distant	Missing	Alive	Dead	0–4	5–9	10–14	15–19	2000–2004	2005–2009	2010–2014	2015–2017
Females	**White**	1497 (28.4)	1233 (86.7)	160 (11.2)	30 (2.1)	74	1249 (83.4)	248 (16.6)	359 (24.0)	403 (26.9)	421 (28.1)	314 (21.0)	446 (29.8)	404 (27.0)	427 (28.5)	220 (14.7)
	Black	297 (5.6)	234 (82.1)	43 (15.1)	8 (2.8)	12	220 (74.1)	77 (25.9)	83 (28.0)	91 (30.6)	67 (22.6)	56 (18.9)	70 (23.6)	82 (27.6)	101 (34.0)	44 (14.8)
	Hispanic	583 (11.1)	469 (84.1)	71 (12.7)	18 (3.2)	25	456 (78.2)	127 (21.8)	197 (33.8)	170 (29.2)	115 (19.7)	101 (17.3)	159 (27.3)	167 (28.6)	171 (29.3)	86 (14.8)
	API	153 (2.9)	125 (83.9)	19 (12.8)	5 (3.4)	4	119 (77.8)	34 (22.2)	53 (34.6)	34 (22.2)	36 (23.5)	30 (19.6)	37 (24.2)	44 (28.8)	43 (28.1)	29 (19.0)
Males	**White**	1643 (31.2)	1364 (86.1)	178 (11.2)	42 (2.7)	59	1339 (81.5)	304 (18.5)	396 (24.1)	407 (24.8)	433 (26.4)	407 (24.8)	504 (30.7)	447 (27.2)	476 (29.0)	216 (13.2)
	Black	292 (5.5)	242 (86.7)	31 (11.1)	6 (2.2)	13	212 (72.6)	80 (27.4)	79 (27.1)	66 (22.6)	80 (27.4)	67 (23.0)	86 (29.5)	75 (25.7)	82 (28.1)	49 (16.8)
	Hispanic	632 (12.0)	514 (83.9)	83 (13.5)	16 (2.6)	19	494 (78.2)	138 (21.8)	171 (27.1)	174 (27.5)	152 (24.1)	135 (21.4)	167 (26.4)	178 (28.2)	178 (28.2)	109 (17.3)
	API	174 (3.3)	151 (89.4)	13 (7.7)	5 (3.0)	5	122 (70.1)	52 (29.9)	46 (26.4)	38 (21.8)	43 (24.7)	47 (27.0)	44 (25.3)	43 (24.7)	54 (31.0)	33 (19.0)
Medulloblastoma (N = 1605)																
Females	**White**	320 (19.9)	233 (74.4)	25 (8.0)	55 (17.6)	2	228 (71.3)	92 (28.8)	109 (34.1)	111 (34.7)	55 (17.2)	45 (14.1)	90 (28.1)	97 (30.3)	75 (23.4)	58 (18.1)
	Black	60 (3.7)	45 (77.6)	4 (6.9)	9 (15.5)	2	39 (65.0)	21 (35.0)	18 (30.0)	24 (40.0)	11 (18.3)	7 (11.7)	14 (23.3)	16 (26.7)	21 (35.0)	9 (15.0)
	Hispanic	156 (9.7)	104 (67.1)	24 (15.5)	27 (17.4)	1	116 (74.4)	40 (25.6)	61 (39.1)	60 (38.5)	22 (14.1)	13 (8.3)	44 (28.2)	39 (25.0)	45 (28.9)	28 (18.0)
	API	45 (2.8)	31 (70.5)	6 (13.6)	7 (15.9)	1	31 (68.9)	14 (31.1)	16 (35.6)	17 (237.8)	7 (15.6)	5 (11.1)	7 (15.6)	14 (31.1)	16 (35.6)	8 (17.8)
Males	**White**	609 (37.9)	439 (74.0)	52 (8.8)	102 (17.2)	16	436 (71.6)	173 (28.4)	180 (29.6)	229 (37.6)	131 (21.5)	69 (11.3)	154 (25.3)	179 (29.4)	174 (28.6)	102 (16.8)
	Black	67 (4.2)	49 (76.6)	3 (4.7)	12 (18.8)	3	46 (68.7)	21 (31.3)	19 (28.4)	27 (40.3)	12 (17.9)	9 (13.4)	18 (26.9)	13 (19.4)	20 (29.9)	16 (23.9)
	Hispanic	268 (16.7)	196 (74.2)	26 (9.9)	42 (15.9)	4	178 (66.4)	90 (33.6)	107 (39.9)	93 (34.7)	41 (15.3)	27 (10.1)	78 (29.1)	72 (26.9)	69 (25.8)	49 (18.3)
	API	80 (5.0)	53 (68.0)	7 (9.0)	18 (23.1)	2	61 (76.3)	19 (23.8)	30 (37.5)	33 (41.3)	13 (16.3)	4 (5.0)	13 (16.3)	20 (25.0)	25 (31.3)	22 (27.5)
PNET (N = 568)																
Females	**White**	136 (23.9)	71 (55.5)	32 (25.0)	25 (19.5)	8	75 (55.2)	61 (44.9)	59 (43.4)	29 (21.3)	22 (16.2)	26 (19.1)	54 (39.7)	32 (23.5)	38 (27.9)	12 (8.8)
	Black	31 (5.5)	19 (67.9)	2 (7.1)	7 (25.0)	3	11 (35.5)	20 (64.5)	14 (45.2)	2 (6.5)	10 (32.3)	5 (16.1)	15 (48.4)	12 (38.7)	3 (9.7)	1 (3.2)
	Hispanic	66 (11.6)	38 (58.5)	15 (23.1)	12 (18.5)	1	41 (62.1)	25 (37.9)	29 (43.9)	17 (25.8)	10 (15.2)	10 (15.2)	32 (48.5)	20 (30.3)	10 (15.2)	4 (6.1)
	API	24 (4.2)	16 (66.7)	3 (12.5)	5 (20.8)	0	12 (50.0)	12 (50.0)	12 (50.0)	2 (8.3)	5 (20.8)	5 (20.8)	12 (50.0)	3 (12.5)	6 (25.0)	3 (12.5)
Males	**White**	168 (29.6)	90 (58.8)	28 (18.3)	35 (33.9)	15	92 (54.8)	76 (45.2)	71 (42.3)	39 (23.2)	29 (17.3)	29 (17.3)	80 (47.6)	47 (28.0)	31 (18.5)	10 (6.0)
	Black	36 (6.3)	20 (64.5)	3 (9.7)	8 (25.8)	5	16 (44.4)	20 (55.6)	14 (38.9)	9 (25.0)	8 (22.2)	5 (13.9)	12 (33.3)	11 (30.6)	8 (22.2)	5 (13.9)
	Hispanic	89 (15.7)	53 (63.1)	20 (23.8)	11 (13.1)	5	48 (53.9)	41 (46.1)	37 (41.6)	22 (24.7)	16 (18.0)	14 (15.7)	32 (36.0)	32 (36.0)	17 (19.1)	8 (9.0)
	API	18 (3.2)	10 (55.6)	4 (22.2)	4 (22.2)	0	4 (22.2)	14 (77.8)	7 (28.9)	5 (27.8)	2 (11.1)	4 (22.2)	6 (33.3)	6 (33.3)	5 (27.8)	1 (5.6)
Neuroblastoma (N = 3112)																
Females	**White**					194					36 (4.2)	10 (1.2)	270 (31.4)	238 (27.7)	224 (26.1)	127 (14.8)

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Table 1 (*continued*)

		Cases	Stage of disease				Vital status*		Age in years				Year of diagnosis			
		N (%)	Local	Regional	Distant	Missing	Alive	Dead	0–4	5–9	10–14	15–19	2000–2004	2005–2009	2010–2014	2015–2017
		859 (27.6)	163 (24.5)	198 (29.8)	304 (45.7)		709 (82.5)	150 (17.5)	717 (83.5)	96 (11.2)						
	Black	198 (6.4)	46 (26.7)	34 (19.8)	92 (53.5)	26	145 (73.2)	53 (26.8)	147 (74.2)	32 (16.2)	15 (7.6)	4 (2.0)	42 (21.2)	68 (34.3)	68 (34.3)	20 (10.1)
	Hispanic	308 (9.9)	68 (36.7)	77 (30.2)	110 (43.1)	53	235 (76.3)	73 (23.7)	263 (85.4)	32 (10.4)	11 (3.6)	2 (0.7)	80 (26.0)	92 (29.9)	90 (29.2)	46 (14.9)
	API	123 (4.0)	26 (24.3)	22 (20.6)	59 (55.1)	16	29 (23.6)	62 (23.8)	106 (86.2)	15 (12.2)	1 (0.8)	1 (0.8)	22 (17.9)	30 (24.4)	45 (36.6)	26 (21.1)
Males	**White**	948 (30.5)	171 (22.8)	189 (25.2)	390 (52.0)	198	732 (77.2)	216 (22.8)	778 (82.1)	124 (13.1)	20 (3.2)	16 (1.7)	268 (28.3)	304 (32.1)	242 (25.5)	134 (14.1)
	Black	209 (6.7)	40 (23.0)	34 (19.5)	100 (57.5)	35	151 (72.3)	58 (27.8)	179 (85.7)	19 (9.1)	8 (3.8)	3 (1.4)	52 (24.9)	59 (28.2)	61 (29.2)	37 (17.7)
	Hispanic	354 (11.4)	76 (25.7)	71 (24.0)	149 (50.3)	58	275 (77.7)	79 (22.3)	298 (84.2)	37 (10.5)	13 (3.7)	6 (1.7)	85 (24.0)	94 (26.6)	119 (33.6)	56 (15.8)
	API	113 (6.7)	15 (15.6)	18 (18.8)	63 (65.6)	17	76 (67.3)	37 (32.7)	99 (87.6)	13 (11.5)	0 (0.0)	1 (0.9)	31 (27.4)	31 (27.4)	28 (24.8)	23 (20.4)
Retinoblastoma (N = 1015)																
Females	**White**	193 (19.0)	118 (87.4)	15 (11.1)	2 (1.5)	58	188 (97.4)	5 (2.6)	188 (97.4)	5 (2.6)	0 (0.0)	0 (0.0)	57 (29.5)	59 (30.6)	53 (27.5)	24 (12.4)
	Black	79 (7.8)	38 (70.4)	14 (25.9)	2 (3.7)	25	72 (91.4)	7 (8.9)	77 (97.5)	1 (1.3)	1 (1.3)	0 (0.0)	24 (30.4)	18 (22.8)	29 (26.7)	8 (10.1)
	Hispanic	158 (15.6)	87 (71.9)	30 (24.8)	4 (3.3)	37	157 (99.4)	1 (0.6)	148 (93.7)	8 (5.1)	2 (1.3)	0 (0.0)	40 (25.3)	54 (34.2)	47 (29.8)	17 (10.8)
	API	49 (4.8)	26 (66.7)	13 (33.3)	0 (0.0)	10	48 (98.0)	1 (2.0)	48 (98.0)	1 (2.0)	0 (0.0)	0 (0.0)	10 (20.4)	15 (30.6)	15 (30.6)	9 (18.4)
Males	**White**	215 (21.2)	118 (86.8)	16 (11.8)	2 (1.5)	79	207 (96.3)	8 (3.7)	205 (95.4)	9 (4.2)	1 (0.5)	0 (0.0)	97 (40.5)	52 (24.2)	46 (21.4)	30 (14.0)
	Black	79 (7.8)	39 (75.0)	13 (25.0)	0 (0)	27	76 (96.2)	3 (3.8)	77 (97.5)	2 (2.5)	1 (1.9)	0 (0.0)	25 (31.7)	26 (32.9)	17 (21.5)	11 (13.9)
	Hispanic	188 (18.5)	98 (69.0)	42 (29.6)	2 (1.4)	46	183 (97.3)	5 (2.7)	177 (94.2)	9 (4.8)	2 (1.1)	0 (0.0)	53 (28.2)	60 (31.9)	49 (26.1)	26 (13.8)
	API	54 (5.3)	26 (74.3)	9 (25.7)	0 (0.0)	19	52 (96.3)	2 (3.7)	53 (98.2)	1 (1.9)	0 (0.0)	0 (0.0)	19 (35.2)	13 (24.1)	12 (22.2)	10 (18.5)
Wilms tumor (N = 2441)																
Females	**White**	647 (26.5)	268 (42.7)	201 (32.06)	158 (25.2)	20	592 (91.5)	55 (8.5)	450 (70.0)	156 (24.1)	26 (4.0)	15 (2.3)	172 (26.6)	176 (27.2)	185 (28.6)	114 (17.6)
	Black	223 (9.1)	79 (37.3)	73 (34.4)	60 (28.3)	11	205 (91.9)	18 (8.1)	141 (63.2)	74 (33.2)	6 (2.7)	2 (0.9)	55 (24.7)	62 (27.8)	70 (31.4)	36 (16.1)
	Hispanic	361 (14.8)	140 (40.2)	113 (32.5)	95 (27.3)	13	322 (89.2)	39 (10.8)	279 (77.3)	69 (19.1)	10 (2.8)	3 (0.8)	78 (21.6)	114 (31.6)	98 (27.2)	71 (19.7)
	API	58 (2.4)	31 (54.4)	16 (28.1)	10 (17.5)	1	52 (89.7)	6 (10.3)	48 (82.8)	9 (15.5)	1 (1.7)	0 (0.0)	11 (19.0)	15 (25.9)	19 (32.8)	13 (22.4)
Males	**White**	601 (24.6)	245 (42.4)	195 (22.7)	138 (23.9)	23	557 (92.7)	44 (7.3)	467 (77.7)	109 (18.1)	19 (3.2)	6 (1.0)	176 (29.3)	176 (29.3)	167 (27.8)	82 (13.6)
	Black	192 (7.9)	88 (46.8)	57 (30.3)	43 (22.9)	4	174 (90.6)	18 (9.4)	152 (79.2)	34 (17.7)	5 (2.6)	1 (0.5)	51 (26.6)	48 (25.0)	59 (30.7)	34 (17.7)
	Hispanic	303 (12.4)	143 (47.8)	84 (28.1)	72 (24.1)	4	265 (87.5)	38 (12.5)	233 (76.9)	63 (20.8)	4 (1.3)	3 (1.0)	80 (26.4)	86 (28.4)	78 (25.7)	59 (19.5)
	API	56 (2.3)	24 (45.3)	15 (28.3)	14 (26.4)	3	48 (85.7)	8 (14.3)	41 (73.2)	11 (19.6)	2 (3.6)	2 (3.6)	18 (32.1)	18 (32.1)	9 (16.1)	11 (19.6)
Hepatoblastoma (N = 729)																
Females	**White**			37 (27.4)		2				9 (6.6)	3 (2.2)	2 (1.5)	39 (28.5)	31 (22.6)	39 (28.5)	28 (20.4)

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Table 1 (*continued*)

		Cases	Stage of disease				Vital status*		Age in years				Year of diagnosis			
		N (%)	Local	Regional	Distant	Missing	Alive	Dead	0–4	5–9	10–14	15–19	2000–2004	2005–2009	2010–2014	2015–2017
		137 (18.8)	65 (48.2)		33 (24.4)		115 (83.9)	22 (16.1)	123 (89.8)							
	Black	20 (2.7)	6 (31.6)	8 (42.1)	5 (26.3)	1	11 (55.0)	9 (45.0)	18 (90.0)	2 (10.0)	0 (0.0)	0 (0.0)	3 (15.0)	3 (15.0)	9 (45.0)	5 (25.0)
	Hispanic	97 (13.3)	47 (49.0)	30 (31.3)	19 (19.8)	1	82 (84.5)	15 (15.5)	94 (96.9)	2 (2.1)	0 (0.0)	1 (1.0)	23 (23.7)	28 (28.9)	26 (26.8)	20 (20.6)
	API	31 (4.3)	18 (62.1)	10 (34.5)	1 (3.5)	2	27 (87.1)	4 (12.9)	27 (87.1)	2 (6.5)	2 (6.5)	0 (0.0)	8 (25.8)	4 (12.9)	12 (38.7)	7 (22.6)
Males	**White**	194 (26.6)	83 (44.6)	59 (31.7)	44 (23.7)	8	151 (77.8)	43 (22.2)	175 (90.2)	13 (6.7)	6 (3.1)	0 (0.0)	56 (28.9)	48 (24.7)	61 (31.4)	29 (15.0)
	Black	36 (4.9)	19 (52.8)	13 (36.1)	4 (11.1)	0	23 (63.9)	13 (36.1)	33 (91.7)	1 (2.8)	2 (5.6)	0 (0.0)	6 (16.7)	10 (27.8)	15 (41.7)	5 (13.9)
	Hispanic	156 (21.4)	75 (49.7)	43 (28.5)	33 (21.9)	5	131 (84.0)	25 (16.0)	147 (94.2)	6 (3.9)	2 (1.3)	1 (0.6)	32 (20.5)	41 (26.3)	51 (32.7)	32 (20.5)
	API	58 (8.0)	24 (42.9)	21 (37.5)	11 (19.6)	2	47 (81.0)	11 (19.0)	55 (94.8)	3 (5.2)	0 (0.0)	0 (0.0)	14 (24.1)	18 (31.0)	15 (25.9)	11 (19.0)
Osteosarcoma (N = 2074)																
Females	**White**	408 (19.7)	116 (37.7)	131 (42.5)	61 (19.8)	100	303 (74.3)	105 (25.7)	8 (2.0)	68 (16.7)	198 (48.5)	134 (32.8)	116 (28.4)	120 (29.4)	116 (28.4)	56 (13.7)
	Black	153 (7.4)	41 (36.3)	46 (40.7)	26 (23.0)	40	98 (64.1)	55 (36.0)	3 (2.0)	27 (17.7)	65 (42.5)	58 (37.9)	47 (30.7)	40 (26.1)	48 (31.4)	18 (11.8)
	Hispanic	274 (13.2)	66 (31.4)	86 (41.0)	58 (27.6)	64	184 (67.2)	90 (32.9)	9 (3.3)	46 (16.8)	144 (52.6)	75 (27.4)	76 (27.7)	86 (31.4)	72 (26.3)	40 (14.6)
	API	74 (3.6)	25 (44.6)	19 (33.9)	12 (21.4)	18	50 (67.6)	24 (32.4)	1 (1.4)	15 (20.3)	34 (46.0)	24 (32.4)	19 (25.7)	20 (27.0)	16 (21.6)	19 (25.7)
Males	**White**	533 (25.7)	167 (41.3)	149 (36.9)	88 (21.8)	129	340 (63.8)	193 (36.2)	10 (1.9)	64 (12.0)	193 (36.2)	266 (49.9)	142 (26.6)	154 (28.9)	143 (26.8)	94 (17.6)
	Black	176 (8.5)	47 (37.0)	50 (39.4)	30 (23.6)	49	115 (65.3)	61 (34.7)	3 (1.7)	26 (14.8)	55 (31.3)	92 (52.3)	55 (31.3)	52 (29.6)	44 (25.0)	25 (14.2)
	Hispanic	364 (17.6)	80 (27.2)	135 (45.9)	79 (26.9)	70	236 (64.8)	128 (35.2)	5 (1.4)	46 (12.6)	156 (42.9)	157 (43.1)	82 (22.5)	109 (30.0)	96 (26.4)	77 (21.2)
	API	92 (4.4)	18 (28.6)	29 (46.0)	16 (25.4)	29	63 (68.5)	29 (31.5)	1 (1.1)	17 (18.5)	27 (29.4)	47 (51.1)	31 (22.7)	16 (17.4)	30 (32.6)	15 (16.3)
Ewing sarcoma (N = 1158)																
Females	**White**	302 (26.1)	77 (33.2)	78 (33.6)	77 (33.2)	70	214 (70.9)	88 (29.1)	26 (8.6)	61 (20.2)	117 (38.7)	98 (32.5)	81 (26.8)	81 (26.8)	86 (28.5)	54 (17.9)
	Black	12 (1.0)	3 (27.5)	3 (37.5)	2 (25.0)	4	5 (41.7)	7 (58.3)	0 (0.0)	3 (25.0)	5 (41.7)	4 (33.3)	6 (50.0)	2 (16.7)	2 (16.7)	2 (16.7)
	Hispanic	110 (9.5)	21 (24.1)	31 (35.6)	35 (40.2)	23	79 (71.8)	31 (28.2)	12 (10.9)	25 (22.7)	46 (41.8)	27 (24.6)	26 (23.6)	27 (24.6)	41 (37.3)	16 (14.6)
	API	29 (2.5)	6 (25.0)	7 (29.2)	11 (45.8)	5	20 (69.0)	9 (31.0)	3 (10.3)	5 (17.2)	9 (31.0)	12 (41.4)	5 (17.2)	8 (27.6)	10 (34.5)	6 (20.7)
Males	**White**	467 (40.3)	112 (33.6)	115 (34.5)	106 (31.8)	134	329 (70.5)	138 (29.6)	28 (6.0)	89 (19.1)	175 (37.5)	175 (37.5)	138 (29.6)	134 (28.7)	127 (27.2)	68 (14.6)
	Black	21 (1.8)	4 (23.5)	8 (47.1)	5 (29.4)	4	13 (61.9)	8 (38.1)	1 (4.8)	3 (14.3)	7 (33.3)	10 (47.6)	2 (9.5)	8 (38.1)	9 (42.9)	2 (9.5)
	Hispanic	171 (14.8)	40 (29.2)	47 (34.3)	50 (36.5)	34	105 (61.4)	66 (38.6)	20 (11.7)	23 (13.5)	58 (33.9)	70 (40.9)	39 (22.8)	58 (33.9)	41 (24.0)	33 (19.3)
	API	46 (4.0)	8 (25.0)	15 (46.9)	9 (28.1)	14	28 (60.9)	18 (39.1)	4 (8.7)	5 (10.9)	11 (23.9)	26 (56.5)	13 (28.3)	12 (26.1)	12 (26.1)	9 (19.6)
Rhabdomyosarcoma (N = 1940)																
Females	**White**	416 (21.4)	124 (33.7)	132 (35.9)	112 (30.4)	48	288 (69.2)	128 (30.8)	171 (41.1)	95 (22.8)	78 (18.8)	72 (17.3)	113 (27.2)	118 (28.4)	114 (27.4)	71 (17.1)

(*continued on next page*)

Table 1 (*continued*)

		Cases	Stage of disease				Vital status*		Age in years				Year of diagnosis			
		N (%)	Local	Regional	Distant	Missing	Alive	Dead	0–4	5–9	10–14	15–19	2000–2004	2005–2009	2010–2014	2015–2017
	Black	127 (6.6)	31 (28.7)	46 (42.6)	31 (28.7)	19	79 (62.2)	48 (37.8)	38 (29.9)	25 (19.7)	37 (29.1)	27 (21.3)	44 (34.7)	31 (24.4)	31 (24.4)	21 (16.5)
	Hispanic	234 (12.1)	76 (35.2)	65 (30.1)	75 (34.7)	18	147 (62.8)	87 (37.2)	94 (40.2)	58 (24.8)	51 (21.8)	31 (13.3)	64 (27.4)	64 (27.4)	67 (28.6)	39 (16.7)
	API	50 (2.6)	23 (48.9)	6 (12.8)	18 (38.3)	3	31 (62.0)	19 (38.0)	17 (34.0)	12 (24.0)	10 (20.0)	11 (22.0)	9 (18.0)	10 (20.0)	17 (34.0)	14 (28.0)
Males	**White**	561 (28.9)	181 (36.4)	169 (34.0)	147 (29.6)	64	386 (68.8)	175 (31.2)	194 (34.6)	125 (22.3)	127 (22.6)	115 (20.5)	184 (32.8)	155 (27.6)	136 (24.2)	86 (15.3)
	Black	176 (9.1)	53 (32.1)	52 (31.5)	60 (36.4)	11	115 (65.3)	61 (34.7)	65 (36.9)	45 (25.6)	34 (19.3)	32 (18.2)	39 (22.2)	63 (35.8)	51 (29.0)	23 (13.1)
	Hispanic	289 (14.9)	80 (30.0)	92 (34.5)	95 (35.6)	22	187 (64.7)	102 (35.3)	104 (36.0)	84 (29.1)	53 (18.3)	48 (16.6)	74 (25.6)	84 (29.1)	87 (30.1)	44 (15.2)
	API	87 (4.5)	27 (33.8)	31 (38.8)	22 (27.5)	7	57 (65.5)	30 (34.5)	33 (37.9)	18 (20.7)	19 (21.8)	17 (19.5)	20 (23.0)	26 (29.9)	26 (29.9)	15 (17.2)
Thyroid carcinoma (N = 3340)																
Females	**White**	1608 (48.1)	838 (52.8)	698 (44.0)	51 (3.2)	21	1597 (99.3)	11 (0.7)	7 (0.4)	48 (3.0)	311 (19.3)	1242 (77.2)	364 (22.6)	397 (24.7)	523 (32.5)	324 (20.2)
	Black	126 (3.8)	84 (66.7)	36 (28.6)	6 (4.8)	0	123 (97.6)	3 (2.4)	0 (0.0)	3 (2.4)	20 (15.9)	103 (81.8)	16 (12.7)	35 (27.8)	51 (40.5)	24 (19.1)
	Hispanic	722 (21.6)	301 (42.3)	385 (54.1)	26 (3.7)	10	715 (99.0)	7 (1.0)	5 (0.7)	33 (4.6)	160 (22.2)	524 (72.6)	116 (16.1)	167 (23.1)	256 (35.5)	183 (25.4)
	API	263 (7.9)	118 (45.6)	132 (51.0)	9 (3.5)	4	263 (100.0)	0 (0.0)	0 (0.0)	7 (2.7)	60 (22.8)	196 (74.5)	49 (18.6)	61 (23.2)	88 (33.5)	65 (24.7)
Males	**White**	378 (11.3)	177 (47.5)	177 (45.5)	19 (5.1)	5	370 (97.9)	8 (2.1)	5 (1.3)	26 (6.9)	90 (23.8)	257 (28.0)	79 (20.9)	102 (27.0)	126 (33.3)	71 (18.8)
	Black	38 (1.1)	22 (57.9)	12 (31.6)	4 (10.5)	0	36 (94.7)	2 (5.3)	0 (0.0)	4 (10.5)	13 (34.2)	21 (55.3)	8 (21.1)	7 (18.4)	12 (31.6)	11 (29.0)
	Hispanic	156 (4.7)	53 (34.4)	91 (59.1)	10 (6.5)	2	152 (97.4)	4 (2.6)	1 (0.6)	11 (7.1)	48 (30.8)	96 (61.5)	25 (16.0)	42 (26.9)	52 (33.3)	37 (23.7)
	API	49 (1.5)	20 (41.7)	27 (56.3)	1 (2.1)	1	49 (100.0)	0 (0.0)	0 (0.0)	3 (6.1)	10 (20.4)	36 (73.5)	3 (6.1)	10 (20.4)	21 (42.9)	15 (30.6)

* Determined at the last date of contact (12/31/2017).

Table 2
Five-year overall survival percentages (%) and 95 % confidence interval (95 % CI) by race/ethnicity and sex for each cancer, SEER 2000–2017.

	White		Hispanic		Black		API		Percent (%) difference highest-lowest
	female % (95 % CI)	male % (95 % CI)	female % (95 % CI)	male % (95 % CI)	female % (95 % CI)	male % (95 % CI)	female % (95 % CI)	male % (95 % CI)	
ALL	**91.6 (90.5, 92.6)**	88.9 (87.8, 90.0)	85.1 (83.6, 86.6)	83.0 (81.6, 84.4)	85.6 (82.1, 89.2)	**82.7 (79.4, 86.0)**	89.3 (86.4, 92.3)	86.3 (83.4, 89.2)	8.9
AML	**66.3 (62.6, 69.9)**	65.4 (61.9, 68.8)	62.4 (57.8, 67.0)	60.4 (56.0, 64.9)	**53.6 (46.1, 61.1)**	55.8 (48.8, 62.8)	59.7 (51.2, 68.3)	63.9 (55.9, 71.9)	12.7
Hodgkin lymphoma	96.6 (95.5, 97.6)	**97.2 (96.3, 98.1)**	96.0 (94.2, 97.9)	95.3 (93.6, 97.1)	**93.3 (90.2, 96.5)**	95.0 (92.5, 97.6)	94.1 (89.5, 98.7)	96.9 (94.2, 99.6)	3.9
Non-Hodgkin lymphoma	86.6 (83.8, 89.3)	**87.5 (85.6, 89.5)**	83.2 (78.9, 87.4)	84.4 (81.3, 87.4)	**81.5 (76.1, 86.9)**	83.0 (78.7, 87.2)	86.8 (80.7, 92.9)	86.3 (81.3, 91.4)	6.0
Burkitt lymphoma	90.3 (84.7, 96.0)	90.6 (88.0, 93.1)	**95.6 (89.7, 101.6)**	91.5 (86.9, 96.1)	**83.1 (67.7, 98.5)**	84.2 (75.6, 92.8)	91.3 (75.0, 107.6)	89.4 (81.9, 96.8)	12.5
Ependymomas	**85.9 (81.2, 90.7)**	77.4 (72.2, 82.7)	70.8 (63.1, 78.5)	71.3 (63.9, 78.7)	72.3 (59.8, 84.8)	**61.5 (48.9, 74.1)**	79.3 (62.9, 95.6)	75.5 (60.4, 90.6)	24.4
Astrocytomas	**84.2 (82.2, 86.1)**	82.0 (80.1, 84.0)	78.0 (74.4, 81.5)	77.4 (73.9, 80.9)	75.0 (69.8, 80.2)	71.2 (65.7, 76.7)	76.1 (68.8, 83.4)	**68.4 (61.0, 75.8)**	15.8
Medulloblastoma	74.4 (69.3, 79.5)	73.7 (69.9, 77.5)	75.2 (68.0, 82.4)	**67.1 (61.0, 73.2)**	69.7 (57.6, 81.9)	71.0 (58.3, 83.7)	67.3 (52.4, 82.2)	**80.9 (71.4, 90.3)**	13.8
PNET	61.5 (53.1, 69.9)	60.0 (52.5, 67.5)	**67.1 (55.2, 79.0)**	55.4 (44.9, 65.8)	37.5 (20.2, 54.8)	43.7 (26.7, 60.7)	54.2 (32.9, 75.5)	**15.2 (0.00, 33.5)**	51.9
Neuroblastoma	**82.6 (79.9, 85.3)**	78.1 (75.2, 80.9)	73.9 (68.5, 79.4)	76.2 (71.3, 81.1)	72.6 (66.0, 79.3)	69.4 (62.5, 76.3)	74.4 (65.7, 83.1)	**66.1 (56.5, 75.7)**	16.5
Retinoblastoma	98.1 (96.0, 100.3)	96.4 (93.8, 99.0)	**99.3 (98.0, 100.6)**	96.8 (94.0, 99.6)	**92.0 (85.9, 98.1)**	95.5 (90.5, 100.5)	97.6 (92.8, 102.3)	95.5 (89.3, 101.6)	7.3
Nephroblastoma	91.2 (88.8, 93.5)	**93.4 (91.2, 95.5)**	88.6 (85.0, 92.2)	**87.3 (83.2, 91.4)**	91.4 (87.5, 95.3)	90.3 (85.8, 94.8)	92.5 (85.3, 99.6)	89.7 (81.2, 98.3)	6.1
Hepatoblastoma	85.0 (78.8, 91.3)	76.9 (70.7, 83.2)	83.3 (75.6, 91.1)	82.6 (76.3, 89.0)	**50.2 (26.4, 74.0)**	65.6 (48.8, 82.4)	**86.7 (74.5, 98.8)**	80.3 (69.2, 91.4)	36.5
Osteosarcoma	**76.1 (71.7, 80.5)**	63.7 (59.2, 68.2)	66.4 (60.2, 72.5)	**62.4 (56.9, 67.9)**	64.0 (56.0, 72.0)	67.5 (60.2, 74.8)	69.1 (57.3, 80.8)	67.7 (57.3, 78.1)	13.7
Ewing sarcoma	70.8 (65.2, 76.5)	72.0 (67.6, 76.5)	69.9 (60.4, 79.4)	62.2 (54.2, 70.3)	**53.4 (23.0, 83.8)**	**75.2 (56.3, 94.1)**	64.0 (44.9, 83.1)	61.4 (46.4, 76.5)	21.8
Rhabdomyosarcoma	67.1 (62.2, 72.0)	**68.7 (64.6, 72.8)**	62.4 (55.8, 68.9)	64.1 (58.0, 70.2)	62.0 (53.1, 71.0)	62.9 (55.1, 70.6)	**51.5 (35.1, 67.9)**	62.0 (50.7, 73.3)	17.2
Thyroid carcinoma	99.5 (99.1, 99.9)	98.5 (97.1, 99.8)	99.4 (98.7, 100.1)	97.5 (94.7, 100.3)	98.3 (95.9, 100.6)	**93.2 (84.0, 102.5)**	**100.0 (100.0, 100.0)**	**100.0 (100.0, 100.0)**	6.8

*Bold text indicates highest and lowest survival percentages within each row.

for PNET. Twelve cancers displayed a statistically significant (Log-Rank $p < 0.05$) difference in 18-year survival by race/ethnicity-sex (Supplemental Figures 3 and 4) including ALL, AML, Hodgkin lymphoma, non-Hodgkin lymphoma, ependymoma, astrocytoma, PNET, neuroblastoma, hepatoblastoma, osteosarcoma, Ewing sarcoma, and thyroid carcinoma.

3.2. Differences in the risk of death

First, we assessed racial/ethnic differences in the risk of death within each sex (Table 3). Among both males and females with ALL, compared to White males and females all minority groups had a statistically significant increased risk of death (HR range: 1.39–1.78). For AML, Black females (HR: 1.56, 95 % CI: 1.22, 2.01) and males (HR: 1.37, 95 % CI: 1.08, 1.74) had a higher risk of death than White females and males, respectively. Hispanic and Black females and males had a 40–60 % increased risk of death compared to White for non-Hodgkin lymphoma. Among females, Hispanic and Black individuals had a 70 % increased risk of death compared to Whites for ependymoma whereas only Black males had an increased risk of death (HR: 2.14, 95 % CI: 1.35, 3.41) compared to White males. In astrocytoma all minority groups in both sexes had statistically significant increased risks of death compared to White females and males with HRs ranging from 1.27 to 1.92. In females, Hispanics had a higher risk of death for neuroblastoma (HR: 1.67, 95 % CI: 1.20, 2.32). In males, Hispanic ethnicity was inversely associated with death after a retinoblastoma diagnosis (HR: 0.26, 95 % CI: 0.07, 0.94). In both females and males, Black race was associated with death after a hepatoblastoma diagnosis (female HR: 3.36, 95 % CI: 1.42, 7.94; male HR: 2.69, 95 % CI: 1.37, 5.31). Among females, Black and API race/ethnicity was associated with a 64 % and 75 %, respectively, increased risk of death after an osteosarcoma diagnosis. Black race in

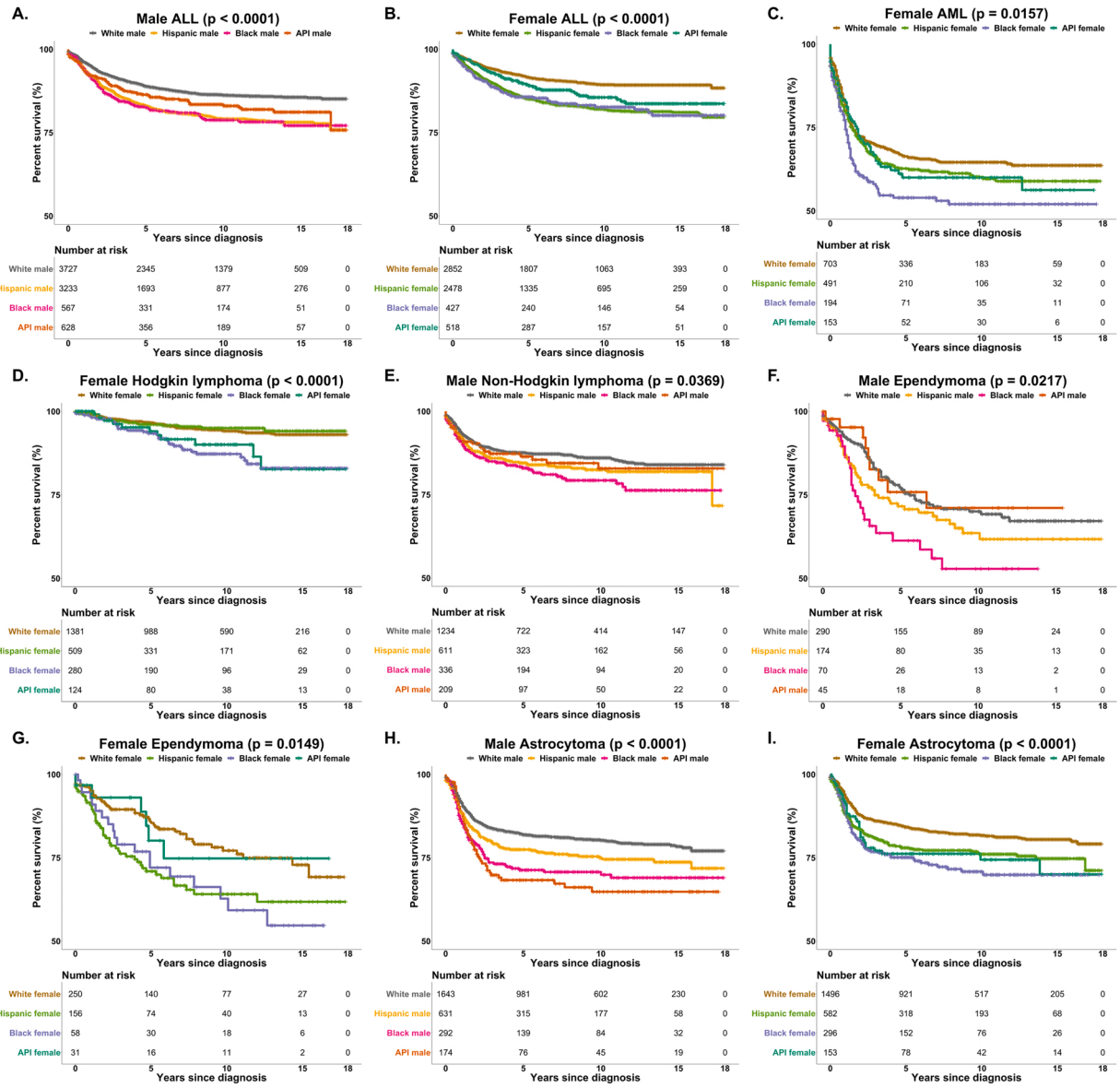

Fig. 1. a and 1b. Kaplan-Meier survival curves (Log-Rank p-values) for childhood cancers with statistically significant survival by race/ethnicity within sex for 18-year overall survival, SEER (2000–2017).

females and Hispanic ethnicity in males was associated with death after Ewing sarcoma (Black female HR: 5.18, 95 % CI: 1.94, 13.86; Hispanic male HR: 1.58, 95 % CI: 1.11, 2.25). Among females, Black race was associated with nearly 4 times the risk of death seen in White females with thyroid carcinoma.

Then, we characterized sex differences in the risk of death within race/ethnicity (Table 3). Male sex was associated with death for ALL (HR: 1.22, 95 % CI: 1.04, 1.42) and osteosarcoma (HR: 1.35, 95 % CI: 1.01, 1.81) among Whites, medulloblastoma among Hispanics (HR: 1.48, 95 % CI: 1.01, 2.18), and PNET among APIs (HR: 6.20, 95 % CI: 2.30, 16.69). Results were also elevated among Black and API males for ALL, though the confidence intervals included the null, which may be due to sample size constraints.

Finally, for completeness, we estimated HR (95 % CI) for race/ethnicity-sex groupings (White-female referent Supplemental Table 2). Elevated HRs excluded the null for 12/17 cancers among race/ethnicity-sex strata. However, there was no evidence of a statistically significant interaction between race/ethnicity and sex for any cancer though osteosarcoma and Ewing sarcoma had a p-interaction= 0.05.

4. Discussion

In our study considering both race/ethnicity and sex in pediatric cancer survival for 17 cancer types using population-based data, statistically significant differences in the risk of death by race/ethnicity were observed for 12 malignancies among males and 11 malignancies among females. When considering sex differences in the risk of death, only four cancers showed statistically significant differences within race/ethnicity groups. As expected, our study contained a higher proportion of males, who have a higher incidence of pediatric cancers [8, 23]. When stratifying by race/ethnicity-sex groups, there were significant differences in overall survival for ALL, AML, Hodgkin lymphoma, non-Hodgkin lymphoma, ependymoma, astrocytoma, PNET, neuroblastoma, hepatoblastoma, osteosarcoma, Ewing sarcoma, and thyroid carcinoma. White-females never had a statistically worse outcome than any other racial/ethnic group. In adjusted models, racial/ethnic-sex groups had significantly worse survival than White-females suggesting a interplay or compound effect of race/ethnicity and sex in the observed survival disparities for some childhood cancers. There was no evidence

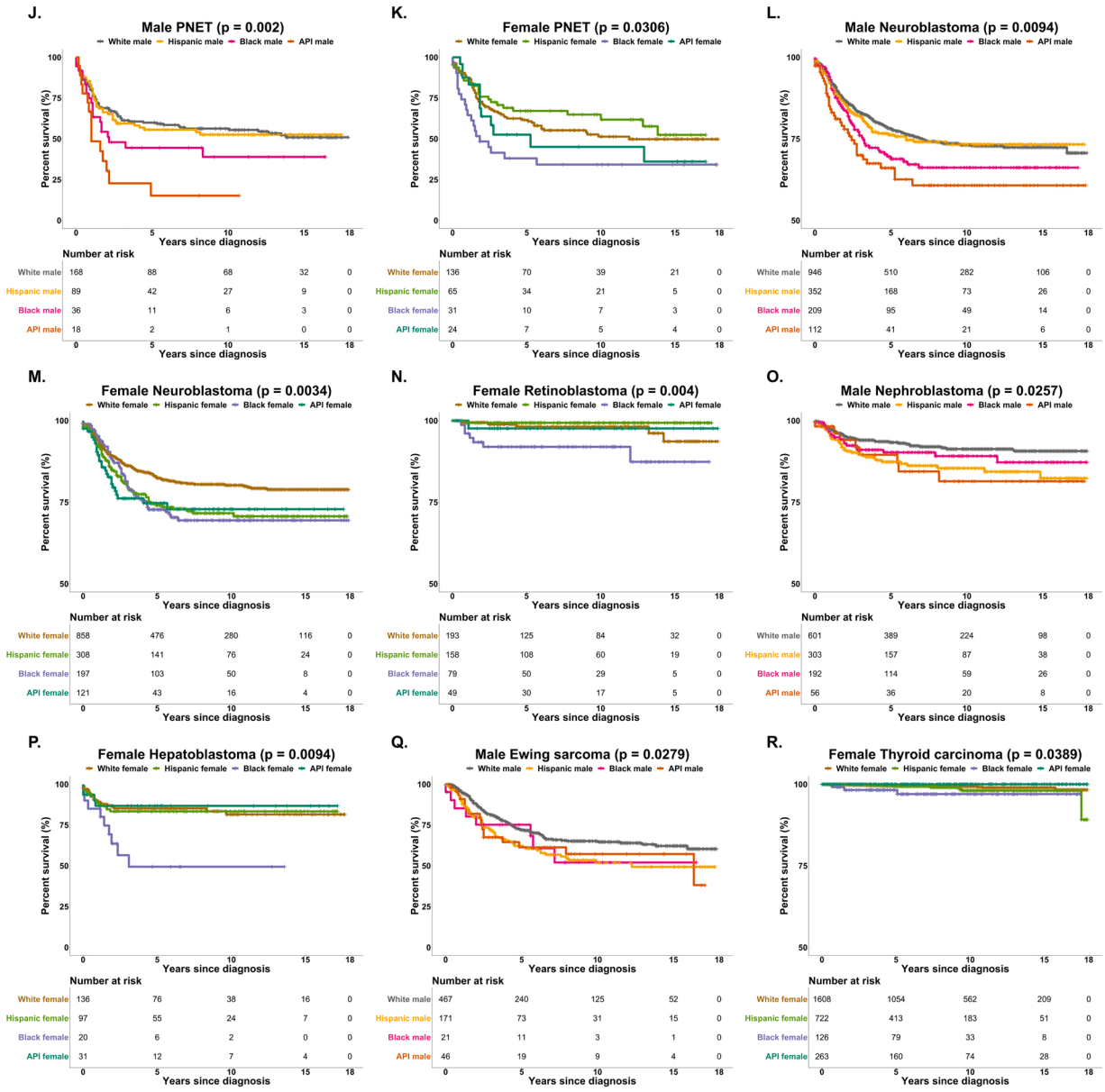

Fig. 1. (*continued*).

of statistical interaction between race/ethnicity and sex in any cancer (all $p > 0.05$). As we did not find evidence of statistical interaction between race/ethnicity and sex, we estimated differences in survival by race/ethnicity within sexes and observed many differences in survival and the risk of death particularly for ALL and astrocytomas where all minority groups had statistically significantly increased risks of death compared to the White males and females. We also estimated sex differences in survival by race/ethnicity groups and found that there were sex differences in ALL and osteosarcoma survival in White children, medulloblastoma in Hispanic individuals, and PNET API children. These are important findings that demonstrate disparities in pediatric cancer by race/ethnicity in each sex and by sex within racial/ethnic groups that are masked in traditional analyses where race/ethnicity or sex are simply adjusted for rather than stratified upon.

As others have reported, Black and Hispanic children often fared worse than White-children in our study [2,9,10,12,13]. However, most other studies adjusted for sex and we have now included race/ethnicity and sex stratified models to obtain a clearer view of both factors with respect to childhood cancer outcome. In our previous report of sex differences in childhood cancer survival, we observed that males had worse survival for ALL, ependymoma, neuroblastoma, osteosarcoma, thyroid carcinoma, and malignant melanoma, which was not included here due to small sample sizes among minority children. In the current work the five remaining cancers all displayed differential 18-year survival when both race/ethnicity and sex were considered. Sex appeared to drive differences most strongly in White children for ALL and osteosarcoma, Hispanic children with medulloblastoma, and API children with PNET. Conversely, race/ethnicity appeared to drive most other survival differences in both male and female groups for minority children with, ALL, AML, non-Hodgkin lymphoma, ependymoma, astrocytoma, PNET (males), neuroblastoma, nephroblastoma (females), hepatoblastoma, osteosarcoma (females), Ewing sarcoma, rhabdomyosarcoma, and thyroid carcinoma (females). These findings highlight the marked complexity of pediatric cancer survival disparities when we jointly consider both race/ethnicity and sex.

Biologic mechanisms underlying the observed sex and racial/ethnic differences could be due to diagnosis delay, tumor biology, response to treatment, genomic differences, and/or differences in immune system

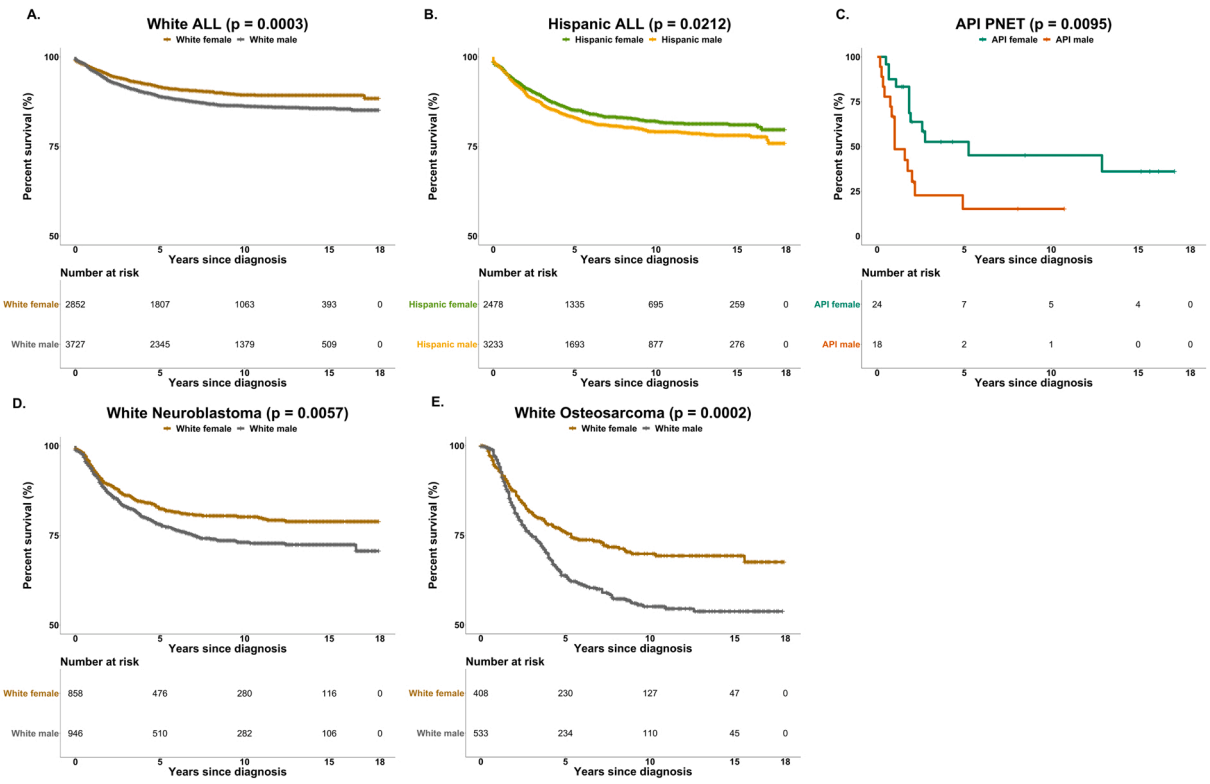

Fig. 2. Kaplan-Meier survival curves (Log-Rank p-values) for childhood cancers with statistically significant survival by sex within race/ethnicity for 18-year overall survival, SEER (2000–2017).

function. In a literature review on diagnosis delay for pediatric cancers, [24] delays were noted for girls with non-Hodgkin lymphoma, boys with Ewing sarcoma, and non-White children for osteosarcoma. Clinical studies with detailed data on symptom onset and date of diagnosis will be of great value in resolving the role of diagnosis delay in our observed racial/ethnic-sex disparities. Racial/ethnic differences in tumor biology defined by histology, genomics and molecular subtypes, have been established in adult breast cancers and are often prognostic [25,26]. Therefore, such phenomena may exist in pediatric malignancies warranting further investigation in appropriately structured studies.

Variation in germline genomics and immune system function between racial/ethnic groups and sex have been reported in adults but remain unexplored in children [27,28]. Germline genomic differences by race/ethnicity may lead to differences in chemotherapeutic sensitivity affecting remission, relapse and death [29,30]. These differences underscore the need to increase racial/ethnic and sex diversity in clinical trials of children and adolescents, which underrepresent males and minorities [31]. There are well-documented sex differences in immunologic function with females having more efficient innate and adaptive immunity, which is hypothesized to lead to better tumor surveillance and clearance [32,33]. In adult breast and prostate cancer, [34,35] there are observed differences in immune function by race that are not necessarily biologic in origin. Instead, decreased immune function may depend on the built environment that often perpetuates racism leading to sustained increased stress [34,36]. As we work toward health equity, considering the role of race/ethnicity and sex in pediatric cancer incidence and outcome is going to be critical to this success.

While biology likely plays a significant role in the observed sex and racial/ethnic differences in childhood cancer outcome, social and behavioral factors that may differ by sex and race/ethnicity cannot be discounted and are equally important. Obesity may be an important risk factor in childhood cancer incidence and outcome. Obesity is an established risk factor for adult malignancies [37] and is ever increasing in children and adolescents around the world, particularly among adolescents, [38] which likely impacts childhood cancer incidence [39]. In an analysis from the Children's Oncology Group, obesity was associated with ALL among males and Hispanic children and was found to be associated with high-risk disease [40]. These findings suggest obesity could play an important role in disease development and severity, which impacts outcomes, by sex and race/ethnicity. In children from poorer households, social factors including access to health insurance and health care may play a particularly important role in determining disparities by race/ethnicity given their consequences on diagnosis delay or treatment interruption [41]. For ALL, Black patients have worse survival than White [2] that is only partially due to higher rates of non-adherence to maintenance therapy [42]. Maintenance to therapy could be affected by socioeconomic status (SES) and caregiver demands on poorer parents with inflexible life situations. In a mediation analysis of race and SES in SEER the survival disparity between Black and White children with many cancers, including ALL, AML and neuroblastoma was partially attributable to SES, but a residual effect of Black race often persisted, suggesting a genetic and/or sociocultural contribution as well [13]. Other analyses have identified associations between self-reported racism and engaging in cancer-related health behaviors in adults, such as smoking, low exercise, obesity, and prostate cancer screening avoidance, [43] which may have similar consequences on medical access and obesity for children and adolescents. Additionally, for minority children living in impoverished areas, chronic exposure to systemic and medical racism and the accompanying prolonged stress response may underlie the observed disparities in long-term outcomes and warrants investigation in studies with detailed information on socioeconomics, quality of life, treatment completion, and outcomes [44]. Finally, participation in clinical trials tends to improve outcomes for children with cancer [45] and varies by race/ethnicity [31] thereby likely impacting observed disparities.

Despite presenting a large, population-based study of over 50,000 children with 17 cancers, our study has limitations. As this is SEER data, we are unable to assess clinical data, such as molecular subtype, and lack

Table 3
Hazard ratios (HR) and 95 % confidence intervals (95 % CI) for associations between race/ethnicity within sexes and sex within race/ethnicity and death after a childhood cancer diagnosis, SEER 18 (2000–2017).

	White, female N (%)	White, male N (%) HR (95 % CI)	Hispanic, female N (%) HR (95 % CI)	Hispanic, male N (%) HR (95 % CI)	Black, female N (%) HR (95 % CI)	Black, male N (%) HR (95 % CI)	API, female N (%) HR (95 % CI)	API, male N (%) HR (95 % CI)
Comparisons by race/ethnicity within sex								
	Females				**Males**			
	White	**Hispanic**	**Black**	**API**	**White**	**Hispanic**	**Black**	**API**
ALL	Referent	**1.78 (1.52, 2.10)**	**1.70 (1.29, 2.24)**	**1.42 (1.07, 1.89)**	Referent	**1.58 (1.39, 1.79)**	**1.57 (1.26, 1.95)**	**1.39 (1.11, 1.75)**
AML	Referent	1.19 (0.98, 1.45)	**1.56 (1.22, 2.01)**	1.21 (0.90, 1.62)	Referent	1.15 (0.96, 1.39)	**1.37 (1.08, 1.74)**	1.00 (0.74, 1.34)
Hodgkin lymphoma	Referent	1.02 (0.62, 1.68)	**2.52 (1.63, 3.88)**	**2.08 (1.10, 3.96)**	Referent	**1.51 (1.02, 2.24)**	1.55 (0.94, 2.57)	1.28 (0.66, 2.50)
Non-Hodgkin lymphoma	Referent	**1.42 (1.01, 2.00)**	**1.48 (1.03, 2.14)**	1.06 (0.63, 1.78)	Referent	**1.39 (1.07, 1.81)**	**1.60 (1.19, 2.17)**	1.18 (0.77, 1.80)
Burkitt lymphoma	Referent	0.37 (0.08, 1.68)	2.15 (0.62, 7.46)	1.24 (0.14, 10.57)	Referent	0.91 (0.49, 1.67)	1.72 (0.92, 3.22)	0.78 (0.34, 1.82)
Ependymomas	Referent	**1.72 (1.13, 2.61)**	**1.78 (1.02, 3.11)**	1.14 (0.48, 2.68)	Referent	1.40 (0.95, 2.05)	**2.14 (1.35, 3.41)**	1.12 (0.55, 2.26)
Astrocytomas	Referent	**1.49 (1.19, 1.85)**	**1.67 (1.29, 2.17)**	**1.51 (1.05, 2.15)**	Referent	**1.27 (1.04, 1.56)**	**1.69 (1.32, 2.17)**	**1.92 (1.43, 2.58)**
Medulloblastoma	Referent	0.79 (0.54, 1.17)	1.33 (0.82, 2.14)	1.40 (0.79, 2.46)	Referent	1.21 (0.93, 1.57)	1.32 (0.84, 2.08)	0.91 (0.57, 1.47)
PNET	Referent	0.77 (0.48, 1.26)	1.70 (0.98, 2.93)	1.16 (0.62, 2.17)	Referent	1.00 (0.67, 1.50)	1.66 (0.98, 2.82)	**2.81 (1.56, 5.06)**
Neuroblastoma	Referent	**1.67 (1.20, 2.32)**	1.32 (0.92, 1.90)	1.22 (0.74, 1.99)	Referent	1.20 (0.89, 1.63)	1.35 (0.97, 1.88)	1.34 (0.88, 2.04)
Retinoblastoma	Referent	0.13 (0.01, 1.61)	1.46 (0.27, 7.79)	0.71 (0.07, 7.49)	Referent	**0.26 (0.07, 0.94)**	0.26 (0.03, 2.21)	Not estimable
Nephroblastoma	Referent	1.33 (0.88, 2.03)	0.84 (0.48, 1.45)	1.40 (0.56, 3.52)	Referent	**1.99 (1.27, 3.12)**	1.41 (0.81, 2.45)	2.09 (0.93, 4.70)
Hepatoblastoma	Referent	1.08 (0.54, 2.17)	**3.36 (1.42, 7.94)**	1.28 (0.42, 3.88)	Referent	0.76 (0.45, 1.28)	**2.69 (1.37, 5.31)**	0.78 (0.38, 1.64)
Osteosarcoma	Referent	1.11 (0.79, 1.55)	**1.64 (1.12, 2.40)**	**1.75 (1.07, 2.89)**	Referent	1.06 (0.81, 1.39)	0.91 (0.64, 1.30)	0.84 (0.50, 1.42)
Ewing tumor	Referent	0.82 (0.50, 1.33)	**5.18 (1.94, 13.86)**	1.14 (0.52, 2.50)	Referent	**1.58 (1.11, 2.25)**	1.68 (0.73, 3.89)	1.55 (0.81, 2.95)
Rhabdomyosarcoma	Referent	1.29 (0.97, 1.72)	1.26 (0.88, 1.80)	1.43 (0.85, 2.40)	Referent	1.14 (0.88, 1.48)	1.11 (0.82, 1.52)	1.49 (0.98, 2.24)
Thyroid carcinoma	Referent	1.64 (0.63, 4.27)	**3.89 (1.07, 14.17)**	Not estimable	Referent	2.07 (0.54, 8.00)	4.75 (0.87, 25.85)	Not estimable
Comparisons by sex within race/ethnicity								
	White, female	**White, male**	**Hispanic, female**	**Hispanic, male**	**Black, female**	**Black, male**	**API, female**	**API, male**
ALL	Referent	**1.22 (1.04, 1.42)**	Referent	1.04 (0.91, 1.19)	Referent	1.13 (0.82, 1.55)	Referent	1.21 (0.87, 1.69)
AML	Referent	1.05 (0.88, 1.25)	Referent	1.03 (0.84, 1.26)	Referent	0.93 (0.69, 1.26)	Referent	0.84 (0.57, 1.23)
Hodgkin lymphoma	Referent	1.05 (0.75, 1.48)	Referent	1.40 (0.82, 2.39)	Referent	0.58 (0.33, 1.04)	Referent	0.62 (0.26, 1.48)
Non-Hodgkin lymphoma	Referent	0.90 (0.69, 1.18)	Referent	0.81 (0.57, 1.14)	Referent	0.95 (0.64, 1.42)	Referent	0.91 (0.49, 1.71)
Burkitt lymphoma	Referent	1.00 (0.53, 1.87)	Referent	2.55 (0.57, 11.44)	Referent	1.07 (0.33, 3.54)	Referent	0.17 (0.01, 2.34)
Ependymomas	Referent	1.31 (0.89, 1.93)	Referent	1.08 (0.71, 1.63)	Referent	1.68 (0.89, 3.14)	Referent	1.21 (0.39, 3.80)
Astrocytomas	Referent	1.15 (0.97, 1.37)	Referent	0.97 (0.76, 1.24)	Referent	1.10 (0.79, 1.51)	Referent	1.27 (0.82, 1.98)
Medulloblastoma	Referent	1.00 (0.77, 1.29)	Referent	**1.48 (1.01, 2.18)**	Referent	0.95 (0.51, 1.76)	Referent	0.58 (0.28, 1.18)
PNET	Referent	1.05 (0.74, 1.51)	Referent	1.30 (0.77, 2.20)	Referent	1.00 (0.50, 2.01)	Referent	**6.20 (2.30, 16.69)**
Neuroblastoma	Referent	1.13 (0.87, 1.45)	Referent	0.85 (0.59, 1.24)	Referent	1.27 (0.83, 1.96)	Referent	1.18 (0.65, 2.15)
Retinoblastoma	Referent	3.45 (0.85, 14.03)	Referent	3.89 (0.38, 39.74)	Referent	0.88 (0.07, 10.60)	Referent	Not estimable
Nephroblastoma	Referent	0.79 (0.52, 1.19)	Referent	1.10 (0.70, 1.74)	Referent	1.47 (0.75, 2.91)	Referent	1.33 (0.40, 4.45)
Hepatoblastoma	Referent	1.58 (0.92, 2.72)	Referent	0.99 (0.51, 1.95)	Referent	1.07 (0.38, 3.04)	Referent	0.79 (0.19, 3.40)
Osteosarcoma	Referent	**1.35 (1.01, 1.81)**	Referent	1.17 (0.85, 1.60)	Referent	0.76 (0.49, 1.18)	Referent	0.81 (0.40, 1.66)
Ewing tumor	Referent		Referent		Referent		Referent	

(*continued on next page*)

Table 3 (*continued*)

	White, female N (%)	White, male N (%) HR (95 % CI)	Hispanic, female N (%) HR (95 % CI)	Hispanic, male N (%) HR (95 % CI)	Black, female N (%) HR (95 % CI)	Black, male N (%) HR (95 % CI)	API, female N (%) HR (95 % CI)	API, male N (%) HR (95 % CI)
		0.78 (0.56, 1.10)		1.60 (0.96, 2.66)		0.82 (0.06, 11.63)		0.86 (0.27, 2.80)
Rhabdomyosarcoma	Referent	0.97 (0.76, 1.23)	Referent	0.88 (0.65, 1.18)	Referent	0.80 (0.53, 1.21)	Referent	1.08 (0.56, 2.08)
Thyroid carcinoma	Referent	2.05 (0.71, 5.94)	Referent	3.47 (0.96, 12.47)	Referent	Not estimable	Referent	Not estimable

*Models adjusted for age at diagnosis (<1, 1–4, 5–9, 10–14, 15–19 years), year of diagnosis (2000–2004, 2005–2009, 2010–2014, 2015–2017), stage of disease (local, regional, distant; not available for I Leukemias). Bold text indicates Hazard Ratios (HR) that exclude the null value of 1.

adequate treatment data to infer the role of treatment received [46] on the observed disparities. We are using race/ethnicity classifications as reported in SEER, but recognize these categories inadequately capture the cultural diversity of groups and do not fully represent 1) the true identity of each case as it was unclear how the data was collected (physician report or patient self-report, etc.) or 2) the social or genomic underpinnings of race/ethnicity that may be important for response to therapy and disease outcome. Further, we did not have insurance status information or SES classifiers that allow us to infer the role of access to care in the observed disparities. For this analysis, we decided to use overall survival, which could include cancer-related, treatment-related, or other causes of death. As competing risks are low in this young and otherwise healthy population, we felt that capturing overall cause of death would more clearly highlight disparities in outcomes that span disease-related and treatment-related toxicities. Differences in outcome types should be further evaluated in properly designed studies with detailed outcome and treatment data. Survival data at the end of the Kaplan Meier curves are based on small numbers of cases and are patients who were diagnosed at the earliest time points in this study. Additionally, SEER requires follow-up data for 90 % of cases diagnosed under the age of 20 years, which leaves some cases missing follow-up; however, we were unable to determine the degree of this missingness in our dataset and cannot determine whether it varies by race/ethnicity. We cannot draw conclusions about equal access to care by race/-ethnicity, which may impact the observed disparities. While we did not observe evidence of statistical interaction using the standard p-value cutoff of 0.05 for the race/ethnicity-sex test, several cancers had smaller, though non-significant p-values (Supplemental Table 2) including Ewing and osteosarcoma (both $p = 0.05$), Hodgkin lymphoma (0.11), and medulloblastoma and PNET (both $p = 0.14$) that may reach statistical significance if the sample size in each stratum were increased. This could be assessed in the future using additional volumes of SEER data or in other larger studies. Finally, as the use of multiple testing corrections is a debated methodological issue, the lack of multiple testing in our analyses may be a limitation of our paper for some, but is generally seen as acceptable in observational research [22,47–49]. Further, as the sex-stratified and race-stratified analyses of any of the 17 given malignancies are independent of their parallels, [22,47] we did not use multiple testing in our analyses. However, the alpha values of the race-stratified and sex-stratified disjunction tests within each of the 17 cancers could be corrected by the two tests in the sex-stratified models (Bonferroni alpha=0.025) and by the four tests in the race/ethnicity stratified models (Bonferroni alpha = 0.0125).

To conclude, we observed racial/ethnic and sex disparities in overall 18-year survival after diagnosis for 12 malignancies among children aged 0–19 years. Notably, racial/ethnic differences were observed for all minorities with ALL and astrocytoma. There were differences in the association between race/ethnicity and death for children with AML, non-Hodgkin lymphoma, ependymoma, astrocytoma, PNET (males), neuroblastoma, nephroblastoma (females), hepatoblastoma, osteosarcoma (females), Ewing sarcoma, rhabdomyosarcoma, and thyroid carcinoma (females). Meanwhile, sex differences were largely present in White children with ALL, osteosarcoma, Hispanic children and medulloblastoma and PNET in API. These findings highlight the need for detailed, population-based studies with clinical and genetic information to allow us to disentangle the roles of race/ethnicity and sex in pediatric cancer survival.

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Data Availability

All data are publicly available through SEER.

CRediT authorship contribution statement

Kristin J. Moore: Data analysis and interpretation, Drafting, editing and approval of final manuscript. **Freddy Barragan:** Data analysis and interpretation, Drafting, editing and approval of final manuscript. **Lindsay A Williams:** Study conceptualization and oversight, Data analysis and interpretation, Drafting, editing and approval of final manuscript.

Conflicts of interest

The authors declare no conflicts of interest.

Appendix A. Supporting information

Supplementary data associated with this article can be found in the online version at doi:10.1016/j.canep.2022.102262.

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