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Racial and Ethnic Disparities in Neurocognitive, Emotional and Quality of Life Outcomes in Survivors of Childhood Cancer: A Report from the Childhood Cancer Survivor Study

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Abstract

Background—Survivors of childhood cancer are at risk of neurocognitive impairment, emotional distress and poor health-related quality of life (HRQOL); however, the effect of race/ethnicity is understudied. We aimed to identify race/ethnicity-based disparities in neurocognitive, emotional and HRQOL outcomes among survivors of childhood cancer.

Methods—Self-reported measures of neurocognitive function, emotional distress (BSI-18), and HRQOL (SF-36) were compared between minority (Hispanic [n=821], non-Hispanic black [NHB: n=600]) and non-Hispanic white (NHW: n=12,287) survivors from the Childhood Cancer Survivor Study, median age 30.9 years (range 16.0-54.1). Using a sample of 3,055 siblings, the magnitude of same race/ethnicity survivor-sibling differences were compared between racial/ethnic groups, adjusting for demographic and treatment characteristics and current socioeconomic status (SES).

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Results—No clear pattern of disparity in neurocognitive outcomes by race/ethnicity was observed. The magnitude of the survivor-sibling difference in mean score for depression was greater in Hispanics than NHWs (3.59 vs. 1.09, p=0.004). NHBs and Hispanics had greater survivor-sibling differences in HRQOL than NHWs for mental health (NHB: −5.78 vs −0.69, p=0.001; Hispanic: −3.87 vs. −0.69, p=0.03) and social function (NHB: −7.11 vs −1.47, p<0.001; Hispanic: −5.33 vs. −1.47, p=0.001). NHBs had greater survivor-sibling differences in physical subscales of HRQOL than NHWs. Findings were, in general, not attenuated by current SES.

Conclusion—Although no pattern of disparity in neurocognitive outcomes was observed, differences across many HRQOL outcomes among minorities compared to NHWs, not attenuated by current SES, were identified. This suggests further research into environmental and sociocultural factors during and immediately after treatment is needed.

Precis:

Disparities across many domains of health-related quality of life among minority survivors of childhood cancer compared to non-Hispanic whites were identified and are not fully explained by socioeconomic status. Fortunately, no pattern of differences in neurocognitive outcomes by race/ethnicity were identified.

Keywords

Pediatric; Cancer; Survivor; Race; Ethnicity; Disparity; Psychological

INTRODUCTION

Given the improvement in survival of childhood cancer observed over the last five decades, the number of pediatric cancer survivors living in the United States is predicted to exceed 500,000 by 2020.[1] However, survival comes at a cost, including increased risk for late mortality and chronic health conditions.[2,3] Childhood cancer survivors are known to be at increased risk of neurocognitive impairment compared to siblings, with 20-40% of survivors having measurable deficits.[4,5] Additionally, certain populations of survivors have been found to be at increased risk for poor emotional and health-related quality of life (HRQOL) outcomes.[6-10]

Risk factors for neurocognitive impairment, emotional distress and poor HRQOL are reasonably well established. Survivors treated at a younger age or who received CNS-directed chemotherapy or cranial radiation have consistently been found to be at higher risk for neurocognitive impairment.[4,5,11] Risk factors for emotional distress include a brain tumor diagnosis, adolescent age at diagnosis, more intensive treatment, female sex, and remaining unmarried.[5,7,10] Similarly, female sex, lower socioeconomic status (SES), major medical problems or prior treatment with cranial radiation are risk factors for poor HRQOL.[6-8] However, the impact of race and ethnicity on these outcomes is not established, attributable largely to the small numbers of minority survivors who have been systematically assessed.[4,6]

The demographics of the United States are shifting and by 2044 over 50% of individuals are expected to belong to a racial/ethnic background other than non-Hispanic white (NHW).[12]

In both the general population and childhood cancer survivors, minorities report lower income, education and rates of health insurance coverage compared to NHWs.[13-17] Racial and ethnic differences in overall and event-free survival of childhood cancer are not fully explained by differences in disease biology or pharmacogenetics and, likely, are in part due to socioeconomic and sociocultural factors.[16] Evaluation of racial and ethnic disparities in childhood cancer survivors focused on late mortality and chronic health condition outcomes has identified that, although differences exist, they are abrogated after adjusting for SES differences between groups.[17,18] However, there is a paucity of literature published on the effects of race and ethnicity on long-term psychological outcomes of childhood cancer survivors. The successful expansion of the Childhood Cancer Survivor Study (CCSS) to include survivors diagnosed 1970-1999 provides a unique opportunity for evaluating the impact of race and ethnicity on neurocognitive, emotional and HRQOL outcomes of childhood cancer survivors.

METHODS

Population

The CCSS is a retrospective cohort study with longitudinal follow-up of survivors of childhood cancer treated at 31 institutions in the US and Canada. Study eligibility included diagnosis of cancer before age 21 years, initial treatment between January 1, 1970 and December 31, 1999, and alive at five years after diagnosis of leukemia, CNS malignancy, Hodgkin lymphoma, non-Hodgkin lymphoma, Wilms tumor, neuroblastoma, soft tissue sarcoma, or bone tumor representing approximately 20% of US children diagnosed with cancer during this time-period. A random sample of siblings of CCSS participants served as a comparison population. The cohort methodology, study design and characteristics have been described in detail previously.[19,20]

The CCSS was approved by institutional review boards at participating centers. Participants provided informed consent for the study and release of information from medical records. For eligible survivors, cancer diagnosis and treatment information were obtained from medical records at the treating institution. All participants completed a baseline questionnaire assessing demographic and health condition outcomes. Race/ethnicity status was obtained through self-report of white, black, American Indian or Alaska Native (AIAN), Asian or Pacific Islander (API), or other categories, with the option to write in their race. Hispanic ethnicity was reported through a separate yes/no question. For this study, excluding small numbers of AIAN (N=142), API (N=365) or other (N=520), participants were grouped into three mutually exclusive race/ethnicity populations: NHW, NHB and Hispanics. The recent expansion of the CCSS cohort to include those diagnosed 1987-1999 more than doubled the number of NHB and Hispanic survivor participants. A proxy (parent, spouse, next of kin) completed the baseline questionnaire for survivors who died more than five years after diagnosis, were under age 18, or unable to complete the questionnaire. Study questionnaires are available at http://ccss.stjude.org. Survivors and siblings with complete race/ethnicity information on baseline questionnaire and who completed a subsequent follow-up questionnaire that included assessment of psychological outcomes were considered eligible for this analysis (Table 1, Figure 1).

Outcome Measures

The CCSS Neurocognitive Questionnaire (CCSS-NCQ) was designed to assess self-reported neurocognitive symptoms in childhood cancer survivors sensitive to therapeutic exposures and has been previously validated in the CCSS cohort.[21] It contains four subscales including task efficiency, emotional regulation, organization, and memory derived from a 25-item questionnaire. Participants were asked to report the degree to which they experienced any of 25 specific problems over the past 6 months using a Likert scale from 1 to 3. Scores were converted to standardized T-scores so that the overall sibling cohort had a mean=50 and standard deviation (SD) of 10. Scores were reported as a continuous variable where higher scores indicate worse neurocognitive function.

The Brief Symptom Inventory-18 (BSI-18) is an 18-item survey that measures symptoms of emotional distress over the past week and has been validated in the CCSS.[22,23] A summary score, the Global Severity Index (GSI), and three subscale scores for anxiety, depression and somatic complaints were reported as continuous variables where higher scores indicate more emotional distress. The Medical Outcomes Short Form-36 (SF-36) is a 36 item-survey used to evaluate HRQOL based on questions about the previous four weeks.[24] There are two summary scales (mental, physical) and eight subscales representing various aspects of well-being where lower scores indicate poor HRQOL. The SF-36 has been validated in childhood cancer survivors and utilized in the CCSS.[6,25] For both the BSI-18 and the SF-36, scores were reported as standardized T-scores with a general population mean=50 and SD=10. Participants <18 years of age were excluded from analyses utilizing the BSI-18 and CCSS-NCQ. Proxy reports were included in analyses utilizing the SF-36 and CCSS-NCQ because of the observable nature of the symptoms assessed but excluded from the analysis of emotional distress utilizing the BSI-18.

Cancer Therapeutic Exposures and Additional Factors

Cancer diagnosis and treatment data were abstracted from medical records including systemic and intrathecal (IT) methotrexate exposure, corticosteroid exposure and cranial radiation therapy (CRT), defined as maximum tumor dose (maxTD) of radiotherapy to one of four brain quadrants.[19,26] The maxTD for each brain segment was determined by summing the total prescribed dose from all overlapping treatment fields; the maxTD was applied only if ≥50% of a given brain segment was within the field(s). Demographic and socioeconomic characteristics including age at questionnaire completion, sex, current household income, education level and insurance status were available from the questionnaires. The presence of a severe/disabling or life-threatening medical condition (grade 3-4), scored applying the Common Terminology Criteria for Adverse Events (CTCAE, version 4.03, National Cancer Institute) intended for scoring both acute and chronic conditions in patients and survivors of cancer, was included.[27]

Statistical Analysis

Descriptive statistics from the time of last contact for survivors and siblings were calculated. Comparisons of the primary outcomes in the form of standardized T-scores were made between siblings and survivors stratified by CRT exposure, within each racial/ethnic group, using multiple linear regression, adjusting for sex, age at follow-up, era of diagnosis,

methotrexate exposure (intravenous and IT), corticosteroid exposure and presence of any CTCAE grade 3-4 chronic medical condition. Modifications by generalized estimating equations (GEE) were used to account for possible within-family correlation between survivors and siblings from the same family. To assess disparities between minority populations and NHWs the magnitude of the survivor-sibling differences for NHBs and Hispanics were compared with the survivor-sibling differences for NHWs, using the same regression method. This was done to standardize, on a population level, for SES differences that existed at the time of diagnosis based on the assumption that survivors and siblings of the same race/ethnicity group experienced similar SES exposures. To assess whether current SES attenuated differences in emotional and HRQOL outcomes, variables for education level, household income and health insurance status at the time of follow-up were added to the model in a subsequent step. The results from these regression analyses were reported as estimated means, differences in means and associated standard errors (SE) with p-values of the differences obtained from the robust variance of GEE.

RESULTS

Comparisons of Survivors and Siblings

A total of 13,708 five-year survivors and 3,055 siblings completed the baseline and follow-up questionnaires (Figure 1). The median age at diagnosis for survivors was 7.2 years (range 0.0-21.0) and the median age at follow-up survey was 30.9 years (range 16.0-54.1) for survivors and 33.4 years (range 9.6-58.4) for siblings. NHB (n=600, 4.4%) and Hispanic (n=821, 6.0%) survivors were more likely than NHW survivors to report a household income <$20,000 (27.6%, 15.8%, 10.1% respectively) and less likely to have health insurance (79.5%, 85.8%, 90.3%) or obtain a college degree (28.2%, 35.5%, 48.2%, Table 1). NHB survivors were more likely than Hispanic or NHW survivors to have been diagnosed with a kidney tumor (14.1%, 7.1%, 8.1% respectively) or have received a cumulative intravenous methotrexate dose ≥4.3 g/m^2 (23.1%, 11.8%, 13.2%) while all other cancer diagnosis and treatment variables differed between groups by <5%.

Neurocognitive Outcomes

Within racial/ethnic groups, survivors were more likely than siblings to have higher scores for task efficiency (NHW, NHB; Hispanic who received CRT), emotional regulation (NHW only) and memory (NHW; NHB and Hispanic who received CRT; Figure 2A). For task efficiency, the comparison of the magnitude of the survivor-sibling difference among NHB survivors with that among NHW survivors overall (7.00 vs. 3.54; p=0.04; Table 2) and among those who did not receive CRT (5.96 vs. 1.68; p=0.02) achieved statistical significance. However, for the remaining neurocognitive subscales, the magnitude of the survivor-sibling differences among NHBs and Hispanics was not greater than that observed among NHWs, overall or among those exposed to CRT.

Emotional Outcomes

Within racial/ethnic groups, survivors were more likely than siblings to have higher scores for depression (NHW, Hispanic), somatization (NHW, NHB) and the global severity index (NHW, Hispanic; Figure 2B). The survivor-sibling difference in mean score for depression,

adjusted for clinical and demographic characteristics, was significantly larger for Hispanics compared to NHWs, overall (3.59 vs. 1.09, p=0.004) and among those not exposed to CRT (3.52 vs. 0.91, p=0.004). Although the survivor-sibling differences among the group exposed to CRT was greater among Hispanics than NHWs (3.78 vs 1.57), it did not achieve statistical significance (p=0.09; Table 3). No significant survivor-sibling differences in emotional distress were observed when NHBs were compared to NHWs.

Health-Related Quality of Life

Survivor-sibling differences in many HRQOL domains were greater for minority survivors than NHWs (Figure 3, Supplemental Table 1). Specifically, the survivor-sibling difference in mean score for social function was significantly greater for both NHBs (−7.11 vs. −1.47, p=<0.001) and Hispanics (−5.33 vs. −1.47, p=0.001) compared to NHWs, overall and among those exposed to CRT (−7.70 vs. −1.97, p=<0.001 for NHBs and −5.75 vs. −1.97, p=0.01 for Hispanics). For mental health, the survivor-sibling difference in mean score was greater in magnitude for Hispanics (−3.87 vs. −0.69, p=0.03) and NHBs (−5.78 vs. −0.69, p=0.001) when compared to NHWs overall and among those exposed to CRT for NHBs only (−6.26 vs. −0.84, p=0.003). Among survivors exposed to CRT, survivor-sibling differences in mean score were greater in magnitude for NHBs compared to NHWs for physical function (−7.58 vs −3.69, p=0.02) and pain (−2.33 vs. 0.99, p=0.03). Additional differences were observed on the role physical and role emotional subscales as well as the mental and physical component summaries.

Finally, current SES was added to the models to assess whether it mediated observed disparities in emotional and HRQOL outcomes (Supplemental Table 2). This addition abrogated previously observed disparities in the magnitude of survivor-sibling differences for pain in NHBs and for mental health in Hispanics. However, the observed disparities in the magnitude of survivor-sibling differences between minority groups and NHWs remained significant, with little attenuation, for depression among Hispanics and most HRQOL subscales including social function for Hispanics and NHBs, role emotional for Hispanics, and mental health, role physical and physical function for NHBs.

DISCUSSION

In this study, we did not identify consistent differences in neurocognitive outcomes by race or ethnicity. However, for depression and many domains of HRQOL outcomes, the magnitude of the differences between minority survivors and siblings was significantly larger than that of NHW survivors and siblings. Further, although differences in current socioeconomic indicators including household income, insurance status and education were observed between groups, they did not account for these disparities. Taken together, these findings suggest unmeasured environmental and sociocultural factors, potentially including chronic stressors or ability to reintegrate into their community following cancer treatment, differentially impact minority survivors during and after therapy for childhood cancer and may place them at risk for poor emotional and quality of life outcomes.

Survivor-sibling differences in HRQOL were greater for minority survivors than NHWs across multiple domains. Both Hispanics and NHBs had significantly larger gaps between

survivors and siblings for mental health scores across a variety of domains compared to NHWs. NHBs also reported disparities in physical well-being compared to NHWs. Multiple studies in survivors of adult-onset cancers, primarily breast cancer, have previously reported that black survivors report worse physical and functional well-being after cancer therapy than white survivors,[28,29] even after adjustment for socioeconomic and demographic factors.[30] To our knowledge, ours is the first study to report this disparity also exists in adult survivors of childhood cancers. Additionally, Hispanic survivors of breast cancer have been found to have no difference in physical function scores compared to NHWs,[30] but have reported more distress and poorer social and mental HRQOL compared to NHW survivors.[28] In a large meta-analysis of psychosocial outcomes in survivors of adult-onset cancers, distress, depression and social and mental HRQOL were found to be worse in Hispanics compared to NHWs and were largely unchanged after adjustment for socioeconomic status.[31] These reported disparities in HRQOL of minority survivors of adult-onset cancers are generally consistent with our findings in minority survivors of childhood cancers.

With regard to emotional distress, the magnitude of the survivor-sibling difference for depression was larger for Hispanics compared to NHWs. However, all survivor and sibling groups, including Hispanics, reported mean scores for depression and the GSI that were at or below the expected population norm of 50. This is concordant with prior reports from the CCSS observing that although survivors report more emotional distress than siblings, both groups score lower than community norms, indicating less symptoms of emotional distress than the general population.[7,9] Consistent with our findings in survivors, a recent study in pediatric cancer patients found no difference in reported symptoms of depression or anxiety in black patients or their caregivers compared to white.[32] In the overall US population, both Hispanics and NHBs reported higher rates of depressive symptoms than NHWs; however, after accounting for poverty, population rates of depression did not differ significantly by race or ethnicity.[33]

Fortunately, there were no overall disparities in neurocognitive outcomes among minority survivors compared to NHW survivors; however, the magnitude of reported survivor-sibling differences in task efficiency for NHBs compared to NHWs was significant. In assessing the implications of this finding, we must observe that the absolute mean score for task efficiency comparing NHB and NHW survivors did not differ substantially in magnitude overall (53.76 NHB vs 54.45 NHW) or among survivors not-exposed to CRT (52.73 NHB vs 52.60 NHW). Therefore this finding would not be expected to represent a clinically significant difference in attention or processing speed. However, the sibling score for task efficiency in NHB (46.77) was substantially below the anticipated standardized sibling mean of 50, and below that of NHW and Hispanic siblings, suggesting that NHB siblings report above average function in task efficiency. This finding should be confirmed in future studies before any further conclusions can be drawn.

Prior studies evaluating race and health outcomes in the general population and adult-onset cancer patients have observed greater levels of psychological distress in participants reporting race-related stress, specifically everyday discrimination, which is reported more frequently in blacks than whites.[34,35] Additional general stressors such as financial stress or stress from life events negatively affect health outcomes in the general population where,

although blacks report these stressors more often, it appears that whites were more adversely impacted by them.[35] Among survivors of childhood cancer, financial hardship has been observed to negatively impact HRQOL.[36] The most significant predictors of financial hardship included lower household income and lower educational attainment, both social determinants that are disproportionately experienced by minority survivors compared to NHWs. While both NHBs and Hispanics may experience more race or ethnicity related stressors, all survivors and many siblings experience general stress related to their cancer experience and many go on to experience financial stress or chronic stress related to comorbidities. Thus, the specific cause of the differences in HRQOL for minorities compared to NHWs is unclear and further study into the effects of stressors on psychological outcomes of childhood cancer survivors is needed.

To our knowledge, this is the largest evaluation of psychological outcomes of minority survivors of childhood cancer to date, including detailed history of cancer therapy and a comparison population of siblings. The utilization of siblings to determine the "gap" between survivors and their same race/ethnicity siblings allowed us to account for differences in environment between racial/ethnic groups that may have been present prior to diagnosis, throughout therapy and into survivorship that were not otherwise captured in the available dataset. However, we did not have access to any direct measures of socioeconomic status at the time of diagnosis or surrogate measures, such as parental education. Additional limitations to consider when interpreting findings include that all neurocognitive and emotional outcomes were self-reported, and the number of minority siblings available for the comparison groups is still relatively small, which may have led to inadequate power to identify differences in neurocognitive outcomes. We must consider the possibility of participation bias leading to decreased generalizability of our findings to all childhood cancer survivors. We have previously reported baseline participation rates for survivors diagnosed 1987-1999 by race/ethnicity including 67% among Hispanic, 57% among NHB and 70% among NHW survivors and observed superior participation rates in the CCSS compared to other survey-based cancer survivor studies.[17] Further, although rates of follow-up completion among non-deceased participants differed across racial/ethnic groups (NHW=69%, NHB=45%, Hispanic=50%), attrition does not appear to differ, overall, by socioeconomic indicators. (Supplemental Tables 3 and 4) For these reasons, our research is important to both draw attention to the disparities identified in emotional and HRQOL outcomes of childhood cancer survivors from racial and ethnic minorities and also motivate innovative strategies for comprehensive investigation of race/ethnicity specific outcomes and associated risk factors in future research.

In conclusion, although differences in long-term neurocognitive outcomes by race or ethnicity were not identified, disparities in health-related quality of life outcomes years after cancer therapy appear widespread in minority survivors. This may suggest that, the stressors a survivor experiences, their ability to cope, access to social support networks, and the expectations they or their community have for employment, financial independence, physical function or emotional adjustment after cancer therapy differ between racial and ethnic groups, leading to the reported health-related quality of life disparities. Clinicians should be aware that minority survivors of childhood cancer appear to represent a high-risk population for poor HRQOL outcomes and the need for annual, long-term follow-up

including a comprehensive psychological assessment, which is recommended for all survivors,[37] should be emphasized among this group. Further research to validate these results and evaluate the role of differential stressors, supports and expectations between minority childhood cancer survivors and NHWs is needed to better understand these findings and develop intervention strategies to close the identified gaps in minority survivor quality of life.

Supplementary Material

Refer to Web version on PubMed Central for supplementary material.

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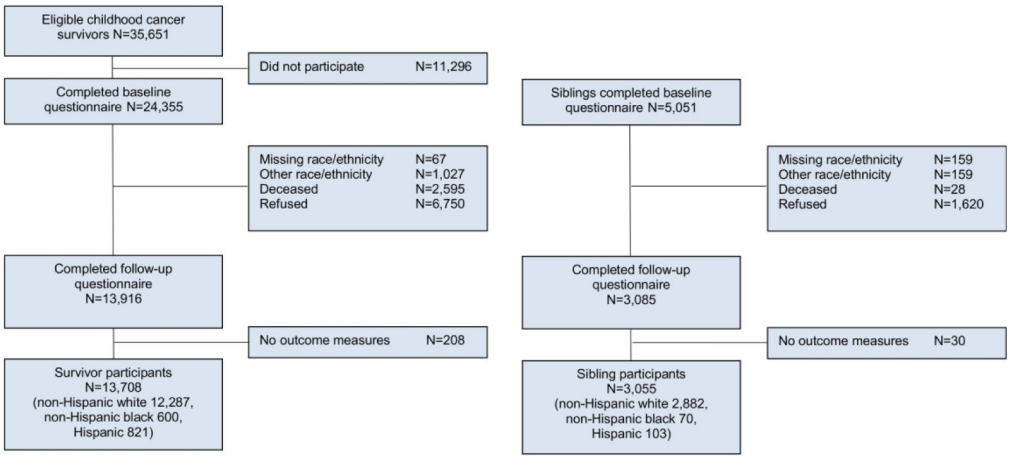
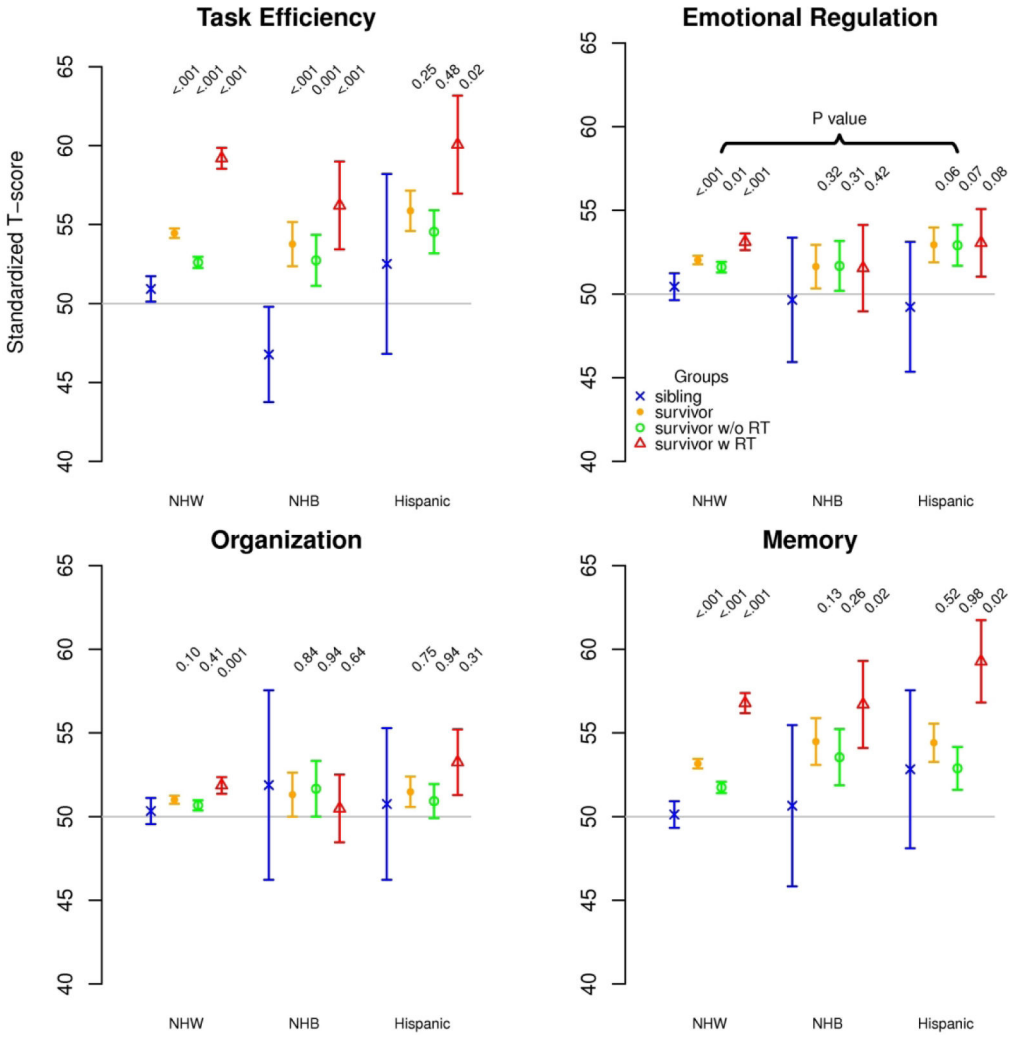


Figure 1.
Study population



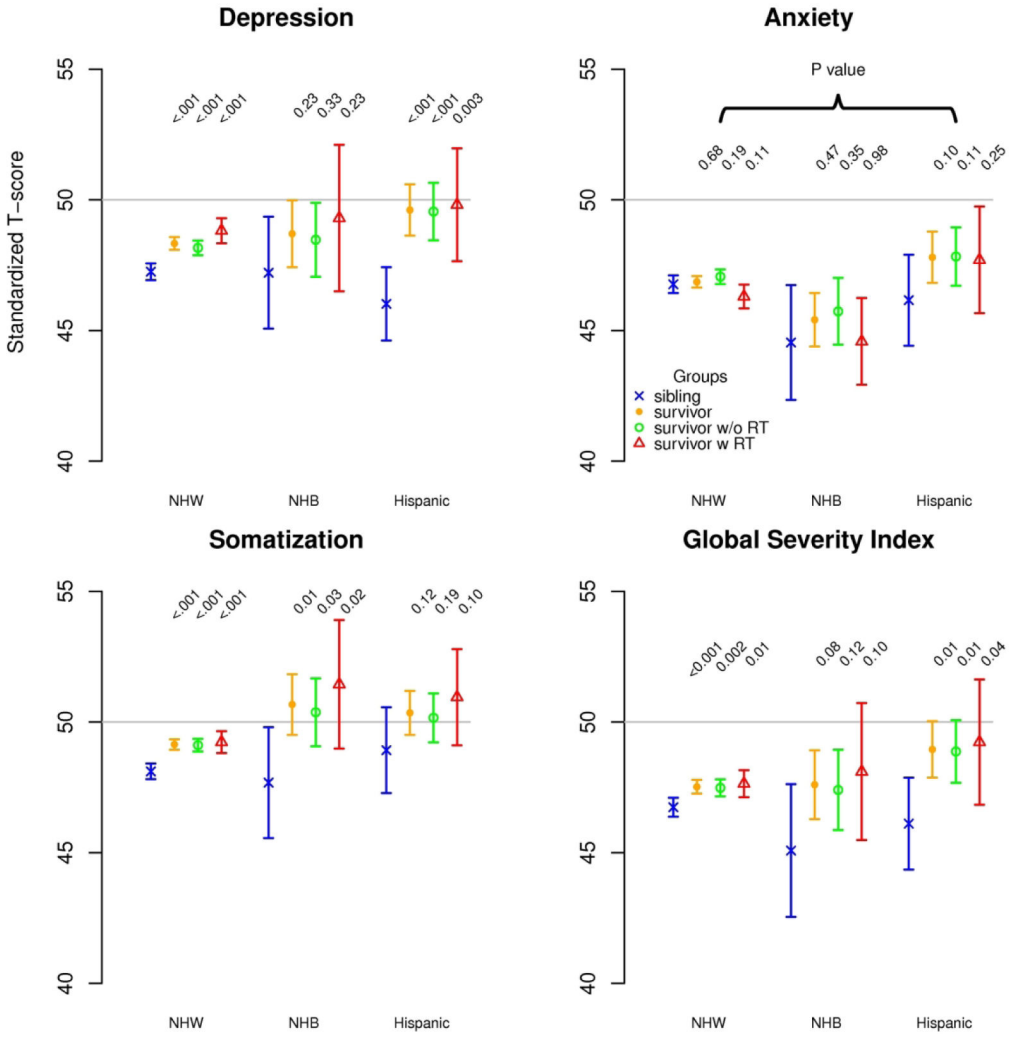


Figure 2.

(A) Neurocognitive outcomes of survivors and siblings within each racial/ethnic group as standardized T-scores, sibling mean=50 SD=10. (B) Emotional (BSI-18) outcomes of survivors and siblings within each racial/ethnic group as standardized T-scores, general population mean=50 SD=10. For both outcomes, higher scores indicate worse function; P-values compare each survivor group to same race/ethnicity sibling group adjusted for sex, age at follow-up, year at diagnosis, methotrexate exposure (intravenous and intrathecal), corticosteroid exposure and any CTCAE grade 3-4 chronic medical condition. NHW=non-Hispanic white, NHB=non-Hispanic black, RT=cranial radiation therapy

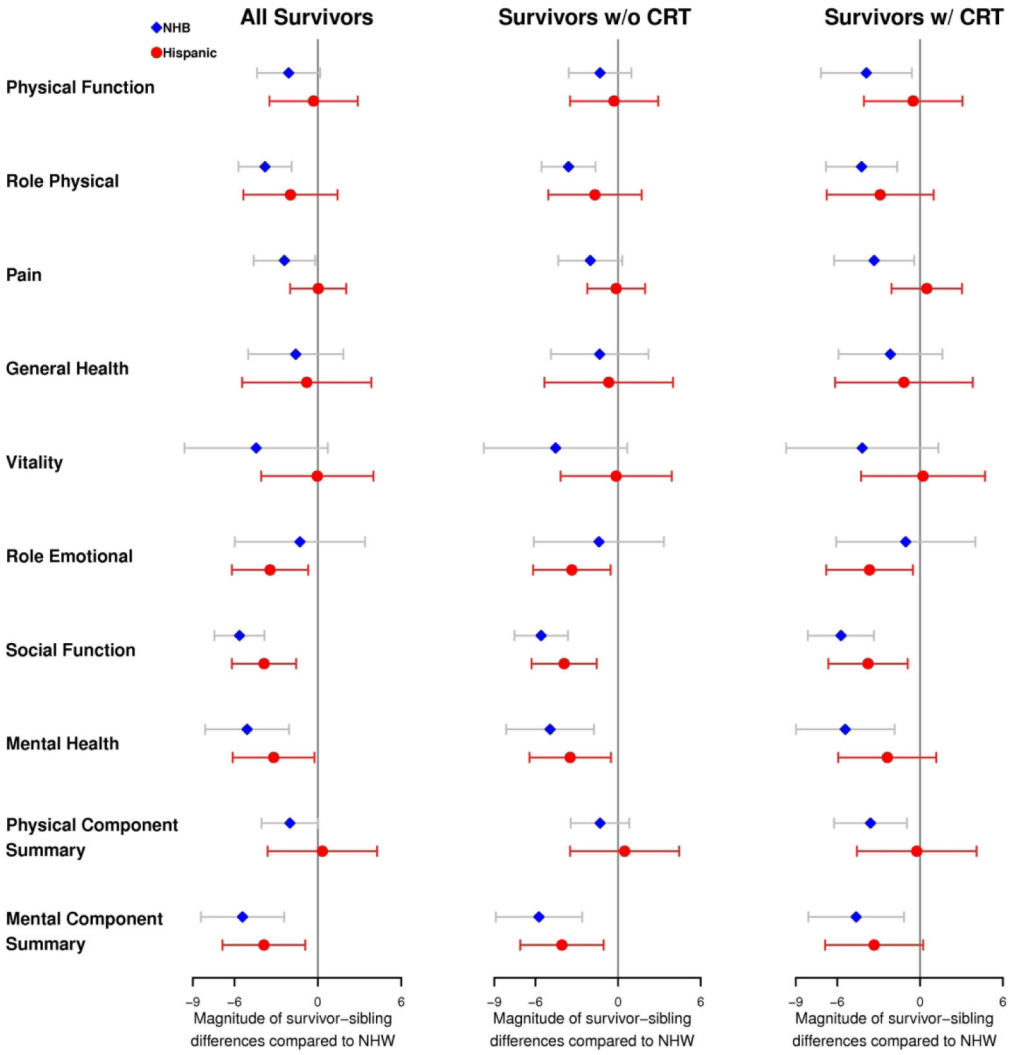


Figure 3.

Health-related quality of life outcomes. Magnitude of the survivor-sibling difference in mean score for Hispanic and non-Hispanic black (NHB) compared to survivor-sibling difference for non-Hispanic white (NHW). CRT=cranial radiation therapy

Table 1.

Demographic and treatment characteristics among survivors of childhood cancer and siblings.

Characteristic		Survivors, n(%)				Siblings, n(%)			
		White, NH (n=12,287)	Black, NH (n=600)	Hispanic (n=821)	*P*	White, NH (n=2882)	Black, NH (n=70)	Hispanic (n=103)	*P*
Sex					0.03				0.84
	Male	6139 (49.8)	298 (48.8)	373 (45.4)		1311 (45.5)	31 (44.3)	44 (42.7)	
	Female	6148 (50.2)	302 (51.2)	448 (54.6)		1571 (54.5)	39 (55.7)	59 (57.3)	
Age at diagnosis (years)					<0.001				
	0-4	4709 (40.2)	240 (41.1)	308 (39.5)					
	5-9	2733 (23.3)	134 (23.9)	233 (29.3)					
	10-14	2663 (20.2)	142 (22.5)	156 (17.8)					
	15-20	2182 (16.3)	84 (12.5)	124 (13.4)					
Year of diagnosis					<0.001				
	1970-79	3842 (28.4)	114 (16.7)	155 (16.4)					
	1980-89	5313 (41.6)	274 (42.3)	322 (36.7)					
	1990-99	3132 (30.1)	212 (41.0)	344 (46.9)					
Age at follow-up (years)					<0.001				0.03
	<25	2649 (22.6)	150 (26.3)	201 (26.6)		544 (18.9)	21 (30.4)	29 (28.2)	
	25-34	5227 (44.2)	271 (45.3)	369 (45.6)		956 (33.3)	25 (36.2)	37 (35.9)	
	35-44	3734 (28.2)	159 (25.5)	227 (25.2)		1022 (35.6)	17 (24.6)	30 (2.1)	
	45-54	676 (5.0)	20 (2.9)	24 (2.6)		338 (11.8)	6 (8.7)	6 (5.8)	
	≥55					11 (0.4)	0 (0.0)	1 (1.0)	
Cancer diagnosis					<0.001				
	Acute lymphoblastic leukemia	3216 (33.0)	133 (31.4)	232 (37.8)					
	Acute myeloid leukemia	421 (3.1)	20 (2.9)	48 (5.1)					
	Other leukemia	118 (0.9)	5 (0.7)	13 (1.4)					
	Astrocytoma	1279 (9.4)	54 (7.9)	87 (9.2)					
	Medulloblastoma, PNET	468 (3.5)	34 (5.0)	29 (3.1)					
	Other CNS tumors	331 (2.4)	23 (3.4)	21 (2.2)					
	Hodgkin lymphoma	1569 (11.6)	67 (9.8)	106 (11.2)					
	Non-Hodgkin lymphoma	992 (7.3)	45 (6.6)	54 (5.7)					

Characteristic	Survivors, n(%)				Siblings, n(%)			
	White, NH (n=12,287)	Black, NH (n=600)	Hispanic (n=821)	*P*	White, NH (n=2882)	Black, NH (n=70)	Hispanic (n=103)	*P*
Kidney tumors	1097 (8.1)	96 (14.1)	67 (7.1)					
Neuroblastoma	864 (6.4)	32 (4.7)	57 (6.0)					
Soft tissue sarcoma	919 (6.8)	48 (7.1)	38 (4.0)					
Ewing sarcoma	377 (2.8)	3 (0.4)	16 (1.7)					
Osteosarcoma	575 (4.2)	40 (5.9)	51 (5.4)					
Other bone tumors	61 (0.5)	0 (0.0)	2 (0.2)					
Cranial radiation (maxTD, Gy)				0.002				
None	7902 (70.3)	341 (68.7)	536 (73.1)					
>0-<20[†]	1121 (10.5)	49 (13.6)	64 (9.9)					
20-<30	969 (8.2)	32 (5.6)	54 (7.7)					
30- <50	335 (2.7)	6 (1.1)	15 (1.8)					
≥50	1037 (8.2)	63 (11.1)	65 (7.6)					
Intravenous methotrexate, g/m^2				<0.001				
None	9060 (75.2)	361 (65.5)	584 (75.4)					
<4.3	1265 (11.7)	53 (11.4)	81 (12.8)					
≥4.3	1094 (13.2)	73 (23.1)	74 (11.8)					
Intrathecal methotrexate, mg/m^2				0.02				
None	7756 (62.6)	347 (62.1)	503 (60.6)					
<230	2602 (24.7)	103 (24.7)	145 (22.7)					
≥230	900 (12.7)	32 (13.3)	75 (16.7)					
Systemic corticosteroid				0.60				
None	6697 (53.4)	301 (52.6)	436 (51.3)					
Prednisone only	4510 (43.6)	178 (44.6)	301 (46.2)					
Any dexamethasone	383 (3.0)	16 (2.8)	22 (2.5)					
Health insurance status				<0.001				<0.001
Yes	11021 (90.3)	478 (79.5)	696 (85.8)		2630 (91.6)	61 (87.1)	83 (81.4)	
No	1182 (9.7)	116 (20.5)	123 (14.2)		241 (8.4)	9 (12.9)	19 (18.6)	
Household income ($[ǂ])				<0.001				0.003
<20,000	1036 (10.1)	115 (27.6)	105 (15.8)		125 (4.8)	5 (10.6)	8 (9.1)	

Characteristic	Survivors, n(%)				Siblings, n(%)			
	White, NH (n=12,287)	Black, NH (n=600)	Hispanic (n=821)	*P*	White, NH (n=2882)	Black, NH (n=70)	Hispanic (n=103)	*P*
20-39,999	1464 (14.2)	109 (23.0)	144 (21.5)		242 (9.2)	4 (8.5)	11 (12.5)	
40-59,999	1670 (15.9)	89 (17.7)	127 (18.4)		313 (12.0)	10 (21.3)	12 (13.6)	
60-79999	1560 (14.5)	62 (13.2)	101 (14.7)		346 (13.2)	7 (14.9)	17 (19.3)	
80-99999	1279 (11.9)	31 (5.8)	59 (8.5)		327 (12.5)	8 (17.0)	15 (17.0)	
≥100,000	3741 (33.5)	63 (12.8)	158 (21.1)		1266 (48.3)	13 (27.7)	25 (28.4)	
Educational attainment				<0.001				<0.001
<High school graduate or GED	564 (4.6)	42 (7.8)	52 (6.1)		110 (3.8)	5 (7.1)	3 (2.9)	
High school graduate	1778 (14.2)	128 (20.9)	147 (18.4)		342 (11.9)	14 (20.0)	12 (11.7)	
Any college/post-high school training	4041 (33.0)	264 (43.1)	334 (40.0)		925 (32.1)	30 (42.9)	52 (50.5)	
College or post-graduate degree	5871 (48.2)	163 (28.2)	287 (35.5)		1504 (52.2)	21 (30.0)	36 (35.0)	
Employment				<0.001				0.69
Unable to work	985 (7.8)	95 (15.1)	96 (11.4)		41 (1.4)	0 (0.0)	2 (1.9)	
Unemployed	1398 (11.4)	81 (13.6)	113 (13.7)		284 (9.9)	8 (11.4)	13 (12.6)	
Employed/student	9904 (80.8)	424 (71.2)	612 (75.0)		2557 (88.7)	6 (88.6)	88 (85.4)	
Major medical condition				0.33				0.93
Yes	3409 (26.4)	167 (26.6)	251 (28.5)		236 (8.2)	5 (7.1)	9 (8.7)	
No	8878 (73.6)	433 (73.4)	570 (71.5)		2646 (91.8)	65 (92.9)	94 (91.3)	

Analyses including percentages were weighted to account for under-sampling of acute lymphoblastic leukemia survivors in latter era (1987–1999)

†Direct cranial radiation doses (not including stray/scatter).

‡Adjusted to 2016-dollar value. NH=non-Hispanic; maxTD=maximum tumor dose

Table 2.

Neurocognitive outcomes across racial/ethnic groups of childhood cancer survivors.

	White, non-Hispanic		Black, non-Hispanic			Hispanic		
	Mean	**P**	**Mean**	**P**	**P***	**Mean**	**P**	**P***
Task efficiency								
Sibling	50.92		46.77			52.51		
Survivor	54.45		53.76			55.87		
Difference from sibling	3.54	<0.001	7.00	<0.001	0.04	3.36	0.25	0.95
Survivor no CRT	52.60		52.73			54.54		
Difference from sibling	1.68	<0.001	5.96	0.001	0.02	2.04	0.48	0.90
Survivor with CRT	59.20		56.21			60.06		
Difference from Sibling	8.28	<0.001	9.45	<0.001	0.57	7.55	0.02	0.83
Emotional regulation								
Sibling	50.44		49.65			49.23		
Survivor	52.03		51.64			52.94		
Difference from sibling	1.59	<0.001	1.99	0.32	0.85	3.72	0.06	0.29
Survivor no CRT	51.61		51.68			52.91		
Difference from sibling	1.16	0.006	2.03	0.31	0.67	3.68	0.07	0.22
Survivor with CRT	53.12		51.55			53.06		
Difference from sibling	2.68	<0.001	1.90	0.42	0.74	3.83	0.08	0.60
Organization								
Sibling	50.33		51.88			50.75		
Survivor	51.00		51.31			51.48		
Difference from sibling	0.68	0.10	−0.57	0.84	0.67	0.73	0.75	0.98
Survivor no CRT	50.67		51.66			50.92		
Difference from sibling	0.34	0.41	−0.22	0.94	0.85	0.17	0.94	0.94
Survivor with CRT	51.86		50.48			53.25		
Difference from Sibling	1.53	0.001	−1.40	0.64	0.33	2.50	0.31	0.70
Memory								
Sibling	50.12		50.65			52.83		
Survivor	53.16		54.48			54.41		

	White, non-Hispanic		Black, non-Hispanic			Hispanic		
	Mean	**P**	**Mean**	**P**	**P***	**Mean**	**P**	**P***
Difference from sibling	3.04	<0.001	3.83	0.13	0.76	1.58	0.52	0.55
Survivor no CRT	51.74		53.54			52.88		
Difference from sibling	1.63	<0.001	2.89	0.26	0.63	0.05	0.98	0.53
Survivor with CRT	56.78		56.70			59.27		
Difference from Sibling	6.66	<0.001	6.05	0.02	0.82	6.44	0.02	0.93

P=p-value comparing survivors to same race/ethnicity siblings; P*=p-value comparing survivor-sibling difference between racial/ethnic groups, referenced to non-Hispanic white survivor-sibling difference.

Adjusted for sex, age at follow-up, year at diagnosis, methotrexate exposure (intravenous and intrathecal), corticosteroid exposure and any CTCAE grade 3-4 chronic medical condition.

Table 3.

Emotional outcomes across racial/ethnic groups of childhood cancer survivors.

	White, non-Hispanic		Black, non-Hispanic			Hispanic		
	Mean	**P**	**Mean**	**P**	**P***	**Mean**	**P**	**P***
Depression								
Sibling	47.25		47.21			46.02		
Survivor	48.33		48.70			49.61		
Survivor-sibling difference	1.09	<0.001	1.49	0.23	0.75	3.59	<0.001	**0.004**
Survivor no CRT	48.16		48.47			49.55		
Survivor-sibling difference	0.91	<0.001	1.26	0.33	0.79	3.52	<0.001	**0.004**
Survivor with CRT	48.82		49.30			49.81		
Survivor-sibling difference	1.57	<0.001	2.09	0.23	0.77	3.78	0.003	0.09
Anxiety								
Sibling	46.77		44.54			46.16		
Survivor	46.86		45.41			47.80		
Survivor-sibling difference	0.09	0.68	0.87	0.47	0.52	1.64	0.10	0.13
Survivor no CRT	47.06		45.73			47.83		
Survivor-sibling difference	0.29	0.19	1.19	0.35	0.48	1.67	0.11	0.19
Survivor with CRT	46.30		44.58			47.70		
Survivor-sibling difference	−0.47	0.11	0.04	0.98	0.71	1.54	0.25	0.14
Somatization								
Sibling	48.11		47.68			48.92		
Survivor	49.14		50.67			50.35		
Survivor-sibling difference	1.03	<0.001	3.00	0.01	0.11	1.43	0.12	0.67
Survivor no CRT	49.11		50.37			50.16		
Survivor-sibling difference	1.00	<0.001	2.70	0.03	0.18	1.24	0.19	0.80
Survivor with CRT	49.23		51.44			50.95		
Survivor-sibling difference	1.12	<0.001	3.76	0.02	0.11	2.03	0.10	0.47
Global severity index								
Sibling	46.74		45.08			46.11		
Survivor	47.52		47.60			48.95		

	White, non-Hispanic		Black, non-Hispanic			Hispanic		
	Mean	**P**	**Mean**	**P**	**P***	**Mean**	**P**	**P***
Survivor-sibling difference	0.78	<0.001	2.52	0.08	0.23	2.85	0.005	0.05
Survivor no CRT	47.48		47.40			48.87		
Survivor-sibling difference	0.74	0.002	2.33	0.12	0.30	2.76	0.009	0.06
Survivor with CRT	47.64		48.10			49.23		
Survivor-sibling difference	0.90	0.005	3.02	0.10	0.25	3.12	0.04	0.14

P=p-value comparing survivors to same race/ethnicity siblings; P*=p-value comparing survivor-sibling difference between racial/ethnic groups, referenced to non-Hispanic white survivor-sibling difference.

Adjusted for sex, age at follow-up, year at diagnosis, methotrexate exposure (intravenous and intrathecal), corticosteroid exposure and any CTCAE grade 3-4 chronic medical condition.