Differences in Long-Term Outcomes by Race/Ethnicity in Childhood Cancer Survivors: A Report from the Childhood Cancer Survivor Study

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1. Overall Goal and Background

The goal of the proposed analysis is to examine differences in risk of developing late effects by race/ethnicity in the CCSS cohort. The idea was proposed by the CCCSS Steering Committee as a strategic plan for addressing minority issues in childhood cancer survivorship. We have collected some preliminary data and made this proposal.

CCSS has investigated extensively a wide range of long-term outcomes of childhood cancer such as mortality, second neoplasms (SNs), chronic conditions, and health status. Many of the CCSS investigations have included race/ethnicity as a variable for adjustment, but only one study by Castellino *et al*. studied specifically the differences in late effects by race/ethnicity using the baseline questionnaire, evaluating all-cause mortality, second malignant neoplasms (SMNs), health status (general health, mental health, limitations of activity, functional impairment, pain as a result of cancer, anxiety/fears as a result of a cancer), health care utilization (medical care within 2 years: general medial contact, general physical examination, cancer-related medical visit, cancer centre visit, emergency room visit, and hospitalization), and health behaviors (positive health behaviors [dental examination within 1 year, for females: pap smear within 3 years, monthly breast self-examination, clinical breast examination within 1 year; for male: monthly testicular self-examination], risky health behaviors [current smoker, binge drinking, heavy drinking, potential problem drinking, physical inactivity]). Due to the fact that health in general population declines with age and the risk of subsequent malignancies and many other adverse outcomes increase over time, it is important to update the impact of race/ethnicity on health outcomes, including the additional follow-up time (questionnaires) beyond the baseline questionnaire. In addition, other than studies that evaluated differential survival rates as a function of race/ethnicity (Bhatia *et al*, Pui *et al*., Rubnitz *et al*., Linabery *et al*., and Kadan-Lottick *et al.*) and the previously mentioned study by Castellino *et al*., there is little literature

evaluating the effects of race/ethnicity on long-term health outcomes of childhood cancer survivors and there is a pressing need (this issue was specifically mentioned in the competitive renewal by NCI) to investigate them (e.g., cause-specific mortality by race/ethnicity).

The purpose of this study is to examine the differences in the rates of developing late effects between groups defined by race/ethnicity in the CCSS cohort by updating the previous study using additional follow-up time and questionnaires, expanding the outcomes to include overall and cause-specific mortality, SNs including SMNs, chronic health conditions, and health status.

2. SUBJECT POPULATION

The study population will include survivors in the original CCSS cohort who had complete information for race/ethnicity in the baseline questionnaire. Analyses on the health status will be further restricted to those who were ≥18 years old and alive at the time of the interview. Analyses including treatment variables will be further restricted to those who signed medical record releases and have treatment exposure data abstracted by the CCSS institutions.

3. SPECIFIC AIMS and HYPOTHESES

The specific aim of this proposal is to provide a comprehensive summary of the differences by race/ethnicity in the outcomes of childhood cancer survivors. Because treatment differs by diagnosis and different race/ethnic groups have different frequencies of diagnosis, initially we will conduct a stratified analysis where the strata are formed by diagnosis (and age and radiation exposure, possibly, depending on discussions with clinicians).

A. Mortality

Hypotheses: While the all-cause Standardized Mortality Ratio (SMR) will be greater than 1.0 in all the race/ethnicity groups, non-Hispanic (NH) White survivors will have the lowest SMR. The overall survival will be lower in NH Black and Hispanics than NH White and other race/ethnicity groups. The survival patterns among the race/ethnicity groups differ by sex: black female survivors will have the highest survival and black male survivors will have the lowest survival. The cumulative incidence of cause-specific mortality will be different such that the leading causes of death vary by race. The mortality rates will be compared by race/ethnicity adjusting for socioeconomic status (SES).

B. Subsequent neoplasm/malignancies

We will investigate the difference in risk of developing overall and specific SNs (SMN, non-melanoma skin cancers (NMSC) and meningiomas) by race/ethnicity. For each of the SN outcome, the effect of race/ethnicity will also be studied in siblings and compared to survivors. We will investigate the occurrence and patterns of multiple SNs by race/ethnicity.
Hypotheses: The Standardized Incidence Ratio (SIR) of all SMN will be greater than 1 in all race/ethnicity groups. NH White survivors have higher likelihood of developing SNs/SMNs than NH Black and Hispanics. These differences may disappear after adjusting for SES.

C. Severe Chronic medical conditions

The effect of race/ethnicity on risks of overall (any organ system) and each organ system class of severe chronic medical conditions will be studied among survivors. Due to the less common occurrence of severe chronic medical conditions in siblings, only the overall outcome (any organ system) and outcomes by certain more prevalent organ systems (vision

endocrine cardiac, GI, other hematologic) will be investigated in siblings by race/ethnicity and differential impact of race/ethnicity for survivors versus siblings will be evaluated to the extent possible. The comparison between race/ethnicity groups will also be carried out both adjusted and unadjusted by SES.

Hypotheses: Minority cancer survivors will have an increased likelihood of some grade 3-5 chronic conditions. Specifically, comparing to NH White survivors, NH Blacks will have a higher risk of cardiovascular disease and Hispanics will have a higher risk of endocrine diseases. These differences may disappear after adjusting for SES.

D. Health status

Six domains of health status were described previously (Hudson *et al*.): general health, mental health, limitations of activity, functional impairment, pain as a result of cancer, and anxiety/fears as a result of a cancer. We will investigate the effect of race/ethnicity on the change of health status over age in each domain of the health status in the survivors. The effect will also be compared between survivors and siblings for the four domains that were measured in siblings (general health, mental health, activity limitations, and functional impairment), assessing interactions to evaluate whether trajectories over age vary by race differently for survivors than for siblings.

Hypotheses: All minority groups of cancer survivors and siblings will have worse general health and functional health than NH White and the age-dependent changes in health status will vary across the race/ethnicity groups.

4. STATISTICAL ANALYSIS FRAMEWORK

Sociodemographic and treatment variables among race/ethnicity groups will be compared descriptively using χ^2 tests for categorical variables and ANOVA for continuous variables. For each specific outcome, we will initially utilize models that were previously developed and published by CCSS in its outcome-specific papers. Where feasible, will start the assessment of each outcome stratified by diagnosis, and explore the possibility of aggregating. In addition, we will examine the role of SES and impact of adjustment for SES. Variables such as health care utilization and health behavior that may differ by race/ethnicity and that are associated to the specific outcome will also be adjusted for. The effect of race/ethnicity will be examined with and without adjusting for specific treatment exposures to assess whether the race/ethnicity effect can be attributable to differences in treatment exposures. Specific analysis methods for different outcomes are described below.

A. Mortality: Overall and specific cause of deaths prior to December 31, 2007 will be determined using the NDI. Survivors are censored on the earlier of the latest questionnaire date and December 31, 2007. Information on the underlying cause of death was obtained from death certificates for residents in the United States. The cause-specific analyses will exclude Canadian residents as the cause information cannot be determined. As in the previous analysis, cause of death will be categorized as the following categories: recurrence, SMN, cardiac, pulmonary, external causes, and other.

Overall and cause-specific mortality rates and Standardized Mortality Ratios (SMR), using the age-, sex-, calendar year-, and race/ethnicity- specific US mortality rates (some modeling is needed as Hispanic-specific rates are available only after 1999), will be

calculated for Non-Hispanic White, Non-Hispanic Black, and Hispanics, and compared across the three groups. Kaplan Meier curves of overall survival will be presented and compared across race/ethnicity stratified by sex. Cumulative incidence of death due to each cause will be estimated by race/ethnicity. Poisson regression models will be used to access the effect of race on all-cause and cause-specific mortality rates (or SMRs) adjusting for potential confounders (e.g., attainted age, age at diagnosis, year of diagnosis, treatment, and socioeconomics) determined in the CCSS mortality paper (Mertens *et al*.), using the logarithm of person-years (or expected counts of deaths) as the offset. Comparing the rate/ethnicity effects in the analysis of overall/cause-specific mortality rates vs. that of overall/cause-specific SMRs will distinguish whether the difference by race/ethnicity in the survivors was due to differences of mortality rates in the general population for specific race/ethnicity groups or due to survivor-related factors such as cancer treatment. The interaction between race/ethnicity and sex will be checked because the race/ethnicity effect on mortality rates seems to differ by sex (Castellino *et al*.).

B. SNs/SMNs: Cumulative incidence of SN and SMN with death as a competing risk event will be estimated with the SNs/SMNs before study entry being used as prevalence. To investigate the occurrence of multiple SNs and SMNs by race/ethnicity, the Total Cumulative Incidence will be calculated. Standardized Incidence Ratios (SIR) will be calculated with the expected number being calculated using age-, sex-, and calendar year-rates from the National Cancer Institute's Surveillance, Epidemiology and End Results (SEER) data. Relative rates (RRs) of developing SNs and SMNs will be estimated by the use of two Poisson multivariable regressions models, adjusting potential confounders determined in the SN paper (Neglia et al. and Friedman et al.). The calculation of SIRs will use subjects free of SMNs at study entry and use all the subsequent malignancies. The calculation of RRs will use subjects free of SN/SMNs at study entry and only use the first occurrence of SN/SNN after study entry. The regression models will be repeated by including siblings in the study subjects and an interaction term between the survivor status and race/ethnicity in the model. However, given the low proportion of siblings developing SN and SMN (2% and 1% respectively), we may be limited to draw solid conclusions.

C. Chronic Conditions: The Common Terminology Criteria for Adverse Events (CTCAE) Grades completed by Oeffinger and Armstrong (Armstrong *et al,* Oeffinger *et al*) will be used. Cumulative incidence and total cumulative incidence of any grade 3-5 overall chronic condition will be evaluated, treating death as a competing risk and including the conditions before study entry as prevalence. Among subjects free of any chronic condition at study entry, Cox regression models will be used to compare the hazards of severe chronic medical conditions of minority survivors to white survivors after 5 years post diagnosis, adjusted for age at diagnosis and sex and with some examination of the impact of adjustment for treatment factors (which may also differ by race/ethnicity). Age is used as the time scale in these models, with survivors entering the analysis at the age at which they enter the cohort and, for models with siblings, siblings will enter at age 5. In addition to the above summary measure of chronic conditions, specific conditions/organ systems will be examined in the same fashion. In order to compare the effect of race/ethnicity between survivors and siblings, the full cohort of both survivors and siblings will be included together in a set of models with sufficient outcome events, and an interaction term between race/ethnicity and

survivor status will be included in these models, adjusting for age and sex, though the number of events may be too small in the siblings.

D. Health status: Health statuses were measured in 3 questionnaires and the participants contributed data from one, two or three questionnaires. For each of the 4 domains that were measured in both survivors and siblings, generalized linear models with a log-link function will be used to estimate the prevalence ratios (PR) of race/ethnicity and compare these effects between survivors and siblings, with random effects to account for within-family and with-person correlation. Because health status worsens as age increases, with changes that may differ between survivors and siblings, and the effect of race/ethnicity on health status is not clear in both survivors and siblings, we will consider a full model that contains the 3-way interaction among race/ethnicity, age, and survivor status. Essentially, we are checking the changes in health status over age in 6 groups determined by race/ethnicity (NH White, NH Black, and Hispanic) and survivor status (survivors vs. siblings). To allow for a flexible pattern of change in health status over age, age will be included in the model as cubic splines. The percentages with adverse health status outcomes will then be estimated as a function of age and will be plotted by using age as the x-axis for each race/ethnicity stratified by survivor status. We may not have enough power to determine the difference in the 6 groups over age and the final model will be determined based on significance of various interaction terms. If needed, a similar model will be fitted by using the survivors only adjusting for treatment-related factors.

There may have been differential dropout by race/ethnicity since baseline. We suspect more minorities have dropped out and we will evaluate whether that might influence the results using the inverse probability weighting (IPW) technique to evaluate the potential for bias due to non-participation (Little & Rubin, 2002).

REMARKS:

1. In preliminary analysis, we found NH Black survivors had higher hazard of developing cardiovascular disease. It is known that NH Blacks have higher risk of cardiovascular disease in the general population. A similar analysis was then performed in siblings and a higher hazard was indeed seen in black siblings HR=2.2 (95% CI: 0.5-9.6). However, the small number of events in siblings restricted our ability to draw a solid conclusion.
2. The 14358 survivors from the baseline were classified into 4 groups: NH-White (N=12397), NH-Black (N=694), Hispanics (N=750), and others (N=517 including 50 with unknown race/ethnicity). The other groups are too small. Even though we have included it in the preliminary results below, we will not include it in the manuscript.

EXAMPLE TABLES and FIGURES with PRELIMINARY DATA

(As described in Statistical Analysis Framework above, we will modify the previously-used CCSS models with relevant considerations specific to making inference on race/ethnicity effects. These are noted as footnotes of each table below.)

Table 1A. Demographic and Treatment Characteristics of the Participants

type	White, NH N=12397	Black, NH N=694	Hispanic/Latin N=750	Other N=517
Sex of patient				
Male	6653 (53.7)	376 (54.2)	389 (51.9)	295 (57.1)
Female	5744 (46.3)	318 (45.8)	361 (48.1)	222 (42.9)
Age at diagnosis				
0-4	4895 (39.5)	315 (45.4)	322 (42.9)	222 (42.9)
5-9	2703 (21.8)	152 (21.9)	204 (27.2)	143 (27.7)
10-14	2534 (20.4)	148 (21.3)	129 (17.2)	100 (19.3)
15-20	2265 (18.3)	79 (11.4)	95 (12.7)	52 (10.1)
Year of diagnosis				
70-73	1721 (13.9)	70 (10.1)	84 (11.2)	48 (9.3)
74-77	2596 (20.9)	108 (15.6)	142 (18.9)	67 (13.0)
78-81	3272 (26.4)	176 (25.4)	168 (22.4)	141 (27.3)
82-86	4808 (38.8)	340 (49.0)	356 (47.5)	261 (50.5)
Diagnosis group				
Acute lymphoblastic leukemia	3682 (29.7)	164 (23.6)	294 (39.2)	189 (36.6)
Acute myeloid leukemia	299 (2.4)	20 (2.9)	18 (2.4)	19 (3.7)
Other leukemia	115 (0.9)	8 (1.2)	11 (1.5)	11 (2.1)
Astrocytomas	1074 (8.7)	39 (5.6)	43 (5.7)	26 (5.0)
Medulloblastoma, PNET	321 (2.6)	25 (3.6)	18 (2.4)	16 (3.1)
Other CNS tumors	277 (2.2)	10 (1.4)	16 (2.1)	11 (2.1)
Hodgkins disease	1721 (13.9)	69 (9.9)	91 (12.1)	46 (8.9)
Non-Hodgkins lymphoma	933 (7.5)	46 (6.6)	55 (7.3)	46 (8.9)
Kidney tumors	1046 (8.4)	120 (17.3)	60 (8.0)	30 (5.8)
Neuroblastoma	829 (6.7)	52 (7.5)	37 (4.9)	36 (7.0)
Soft tissue sarcoma	1065 (8.6)	78 (11.2)	56 (7.5)	47 (9.1)
Ewings sarcoma	377 (3.0)	6 (0.9)	12 (1.6)	9 (1.7)
Osteosarcoma	608 (4.9)	57 (8.2)	37 (4.9)	31 (6.0)
Other bone tumors	50 (0.4)	0 (0.0)	2 (0.3)	0 (0.0)
Received radiation therapy				
Yes	7441 (67.2)	299 (64.7)	392 (65.4)	281 (65.7)
No	3629 (32.8)	163 (35.3)	207 (34.6)	147 (34.3)
Chemotherapy	*Clinically meaningful dose categories will be used*			
Alkylating agent (non-Pt) dose				
Anthracycline dose				
Epipodophyllotoxin dose				
Bleomycin dose				
Socioeconomic status				
Health Insurance	*To be filled in the analysis*			
Household Income				
Highest education				
Positive Health behaviors				

Dental examination within 1 year
Female: pap smear within 3 years
Female: monthly breast self-examination
Female: clinical breast examination within 1 year
Male: monthly testicular self-examination
Risky health behaviors
Current smoker
Binger drinking
Heavy drinking
Potential problem drinking
Physical inactivity
Health care utilization
General medial contact
General physical examination
Cancer-related medical visit
Cancer centre visit
Emergency room visit

Note: We will conduct stratified analyses with strata formed by diagnosis and the table will be done with samples formed by diagnosis.

Table 1 Supplement A: dose (mg/m²) of Bleomycin by race/ethnicity stratified by diagnose

Race	No	Quartile 1	Quartile 2	Quartile 3	Quartile 4
Leukemia					
White,NH	3700 (100.0)	1 (0.0)	0	0	0
Black,NH	133 (100.0)	0	0	0	0
Hispanic/Latine	250 (99.6)	1 (0.4)	0	0	0
Other	187 (100.0)	0	0	0	0
CNS					
White,NH	1484 (99.8)	2 (0.1)	0	0	1 (0.1)
Black,NH	46 (100.0)	0	0	0	0
Hispanic/Latine	69 (100.0)	0	0	0	0
Other	45 (100.0)	0	0	0	0
HD					
White,NH	1219 (83.2)	85 (5.8)	86 (5.9)	58 (4.0)	18 (1.2)
Black,NH	27 (64.3)	6 (14.3)	3 (7.1)	3 (7.1)	3 (7.1)
Hispanic/Latine	55 (80.9)	2 (2.9)	5 (7.4)	3 (4.4)	3 (4.4)
Other	27 (75.0)	4 (11.1)	2 (5.6)	2 (5.6)	1 (2.8)
NHL					
White,NH	764 (96.1)	16 (2.0)	6 (0.8)	4 (0.5)	5 (0.6)
Black,NH	30 (93.8)	1 (3.1)	0	1 (3.1)	0
Hispanic/Latine	41 (97.6)	1 (2.4)	0	0	0
Other	33 (97.1)	1 (2.9)	0	0	0
Kidney (Wilms)					
White,NH	928 (99.9)	1 (0.1)	0	0	0
Black,NH	80 (100.0)	0	0	0	0
Hispanic/Latine	50 (100.0)	0	0	0	0
Other	24 (100.0)	0	0	0	0
Neuroblastoma					
White,NH	735 (99.7)	0	0	1 (0.1)	1 (0.1)
Black,NH	32 (100.0)	0	0	0	0
Hispanic/Latine	32 (100.0)	0	0	0	0
Other	30 (100.0)	0	0	0	0
Soft tissue sarcoma					
White,NH	912 (95.9)	9 (0.9)	7 (0.7)	7 (0.7)	16 (1.7)
Black,NH	54 (96.4)	0	0	0	2 (3.6)
Hispanic/Latine	41 (97.6)	0	0	0	1 (2.4)
Other	39 (95.1)	1 (2.4)	0	0	1 (2.4)
Bone cancer					
White,NH	714 (78.6)	18 (2.0)	36 (4.0)	55 (6.1)	85 (9.4)
Black,NH	27 (69.2)	0	3 (7.7)	4 (10.3)	5 (12.8)
Hispanic/Latine	28 (71.8)	0	1 (2.6)	6 (15.4)	4 (10.3)
Other	15 (46.9)	2 (6.3)	3 (9.4)	6 (18.8)	6 (18.8)

Table 1 Supplement B: dose (mg/m²) of Anthracycline by race/ethnicity stratified by diagnose

Race	No	Quartile 1	Quartile 2	Quartile 3	Quartile 4
Leukemia					
White,NH	1938 (55.0)	556 (15.8)	363 (10.3)	314 (8.9)	350 (9.9)
Black,NH	60 (49.6)	23 (19.0)	13 (10.7)	9 (7.4)	16 (13.2)
Hispanic/Latine	124 (53.7)	37 (16.0)	17 (7.4)	23 (10.0)	30 (13.0)
Other	93 (51.7)	33 (18.3)	19 (10.6)	17 (9.4)	18 (10.0)
CNS					
White,NH	1483 (99.5)	2 (0.1)	2 (0.1)	2 (0.1)	1 (0.1)
Black,NH	46 (100.0)	0	0	0	0
Hispanic/Latine	69 (100.0)	0	0	0	0
Other	45 (100.0)	0	0	0	0
HD					
White,NH	1184 (80.2)	96 (6.5)	99 (6.7)	81 (5.5)	17 (1.2)
Black,NH	25 (59.5)	11 (26.2)	3 (7.1)	3 (7.1)	0
Hispanic/Latine	45 (67.2)	4 (6.0)	7 (10.4)	9 (13.4)	2 (3.0)
Other	27 (75.0)	3 (8.3)	4 (11.1)	2 (5.6)	0
NHL					
White,NH	359 (47.6)	88 (11.7)	99 (13.1)	116 (15.4)	92 (12.2)
Black,NH	10 (32.3)	3 (9.7)	8 (25.8)	7 (22.6)	3 (9.7)
Hispanic/Latine	16 (40.0)	2 (5.0)	4 (10.0)	9 (22.5)	9 (22.5)
Other	15 (44.1)	2 (5.9)	3 (8.8)	9 (26.5)	5 (14.7)
Kidney (Wilms)					
White,NH	557 (61.6)	69 (7.6)	158 (17.5)	102 (11.3)	18 (2.0)
Black,NH	39 (50.0)	4 (5.1)	22 (28.2)	12 (15.4)	1 (1.3)
Hispanic/Latine	28 (62.2)	3 (6.7)	4 (8.9)	9 (20.0)	1 (2.2)
Other	14 (60.9)	1 (4.3)	3 (13.0)	5 (21.7)	0
Neuroblastoma					
White,NH	549 (75.6)	67 (9.2)	56 (7.7)	31 (4.3)	23 (3.2)
Black,NH	17 (54.8)	6 (19.4)	6 (19.4)	0	2 (6.5)
Hispanic/Latine	20 (66.7)	7 (23.3)	1 (3.3)	0	2 (6.7)
Other	18 (62.1)	4 (13.8)	3 (10.3)	1 (3.4)	3 (10.3)
Soft tissue sarcoma					
White,NH	548 (59.6)	37 (4.0)	95 (10.3)	95 (10.3)	144 (15.7)
Black,NH	30 (55.6)	2 (3.7)	3 (5.6)	6 (11.1)	13 (24.1)
Hispanic/Latine	26 (63.4)	3 (7.3)	3 (7.3)	5 (12.2)	4 (9.8)
Other	20 (51.3)	3 (7.7)	3 (7.7)	6 (15.4)	7 (17.9)
Bone cancer					
White,NH	179 (21.3)	40 (4.8)	92 (11.0)	205 (24.4)	324 (38.6)
Black,NH	4 (10.8)	2 (5.4)	5 (13.5)	14 (37.8)	12 (32.4)
Hispanic/Latine	6 (15.8)	4 (10.5)	7 (18.4)	10 (26.3)	11 (28.9)
Other	1 (3.7)	1 (3.7)	10 (37.0)	9 (33.3)	6 (22.2)

Table 1 Supplement C: dose (mg/m²) of Alkylating agent by race/ethnicity stratified by diagnose

Race	No	Quartile 1	Quartile 2	Quartile 3	Quartile 4
Leukemia					
White,NH	1786 (52.5)	656 (19.3)	360 (10.6)	385 (11.3)	213 (6.3)
Black,NH	42 (35.9)	28 (23.9)	16 (13.7)	27 (23.1)	4 (3.4)
Hispanic/Latine	86 (39.1)	67 (30.5)	17 (7.7)	27 (12.3)	23 (10.5)
Other	77 (44.8)	50 (29.1)	24 (14.0)	14 (8.1)	7 (4.1)
CNS					
White,NH	1164 (82.4)	153 (10.8)	41 (2.9)	34 (2.4)	20 (1.4)
Black,NH	36 (78.3)	6 (13.0)	3 (6.5)	1 (2.2)	0
Hispanic/Latine	49 (74.2)	9 (13.6)	5 (7.6)	3 (4.5)	0
Other	35 (81.4)	5 (11.6)	0	1 (2.3)	2 (4.7)
HD					
White,NH	585 (46.7)	76 (6.1)	217 (17.3)	254 (20.3)	120 (9.6)
Black,NH	15 (39.5)	5 (13.2)	7 (18.4)	7 (18.4)	4 (10.5)
Hispanic/Latine	19 (33.3)	2 (3.5)	11 (19.3)	19 (33.3)	6 (10.5)
Other	12 (38.7)	2 (6.5)	5 (16.1)	8 (25.8)	4 (12.9)
NHL					
White,NH	101 (14.0)	97 (13.5)	209 (29.0)	163 (22.6)	150 (20.8)
Black,NH	3 (9.7)	10 (32.3)	6 (19.4)	8 (25.8)	4 (12.9)
Hispanic/Latine	4 (10.8)	1 (2.7)	8 (21.6)	10 (27.0)	14 (37.8)
Other	5 (16.1)	2 (6.5)	8 (25.8)	5 (16.1)	11 (35.5)
Kidney (Wilms)					
White,NH	844 (91.9)	14 (1.5)	23 (2.5)	14 (1.5)	23 (2.5)
Black,NH	72 (91.1)	1 (1.3)	2 (2.5)	2 (2.5)	2 (2.5)
Hispanic/Latine	47 (95.9)	2 (4.1)	0	0	0
Other	21 (91.3)	0	1 (4.3)	0	1 (4.3)
Neuroblastoma					
White,NH	311 (46.3)	50 (7.4)	79 (11.8)	105 (15.6)	127 (18.9)
Black,NH	10 (33.3)	4 (13.3)	8 (26.7)	3 (10.0)	5 (16.7)
Hispanic/Latine	10 (37.0)	1 (3.7)	7 (25.9)	5 (18.5)	4 (14.8)
Other	14 (48.3)	2 (6.9)	3 (10.3)	6 (20.7)	4 (13.8)
Soft tissue sarcoma					
White,NH	316 (36.9)	42 (4.9)	59 (6.9)	123 (14.4)	316 (36.9)
Black,NH	13 (25.5)	4 (7.8)	0	11 (21.6)	23 (45.1)
Hispanic/Latine	13 (34.2)	0	1 (2.6)	8 (21.1)	16 (42.1)
Other	13 (35.1)	2 (5.4)	2 (5.4)	6 (16.2)	14 (37.8)
Bone cancer					
White,NH	287 (34.5)	52 (6.2)	189 (22.7)	93 (11.2)	212 (25.5)
Black,NH	13 (34.2)	3 (7.9)	15 (39.5)	4 (10.5)	3 (7.9)
Hispanic/Latine	12 (30.8)	1 (2.6)	12 (30.8)	4 (10.3)	10 (25.6)
Other	4 (14.3)	4 (14.3)	12 (42.9)	1 (3.6)	7 (25.0)

Table 1 Supplement D: dose (mg/m²) of Epipodophyllotoxin by race/ethnicity stratified by diagnose

Race	No	Quartile 1	Quartile 2	Quartile 3	Quartile 4
Leukemia					
White,NH	3188 (87.8)	106 (2.9)	89 (2.5)	93 (2.6)	153 (4.2)
Black,NH	94 (74.6)	2 (1.6)	5 (4.0)	7 (5.6)	18 (14.3)
Hispanic/Latine	222 (91.7)	3 (1.2)	3 (1.2)	7 (2.9)	7 (2.9)
Other	163 (88.6)	3 (1.6)	8 (4.3)	7 (3.8)	3 (1.6)
CNS					
White,NH	1453 (98.2)	7 (0.5)	10 (0.7)	7 (0.5)	3 (0.2)
Black,NH	45 (100.0)	0	0	0	0
Hispanic/Latine	66 (95.7)	0	2 (2.9)	1 (1.4)	0
Other	44 (100.0)	0	0	0	0
HD					
White,NH	1495 (99.1)	3 (0.2)	8 (0.5)	1 (0.1)	2 (0.1)
Black,NH	39 (92.9)	2 (4.8)	0	0	1 (2.4)
Hispanic/Latine	68 (98.6)	1 (1.4)	0	0	0
Other	36 (100.0)	0	0	0	0
NHL					
White,NH	747 (93.6)	17 (2.1)	16 (2.0)	17 (2.1)	1 (0.1)
Black,NH	29 (90.6)	0	0	2 (6.3)	1 (3.1)
Hispanic/Latine	41 (97.6)	0	0	1 (2.4)	0
Other	30 (88.2)	3 (8.8)	1 (2.9)	0	0
Kidney (Wilms)					
White,NH	906 (97.9)	4 (0.4)	2 (0.2)	9 (1.0)	4 (0.4)
Black,NH	78 (97.5)	0	1 (1.3)	1 (1.3)	0
Hispanic/Latine	50 (100.0)	0	0	0	0
Other	23 (95.8)	0	1 (4.2)	0	0
Neuroblastoma					
White,NH	662 (91.1)	25 (3.4)	19 (2.6)	19 (2.6)	2 (0.3)
Black,NH	27 (84.4)	2 (6.3)	2 (6.3)	1 (3.1)	0
Hispanic/Latine	29 (90.6)	2 (6.3)	1 (3.1)	0	0
Other	23 (76.7)	3 (10.0)	3 (10.0)	1 (3.3)	0
Soft tissue sarcoma					
White,NH	892 (94.2)	16 (1.7)	20 (2.1)	14 (1.5)	5 (0.5)
Black,NH	55 (98.2)	0	1 (1.8)	0	0
Hispanic/Latine	42 (100.0)	0	0	0	0
Other	38 (95.0)	0	1 (2.5)	1 (2.5)	0
Bone cancer					
White,NH	892 (97.2)	4 (0.4)	7 (0.8)	13 (1.4)	2 (0.2)
Black,NH	39 (97.5)	0	0	1 (2.5)	0
Hispanic/Latine	42 (100.0)	0	0	0	0
Other	30 (93.8)	0	2 (6.3)	0	0

Tables for Mortality analyses

Table 2: SMR (95% CI) by Race/ethnicity

Race	N (%)			SMR					
	Overall	Alive	Dead	All-cause	SN	Cardiac	Pulmonary	External	Other
White, NH	12397 (86.3)	10640 (86.4)	1757 (86.1)	6.0 (5.8 - 6.3)	11.4 (10.3 - 12.7)	5.0 (4.1 - 6.0)	7.4 (5.5 - 9.7)	0.8 (0.7 - 1.0)	4.6 (4.1 - 5.1)
Black, NH	694 (4.8)	582 (4.7)	112 (5.5)	8.0 (6.6 - 9.7)	16.8 (10.6 - 25.2)	13.4 (7.1 - 23.0)	15.6 (5.0 - 36.4)	0.9 (0.3 - 1.8)	5.7 (3.4 - 9.0)
Hispanic	750 (5.2)	645 (5.2)	105 (5.1)	6.8 (5.6 - 8.3)	10.9 (6.3 - 17.4)	12.8 (7.0 - 21.5)	5.6 (0.6 - 20.1)	0.9 (0.4 - 1.8)	4.9 (2.8 - 7.8)
Other	517 (3.6)	451 (3.7)	66 (3.2)	6.4 (4.9 - 8.1)	10.8 (5.2 - 19.9)	2.9 (0.3 - 10.6)	4.4 (0.1 - 24.6)	0.8 (0.3 - 1.8)	5.8 (3.1 - 9.9)

Table 3: Relative rate of mortality due to subsequent malignancy, cardiac disease, pulmonary disease, and other causes excluding recurrence and external causes*

	All cause		Subsequent neoplasm		Cardiac cause		Pulmonary cause		Other cause	
Race/ethnicity	RR	P-value	RR	P-value	RR	P-value	RR	P-value	RR	P-value
1. Basic model*										
White,NH	Ref		Ref		Ref		Ref		Ref	
Black,NH	1.3 (1.1 - 1.6)	0.008	1.3 (0.9 - 2.0)	0.18	2.6 (1.5 - 4.7)	0.001	2.2 (0.9 - 5.6)	0.09	1.1 (0.7 - 1.8)	0.64
Hispanic	1.1 (0.9 - 1.3)	0.33	0.9 (0.5 - 1.5)	0.64	2.5 (1.5 - 4.4)	0.001	0.8 (0.2 - 3.2)	0.71	0.9 (0.6 - 1.5)	0.81
Other	1.0 (0.8 - 1.3)	0.72	0.8 (0.4 - 1.5)	0.55	0.6 (0.1 - 2.4)	0.46	0.7 (0.1 - 4.8)	0.68	1.1 (0.6 - 1.9)	0.76
2. Adjusted for diagnosis										
White,NH	Ref		Ref		Ref		Ref		Ref	
Black,NH	1.4 (1.1 - 1.7)	0.001	1.4 (0.9 - 2.2)	0.11	2.8 (1.6 - 5.0)	<.001	2.4 (1.0 - 6.1)	0.06	1.2 (0.7 - 1.9)	0.52
Hispanic	1.1 (0.9 - 1.4)	0.27	0.9 (0.6 - 1.5)	0.75	2.6 (1.5 - 4.5)	<.001	0.8 (0.2 - 3.3)	0.77	1.0 (0.6 - 1.6)	0.94
Other	1.1 (0.8 - 1.4)	0.64	0.9 (0.5 - 1.6)	0.63	0.6 (0.2 - 2.5)	0.51	0.7 (0.1 - 5.0)	0.71	1.1 (0.6 - 2.0)	0.67
3. Adjusted for treatment [1], subset of sample with MRAF [2]										
White,NH	Ref		Ref		Ref		Ref		Ref	
Black,NH	1.6 (1.2 - 2.1)	<.001	1.8 (1.1 - 3.0)	0.017	1.5 (0.5 - 4.1)	0.44	2.6 (0.8 - 8.5)	0.12	1.7 (1.0 - 3.0)	0.06
Hispanic	1.2 (0.9 - 1.6)	0.18	1.1 (0.6 - 2.0)	0.67	1.8 (0.8 - 4.1)	0.18	0.0	>.99	1.1 (0.6 - 2.0)	0.88
Other	1.3 (1.0 - 1.8)	0.07	0.9 (0.4 - 1.9)	0.76	0.9 (0.2 - 3.9)	0.94	1.1 (0.1 - 7.9)	0.94	1.3 (0.7 - 2.6)	0.41
4. Adjusted for TX & DX, subset of sample with MRAF [2]										
White,NH	Ref		Ref		Ref		Ref		Ref	
Black,NH	1.7 (1.3 - 2.2)	<.001	1.9 (1.2 - 3.1)	0.012	1.6 (0.6 - 4.3)	0.38	2.8 (0.8 - 9.3)	0.10	1.7 (1.0 - 3.0)	0.06
Hispanic	1.2 (0.9 - 1.6)	0.17	1.1 (0.6 - 2.0)	0.69	1.8 (0.8 - 4.1)	0.19	0.0	>.99	1.1 (0.6 - 2.0)	0.84
Other	1.4 (1.0 - 1.9)	0.047	0.9 (0.4 - 2.0)	0.84	1.0 (0.3 - 4.3)	0.95	1.1 (0.1 - 7.9)	0.95	1.4 (0.7 - 2.7)	0.34

5. Basic model, subset of sample with MRAF [2]										
White,NH	Ref		Ref		Ref		Ref		Ref	
Black,NH	1.6 (1.3 - 2.1)	<.001	1.8 (1.1 - 3.0)	0.016	1.5 (0.5 - 4.1)	0.45	1.8 (1.1 - 3.0)	0.016	1.7 (1.0 - 3.0)	0.06
Hispanic	1.2 (0.9 - 1.6)	0.12	1.2 (0.7 - 2.1)	0.56	2.0 (0.9 - 4.6)	0.10	1.2 (0.7 - 2.1)	0.56	1.0 (0.6 - 2.0)	0.88
Other	1.4 (1.0 - 1.9)	0.046	0.9 (0.4 - 1.9)	0.80	1.0 (0.2 - 4.0)	0.98	0.9 (0.4 - 1.9)	0.80	1.4 (0.7 - 2.6)	0.38
6. Adjusted for diagnosis, subset of sample with MRAF [2]										
White,NH	Ref		Ref		Ref		Ref		Ref	
Black,NH	1.7 (1.3 - 2.3)	<.001	2.0 (1.2 - 3.3)	0.006	1.7 (0.6 - 4.7)	0.31	2.9 (0.9 - 9.6)	0.08	1.8 (1.0 - 3.2)	0.037
Hispanic	1.3 (1.0 - 1.7)	0.08	1.2 (0.7 - 2.1)	0.55	2.0 (0.9 - 4.6)	0.10	0.0 (0.0 - .)	1.00	1.1 (0.6 - 2.1)	0.73
Other	1.4 (1.0 - 1.9)	0.030	0.9 (0.4 - 2.0)	0.86	1.1 (0.3 - 4.4)	0.92	1.1 (0.2 - 8.3)	0.91	1.4 (0.7 - 2.8)	0.30

MRAF: medical records abstraction form.

*All models adjusted for sex, age at diagnosis, treatment era, and attained age as cubic splines.

[1] Treatment includes radiation therapy, alkylating agent score, anthracycline exposure, epipodophyllotoxin exposure, Bleomycin exposure.

[2] The regression used only the survivors who signed medical records abstraction form and had treatment information available.

Note: Regression models will be repeated with the additional adjustment of socioeconomic variables including SES.

Tables for SN/SMN analysis

Race	N (%)		
	Overall cohort (n=14358)	SN (n=1685)	SMN (n=830)
White, NH	12397 (86.3)	1555 (92.3)	749 (90.2)
Black, NH	694 (4.8)	36 (2.1)	29 (3.5)
Hispanic	750 (5.2)	57 (3.4)	35 (4.2)
Other	517 (3.6)	37 (2.2)	17 (2.0)

Table 4: Multivariable analysis of overall SNs and SMNs*

Race	Unadjusted for treatment				Unadjusted for treatment, Survivors' subset with MRAF^				Adjusted for treatment			
	SN*		SMN*		SN*		SMN*		SN†		SMN†	
	RR (95% CI)	P	RR (95% CI)	P	RR (95% CI)	P	RR (95% CI)	P	RR (95% CI)	P	RR (95% CI)	P
White, NH	Ref		Ref						Ref		Ref	
Black, NH	0.6 (0.4 - 0.8)	0.002	0.9 (0.6 - 1.3)	0.62	0.8 (0.5 - 1.1)	0.16	1.2 (0.8 - 1.8)	0.47	0.7 (0.5 - 1.1)	0.10	1.1 (0.7 - 1.7)	0.67
Hispanic	0.8 (0.6 - 1.0)	0.046	1.0 (0.7 - 1.4)	0.85	0.9 (0.6 - 1.2)	0.30	1.2 (0.8 - 1.7)	0.41	0.9 (0.6 - 1.2)	0.39	1.2 (0.8 - 1.7)	0.46
Other	0.8 (0.6 - 1.1)	0.14	0.7 (0.4 - 1.2)	0.20	0.8 (0.5 - 1.1)	0.20	0.7 (0.4 - 1.2)	0.21	0.8 (0.5 - 1.1)	0.14	0.7 (0.4 - 1.2)	0.19

* Adjusted for sex, age at diagnosis, treatment era, primary cancer diagnosis, radiation therapy, splenectomy, alkylating agent score, anthracycline exposure, epipodophyllotoxin exposure, platinum exposure, and age as cubic splines.

^ The regression used only the survivors who signed medical records abstraction form and had treatment information available.

† Adjusted for sex, age at diagnosis, treatment era, primary cancer diagnosis, and age as cubic splines.

Note: Regression models will be repeated with the additional adjustment of socioeconomic variables including SES.

Tables for Chronic conditions analyses

Table 5. Hazard ratios comparing minority/ethnic groups to White, Non-Hispanic for grade 3-5 chronic conditions in CCSS survivors, overall and by organ system

Reference Gp: White, NH		Adjusted for sex and age at dx		Adjusted for sex, age at dx, & diagnosis[1]		Adjusted for sex, age at dx, & treatment[2]		Adjusted for sex, age at dx, subset w/MRAF[3]	
Organ system	**Ethnicity**	**HR (95% CI)**	**p-value**	**HR (95% CI)**	**p-value**	**HR (95% CI)**	**p-value**	**HR (95% CI)**	**p-value**
All conditions	Black, NH	1.0 (0.9-1.2)	0.70	1.1 (0.9-1.3)	0.42	1.0 (0.8-1.3)	0.92	1.0 (0.8-1.2)	0.99
	Hispanic	1.2 (1.0-1.3)	0.0695	1.2 (1.0-1.4)	0.0278	1.2 (1.0-1.4)	0.0218	1.2 (1.0-1.4)	0.0190
	Other	1.1 (0.9-1.3)	0.42	1.1 (0.9-1.3)	0.27	1.1 (0.9-1.3)	0.41	1.1 (0.9-1.3)	0.43
Neoplasms	Black, NH	0.9 (0.7-1.3)	0.62	1.0 (0.7-1.4)	0.87	1.1 (0.7-1.5)	0.75	1.0 (0.7-1.5)	0.81
	Hispanic	1.0 (0.8-1.4)	0.89	1.0 (0.8-1.4)	0.86	1.2 (0.9-1.6)	0.25	1.2 (0.9-1.6)	0.28
	Other	0.8 (0.5-1.2)	0.27	0.8 (0.5-1.2)	0.30	0.9 (0.6-1.4)	0.55	0.9 (0.6-1.3)	0.53
Hearing	Black, NH	1.0 (0.6-1.6)	0.92	1.1 (0.7-1.7)	0.81	1.0 (0.5-1.8)	0.95	1.0 (0.5-1.7)	0.89
	Hispanic	0.9 (0.6-1.5)	0.69	1.0 (0.6-1.7)	0.85	1.2 (0.7-1.9)	0.57	1.0 (0.6-1.7)	0.98
	Other	1.3 (0.8-2.1)	0.35	1.4 (0.9-2.2)	0.18	1.3 (0.8-2.1)	0.37	1.3 (0.7-2.1)	0.40
Vision	Black, NH	0.6 (0.3-1.1)	0.10	0.6 (0.3-1.2)	0.14	0.6 (0.3-1.4)	0.24	0.6 (0.3-1.4)	0.22
	Hispanic	1.2 (0.7-1.9)	0.56	1.2 (0.7-1.9)	0.54	1.2 (0.7-2.1)	0.43	1.2 (0.7-2.0)	0.53
	Other	1.3 (0.7-2.3)	0.39	1.3 (0.7-2.2)	0.42	1.4 (0.8-2.6)	0.25	1.4 (0.8-2.5)	0.27
Endocrine	Black, NH	0.9 (0.6-1.2)	0.44	0.9 (0.7-1.3)	0.60	0.8 (0.5-1.2)	0.33	0.8 (0.5-1.2)	0.22
	Hispanic	1.3 (1.0-1.7)	0.0742	1.3 (1.0-1.7)	0.0690	1.5 (1.1-2.0)	0.0077	1.5 (1.1-1.9)	0.0118
	Other	0.9 (0.6-1.3)	0.67	0.9 (0.6-1.4)	0.69	0.9 (0.6-1.3)	0.50	0.9 (0.6-1.3)	0.53
Respiratory	Black, NH	1.2 (0.6-2.3)	0.63	1.3 (0.7-2.5)	0.47	1.1 (0.5-2.6)	0.77	1.1 (0.5-2.6)	0.74
	Hispanic	1.1 (0.6-2.1)	0.73	1.1 (0.6-2.2)	0.68	0.6 (0.2-1.6)	0.28	0.5 (0.2-1.5)	0.23
	Other	1.1 (0.5-2.4)	0.90	1.1 (0.5-2.4)	0.87	1.0 (0.4-2.4)	0.98	1.0 (0.4-2.5)	0.94
Cardiac	Black, NH	1.8 (1.3-2.4)	0.0004	1.9 (1.4-2.5)	<.0001	1.5 (1.0-2.2)	0.0556	1.5 (1.0-2.2)	0.0495
	Hispanic	1.3 (0.9-1.7)	0.17	1.3 (0.9-1.8)	0.14	1.2 (0.8-1.7)	0.36	1.2 (0.8-1.7)	0.30
	Other	1.3 (0.9-1.9)	0.19	1.3 (0.9-2.0)	0.13	1.2 (0.8-1.8)	0.44	1.2 (0.8-1.8)	0.45
GI	Black, NH	0.9 (0.5-1.7)	0.69	0.8 (0.4-1.4)	0.41	1.0 (0.5-2.0)	>0.99	1.0 (0.5-2.0)	>0.99
	Hispanic	1.1 (0.7-2.0)	0.66	1.2 (0.7-2.0)	0.60	1.0 (0.5-2.0)	0.89	1.0 (0.5-1.9)	0.96
	Other	1.0 (0.5-2.0)	0.92	1.1 (0.6-2.1)	0.80	0.9 (0.4-2.0)	0.87	0.9 (0.4-1.9)	0.82
Renal	Black, NH	0.8 (0.3-2.2)	0.71	0.7 (0.3-2.0)	0.53	0.9 (0.3-2.9)	0.89	0.9 (0.3-3.0)	0.91
	Hispanic	0.9 (0.3-2.7)	0.89	1.0 (0.3-2.8)	0.95	1.0 (0.3-3.4)	0.99	0.9 (0.3-3.2)	0.91

	Other	0.8 (0.3-2.6)	0.74	0.9 (0.3-2.8)	0.82	0.7 (0.2-2.7)	0.57	0.7 (0.2-2.7)	0.56
Musculoskeletal	Black, NH	0.8 (0.4-1.6)	0.50	0.7 (0.3-1.5)	0.32	0.8 (0.3-1.9)	0.59	0.8 (0.3-2.1)	0.72
	Hispanic	0.9 (0.5-1.8)	0.81	0.9 (0.5-1.7)	0.75	0.9 (0.4-2.0)	0.85	1.1 (0.5-2.2)	0.85
	Other	0.5 (0.1-1.4)	0.17	0.4 (0.1-1.3)	0.15	0.5 (0.2-1.7)	0.28	0.6 (0.2-1.7)	0.31
Neurological	Black, NH	1.0 (0.6-1.7)	0.96	1.1 (0.7-1.9)	0.70	1.2 (0.6-2.2)	0.66	1.1 (0.6-2.1)	0.74
	Hispanic	1.3 (0.9-1.9)	0.21	1.4 (0.9-2.1)	0.10	1.4 (0.9-2.2)	0.09	1.5 (1.0-2.3)	0.05
	Other	1.2 (0.7-2.0)	0.52	1.3 (0.8-2.2)	0.37	1.3 (0.8-2.3)	0.30	1.3 (0.8-2.3)	0.34
Other Hematologic	Black, NH	0.7 (0.4-1.3)	0.23	0.7 (0.4-1.3)	0.30	0.6 (0.3-1.4)	0.23	0.6 (0.3-1.3)	0.22
	Hispanic	1.2 (0.8-2.0)	0.36	1.3 (0.8-2.0)	0.30	1.1 (0.7-1.9)	0.63	1.3 (0.8-2.1)	0.31
	Other	1.6 (1.0-2.5)	0.0694	1.6 (1.0-2.6)	0.0590	1.6 (1.0-2.7)	0.0649	1.6 (1.0-2.7)	0.0629

[1]Model adjusted for diagnosis used 8 diagnosis groups

[2]Model adjusted for treatment used any radiation, surgery, platinum drug, epipodophyllotoxins, anthracycline and alkylating agent

[3]Model not adjusted for diagnosis or treatment, but uses only those survivors with MRAF information.

Note: Regression models will be repeated with the additional adjustment of socioeconomic variables including SES. For overall outcome and certain more prevalent organ systems, regression model will also be carried out with an interaction term between race/ethnicity and survivor/sibling status.

Tables for health status

Table 6. Relative risk of moderate to extreme health status outcomes by race/ethnicity in CCSS survivors

Variables	General Health PR (95% CI)	Mental Health PR (95% CI)	Functional Health PR (95% CI)	Activity Limitation PR (95% CI)	Pain PR (95% CI)	Anxiety PR (95% CI)	Any Domain PR (95% CI)
Race/ethnicity*							
White, NH	Ref	Ref	Ref	Ref	Ref	Ref	Ref
Black, NH							
Hispanic							
Race/ethnicity^	Ref	Ref	Ref	Ref	Ref	Ref	Ref
White, NH							
Black, NH							
Hispanic							

*Models adjusted for age as cubic splines and sex.

^Similar models additionally adjusted for treatment-related factors

Note: Regression models will be repeated with the additional adjustment of socioeconomic variables including SES.

Table 7. Relative risk of moderate to extreme health status outcomes by race/ethnicity in CCSS survivors and siblings*

Variables	General Health PR (95% CI)	Mental Health PR (95% CI)	Functional Health PR (95% CI)	Activity Limitation PR (95% CI)	Any Domain PR (95% CI)
Survivors					
White, NH	Ref	Ref	Ref	Ref	Ref
Black, NH					
Hispanic					
Siblings					
White, NH	Ref	Ref	Ref	Ref	Ref
Black, NH					
Hispanic					

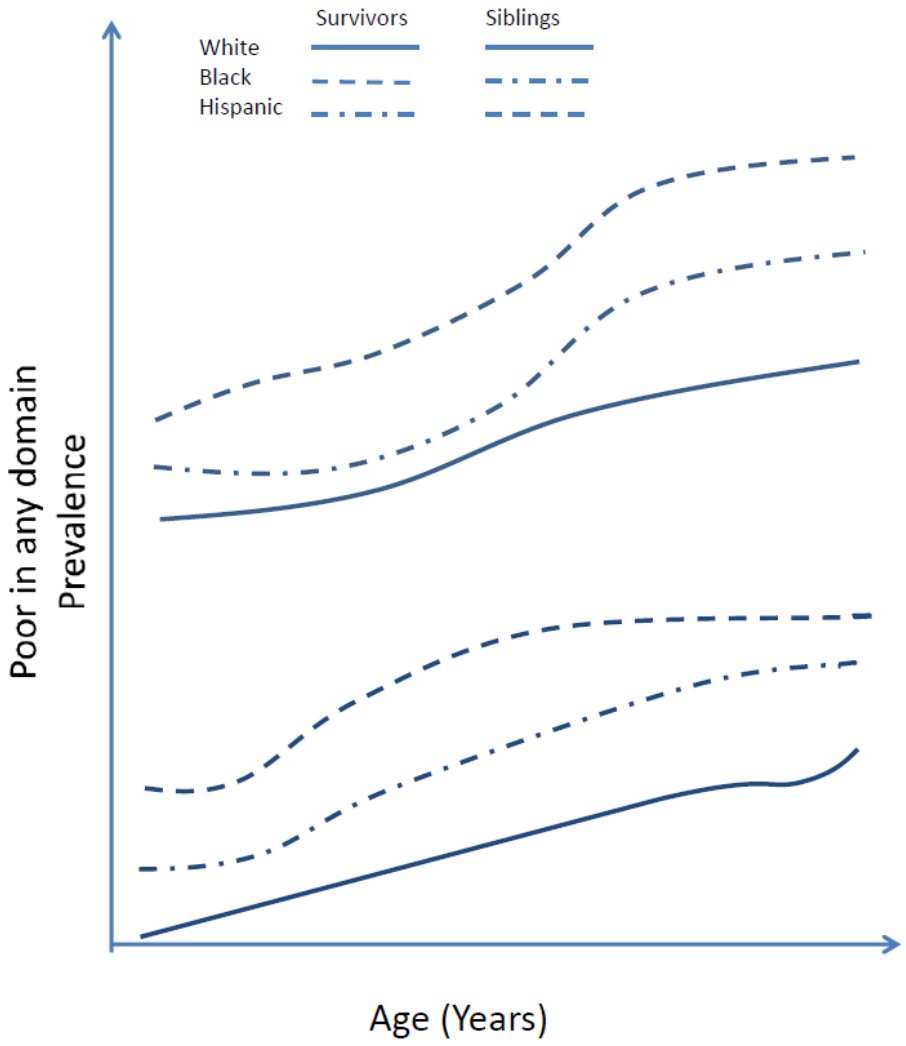
*Models adjusted for age as cubic splines and sex, and included interaction terms XXX (depending on the final model)

Note: Regression models will be repeated with the additional adjustment of socioeconomic variables including SES.

FIGURES:

Survival curves and cumulative incidence curves will use years from the cohort entry (5 years from the initial cancer diagnosis) as the x-axis scale.

Fig 1A: Kaplan-Meier curves of survival probability by race/ethnicity stratified by sex.
Fig 1B: Cumulative incidences of specific cause of death for each race/ethnicity group.
Fig 2A: Cumulative incidences of any SN and any SMN with breakdown by race/ethnicity.
Fig 2B: Cumulative incidence of SN outcomes (SMN, NMSc, and meningioma)
Fig 2C: Total Cumulative incidences of any SN and any SMN with breakdown by race/ethnicity.
Fig 3: Cumulative incidences of any grade 3-5 overall condition, and for some specific chronic conditions which were identified from the model that have different hazard ratio across race/ethnicity groups.
Fig 4: Prevalence of survivors and siblings with adverse health status outcomes by race/ethnicity over age (the figure below is made just as an example).



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