

CHILDHOOD CANCER SURVIVOR STUDY- Analysis Concept Proposal

1. TITLE: Psychological Distress, Health-Related Quality of Life, Social Attainment, and Chronic Health Conditions of Bereaved Siblings from the CCSS

2. WORKING GROUP INVESTIGATORS: This proposed study will be within the Psychology Working Group (with Chronic Disease as a secondary Working Group).

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3. BACKGROUND AND RATIONALE:

Although the majority of childhood cancer patients will be cured of their cancer, deaths childhood cancer is the second leading cause of death among children in the US.[1] This fact, coupled with the statistic of the average size of families in the US includes two children,[2] has resulted in a large and increasing population of bereaved siblings following a diagnosis of childhood cancer. Death may occur in association with the underlying diagnosis and treatment or after a period of survivorship in association with late mortality due to subsequent malignancy as well as treatment-related toxicities. [3]

Not surprisingly, despite resiliency and reassuring psychosocial health overall, siblings who have lost a brother or sister to childhood cancer demonstrate increased risk for impaired psychosocial health. [4-5] Among 174 siblings who lost a brother or sister to cancer 2 to 9 years earlier, low levels of self-esteem, disordered sleep, and low levels of maturity were reported, and over 50% had not fully grieved the loss of their brother or sister with cancer.[6-7] In another study, 58 siblings an average of 12 years post-bereavement reported that the loss of their sibling with cancer still impacted their current education and career goals. [8] Although some siblings who have lost a brother or sister to childhood cancer may report negative memories and experiences, others demonstrate an ability to revisit these experiences in a positive manner through various means. [9-11] Chronic stress (in general) has also been associated with adverse health outcomes (e.g., cardiovascular disease and events) and may be potentially modifiable. [12-13] The impact of bereavement on chronic health conditions has not been explored among siblings of patients diagnosed with childhood cancer.

Previous studies focusing on siblings who have lost a brother a sister to childhood cancer have largely employed small samples of bereaved siblings with limited domain-specific measures limiting the ability to understand the impact of bereavement on siblings. Moreover, few studies have characterized psychosocial outcomes and physical health among bereaved siblings when they reach adulthood having experienced the death of a brother or sister from childhood cancer. Further information, drawn from large, diagnostically diverse samples of adult siblings that are

bereaved, using non-bereaved siblings impacted by childhood cancer as a comparison group is needed to better characterize the psychosocial burden and physical health burden of bereavement on this population. Moreover, identification of risk factors as well as protective factors for sibling psychosocial health and physical health in adulthood are needed to help inform the development of state-of-the science interventions tailored to the unique needs of this population. [14-16] The aim of this study is to use the CCSS data [17-18] to fill these gaps in our existing knowledge.

4. SPECIFIC AIMS:

Aim 1: We will compare the psychological distress (using BSI-18 data), health-related quality of life (using SF-36 data) of bereaved siblings to non-bereaved siblings from the CCSS adjusted for sociodemographic (age, gender, race/ethnicity, income) and cancer-related factors (time since diagnosis, diagnosis). We will compare the social attainment (using educational attainment, employment status, and marital status data) and chronic health conditions of bereaved siblings to non-bereaved siblings from the CCSS adjusted for sociodemographic (age, gender, race/ethnicity, income) and cancer-related factors (time since diagnosis, diagnosis).

***Hypothesis:** We hypothesize that bereaved siblings will have greater psychological distress, adverse health-related quality of life, compared to non-bereaved siblings from the CCSS adjusted for sociodemographic and cancer-related factors. We hypothesize that bereaved sibling will have diminished social attainment and a greater burden of chronic health conditions compared to non-bereaved siblings from the CCSS adjusted for sociodemographic and cancer-related factors.*

Aim 2: We will evaluate potential sociodemographic and cancer-related factors associated with psychological distress (using BSI-18 data), adverse health-related quality of life (using SF-36 data), diminished social attainment (using educational attainment, employment status, and marital status data), and chronic health conditions among bereaved siblings from the CCSS.

***Hypothesis:** We hypothesize that sociodemographic factors (younger age, birth order - younger sibling/older deceased , female gender, male sibling/female survivor, Black/Asian/Latino race/ethnicity, low household income), sibling health-related factors (presence of chronic health conditions) and cancer-related factors (younger sibling age at diagnosis, shorter time since diagnosis, younger sibling age at bereavement, shorter time since bereavement, diagnosis of brain tumor, bone tumor, or sarcoma, and greater treatment intensity) will be associated with greater psychological distress, adverse health-related quality of life, diminished social attainment, and greater burden of chronic health conditions among bereaved siblings from the CCSS.*

5. ANALYSIS FRAMEWORK:

5.1 Sample:

The proposed analyses will utilize data collected at baseline (from between 1994 and 1998 for survivors diagnosed between 1970 and 1986 (cohort 1) and between 2007 and 2012 for survivors diagnosed between 1987 and 1999 (cohort 2). Data will be drawn from baseline survey data as well as the follow-up 2 (FU2), follow-up 4 (FU4), follow-up 5 (FU5) and follow-up 7 (FU7) surveys. Health-related quality of life data will be drawn only from FU2 and FU5. A total of 913 bereaved siblings (823 cohort 1, 90 cohort 2) have completed baseline questionnaire with a

survivor sibling with a known date of death and will be selected for these analyses. Bereaved siblings must have completed the outcomes of interest after the death of the brother or sister with cancer. We will not exclude siblings who experience bereavement after completion of baseline survey data submission.

5.2 Outcomes of Interest and Predictor Variables:

Outcomes of interest (all Aims)

- A. Sibling psychological distress (BSI-18) defined using continuous t-scores for each subscale and dichotomizing at ≥ 63 .
 - a. Depression
 - b. Anxiety
 - c. Somatization
- B. Sibling health-related quality of life (SF-36) as continuous t-scores for each subscale and dichotomized at < 40 .
 - a. Physical function
 - b. Role physical
 - c. Bodily pain
 - d. General health
 - e. Vitality
 - f. Role emotional
 - g. Social function
 - h. Mental health
- C. Social attainment (Educational attainment, employment status, marital status)
 - a. Educational attainment at last survey (Less than high school or high school graduate vs. some college)
 - b. Employment defined as of last survey (Working full-time or part-time vs. not seeking paid work or unemployed and looking for work or unable to work or retired or student or other)
 - c. Relationship/marital status at last survey (Married or living as married, Divorced or separated or Never married)
- D. Sibling chronic health conditions occurring after bereavement
 - a. At least one severe or life-threatening chronic health condition (Grade 3-4)
 - b. Multiple Grade 2-4 chronic health conditions (≥ 2)
 - c. Specific chronic health conditions (cardiovascular – heart attack, hypertension, stroke) Grade 2- 4

Aim 1: We will compare the psychological distress (using BSI-18 data), and health-related quality of life (using SF-36 data) of bereaved siblings to non-bereaved siblings from the CCSS adjusted for current age and gender. We will compare the social attainment (using educational attainment, employment status, and marital status data with selected analyses restricted to those responses given at age ≥ 25) and burden of chronic health conditions of bereaved siblings to non-bereaved siblings from the CCSS adjusted for current age and gender.

Descriptive and statistical comparisons of bereaved siblings versus non-bereaved siblings overall and within sibling sociodemographic, and cancer-related stratum

- A. Sibling Sociodemographic Factors
 - a. Age at baseline
 - b. Gender
 - c. Race/ethnicity
 - d. Household income
- B. Cancer-Related Factors
 - a. Diagnosis
 - b. Time since diagnosis

Aim 2: We will evaluate potential sociodemographic, and cancer-related factors associated with psychological distress (using BSI-18 data), adverse health-related quality of life (using SF-36 data), diminished social attainment (using educational attainment, employment status, and marital status data with selected analyses restricted to those responses given at age ≥ 25), and burden of chronic health conditions among bereaved siblings from the CCSS.

Multivariable logistic regression will be used to construct multivariable models to assess the associations between sociodemographic and cancer-related factors with outcomes of bereaved sibling psychological distress, health-related quality of life, social attainment, and burden of chronic health conditions

- A. Sibling Sociodemographic Factors
 - a. Age at baseline
 - b. Older/younger than patient
 - c. Gender
 - d. Sibling/survivor gender
 - e. Race/ethnicity
 - f. Household income
- B. Cancer-Related Factors
 - a. Diagnosis
 - b. Treatment
 - c. Age at diagnosis
 - d. Time since diagnosis
 - e. Age at bereavement
 - f. Time since bereavement

5.3 Statistical analysis plan:

Table 1 will provide descriptive statistics of the bereaved and non-bereaved sibling populations, including demographic characteristics, such as, age of the sample, sex, and race/ethnicity. Selected characteristics of the siblings' brothers or sisters will also be provided such as diagnosis, treatment, and time since diagnosis. Data will be reported and comparisons will be made in this table by bereaved and non-bereaved sibling status.

For all Aims, responses to the questions regarding psychological distress (BSI-18), health related quality of life (SF-36), social attainment, chronic health conditions will be used to define outcomes as described above under 5.2.

Aim 1: (Tables 2-7)

All outcomes will be summarized for bereaved and non-bereaved siblings, overall and by demographic characteristics. For BSI-18 subscales (Depression, Anxiety, Somatization) and Health-related quality of life (SF-36 subscales), mean t-scores and associated standard error measurements will be reported. For dichotomized versions of these scores, the frequency and percent of siblings meeting the cutoff for poorer outcome will be reported. Similarly frequencies and percents will be reported for social attainment outcomes (employment, educational attainment and marital status) and burden of chronic health conditions will be reported.

Formal statistical comparisons of these outcomes between bereaved and non-bereaved siblings will be assessed. Continuous outcomes (t-scores for BSI, SF-36 subscales) will be compared using t-tests and linear regression models adjusted for age and gender. For all dichotomized outcomes, modified Poisson models will be used to evaluate prevalence ratios (PRs) and 95% confidence intervals, also adjusted for age and gender. Additional factors can be examined in the context of these models to assess whether there are factors that affect bereaved siblings' outcomes more than their non-bereaved counterparts. Initial stratified summaries will be generated and those factors identified as potentially important will be examined in the context of the multivariable model with an interaction term between the factor and bereaved vs non-bereaved sibling.

Aim 2: (Tables 8-19)

Responses to the questions regarding psychological distress using the BSI-18 including subscale scores (Depression, Anxiety, Somatization) will be analyzed utilizing the outcome dichotomized as: psychological distress ($T > 63$) vs. no psychological distress ($T < 63$). Responses to the questions regarding health-related quality of life using the SF-36 including the subscale scores (Physical Function, Role Physical, Bodily Pain, General Health, Vitality, Role Emotional Social Function, Mental Health) will be analyzed utilizing the outcome dichotomized as: adverse health-related quality of life ($T < 1$ standard deviation below mean) vs. good health-related quality of life ($T > 1$ standard deviation below mean). Responses to the questions regarding social attainment assessment will be analyzed utilizing the outcomes dichotomized as: education level (less than high school vs. high school graduate and/or some college), employed (never employed vs. employed in past and/or employed in past 12 months), and married (married or living as married vs. divorced or separated and/or never married).

Responses to the questions regarding chronic health conditions assessment will be analyzed utilizing the outcomes dichotomized as: severe or life threatening (Grade 3-4, yes versus no), greater number of grade 2-4 chronic health conditions (≥ 2 , yes versus no), and whether they had a grade 2-4 cardiovascular chronic health condition (yes versus no). For each dichotomous outcome all candidate factors summarized above including sibling sociodemographic, and cancer-related factors will be analyzed in modified Poisson univariable models to evaluate prevalence ratios (PRs) (Tables 8-13). Those factors with a p-value of < 0.10 will be considered for risk factors in a full multivariable regression models, with adjustment a priori for age and gender. We will construct multivariable models as depicted in (Table 14-19). Starting with a full model, variables will be eliminated based on model fit (AIC criteria) and eliminating those with at the $p > 0.10$ level until all variables remaining in the model are statistically significant or necessary to include as an adjustment factor. Adjusted prevalence ratios with 95% confidence intervals will be reported. Analyses will be carried out using the SAS statistical software (SAS Institute, Cary, NC).

APPENDIX A

TABLE 1: Characteristics of the Bereaved Sibling Population and Non-Bereaved Sibling Comparison Population

Variable	Bereaved Siblings N = (%)	Non-Bereaved Siblings N = (%)	P-value
Age at Baseline 18-20 20-29 30-39 40+			
Birth Order Sibling Older Sibling Younger			
Gender Male Female			
Sibling / Survivor Gender Sibling M / Survivor M Sibling F / Survivor F Sibling M / Survivor F Sibling F / Survivor M			
Race/ethnicity White Non-white			
Household Income <\$40,000 \$40,000-59,999 Over \$60,000			
Age at Diagnosis Not born yet 0-9 years 10-19 years ≥20 years			
Time Since Diagnosis 5-10 years 10-15 years 15-20 years 20+			
Diagnosis Brain tumor Leukemia Hodgkin Lymphoma Non-Hodgkin Lymphoma Kidney tumor Bone tumor Sarcoma Neuroblastoma			
Treatment Chemotherapy Yes No Radiation Yes No Surgery Yes No			
Age at Bereavement Not born yet 0-9 years 10-19 years ≥20 years			

Time Since Bereavement		
5-10 years		
10-15 years		
15-20 years		
20+		

TABLE 2: Means and SEs on BSI-18 Scores of Bereaved Siblings and Non-Bereaved Siblings from the CCSS

Variable	Bereaved Siblings			Non-Bereaved Siblings		
	Somatization	Depression	Anxiety	Somatization	Depression	Anxiety
	Mean (95%CI)	Mean (95%CI)	Mean (95%CI)	Mean (95%CI)	Mean (95%CI)	Mean (95%CI)
U.S. Population						
All Siblings						
Age at Baseline						
18-20						
20-29						
30-39						
40+						
Gender						
Male						
Female						
Race/Ethnicity						
White						
Non-White						
Household Income						
<\$40,000						
\$40,000-59,999						
Over \$60,000						
Time Since Diagnosis						
5-10 years						
10-15 years						
15-20 years						
20+						
Diagnosis						
Brain tumor						
Leukemia						
Hodgkin Lymphoma						
Non-Hodgkin Lymphoma						
Kidney tumor						
Bone tumor						
Sarcoma						
Neuroblastoma						

TABLE 3A: Means and SEs on SF-36 Scores of Bereaved Siblings and Non-Bereaved Siblings from the CCSS

Variable	Bereaved Siblings				Non-Bereaved Siblings			
	Physical Function	Role Physical	Bodily pain	General Health	Physical Function	Role Physical	Bodily Pain	General Health
	Mean 95% CI	Mean 95% CI	Mean 95% CI	Mean 95% CI	Mean 95% CI	Mean 95% CI	Mean 95% CI	Mean 95% CI
U.S. Population								
Overall								
Age at Baseline								
18-20								
20-29								
30-39								
40+								
Gender								
Male								
Female								
Race/Ethnicity								
White								
Non-White								
Household Income								
<\$40,000								
\$40,000-59,999								
Over \$60,000								
Time Since Diagnosis								
5-10 years								
10-15 years								
15-20 years								
20+								
Diagnosis								
Brain tumor								
Leukemia								
Hodgkin Lymphoma								
Non-Hodgkin Lymphoma								
Kidney tumor								
Bone tumor								
Sarcoma								
Neuroblastoma								

TABLE 3B: Means and SEs on SF-36 Scores of Bereaved Siblings and Non-Bereaved Siblings from the CCSS

Variable	Bereaved Siblings			Non-Bereaved Siblings		
	Role Emotional	Social Function	Mental Health	Role Emotional	Social Function	Mental Health
	Mean 95%CI	Mean 95%CI	Mean 95%CI	Mean 95%CI	Mean 95%CI	Mean 95%CI
U.S. Population						
Overall						
Age						
18-20						
20-29						
30-39						
40+						
Gender						
Male						
Female						
Race/Ethnicity						
White						
Non-White						
Household Income						
<\$40,000						
\$40,000-59,999						
Over \$60,000						
Time Since Diagnosis						
5-10 years						
10-15 years						
15-20 years						
20+						
Diagnosis						
Brain tumor						
Leukemia						
Hodgkin Lymphoma						
Non-Hodgkin Lymphoma						
Kidney tumor						
Bone tumor						
Sarcoma						
Neuroblastoma						

TABLE 4: Frequencies and Proportions of Educational Attainment of Bereaved Siblings and Non-Bereaved Siblings from the CCSS

Variable	Bereaved Siblings		Non-Bereaved Siblings	
	Less than High School / High School Graduate	Some College	Less than High School / High School Graduate	Some College
	N %	N %	N %	N %
Overall				
Age				
18-20				
20-29				
30-39				
40+				
Gender				
Male				
Female				
Race/Ethnicity				
White				
Non-White				
Household Income				
<\$40,000				
\$40,000-59,999				
Over \$60,000				
Time Since Diagnosis				
5-10 years				
10-15 years				
15-20 years				
20+				
Diagnosis				
Brain tumor				
Leukemia				
Hodgkin Lymphoma				
Non-Hodgkin Lymphoma				
Kidney tumor				
Bone tumor				
Sarcoma				
Neuroblastoma				

TABLE 5: Frequencies and Proportions of Employment of Bereaved Siblings and Non-Bereaved Siblings from the CCSS

Variable	Bereaved Siblings		Non-Bereaved Siblings	
	Employed (Full or Part)	Not Employed (Not seeking, Unemployed, Unable, Retired, Student, Other)	Employed (Full or Part)	Not Employed (Not seeking, Unemployed, Unable, Retired, Student, Other)
	N %	N %	N %	N %
Overall				
Age				
25-29				
30-39				
40+				
Gender				
Male				
Female				
Race/Ethnicity				
White				
Non-White				
Household Income				
<\$40,000				
\$40,000-59,999				
Over \$60,000				
Time Since Diagnosis				
5-10 years				
10-15 years				
15-20 years				
20+				
Diagnosis				
Brain tumor				
Leukemia				
Hodgkin Lymphoma				
Non-Hodgkin Lymphoma				
Kidney tumor				
Bone tumor				
Sarcoma				
Neuroblastoma				

TABLE 6: Frequencies and Proportions of Marital Status of Bereaved Siblings and Non-Bereaved Siblings from the CCSS

Variable	Bereaved Siblings		Non-Bereaved Siblings	
	Married or Living as Married	Divorced or Separated or Never Married	Married or Living as Married	Divorced or Separated or Never Married
	N %	N %	N %	N %
Overall				
Age				
25-29				
30-39				
40+				
Gender				
Male				
Female				
Race/Ethnicity				
White				
Non-White				
Household Income				
<\$40,000				
\$40,000-59,999				
Over \$60,000				
Time Since Diagnosis				
5-10 years				
10-15 years				
15-20 years				
20+				
Diagnosis				
Brain tumor				
Leukemia				
Hodgkin Lymphoma				
Non-Hodgkin Lymphoma				
Kidney tumor				
Bone tumor				
Sarcoma				
Neuroblastoma				

TABLE 7: Frequencies and Proportions of Chronic Health Conditions of Bereaved Siblings and Non-Bereaved Siblings from the CCSS

Variable	Bereaved Siblings			Non-Bereaved Siblings		
	Grade 3-4 Chronic Health Condition	> or = 2 Chronic Health Conditions	Cardiovascular Chronic Health Condition	Grade 3-4 Chronic Health Condition	> or = 2 Chronic Health Conditions	Cardiovascular Chronic Health Condition
	N %	N %	N %	N %	N %	N %
Overall						
Age						
18-20						
20-29						
30-39						
40+						
Sibling Gender						
Male						
Female						
Race/Ethnicity						
White						
Non-White						
Household Income						
<\$40,000						
\$40,000-59,999						
Over \$60,000						
Time Since Diagnosis						
5-10 years						
10-15 years						
15-20 years						
20+						
Diagnosis						
Brain tumor						
Leukemia						
Hodgkin Lymphoma						
Non-Hodgkin Lymphoma						
Kidney tumor						
Bone tumor						
Sarcoma						
Neuroblastoma						

TABLE 8: Univariable Models: Predictors of Elevated* BSI-18 Scores among Bereaved Siblings from the CCSS

Variable	Somatization PR (95% CI)	Depression PR (95% CI)	Anxiety PR(95% CI)
Age 18-20 20-29 30-39 40+			
Birth Order Sibling Older Sibling Younger			
Gender Male Female			
Sibling / Survivor Gender Sibling M / Survivor M Sibling F / Survivor F Sibling M / Survivor F Sibling F / Survivor M			
Race/Ethnicity White Non-White			
Household Income <\$40,000 \$40,000-59,999 Over \$60,000			
Age at Diagnosis Not born yet 0-9 years 10-19 years ≥20 years			
Time Since Diagnosis 5-10 years 10-15 years 15-20 years 20+			
Diagnosis Brain tumor Leukemia Hodgkin Lymphoma Non-Hodgkin Lymphoma Kidney tumor Bone tumor Sarcoma Neuroblastoma			
Treatment Chemotherapy Yes No Radiation Yes No Surgery Yes No			
Age at Bereavement Not born yet 0-9 years 10-19 years ≥20 years			
Time Since Bereavement 5-10 years 10-15 years			

15-20 years 20+			
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*Elevated T-score > 63

TABLE 9A: Univariable Models: Predictors of Diminished* SF-36 Scores among Bereaved Siblings from the CCSS

Variable	Physical Function PR (95% CI)	Role Physical PR (95% CI)	Bodily Pain PR(95% CI)	General Health PR (95% CI)	Vitality PR(95% CI)
Age 18-20 20-29 30-39 40+					
Birth Order Sibling Older Sibling Younger					
Gender Male Female					
Sibling / Survivor Gender Sibling M / Survivor M Sibling F / Survivor F Sibling M / Survivor F Sibling F / Survivor M					
Race/Ethnicity White Non-White					
Household Income <\$40,000 \$40,000-59,999 Over \$60,000					
Age at Diagnosis Not born yet 0-9 years 10-19 years >20 years					
Time Since Diagnosis 5-10 years 10-15 years 15-20 years 20+					
Diagnosis Brain tumor Leukemia Hodgkin Lymphoma Non-Hodgkin Lymphoma Kidney tumor Bone tumor Sarcoma Neuroblastoma					
Treatment Chemotherapy Yes No Radiation Yes No Surgery Yes No					
Age at Bereavement Not born yet 0-9 years 10-19 years ≥20 years					
Time Since Bereavement 5-10 years 10-15 years					

15-20 years 20+					
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*Diminished T-score < 1 SD below mean (< 40)

TABLE 9B: Univariable Models: Predictors of Diminished* SF-36 Scores among Bereaved Siblings from the CCSS

Variable	Role Emotional	Social Function	Mental Health
	PR (95% CI)	PR (95% CI)	PR(95% CI)
Age 18-20 20-29 30-39 40+			
Birth Order Sibling Older Sibling Younger			
Gender Male Female			
Sibling / Survivor Gender Sibling M / Survivor M Sibling F / Survivor F Sibling M / Survivor F Sibling F / Survivor M			
Race/Ethnicity White Non-White			
Household Income <\$40,000 \$40,000-59,999 Over \$60,000			
Age at Diagnosis Not born yet 0-9 years 10-19 years >20 years			
Time Since Diagnosis 5-10 years 10-15 years 15-20 years 20+			
Diagnosis Brain tumor Leukemia Hodgkin Lymphoma Non-Hodgkin Lymphoma Kidney tumor Bone tumor Sarcoma Neuroblastoma			
Treatment Chemotherapy Yes No Radiation Yes No Surgery Yes No			
Age at Bereavement Not born yet 0-9 years 10-19 years ≥20 years			
Time Since Bereavement 5-10 years 10-15 years			

15-20 years			
20+			

*Diminished T-score < 1 SD below mean (<40)

TABLE 10: Univariable Models: Predictors of Educational Attainment among Bereaved Siblings from the CCSS

Variable	Some College vs. Less than High School Graduate PR (95% CI)	High School Graduate vs. Less than High School Graduate PR (95% CI)
Age 18-20 20-29 30-39 40+		
Birth Order Sibling Older Sibling Younger		
Gender Male Female		
Sibling / Survivor Gender Sibling M / Survivor M Sibling F / Survivor F Sibling M / Survivor F Sibling F / Survivor M		
Race/Ethnicity White Non-White		
Household Income <\$40,000 \$40,000-59,999 Over \$60,000		
Age at Diagnosis Not born yet 0-9 years 10-19 years ≥20 years		
Time Since Diagnosis 5-10 years 10-15 years 15-20 years 20+		
Diagnosis Brain tumor Leukemia Hodgkin Lymphoma Non-Hodgkin Lymphoma Kidney tumor Bone tumor Sarcoma Neuroblastoma		
Treatment Intense Chemotherapy Yes No Radiation Yes No Surgery Yes No		
Age at Bereavement Not born yet 0-9 years 10-19 years ≥20 years		
Time Since Bereavement 5-10 years 10-15 years 15-20 years		

20+		
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TABLE 11: Univariable Models: Predictors of Employment Status among Bereaved Siblings from the CCSS

Variable	Employed vs. Not Employed PR (95% CI)	Employed vs. Not Employed PR (95% CI)
Age 25-29 30-39 40+		
Birth Order Sibling Older Sibling Younger		
Gender Male Female		
Sibling / Survivor Gender Sibling M / Survivor M Sibling F / Survivor F Sibling M / Survivor F Sibling F / Survivor M		
Race/Ethnicity White Non-White		
Household Income <\$40,000 \$40,000-59,999 Over \$60,000		
Age at Diagnosis Not born yet 0-9 years 10-19 years ≥20 years		
Time Since Diagnosis 5-10 years 10-15 years 15-20 years 20+		
Diagnosis Brain tumor Leukemia Hodgkin Lymphoma Non-Hodgkin Lymphoma Kidney tumor Bone tumor Sarcoma Neuroblastoma		
Treatment Chemotherapy Yes No Radiation Yes No Surgery Yes No		
Age at Bereavement Not born yet 0-9 years 10-19 years ≥20 years		
Time Since Bereavement 5-10 years 10-15 years 15-20 years 20+ years		

TABLE 12: Univariable Models: Predictors of Marital Status among Bereaved Siblings from the CCSS

Variable	Married or Living as Married vs. Not Married PR (95% CI)	Divorced or Separated vs. Not Married PR (95% CI)
Age 25-29 30-39 40+		
Birth Order Sibling Older Sibling Younger		
Gender Male Female		
Sibling / Survivor Gender Sibling M / Survivor M Sibling F / Survivor F Sibling M / Survivor F Sibling F / Survivor M		
Race/Ethnicity White Non-White		
Household Income <\$40,000 \$40,000-59,999 Over \$60,000		
Age at Diagnosis Not born yet 0-9 years 10-19 years >20 years		
Time Since Diagnosis 5-10 years 10-15 years 15-20 years 20+ years		
Diagnosis Brain tumor Leukemia Hodgkin Lymphoma Non-Hodgkin Lymphoma Kidney tumor Bone tumor Sarcoma Neuroblastoma		
Treatment Intense Chemotherapy Yes No Radiation Yes No Surgery Yes No		
Age at Bereavement Not born yet 0-9 years 10-19 years ≥20 years		
Time Since Bereavement 5-10 years		

10-15 years 15-20 years 20+ years		
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TABLE 13: Univariable Models: Predictors of Chronic Health Conditions among Bereaved Siblings from the CCSS

Variable	Any Grade 3-4 Chronic Health Condition PR (95% CI)	> or = 2 Grade 2-4 Chronic Health Conditions PR (95% CI)	Cardiovascular Chronic Health Condition PR (95% CI)
Age 18-20 20-29 30-39 40+			
Birth Order Sibling Older Sibling Younger			
Gender Male Female			
Sibling / Survivor Gender Sibling M / Survivor M Sibling F / Survivor F Sibling M / Survivor F Sibling F / Survivor M			
Race/Ethnicity White Non-White			
Household Income <\$40,000 \$40,000-59,999 Over \$60,000			
Age at Diagnosis Not born yet 0-9 years 10-19 years ≥20 years			
Time Since Diagnosis 5-10 years 10-15 years 15-20 years 20+ years			
Diagnosis Brain tumor Leukemia Hodgkin Lymphoma Non-Hodgkin Lymphoma Kidney tumor Bone tumor Sarcoma Neuroblastoma			
Treatment Chemotherapy Yes No Radiation Yes No Surgery Yes No			
Age at Bereavement Not born yet 0-9 years 10-19 years ≥20 years			

Time Since Bereavement 5-10 years 10-15 years 15-20 years 20+ years			
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TABLE 14: Multivariable Models: Predictors of Elevated* BSI-18 Scores among Bereaved Siblings from the CCSS

Variable	Somatization PR (95% CI)	Depression PR (95% CI)	Anxiety PR(95% CI)
Age 18-20 20-29 30-39 40+			
Birth Order Sibling Older Sibling Younger			
Gender Male Female			
Sibling / Survivor Gender Sibling M / Survivor M Sibling F / Survivor F Sibling M / Survivor F Sibling F / Survivor M			
Race/Ethnicity White Non-White			
Household Income <\$40,000 \$40,000-59,999 Over \$60,000			
Age at Diagnosis Not born yet 0-9 years 10-19 years ≥20 years			
Time Since Diagnosis 5-10 years 10-15 years 15-20 years 20+			
Diagnosis Brain tumor Leukemia Hodgkin Lymphoma Non-Hodgkin Lymphoma Kidney tumor Bone tumor Sarcoma Neuroblastoma			
Treatment Chemotherapy Yes No Radiation Yes No Surgery Yes No			
Age at Bereavement Not born yet 0-9 years 10-19 years ≥20 years			
Time Since Bereavement 5-10 years 10-15 years			

15-20 years			
20+ years			

*Elevated T-score > 63

TABLE 15A: Multivariable Models: Predictors of Diminished* SF-36 Scores of Bereaved Siblings from the CCSS

Variable	Physical Function PR (95% CI)	Role Physical PR (95% CI)	Bodily Pain PR(95% CI)	General Health PR (95% CI)	Vitality PR(95% CI)
Age 18-20 20-29 30-39 40+					
Birth Order Sibling Older Sibling Younger					
Gender Male Female					
Sibling / Survivor Gender Sibling M / Survivor M Sibling F / Survivor F Sibling M / Survivor F Sibling F / Survivor M					
Race/Ethnicity White Non-White					
Household Income <\$40,000 \$40,000-59,999 Over \$60,000					
Age at Diagnosis Not born yet 0-9 years 10-19 years >20 years					
Time Since Diagnosis 5-10 years 10-15 years 15-20 years 20+					
Diagnosis Brain tumor Leukemia Hodgkin Lymphoma Non-Hodgkin Lymphoma Kidney tumor Bone tumor Sarcoma Neuroblastoma					
Treatment Chemotherapy Yes No Radiation Yes No Surgery Yes No					
Age at Bereavement Not born yet 0-9 years 10-19 years ≥20 years					
Time Since Bereavement 5-10 years 10-15 years					

15-20 years					
20+ years					

*Diminished T-score < 1 SD below mean

TABLE 15B: Multivariable Models: Predictors of Diminished* SF-36 Scores of Bereaved Siblings from the CCSS

Variable	Role Emotional	Social Function	Mental Health
	PR (95% CI)	PR (95% CI)	PR(95% CI)
Age 18-20 20-29 30-39 40+			
Birth Order Sibling Older Sibling Younger			
Gender Male Female			
Sibling / Survivor Gender Sibling M / Survivor M Sibling F / Survivor F Sibling M / Survivor F Sibling F / Survivor M			
Race/Ethnicity White Non-White			
Household Income <\$40,000 \$40,000-59,999 Over \$60,000			
Age at Diagnosis Not born yet 0-9 years 10-19 years >20 years			
Time Since Diagnosis 5-10 years 10-15 years 15-20 years 20+			
Diagnosis Brain tumor Leukemia Hodgkin Lymphoma Non-Hodgkin Lymphoma Kidney tumor Bone tumor Sarcoma Neuroblastoma			
Treatment Chemotherapy Yes No Radiation Yes No Surgery Yes No			
Age at Bereavement Not born yet 0-9 years 10-19 years ≥20 years			
Time Since Bereavement 5-10 years 10-15 years			

15-20 years			
20+ years			

*Diminished T-score < 1 SD below mean

TABLE 16: Multivariable Models: Predictors of Educational Attainment of Bereaved Siblings from the CCSS

Variable	Some College vs. High School Graduate / Less than High School Graduate PR (95% CI)	Some College vs. High School Graduate / Less than High School Graduate PR (95% CI)
Age 18-20 20-29 30-39 40+		
Birth Order Sibling Older Sibling Younger		
Gender Male Female		
Sibling / Survivor Gender Sibling M / Survivor M Sibling F / Survivor F Sibling M / Survivor F Sibling F / Survivor M		
Race/Ethnicity White Non-White		
Household Income <\$40,000 \$40,000-59,999 Over \$60,000		
Age at Diagnosis Not born yet 0-9 years 10-19 years >20 years		
Time Since Diagnosis 5-10 years 10-15 years 15-20 years 20+		
Diagnosis Brain tumor Leukemia Hodgkin Lymphoma Non-Hodgkin Lymphoma Kidney tumor Bone tumor Sarcoma Neuroblastoma		
Treatment Chemotherapy Yes No Radiation Yes No Surgery Yes No		
Age at Bereavement Not born yet 0-9 years 10-19 years ≥20 years		
Time Since Bereavement 5-10 years 10-15 years		

15-20 years		
20+ years		

TABLE 17: Multivariable Models: Predictors of Employment Status of Bereaved Siblings from the CCSS

Variable	Employed vs. Not Employed PR (95% CI)	Employed vs. Not Employed PR (95% CI)
Age 25-29 30-39 40+		
Birth Order Sibling Older Sibling Younger		
Gender Male Female		
Sibling / Survivor Gender Sibling M / Survivor M Sibling F / Survivor F Sibling M / Survivor F Sibling F / Survivor M		
Race/Ethnicity White Non-White		
Household Income <\$40,000 \$40,000-59,999 Over \$60,000		
Age at Diagnosis Not born yet 0-9 years 10-19 years ≥20 years		
Time Since Diagnosis 5-10 years 10-15 years 15-20 years 20+		
Diagnosis Brain tumor Leukemia Hodgkin Lymphoma Non-Hodgkin Lymphoma Kidney tumor Bone tumor Sarcoma Neuroblastoma		
Treatment Chemotherapy Yes No Radiation Yes No Surgery Yes No		
Age at Bereavement Not born yet 0-9 years 10-19 years ≥20 years		
Time Since Bereavement 5-10 years 10-15 years 15-20 years 20+ years		

TABLE 18: Multivariable Models: Predictors of Marital Status of Bereaved Siblings from the CCSS

Variable	Married or Living as Married vs. Not Married PR (95% CI)	Divorced or Separated vs. Not Married PR (95% CI)
Age 25-29 30-39 40+		
Birth Order Sibling Older Sibling Younger		
Gender Male Female		
Sibling / Survivor Gender Sibling M / Survivor M Sibling F / Survivor F Sibling M / Survivor F Sibling F / Survivor M		
Race/Ethnicity White Non-White		
Household Income <\$40,000 \$40,000-59,999 Over \$60,000		
Age at Diagnosis Not born yet 0-9 years 10-19 years ≥20 years		
Time Since Diagnosis 5-10 years 10-15 years 15-20 years 20+		
Diagnosis Brain tumor Leukemia Hodgkin Lymphoma Non-Hodgkin Lymphoma Kidney tumor Bone tumor Sarcoma Neuroblastoma		
Treatment Chemotherapy Yes No Radiation Yes No Surgery Yes No		
Age at Bereavement Not born yet 0-9 years 10-19 years ≥20 years		
Time Since Bereavement 5-10 years 10-15 years 15-20 years		

20+ years		
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TABLE 19: Multivariable Models: Predictors of Chronic Health Conditions of Bereaved Siblings from the CCSS

Variable	Grade 3-4 Chronic Health Condition PR (95% CI)	> or = 2 Grade 2-4 Chronic Health Conditions PR (95% CI)	Cardiovascular Grade 2-4 Chronic Health Condition PR (95% CI)
Age 18-20 20-29 30-39 40+			
Birth Order Sibling Older Sibling Younger			
Gender Male Female			
Sibling / Survivor Gender Sibling M / Survivor M Sibling F / Survivor F Sibling M / Survivor F Sibling F / Survivor M			
Race/Ethnicity White Non-White			
Household Income <\$40,000 \$40,000-59,999 Over \$60,000			
Age at Diagnosis Not born yet 0-9 years 10-19 years >20 years			
Time Since Diagnosis 5-10 years 10-15 years 15-20 years 20+			
Diagnosis Brain tumor Leukemia Hodgkin Lymphoma Non-Hodgkin Lymphoma Kidney tumor Bone tumor Sarcoma Neuroblastoma			
Treatment Chemotherapy Yes No Radiation Yes No Surgery Yes No			
Age at Bereavement Not born yet 0-9 years 10-19 years ≥20 years			
Time Since Bereavement			

5-10 years			
10-15 years			
15-20 years			
20+ years			

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