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Psychological Outcomes of Siblings of Cancer Survivors: A Report from the Childhood Cancer Survivor Study

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Abstract

Objective—To identify risk factors for adverse psychological outcomes among adult siblings of long-term survivors of childhood cancer.

Methods—Cross-sectional, self-report data from 3,083 adult siblings (mean age 29 years, range 18-56 years) of 5+ year survivors of childhood cancer were analyzed to assess psychological outcomes as measured by the Brief Symptom Inventory-18 (BSI-18). Sociodemographic and health data, reported by both the siblings and their matched cancer survivors were explored as risk factors for adverse sibling psychological outcomes through multivariable logistic regression.

Results—Self-reported symptoms of psychological distress, as measured by the global severity index of the BSI-18, were reported by 3.8% of the sibling sample. Less than 1.5% of siblings reported elevated scores on two or more of the subscales of the BSI-18. Risk factors for sibling depression included having a survivor brother (OR 2.22, 95% CI 1.42-3.55), and having a survivor with impaired general health (OR 2.15, 95% CI 1.18-3.78). Siblings who were younger than the survivor reported increased global psychological distress (OR 1.81, 95% CI 1.05-3.12), as did siblings of survivors reporting global psychological distress (OR 2.32, 95% CI 1.08-4.59). Siblings of sarcoma survivors reported more somatization than did siblings of leukemia survivors (OR 2.07, 95% CI 1.05-3.98).

Conclusions—These findings suggest that siblings of long-term childhood cancer survivors are psychologically healthy in general. There are, however, small subgroups of siblings at risk for long-term psychological impairment who may benefit from preventive risk-reduction strategies during childhood while their sibling with cancer is undergoing treatment.

Background

Almost 80% of childhood cancer patients will achieve five-year survival with the majority being cured of their disease [1]. As a result, it is estimated that there are over 325,000 survivors of childhood cancer in the United States (US) [2]. In 2010, it was estimated that 1 in 640 individuals in the US between the ages of 20 and 39 was a survivor of childhood cancer [1]. The National Cancer Institute, Office of Cancer Survivorship states that "family members, friends, and caregivers are part of the survivorship experience" [3]. Given the high survival rate for pediatric cancers and the fact that the average US family has two children, [4] there is a large and growing population of siblings impacted by the childhood cancer experience.

Research with siblings of children on active therapy for cancer demonstrates impaired psychosocial health [5-13]. Unfortunately, little is known about these siblings when they reach adulthood and the child with cancer is a long-term survivor [14-16]. Previous literature has reported some siblings of childhood cancer survivors to be at higher risk for depression, post-traumatic stress symptoms, tobacco use, and heavy alcohol use, [17-21] findings that suggest subgroups of siblings with long-term impairment in psychosocial health. Additionally, some siblings report impairment in specific domains of health-related quality of life (HRQOL) despite overall positive HRQOL outcomes when compared to normative data from the US general population [22]. Further information, drawn from large, diagnostically diverse samples, is needed to best identify subgroups of siblings at greatest risk for psychological distress in adulthood.

Younger sibling age at patient diagnosis, shorter time since patient diagnosis, and death of the sibling with cancer (bereavement), as well as sociodemographic factors identified as predictors of distress in the general population (e.g. female sex, lower socioeconomic status) have been suggested as possible risk factors for psychological distress among siblings [9,23-27]. However, few within sibling cohort analyses of psychosocial outcomes have been completed, limiting the identification of at-risk subgroups of siblings [23-25,28].

Other factors that may be associated with sibling psychological distress include survivor physical and psychological health, as well as cancer-related factors (e.g., diagnosis, treatment type or intensity, late adverse chronic health conditions or second cancers). For example, in one study, siblings of survivors with limb disfigurement reported more psychosocial distress compared to siblings of survivors without limb disfigurement [29]. The specific cancer diagnosis and treatment type or intensity may be related to more severe late effects. Furthermore, having a brother or sister who survived cancer and is now experiencing poor health, mentally and/or physically, may put more chronic strain on the family, decrease the amount of support and attention the sibling receives, complicate the survivor-sibling relationships, and serve as a constant reminder of the cancer experience [30-31].

The aim of this study was to use the Childhood Cancer Survivor Study (CCSS) data [32] to identify demographic, health, and cancer-related factors associated with sibling psychological distress. We hypothesized that survivor diagnosis (e.g. bone tumor, sarcoma), treatment type and intensity (e.g. combined chemotherapy, radiation therapy, and surgery), and the presence of survivor late effects (e.g. poor general and psychological health, chronic health conditions, death, second malignant neoplasms) would be associated with increased adverse psychological outcomes among siblings.

Methods

Sample

The National Cancer Institute funded CCSS is a retrospectively ascertained cohort of long-term survivors of childhood cancer diagnosed between January 1, 1970 and December 31, 1986 across 26 collaborating institutions in the US and Canada. A description of the study design, methods, and sample utilized by the CCSS has been published previously [32-33]. Eligibility criteria for the CCSS include: (1) a diagnosis of leukemia, central nervous system malignancy, Hodgkin's lymphoma, non-Hodgkin's lymphoma, kidney tumor, neuroblastoma, bone tumor, or soft tissue sarcoma prior to 21 years of age and, (2) survival to at least 5 years post-diagnosis. A random sample of the 14,363 participating survivors was asked to provide contact information for their nearest aged sibling. Of the 5,791 eligible siblings 4,869 (84.1%) agreed to participate, and 3,899 (80.1% of willing siblings) completed the baseline questionnaire. Details about sibling non-respondents are not available; however, no statistically significant differences were demonstrated between survivor participants and non-participants with respect to sex, type of cancer or treatment, age at diagnosis, and age at the time of completion of a baseline questionnaire [32-33]. Of the participating siblings, this analysis included those who were ≥ 18 years of age at the time of completion of the baseline questionnaire resulting in data from 3,083 siblings.

Data for this study was collected between 1994 and 1998 via a 24-page self-report baseline questionnaire. Completed by both survivors and their siblings, the baseline questionnaire captured demographic information and information on physical and psychological health, and can be viewed at ccss.stjude.org. After survivors' signed a release granting access to their medical records, treatment information was obtained from the survivors' treating institution by trained medical record abstractors using a defined protocol including double abstraction in a sub-sample of medical records across the 26 treatment centers. The protocols and questionnaires utilized by the CCSS underwent approval by the Institutional Review Boards of all collaborating centers.

Outcome Measures

Psychological distress was assessed using the Brief Symptom Inventory 18 (BSI-18) [34]. The BSI-18 is an 18-item standardized self-report inventory that uses a five-point Likert response scale (0 = “not at all”; 4 = “extremely”) exploring the degree to which problems have distressed or bothered the respondent during the last 7 days. The BSI-18 includes a measure of global psychological distress, the global severity index (GSI), a sum across all 18 items with total scores ranging from 0 to 72. It also includes measures of specific domains of psychological distress including subscales for depression, somatization, and anxiety. The three subscales include six-items each with total scores ranging from 0 to 24. The GSI and subscale scores are converted to T-scores using sex-specific community normative data, which have a mean of 50 and standard deviation of 10. Higher T-scores correspond to higher reported psychological distress. Psychometric properties of the BSI-18 have been previously reported for the CCSS sample demonstrating satisfactory reliability and validity [35-36]. Each outcome including the GSI and subscale scores was modeled separately, using dichotomized scoring of sex-specific standardized outcomes, where clinically “elevated” represents T-scores ≥ 63 [34].

Independent Variables

Sociodemographic, health, and cancer-related variables were assessed as potential risk factors for sibling distress. Sibling sociodemographic factors included age at completion of the baseline questionnaire, sex, race/ethnicity, marital status, educational attainment, household income, and employment status. Sibling health-related factors included self-

reported general health using a five-category response scale: poor, fair, good, very good, and excellent. Sibling chronic health conditions were characterized according to the chronic health severity index derived from the NCI Common Terminology Criteria for Adverse Events [37]. Chronic conditions of any grade (0 – 4) were considered as a risk factor. Sibling cancer-related factors included sibling age at diagnosis of the survivor and the presence (or absence) of sibling bereavement for those siblings whose survivor died following study entry.

Survivor factors also included sociodemographic, health, and cancer-related variables. Sociodemographic factors included survivor sex and age at baseline questionnaire completion. The relative ages of the survivor and the sibling age was also considered (i.e. survivor older / sibling older). Survivor health-related factors included self-reported general and psychological health measured as described above for siblings. Survivor cancer-related factors included diagnosis and treatment modality (i.e. chemotherapy, radiation, surgery, or any combination thereof). Late adverse outcomes of cancer and its treatment included chronic health conditions, defined as above for siblings, as well as development of a second cancer and whether the survivor had a limb amputated.

Analysis

Descriptive statistics were generated for sociodemographic, health, and cancer-related variables. The proportion of siblings scoring clinically “elevated” on the GSI (i.e. global psychological distress) and each of the subscales as well as combinations thereof were calculated. Adjusted univariate logistic regression models were used to identify predictors for the GSI and subscales of somatization, depression, and anxiety of the BSI-18. For each outcome, each candidate factor described above was analyzed in a separate model adjusted for: sibling sex (female as reference), sibling age at baseline (0-29 years, 30+ years as reference), and sibling race/ethnicity (white not-Hispanic, other races/ethnicities as reference). Predictor variables significant at $p \leq 0.10$ level were chosen to be included in the multivariable modeling.

Multivariable modeling included the variables as described above. Starting with a full model, variables were eliminated at the $p \geq 0.05$ level until all variables remaining in the model were statistically significant. The adjustment-variables remained in the final multivariable model even if they were not statistically significant. Sibling age was included in the initial modeling as a continuous variable; however, the dichotomized version of this variable did not change coefficients to a significant extent. The variable “survivor older / sibling older” was also evaluated in the modeling as a variable with additional categories (e.g. survivor 10 or more years older, 5-10 years older, etc.); however, small cell counts decreased the power of this analysis so a dichotomized version of this variable was also selected for use. We also tested directly for an interaction between sibling sex and survivor sex as well as for an interaction between sibling sex and sibling age at diagnosis of the survivor. These interactions remained in the model only if they were significant.

Dichotomization of the outcome measure allowed a clinically meaningful interpretation of the findings. Additionally, with such a large sample size there is a danger that very small shifts in a mean will result in statistically significant differences that are not clinically meaningful. Adjusted odds ratios accompanied by 95% confidence intervals were reported for final models. We utilized SAS version 9.2 (Cary, NC) for all analyses.

Results

Provided in Table 1, are the characteristics of the sibling population. The sibling cohort is predominantly White (>90%) and educated (75% with greater than a high school education).

The mean age of siblings at completion of the baseline questionnaire was 29 years (range 18-56 years). Their mean age at the time their sibling was diagnosed with cancer was 10 years (range, -7 to 36 years). The percent of the sibling population reporting elevated scores on the GSI was 3.8%. Elevations on the somatization, depression, and anxiety subscales alone were reported by 2.0 %, 3.3 %, and 1.1 % of the sibling population, respectively. Less than 1.5% of the sibling population reported elevated scores on two or more subscales. Elevated scores on both the depression and anxiety subscales were found in 1.3% of the sibling population; however, elevated scores on both the somatization and anxiety subscales were found in only 0.5%.

Adjusted Analysis of Sociodemographic Factors and Elevated Sibling Distress Scores

Results of adjusted analyses describing sibling sociodemographic factors associated with symptomatic scores on the GSI and individual subscales are provided in Table 2. Lower sibling household income was associated with symptomatic scores on the GSI and each of the subscales. Similar associations between symptomatic scores on the GSI and subscales were found with health impairment and the presence of chronic health conditions. Being an unmarried sibling was associated with increased global psychological distress (OR 2.24, 95% CI 1.45-3.47) and depression (OR 3.70, 95% CI 2.58-5.36). Factors associated with increased somatization included lower (high school or less) sibling education (OR 1.89, 95% CI 1.22-2.86). Sibling employment served as a protective factor for somatization (OR 0.39, 95% CI 0.23-0.68).

Adjusted Analysis of Survivor Factors and Elevated Sibling Distress Scores

Results of adjusted analyses of survivor factors impacting sibling GSI scores and subscales are provided in Table 3. Survivor's global psychological distress was the primary factor associated with sibling global psychological distress (OR 2.16, 95% CI 1.06-4.04). For the subscale of somatization, being a sibling of a survivor of soft tissue sarcoma was associated with greater somatization than being a sibling of a leukemia survivor (OR 2.04, 95% CI 1.10-3.70). Younger sibling age (≤18 years) at the time of survivor's diagnosis of a second malignancy was also a risk factor for sibling somatization (OR 3.37, 95% CI 0.97-8.99). Survivor health impairment (OR 2.18, 95% CI 1.33-3.43) and survivor depression (OR 1.96 (1.14-3.22) were associated with sibling depression. Death of the survivor (OR 1.88, 95% CI 1.19-2.86) and, for bereaved siblings, younger age (≤18 years) at time of the death (OR 2.13, 95% CI 1.11-3.78), were also associated with sibling depression. Survivor's anxiety was associated with sibling anxiety (OR 2.32, 95% CI 1.05-4.57).

Multivariate Analysis of Factors Associated with Elevated Sibling Distress Scores

Multivariable models describing factors associated with elevated sibling scores including the GSI and subscale scores are presented in Table 4. Sibling sociodemographic factors associated with increased risk of global psychological distress include being unmarried (OR 2.23, 95% CI 1.32-3.81), having an income less than $19,999 or a income between $20,000 and $59,000 when compared to a income greater than $60,000 per year lower and middle household incomes (OR 4.33, 95% CI 1.90-10.31 and OR 2.76, 95% CI 1.41-5.93, respectively), and sibling self-reported fair / poor general health(OR 5.35, 95% CI 2.83-9.78). Risk factors for somatization, depression, and anxiety were similar to those for global distress, except that age (being in the younger adult subgroup) at baseline assessment was a risk factor for sibling somatization, the presence of a chronic health condition was a risk factor for sibling somatization and anxiety, and not being married was a risk factor for depression. Being younger than the childhood cancer survivor was associated with increased global psychological distress (OR 1.81, 95% CI 1.05-3.12) and being a sibling of a male survivor was associated with increased depression (OR 2.22, 95% CI 1.42-3.55). Survivor's global psychological distress was a risk factor for sibling global psychological distress (OR

2.32, 95% CI 1.08-4.59), and survivor's self-reported fair/poor general health was a risk factor for sibling depression (OR 2.15, 95% CI 1.18-3.78). Compared to being a sibling of a leukemia survivor, siblings of soft tissue sarcoma survivors were more likely to report greater somatization (OR 2.07, 95% CI 1.05-3.98).

Discussion

This study demonstrates that, as a group, adult siblings of long-term survivors of childhood cancer generally report being psychologically healthy. There are, however, small groups of siblings at risk for psychological distress. Risk factors for sibling psychological distress were found in several survivor variable domains. Psychological distress and adverse self-reported health status among the survivor predicted sibling global distress and depression, respectively, with the former predicting both outcomes and the latter predicting depression. A survivor diagnosis of sarcoma was also associated with a risk for sibling somatization. The relative ages between survivor and sibling were also related to global distress, with elevated risk for siblings younger than the survivor. Survivor male sex was also a risk for sibling depression. Finally, sibling factors that increased risk for psychological distress included sibling age less than 30 years at study entry increasing risk for sibling somatization.

Current psychological distress and self-perceived adverse health status in adult survivors may be salient factors associated with psychological distress in the siblings of these survivors. It is noteworthy that, in addition to the health of the siblings themselves bestowing risk for psychological distress, the current medical and psychological status of their cancer survivor brother or sister may have had salience for adult sibling depression. Given that siblings and their survivors were not assessed simultaneously, and the questionnaires specifically ask about psychological distress over the past 7 days, we cannot be confident that the distress of survivors and siblings co-occurred in time. However, such symptoms in the cancer survivor may lead the sibling to worry about the survivor's well-being and create ongoing sibling psychological distress. It is becoming well known that childhood cancer survivors have elevated rates of early mortality compared to the general population [1-2]. Sibling worry that a brother or sister may die is well documented during cancer treatment and for adolescent siblings of cancer survivors [18]. Long-standing health problems of survivors may continue to fuel such worries and manifest in siblings' distress. For example, Lehna used qualitative methods to record the oral history of a sibling of a long-term survivor [38]. This sibling noted ongoing worries with respect to the growth and fertility of her sibling who had survived cancer over 10 years previously. Additionally, long-standing health concerns among survivors may continue to strain the family [39] which in turn can impact the siblings.

Being a sibling of a sarcoma survivor was a factor associated with siblings' increased somatization when compared to siblings of leukemia survivors. Sarcoma survivors report ongoing long-term psychological distress and pain issues [22,40]. Somatization with multiple pain sites and other symptoms is commonly found in cohorts of chronic pain patients as well as in their family members [41-42]. Coupled with this ongoing pain, treatment of sarcomas often requires intensive chemotherapy, radiation therapy, and surgical therapy, with the latter two imparting risk for untoward effects on the survivor's growing musculoskeletal system. Such visible reminders of the childhood cancer family experience may create risk for somatization in siblings who may then notice and worry about bodily sensations more than otherwise.

Siblings younger than the survivors may have greater risk for psychological distress due to a greater impact of diminished parenting time and attention during the period of their survivor's cancer treatment. Siblings older than the child with cancer may have had greater

opportunity to find other support systems (e.g. peers, teachers). Additionally, older siblings may be more able to derive some benefit from being a sibling of a child with cancer, such as post-traumatic growth [5-8,43-44]. These age differences in responses to the survivorship experience with younger sibling age associated with adverse psychological outcomes also highlight the importance of the developmental context that overshadows the childhood cancer survivorship experiences. For example, diminished parenting time and attention may have a particularly notable impact on the social and emotional development tasks of younger siblings.

Reason for greater depression among siblings of male survivors is unknowable in this cross-sectional study. It could be that females with cancer might provide more support to their siblings than do male survivors, or that male children / adolescents with cancer might be less open and expressive about their feelings during and after treatment that might serve to undermine the survivor-sibling relationship over time. Furthermore, male siblings were less likely to report somatization, a finding that suggests that male siblings may be less focused on bodily symptoms over time and have relative resistance to develop physical manifestations of psychological distress [45], at least compared to female siblings. There was no significant interactive effect between sibling sex and survivor sex; however, indicating that the impact of sibling gender was independent of their survivor's gender. These age- and gender-specific roles in the long-term survivor-sibling relationship warrant further exploration.

Younger sibling age at baseline assessment was a risk for sibling somatization although the reason for this is not readily apparent in our data. In general, research demonstrates that somatic complaints tend to increase with age. The reason for our finding of increased somatization in younger siblings is interesting. It may be that siblings of cancer survivors may be more focused on physical symptoms as a result of the childhood cancer experience which may result in somatic distress at a younger age. Siblings may also experience memories relating to the cancer experience or may also manifest ongoing fears relating to risk of late effects or recurrence which may result in somatic distress at a younger age.

Limitations

This study is a cross-sectional secondary data analysis from a retrospective cohort of siblings ascertained through childhood cancer survivors diagnosed between 1970 and 1986. Thus, the generalizability of the results needs to be carefully considered given the historical nature of the study design and the specific characteristics of the survivor cohort. Since the 1970s and early 1980s, the prognosis for pediatric cancer patients has continued to improve and the intensity of treatments has, to varying degrees, changed [1]. While cancer treatments and healthcare practices have evolved, it is unknown if these changes would influence the degree of impact on siblings. That is, whether the patient is being treated with less intensive therapy or receiving a greater amount of care in the outpatient setting, it is still likely that the parents' attention will be focused on the child with cancer and disruption of the pre-diagnosis family dynamic would still result. The demographic and sociodemographic characteristics of the CCSS cohort also need to be considered. Closely related to sociodemographic factors, siblings and survivors also share a common genetic, family, and cultural background that may contribute to some of the shared variance between siblings and their survivor's psychological health. There may also be biases introduced by the fact that not all of the siblings of the randomly selected survivors participated. Some siblings chose not to participate and in the case of multiple siblings only one sibling was selected. Finally, while care must be taken in interpretation of results when multiple comparisons are made, factors remained significant in our final models even after adjusting for multiple comparisons.

Despite these limitations, this is the largest collection of siblings of long-term survivors of childhood cancer that has ever been analyzed. Sibling studies are typically single institution studies often with well under 100 participants and with limited diagnostic representation. The large cohort in the CCSS with 26 participating institutions throughout North America provides the opportunity to study adults who are long-term survivors of childhood cancer, well-characterized through medical record abstraction by diagnosis and treatment. The CCSS also provides a matched cohort of survivors and nearest age adult siblings so that within family sibling-survivor factors can be analyzed for the impact of this early childhood cancer experience on siblings' current psychological health. Furthermore, survivor risk factors and sibling outcomes are measured with validated instruments.

Conclusion

The main finding from this large case-controlled study of long-term childhood cancer survivors and their siblings is that siblings are a robust and psychologically healthy group of individuals overall. However, there are small subsets of siblings at risk for developing psychological distress and these groups can be predicted from factors such as sibling gender (e.g. female) and current age (e.g. younger), and the sibling/survivor age relationship (e.g. survivor older than sibling). Other identified risk factors include survivor gender (e.g. male), diagnosis (e.g. sarcoma), and current adverse survivor physical and psychological health status. The risk factors that emerged for sibling psychological distress appear to be different than those for survivor psychological distress [46], a difference that indicates that the experiences of siblings during and after the family's cancer treatment may be unique. The findings support the need to examine the effects of childhood cancer on the entire family, especially long-term effects. This should include rich qualitative data in addition to quantitative longitudinal characterization of sibling outcomes over time incorporating the perspectives of multiple family members, family risk factors, and coping styles / developmental stage of siblings and their family members, all of which can impact sibling outcomes. Such an investment will help ensure that optimal family-centered care during childhood cancer treatment can enhance positive outcomes for all, and especially for the small high-risk sibling cohorts identified in this study.

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Table 1

Characteristics of the sibling population (N=3,083)

Characteristic	Frequency*	Percent	Characteristic	Frequency*	Percent
Age at Baseline Questionnaire			Survivor's Age at Diagnosis		
0-29 years	1651	53.6	0-9 years	1644	53.3
≥30 years	1432	46.5	10-19 years	1356	44.0
Age at Survivor Diagnosis			≥ 20 years	83	2.7
Not yet born	123	4.0			
0-9 years	1844	59.8	Survivor's Sex		
10-19 years	884	28.7	Female	1450	47.0
≥ 20 years	232	7.5	Male	1633	53.0
Sex					
Female	1626	52.7	Survivor's Diagnosis		
Male	1457	47.3	Leukemia	980	31.8
Years Since Survivor Diagnosis			Brain Tumor	384	12.5
9-20 years	1940	62.9	Hodgkin Lymphoma	497	16.1
> 20 years	1143	37.1	Non-Hodgkin Lymphoma	261	8.5
Marital Status			Neuroblastoma	232	7.5
Not Married	1331	44.0	Soft tissue sarcoma	149	4.8
Married / Living as Married	1695	56.0	Bone cancer	292	9.5
Employment in Last Year			Kidney	288	9.3
Yes	2813	93.2			
No	206	6.8	Survivor's Treatment#		
Race/Ethnicity			Chemo + RT + Surgery	1323	46.5
Others	239	8.0	Chemo + RT, no Surgery	332	11.7
White	2736	92.0	RT + Surgery, no Chemo	344	12.1
Household Income			Chemo + Surgery, no RT	482	16.9
0-$19,999	357	12.8	Chemo or RT, no Surgery	159	5.6
$20,000-$59,999	1379	49.5	Surgery only	205	7.2
≥ $60,000	1051	37.7			
Education			Survivor's Health		

Characteristic	Frequency*	Percent	Characteristic	Frequency*	Percent
High School or Less	737	25.0	Good/Very good/Excellent	2527	91.3
Greater than High School	2216	75.0	Fair/Poor	241	8.7
Health			Survivor At Least 1 Chronic Health Condition		
Good/Very good/Excellent	2896	94.9	Yes	1924	62.4
Fair/Poor	157	5.1	No	1159	37.6
At Least 1 Chronic Health Condition			Survivor's Global Severity Index Score Elevated		
Yes	1164	37.8	Yes	165	7.4
No	1919	62.2	No	2060	92.6
Sibling's Survivor Deceased			Survivor's Somatization Score Elevated		
Yes	305	9.9	Yes	164	7.4
No	2778	90.1	No	2062	92.6
Sibling's Survivor Second Cancer			Survivor's Depression Score Elevated		
Yes	143	4.6	Yes	216	9.7
No	2940	95.4	No	2011	90.3
			Survivor's Anxiety Score Elevated		
			Yes	134	6.0
			No	2091	94.0

*Frequency counts may not be equal to the total secondary to missing data.

#RT=radiation therapy

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Table 2

Adjusted[*] univariate models - Sociodemographic factors associated with elevated[%] sibling scores (global severity index, somatization, depression, and anxiety)

Sibling Factor	Global Severity Index	Somatization	Depression	Anxiety
	OR (95% CI)	OR (95% CI)	OR (95% CI)	OR (95% CI)
Sibling Age at Survivor Diagnosis				
Not born yet	2.30 (0.65-8.22)	1.12 (0.26-4.26)	1.22 (0.45-3.25)	0.92 (0.24-3.25)
0-9 years	1.30 (0.52-3.64)	1.17 (0.49-3.12)	0.72 (0.36-1.51)	0.69 (0.30-1.75)
10-19 years	0.93 (0.39-2.47)	1.19 (0.53-2.95)	0.76 (0.40-1.52)	0.66 (0.30-1.58
≥20 years (referent)	1.00	1.00	1.00	1.00
Survivor Older/Sibling Older				
Survivor Older	1.24 (0.83-1.84)	1.03 (0.69-1.52)	1.14 (0.83-1.58)	1.08 (0.72-1.63)
Sibling Older (referent)	1.00	1.00	1.00	1.00
Sibling Household Income				
0-$19,999	4.08 (2.20-7.70)**	4.95 (2.73-9.18)**	2.76 (1.66-4.59)**	3.33 (1.80-6.17)**
$20,000-$59,999	2.22 (1.33-3.87)**	2.37 (1.43-4.13)**	1.92 (1.29-2.89)**	1.77 (1.08-3.00)**
≥ $60,000 (referent)	1.00	1.00	1.00	1.00
Sibling Education				
High school or less	1.32 (0.83-2.06)	1.89 (1.22-2.86)**	1.10 (0.75-1.58)	1.45 (0.90-2.27)
Greater than high school (referent)	1.00	1.00	1.00	1.00
Sibling Employment in Last Year				
Yes	0.63 (0.34-1.29)	0.39 (0.23-0.68)**	0.92 (0.52-1.79)	0.72 (0.37-1.56)
No (referent)	1.00	1.00	1.00	1.00
Sibling Marital Status				
Not married	2.24 (1.45-3.47)**	1.12 (0.73-1.69)	3.70 (2.58-5.36)**	1.50 (0.97-2.33)
Married or living as married (referent)	1.00	1.00	1.00	1.00
Sibling Health				
Fair/Poor	7.96 (4.87-12.71)**	9.74 (6.16-15.18)**	5.67 (3.64-8.66)**	4.54 (2.56-7.68)**
Good/Very good/Excellent (referent)	1.00	1.00	1.00	1.00
Sibling At Least 1 Chronic Health Condition				

Sibling Factor	Global Severity Index	Somatization	Depression	Anxiety
	OR (95% CI)	OR (95% CI)	OR (95% CI)	OR (95% CI)
Yes	2.27 (1.53-3.39)**	2.76 (1.87-4.12)**	1.68 (1.22-2.30)**	2.03 (1.36-3.04)**
No (referent)	1.00	1.00	1.00	1.00

** P≤0.05

* Adjusted for sibling sex, sibling age at baseline, and sibling ethnicity.

% Elevated scores correspond to a T score ≥ 63.

Table 3

Adjusted[*] univariate models - Survivor-related factors associated with elevated[%] sibling scores (global severity index, somatization, depression, and anxiety)

Sibling Factor	Global Severity Index	Somatization	Depression	Anxiety
	OR (95% CI)	OR (95% CI)	OR (95% CI)	OR (95% CI)
Survivor Diagnosis				
Bone cancer	1.25 (0.59-2.50)	1.53 (0.75-2.96)	1.22 (0.67-2.11)	1.74 (0.84-3.42)
Brain Tumor	0.96 (0.47-1.84)	0.86 (0.41-1.69)	1.13 (0.67-1.86)	0.94 (0.43-1.90)
Hodgkin Lymphoma	1.16 (0.61-2.14)	1.41 (0.78-2.52)	0.83 (0.48-1.40)	1.49 (0.78-2.78)
Non-Hodgkin Lymphoma	1.31 (0.62-2.57)	1.38 (0.67-2.66)	1.15 (0.62-2.01)	1.72 (0.82-3.39)
Neuroblastoma	1.64 (0.68-3.52)	0.58 (0.14-1.67)	1.40 (0.67-2.69)	1.42 (0.52-3.33)
Kidney	0.64 (0.22-1.53)	0.37 (0.09-1.04)	0.63 (0.27-1.29)	0.92 (0.34-2.11)
Soft tissue sarcoma	1.11 (0.51-2.23)	2.04 (1.10-3.70)**	1.35 (0.77-2.29)	1.32 (0.60-2.71)
Leukemia (referent)	1.00	1.00	1.00	1.00
Survivor Treatment				
Chemo + RT + Surgery	0.65 (0.34-1.34)	0.85 (0.43-1.89)	1.22 (0.65-2.56)	1.03 (0.51-2.38)
Chemo + RT, no Surgery	0.58 (0.24-1.39)	0.87 (0.37-2.16)	0.82 (0.36-1.94)	0.74 (0.29-1.99)
RT + Surgery, no Chemo	0.61 (0.26-1.46)	0.59 (0.23-1.55)	1.18 (0.54-2.69)	0.76 (0.29-2.04)
Chemo + Surgery, no RT	0.58 (0.26-1.32)	0.80 (0.36-1.93)	1.08 (0.52-2.41)	0.71 (0.29-1.83)
Chemo or RT, no Surgery	0.35 (0.08-1.16)	0.29 (0.04-1.15)	1.37 (0.55-3.46)	0.33 (0.05-1.36)
Surgery only (referent)	1.00	1.00	1.00	1.00
Survivor Health				
Fair/Poor	1.42 (0.71-2.61)	1.00 (0.46-1.91)	2.18 (1.33-3.43)**	1.00 (0.44-1.98)
Good/Very good/Excellent (referent)	1.00	1.00	1.00	1.00
Survivor At Least 1 Chronic Health Condition				
Yes	1.03 (0.69-1.55)	1.01 (0.69-1.50)	1.10 (0.80-1.54)	1.24 (0.82-1.91)
No (referent)	1.00	1.00	1.00	1.00
Survivor Psychological Distress[##]				
Yes	2.16 (1.06-4.04)**	0.91 (0.35-1.96)	1.96 (1.14-3.22)**	2.32 (1.05-4.57)**
No (referent)	1.00	1.00	1.00	1.00

Sibling Factor	Global Severity Index	Somatization	Depression	Anxiety
	OR (95% CI)	OR (95% CI)	OR (95% CI)	OR (95% CI)
Sibling's Survivor Second Cancer				
Yes	1.06 (0.37-2.40)	1.86 (0.85-3.60)	0.76 (0.30-1.63)	1.85 (0.81-3.69)
No (referent)	1.00	1.00	1.00	1.00
Sibling Age at Survivor Second Cancer				
0-18 years	0.77 (0.04-3.68)	3.37 (0.97-8.99)**	0.48 (0.03-2.27)	1.75 (0.28-6.00)
19-29 years	0.50 (0.03-2.33)	1.02 (0.17-3.38)	0.60 (0.10-1.96)	1.05 (0.17-3.46)
≥30 years	2.14 (0.50-6.36)	1.76 (0.41-5.20)	1.25 (0.30-3.62)	3.19 (0.91-8.68)**
Survivor Without Second Cancer (referent)	1.00	1.00	1.00	1.00
Sibling's Survivor Deceased				
Yes	1.33 (0.70-2.33)	1.27 (0.68-2.20)	1.88 (1.19-2.86)**	1.27 (0.65-2.26)
No (referent)	1.00	1.00	1.00	1.00
Sibling Age at Survivor Death				
0-18 years	1.91 (0.83-3.83)	1.76 (0.77-3.54)	2.13 (1.11-3.78)**	1.22 (0.42-2.80)
19-29 years	0.48 (0.08-1.57)	0.88 (0.26-2.17)	1.67 (0.80-3.14)	1.01 (0.30-2.51)
≥30 years	1.98 (0.46-5.87)	1.02 (0.16-3.54)	1.74 (0.51-4.53)	2.12 (0.49-6.30)
Survivor Alive (referent)	1.00	1.00	1.00	1.00

** P≤0.05

* Adjusted for sibling-sex, sibling age at baseline, and sibling ethnicity.

% Elevated scores correspond to a T score ≥ 63.

RT=radiation therapy

Psychological Distress= GSI or respective subscale elevation (e.g. for the outcome of sibling depression, survivor psychological distress refers to elevation on the depression subscale).

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Table 4

Multivariate Models For Elevated[%] Sibling Scores (Global Severity Index, Somatization, Depression, Anxiety)

	Global Severity Index	Somatization	Depression	Anxiety
Sibling Factors	**OR (95% CI)**	**OR (95% CI)**	**OR (95% CI)**	**OR (95% CI)**
Sibling Sex				
Male	0.67 (0.39-1.12)	0.58 (0.37-0.90)**	0.98 (0.63-1.51)	1.30 (0.85-1.98)
Female (referent)	1.00	1.00	1.00	1.00
Age at Baseline				
0-29 years	0.74 (0.42-1.28)	1.85 (1.18-2.93)**	0.84 (0.54-1.31)	1.15 (0.75-1.77)
>30 years (referent)	1.00	1.00	1.00	1.00
Race / Ethnicity				
White (non-Hispanic)	2.00 (0.69-8.48)	0.63 (0.33-1.28)	1.27 (0.57-3.41)	0.98 (0.47-2.39)
Other (referent)	1.00	1.00	1.00	1.00
Marital Status				
Not Married	2.23 (1.32-3.81)**	NS	4.26 (2.66-6.96)**	NS
Married (referent)	1.00	Reference	1.00	
Household Income				
0-$19,999	4.33 (1.90-10.31)**	3.95 (2.13-7.47)**	1.93 (0.93-3.98)	2.96 (1.59-5.52)**
$20,000-$59,999	2.76 (1.41-5.93)**	2.06 (1.22-3.63)**	2.10 (1.23-3.74)**	1.65 (1.00-2.82)**
$60,000+ (referent)	1.00	1.00	1.00	1.00
Sibling Health				
Fair / Poor	5.35 (2.83-9.78)**	8.30 (5.01-13.60)**	5.16 (2.87-9.01)**	3.42 (1.86-5.98)**
Good/Very good/Excellent (referent)	1.00	1.00	1.00	1.00
Chronic Health Conditions				
Yes	NS	2.31 (1.51-3.57)**	NS	1.90 (1.24-2.93)**
No (referent)		1.00		1.00
Diagnosis				
Brain tumor	NS	0.80 (0.35-1.68)	NS	NS
Hodgkin lymphoma	NS	1.70 (0.91-3.15)	NS	NS

	Global Severity Index	Somatization	Depression	Anxiety
Sibling Factors	**OR (95% CI)**	**OR (95% CI)**	**OR (95% CI)**	**OR (95% CI)**
Non-Hodgkin lymphoma	NS	1.02 (0.46-2.13)	NS	NS
Kidney tumor	NS	0.34 (0.08-1.03)	NS	NS
Neuroblastoma	NS	0.44 (0.10-1.38)	NS	NS
Soft tissue sarcoma	NS	2.07 (1.05-3.98)**	NS	NS
Bone tumor	NS	1.62 (0.76-3.30)	NS	NS
Leukemia (referent)		1.00		
Survivor Psychological Distress#				
Yes	2.32 (1.08-4.59)**	NS	1.86 (1.00-3.30)**	NS
No (referent)	1.00		1.00	
Survivor Health				
Fair / Poor	NS	NS	2.15 (1.18-3.78)**	NS
Good/Very good/Excellent (referent)			1.00	
Survivor Sex				
Male	NS	NS	2.22 (1.42-3.55)**	NS
Female (referent)			1.00	
Survivor Older	1.81 (1.05-3.12)**	NS	NS	NS
Sibling Older (referent)	1.00			

** P≤0.05

% Elevated scores correspond to a T score > 63.

NS= not significant; therefore, not included in final model aside from age, race/ethnicity, sibling gender.

Psychological Distress= GSI for the outcome of psychological distress, somatization for the outcome of somatization, depression for the outcome of depression, and anxiety for the outcome of anxiety.