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Prevalence and Predictors of Posttraumatic Stress Disorder in Adult Survivors of Childhood Cancer

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Prevalence and Predictors of Posttraumatic Stress Disorder in Adult Survivors of Childhood Cancer

WHAT'S KNOWN ON THIS SUBJECT: Small studies of young adult survivors of childhood cancer found increased prevalence of self-reported symptoms of posttraumatic stress, compared with population normative levels.

WHAT THIS STUDY ADDS: This study used a large cohort of childhood cancer survivors and their healthy siblings from across the United States and Canada to examine the prevalence of self-reported PTSD symptoms associated with evidence of impaired function or clinical distress.

abstract

OBJECTIVE: This study compared the prevalence of symptoms of posttraumatic stress disorder (PTSD), with functional impairment and/or clinical distress, among very long-term survivors of childhood cancer and a group of healthy siblings.

METHODS: A total of 6542 childhood cancer survivors >18 years of age who received diagnoses between 1970 and 1986 and 368 siblings of cancer survivors completed a comprehensive demographic and health survey.

RESULTS: A total of 589 survivors (9%) and 8 siblings (2%) reported functional impairment and/or clinical distress in addition to the set of symptoms consistent with a full diagnosis of PTSD. Survivors had more than fourfold greater risk of PTSD, compared with siblings (odds ratio [OR]: 4.14 [95% confidence interval [CI]: 2.08–8.25]). With controlling for demographic and treatment variables, increased risk of PTSD was associated with educational level of high school or less (OR: 1.51 [95% CI: 1.16–1.98]), being unmarried (OR: 1.99 [95% CI: 1.58–2.50]), having annual income below $20 000 (OR: 1.63 [95% CI: 1.21–2.20]), and being unemployed (OR: 2.01 [95% CI: 1.62–2.51]). Intensive treatment also was associated with increased risk of full PTSD (OR: 1.36 [95% CI: 1.06–1.74]).

CONCLUSIONS: PTSD was reported significantly more often by survivors of childhood cancer than by sibling control subjects. Although most survivors apparently are faring well, a subset reported significant impairment that may warrant targeted intervention. *Pediatrics* 2010;125:e1124–e1134

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KEY WORDS
childhood cancer, young adults, posttraumatic stress disorder

ABBREVIATIONS
PTSD—posttraumatic stress disorder
OR—odds ratio
CI—confidence interval
CCSS—Childhood Cancer Survivor Study
BSI-18—Brief Symptom Inventory 18
Rand SF-36—Rand Health Status Survey Short Form 36

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Studies of survivors of childhood cancer have found a small number of survivors who report symptoms of posttraumatic stress.[1–3] These symptoms include reexperiencing or intrusion of unwanted memories, such as nightmares or flashbacks; avoidance of reminders of the events, such as doctors or hospitals, or numbing of emotional responses; and increased sympathetic arousal, including a heightened startle response to sudden noise and constant monitoring for danger. However, to meet the established criteria for a diagnosis of posttraumatic stress disorder (PTSD), according to the *Diagnostic and Statistical Manual of Mental Disorders, Fourth Edition*,[4] 1 symptom of reexperiencing, 3 symptoms of avoidance, and 2 symptoms of increased arousal must be present. In addition, symptoms must be severe enough to cause clinical distress or functional impairment. Symptoms also must be in response to an event that ended ≥1 month before assessment, was perceived as a threat to the life or bodily integrity of self or a loved one, and elicited feelings of horror, intense fear, or helplessness.

Previous studies of PTSD in survivors of childhood cancer found a minority of survivors reporting significant symptoms, that is, as few as 3% of survivors 8 to 20 years of age[1] to 20% of young adult survivors.[2] Compared with a rate of 8.6% in a study of 965 adults attending a primary care clinic,[5] young adult survivors, but not younger survivors, seemed to have a significantly increased prevalence of PTSD symptoms. Although no formal assessment of clinical distress or functional impairment was performed as part of the diagnosis, the young adult survivors who reported symptoms of PTSD were less likely to be married and reported more psychological distress and poorer quality of life across all domains.[6] Similar impairments in function were described for people with PTSD in the general population.[5,7]

Subsequent studies of PTSD in adult survivors of childhood cancer, with sample sizes ranging from 45 to 368, reported prevalence rates of 13% to 19%.[8–10] PTSD has been associated with female gender, unemployment, lower educational levels, cancer of the central nervous system, and severe late effects or health problems.[11] However, these associations have not been reported consistently across studies. Furthermore, there has been no clear assessment of the prevalence of symptoms of PTSD associated with clinical distress and functional impairment, which, as stated above, are required criteria for the clinical disorder of PTSD. The objectives of this study were to use the unique resource of the Childhood Cancer Survivor Study (CCSS) to examine the prevalence of PTSD in very long-term survivors of childhood cancer, compared with a sibling control group, and to examine the association of PTSD with demographic and cancer-related variables.

METHODS

Sample

The CCSS is a longitudinal cohort study that tracks the health status of survivors of childhood cancer diagnosed between 1970 and 1986, from collaborating centers. The institutional review board at each collaborating center reviewed and approved the CCSS protocol and documents sent to participants. All study participants provided informed consent for participation in the study and for release of information from medical records. Detailed descriptions of the study design and characteristics of the cohort were reported previously.[12–15] Figures 1 and 2 detail how survivors and siblings came to participate in the study. Demographic characteristics of the survivors and siblings participating in this study are presented in Table 1. Table 2 provides cancer-related, descriptive statistics of participating survivors.

Primary Outcome Variable

PTSD was the primary outcome variable, defined as detailed in Table 3. A dichotomous (yes/no), categorical variable was created by using the full diagnostic criteria for PTSD, including the number and distribution of symptoms specified in the *Diagnostic and Statistical Manual of Mental Disorders, Fourth Edition*,[1] and assessment of functional impairment or clinical distress. All survivors and siblings were considered positive for criterion A (exposure to an event threatening the life or bodily integrity of self or loved one) on the basis of the cancer experience and positive for criterion E (symptoms for >1 month after the event) because of the length of time since the cancer treatment.

Posttraumatic stress symptoms were assessed by using the Posttraumatic Stress Diagnostic Scale.[16] This measure includes 17 questions covering the 3 categories of symptoms described above. Each symptom was rated on a scale of 0 to 3 for frequency in the past month (0 = not at all or only 1 time, 1 = once in a while, 2 = one-half of the time, and 3 = almost always). Symptoms rated at ≥1 were counted as present. With these scoring criteria, the Posttraumatic Stress Diagnostic Scale has been shown to have good internal consistency and test-retest reliability, as well as satisfactory convergent and concurrent validity, as assessed with clinical diagnoses of PTSD (through a standardized diagnostic interview) and self-reported measures of depression and anxiety.[17]

The Brief Symptom Inventory 18 (BSI-18) was used to evaluate psychological distress.[18] The BSI-18 is an 18-item,

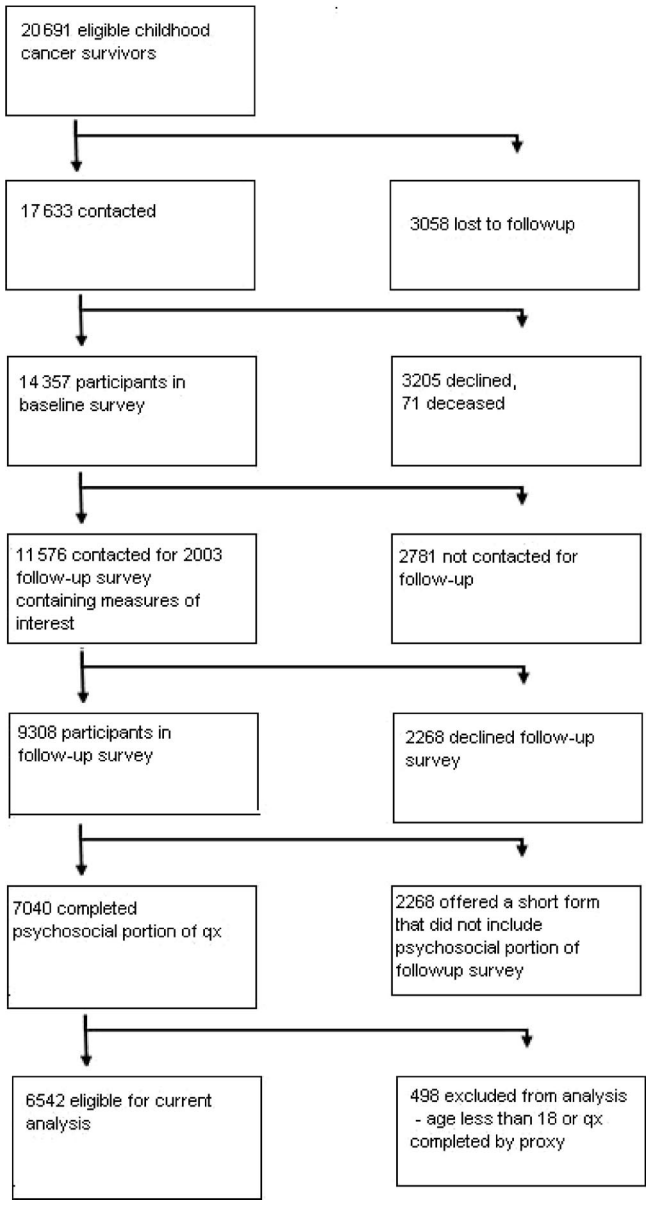

FIGURE 1
Flow diagram of recruitment of the survivor participants in the study. Qx indicates questionnaire.

self-report questionnaire that generates a summary scale, the global stress index, and 3 subscales (depression, anxiety, and somatization). Each item is rated on a 5-point scale, with distress ratings ranging from 0 (not at all) to 4 (extremely). Raw scores are converted to age- and gender-corrected standard *T* scores by using adult, nonpatient, community normative values (mean: 50; SD: 10). A *T* score of ≥63 is used to identify clinical cases. The BSI-18 has been validated with healthy volunteers[18] and in earlier administrations with this cohort of cancer survivors.[19,20]

The Rand Health Status Survey Short Form 36 (Rand SF-36) was used to assess functional impairment. The Rand SF-36 is a self-report measure that evaluates physical functioning, bodily pain, role limitations attributable to physical health problems, role limitations attributable to personal or emotional health problems, general mental health, social functioning, energy/fatigue, and general health perception.[21] Multiitem subscale scores are converted to normative value-referenced *T* scores (mean: 50; SD: 10). Scores of ≤40 are considered to indicate clinical impairment. The Rand SF-36 has undergone extensive reliability and validity testing[22] and has demonstrated sensitivity in the CCSS cohort.[23]

Findings for the BSI-18 and the Rand SF-36 role limitations attributable to emotional health problems were used to determine whether survivors met criterion F of the diagnostic criteria for PTSD. Survivors with BSI-18 global stress index scores of ≥63 or 2 subscale (ie, depression, anxiety, or somatization) scores of ≥63 were determined to meet criterion F on the basis of significant distress. Survivors with scores of ≤40 for the role limitations attributable to emotional health scale from the Rand SF-36 were determined to meet criterion F on the basis of functional limitations.

Independent Variables

Specific cancer diagnosis, age at diagnosis, presence or absence of relapse or new malignancy, year of treatment, years since diagnosis, and intensity of treatment (a yes/no composite variable of chemotherapy, surgery, and radiotherapy, as detailed in Appendix 1) were analyzed as potential cancer-related predictors of PTSD among survivors. In addition, demographic factors, including age at interview, gender, and self-reported employment, marital status, education, ethnicity, and current income, were analyzed as potential correlates of PTSD for survivors.

Statistical Analyses

Descriptive data were examined to determine the distribution of variables of interest, and categories were created to balance appropriate

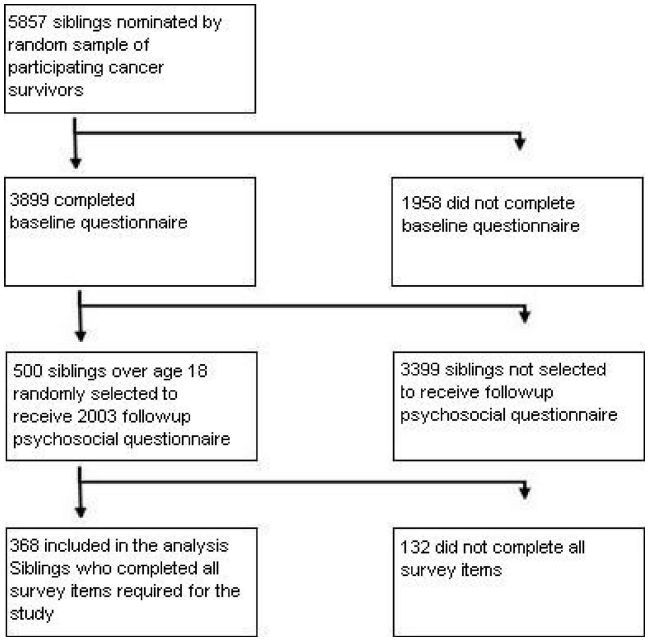

FIGURE 2
Flow diagram of recruitment of the sibling participants in the study.

TABLE 1 Demographic Characteristics of Survivors and Siblings

	n (%)		*P*
	Sibling	Survivor	
Age at interview			
18–29 y	134 (36.4)	2645 (40.4)	<.01
30–39 y	139 (37.8)	2769 (42.3)	
≥40 y	95 (25.8)	1128 (17.2)	
Race			
All others	22 (6.3)	815 (12.5)	<.0001
White non-Hispanic	330 (93.8)	5703 (87.5)	
Gender			
Female	193 (52.4)	3423 (52.3)	.96
Male	175 (47.6)	3119 (47.7)	
Education			
High school graduate or less	54 (14.8)	987 (15.2)	.57
Some college	125 (34.2)	2372 (36.5)	
College graduate or more	187 (51.1)	3140 (48.3)	
Employed			
No	58 (15.8)	1430 (22.0)	<.01
Yes	309 (84.2)	5067 (78.0)	
Personal income			
Below $20 000	109 (34.1)	2688 (42.4)	<.0001
$20 000–39 999	80 (25.0)	1892 (29.8)	
$40 000 or above	131 (40.9)	1766 (27.8)	
Marital status			
Single	102 (28.0)	2671 (41.2)	<.0001
Married or living as married	218 (59.9)	3322 (51.2)	
Widowed, divorced, or separated	44 (12.1)	490 (7.6)	

P values were from robust Wald tests.

distribution of subjects with evaluation of associations relevant to the hypotheses of interest. Races and ethnicities other than non-Hispanic white were collapsed into one "other" category, given the small numbers in each of the other self-reported race/ethnicity categories.

Descriptive demographic and cancer-related characteristics of survivors who completed surveys of interest to this study were compared with those of survivors who did not complete the surveys by using *P* values from χ^2 tests (Appendices 2 and 3). Demographic distributions for the survivor and sibling groups were compared by using *P* values from robust Wald tests.[24] The prevalence of PTSD among survivors was compared with that among siblings by using logistic regression models with robust variance estimates, with adjustment for age at interview, gender, and intrafamily correlation.[25] Given the difference in the racial composition of the survivor and sibling samples, all analyses also adjusted for race.

Similarly, relationships between PTSD and demographic characteristics and treatments among survivors were assessed by using logistic regression models. Variables that were significant at the .05 level in univariate models were used in a multivariate model, with assessment of potential 2-way interactions. Because of strong colinearity between diagnoses, intensive treatment, and specific treatments, 3 models were fit, to examine each of those factors in a separate multivariate model. All reported *P* values are 2-sided.

RESULTS

Siblings were similar to survivors with respect to gender and education level but were more likely to be older at interview ($P < .01$), to be white ($P < .0001$), to be employed ($P < .01$), to be married ($P < .0001$), and to have a higher income ($P < .0001$). The mean age at interview for survivors was 31.85 years (SD: 7.55 years; range: 18–53 years) and that for siblings was 33.44 years (SD: 8.19 years; range: 18–54 years). Survivors had a mean age at diagnosis of 8.21 years (SD: 5.87 years; range: 0–20 years). Other specific descriptive data for survivors and siblings are presented in Tables 1

TABLE 2 Medical Characteristics of Survivors

	n (%)
Diagnosis	
Bone cancer	604 (9.2)
Central nervous system cancer	687 (10.5)
Hodgkin's lymphoma	931 (14.2)
Kidney cancer (Wilms' tumor)	626 (9.6)
Leukemia	2183 (33.4)
Non-Hodgkin's lymphoma	504 (7.7)
Neuroblastoma	406 (6.2)
Soft-tissue sarcoma	601 (9.2)
Age at diagnosis	
0–4 y	2395 (36.6)
5–9 y	1475 (22.5)
10–14 y	1414 (21.6)
15–20 y	1258 (19.2)
Year of diagnosis	
1970–1973	881 (13.5)
1974–1978	1712 (26.2)
1979–1986	3949 (60.4)
Time since diagnosis	
15–19 y	1773 (27.1)
20–24 y	2343 (35.8)
25–29 y	1668 (25.5)
30–34 y	758 (11.6)
Chemotherapy	
None	1246 (20.3)
Anthracyclines or alkylating agents	3676 (59.8)
Other drugs	1223 (19.9)
Radiotherapy	
Radiation to brain	1818 (29.6)
Radiation but not to brain	2060 (33.5)
No radiotherapy	2087 (34.0)
Radiation, site unknown	176 (2.9)
Second malignancy or recurrence	
No	5364 (82.0)
Yes	1178 (18.0)

TABLE 3 Definition of PTSD Used in This Study

	DSM-IV Criteria	PTSD Criteria Used in Study
Criterion A	Exposure to event threatening life or bodily integrity of self or loved one	Diagnosed with cancer or sibling diagnosed with cancer
Criterion B	Reexperiencing (1 symptom required)	Uncontrollable, upsetting thoughts or images Having bad dreams or nightmares Reliving illness Feeling upset when reminded about illness Having physical reactions when reminded about illness
Criterion C	Avoidance (3 symptoms required)	Not thinking, talking, or feeling about illness Avoiding activities, people, or places that are reminders of illness Forgetting important experiences about illness Having less interest in important activities Feeling distant or cut off from people Feeling numb Believing future plans and hopes will not come true
Criterion D	Arousal (2 symptoms required)	Having trouble falling or staying asleep Feeling irritable or having fits of anger Having trouble concentrating Being overly alert Being jumpy or easily startled
Criterion E	Duration	>30 d after traumatic event
Criterion F	Significant distress or functional impairment	Significant distress defined as *T* score of ≥63 on BSI-18 global stress index scale or *T* score of ≥63 for 2 of following 3 BSI-18 factors: depression, anxiety, and somatization; functional impairment defined as *T* score of ≤40 for role limitations attributable to emotional health factor from Rand SF-36

DSM-IV indicates *Diagnostic and Statistical Manual of Mental Disorders, Fourth Edition.*

and 2. Of the 6542 childhood cancer survivors and 368 siblings surveyed, 589 (9%) of the survivors and 8 (2%) of the siblings reported the constellation of symptoms plus clinical distress and/or functional impairment consistent with a diagnosis of PTSD (with adjustment for age at interview, race, gender, and within-family correlation between survivor and sibling, odds ratio [OR]: 4.14 [95% confidence interval [CI]: 2.08–8.25]).

Table 4 presents results of multivariate modeling among survivors. PTSD was significantly associated with being unmarried (single versus married, OR: 1.99 [95% CI: 1.58–2.50]), having an annual income of less than $20 000 (versus more than $40 000, OR: 1.63 [95% CI: 1.21–2.20]), being unemployed (OR: 2.01 [95% CI: 1.62–2.51]), having a high school education or less (high school versus college graduate, OR: 1.51 [95% CI: 1.16–1.98]), and being >30 years of age (30–39 years versus 18–29 years, OR: 1.52 [95% CI: 1.16–2.00]). Because of a suggested interaction between gender and race in the sample ($P = .06$), the strata defined by combinations of these factors were examined as separate risk groups. There were no significant associations of these gender/race combinations with PTSD. Models were stratified on the basis of age at diagnosis because of a significant interaction between radiotherapy and age at diagnosis. Survivors who underwent cranial radiotherapy at <4 years of age were at particularly high risk for PTSD (OR: 2.05 [95% CI: 1.41–2.97]).

The risk for PTSD was not significantly greater for survivors who experienced recurrence of cancer (OR: 1.22 [95% CI: 0.72–1.41]) or a second malignant neoplasm (OR: 1.01 [95% CI: 0.72–1.41]). In a separate multivariate model, the risk for PTSD was significantly greater for survivors treated with more-intensive treatment, as defined in Appendix 1 (OR: 1.36 [95% CI: 1.06–1.74]; data not shown).

Survivors of all diagnostic categories of cancer were at statistically significantly greater risk of PTSD, compared with siblings (Table 5). Greater than twofold (range: 2.4–4.6-fold) increased risks were present for all cancer diagnostic groups.

DISCUSSION

The prevalence of PTSD, including functional impairment and/or clinical distress as well as symptoms, was >4 times greater in young adult cancer survivors than in a comparison group of siblings. The prevalence of PTSD was associated with many of the specific

TABLE 4 Multivariate Model for Risk of PTSD Among Survivors, With Adjustment for All Listed Variables

	n (%)		OR (95% CI)	*P*
	PTSD	No PTSD		
Gender/race				
Male/nonwhite	26 (8)	303 (92)	1.00 (reference)	
Female/nonwhite	49 (13)	315 (87)	1.56 (0.93–2.62)	.09
Male/white non-Hispanic	200 (8)	2153 (92)	1.23 (0.79–1.90)	.36
Female/white non-Hispanic	237 (9)	2410 (91)	1.11 (0.72–1.72)	.62
Age at interview				
18–29 y	195 (8)	2152 (92)	1.00 (reference)	
30–39 y	225 (10)	2130 (90)	1.52 (1.16–2.00)	<.01
≥40 y	92 (9)	899 (91)	1.57 (1.05–2.34)	.03
Education				
College graduate or more	202 (7)	2601 (93)	1.00 (reference)	
High school graduate or less	110 (14)	704 (86)	1.51 (1.16–1.98)	<.01
Some college	200 (10)	1876 (90)	1.12 (0.90–1.39)	.32
Employed				
Yes	311 (7)	4144 (93)	1.00 (reference)	
No	201 (16)	1037 (84)	2.01 (1.62–2.51)	<.0001
Personal income				
$40 000 or above	97 (6)	1497 (94)	1.00 (reference)	
$20 000–39 999	112 (7)	1566 (93)	1.02 (0.76–1.37)	.89
Below $20 000	303 (13)	2118 (87)	1.63 (1.21–2.20)	<.01
Marital status				
Married or living as married	189 (6)	2734 (94)	1.00 (reference)	
Single	259 (11)	2088 (89)	1.99 (1.58–2.50)	<.0001
Widowed, divorced, or separated	64 (15)	359 (85)	2.27 (1.66–3.11)	<.0001
Radiotherapy and age at diagnosis				
0–4 y				
No radiotherapy	53 (6)	820 (94)	1.00 (reference)	
Cranial radiation	85 (13)	587 (87)	2.05 (1.41–2.97)	<.001
Radiation to other site	43 (8)	504 (92)	1.57 (1.02–2.43)	.04
5–9 y				
No radiotherapy	28 (7)	383 (93)	1.00 (reference)	
Cranial radiation	51 (11)	430 (89)	1.25 (0.76–2.04)	.39
Radiation to other site	43 (12)	327 (88)	1.83 (1.09–3.06)	.02
10–14 y				
No radiotherapy	36 (10)	342 (90)	1.00 (reference)	
Cranial radiation	26 (7)	343 (93)	0.58 (0.34–1.00)	.05
Radiation to other site	51 (10)	437 (90)	1.10 (0.69–1.75)	.69
15–20 y				
No radiotherapy	31 (9)	314 (91)	1.00 (reference)	
Cranial radiation	15 (8)	163 (92)	0.82 (0.42–1.59)	.56
Radiation to other site	50 (9)	531 (91)	1.09 (0.67–1.77)	.74
Chemotherapy				
None	94 (8)	1045 (92)	1.00 (reference)	
Anthracyclines or alkylating agents	310 (9)	3098 (91)	1.07 (0.83–1.38)	.59
Other drugs	108 (9)	1038 (91)	1.32 (0.96–1.81)	.08
Second malignant neoplasm				
No	465 (9)	4725 (91)	1.00 (reference)	
Yes	47 (9)	456 (91)	1.01 (0.72–1.41)	.97
Recurrence				
No	446 (9)	4676 (91)	1.00 (reference)	
Yes	66 (12)	505 (88)	1.22 (0.91–1.62)	.18

demographic variables assessed, including marital status, education, employment, income, and age at interview. However, the relationship of PTSD to cancer-related variables was more complex. The best predictors of risk for PTSD among the survivors were a composite variable of intensity of therapy and an interaction of age at diagnosis with cranial radiotherapy. Intensity of treatment, defined in a manner similar to that in this study, was not significantly correlated with PTSD in a previous study of 186 survivors of childhood cancer.[2] However, other studies found that brain tumors and treatments (such as cranial radiotherapy) with an impact on cognitive function were associated with long-term emotional distress for survivors.[26–30] It may be that the intensity of treatment in general, and cranial radiotherapy for very young children in particular, is related to late effects that impair function and cause emotional distress. The association of PTSD with lower education, employment, and income levels for survivors would be consistent with this subgroup having additional burdens and reminders posed by later physical and cognitive effects of cancer treatment.

The prevalence of PTSD in this study is far higher than the 3% reported by cancer survivors who were still children and adolescents[1] and is similar to, or higher than, findings from studies that included adolescents as well as adult survivors, in which an elevated rate of 10.9%[31] or a rate similar to that of control subjects[32] was reported. If the symptoms of PTSD are a result of early trauma associated with specific childhood cancer experiences, how could it be that the symptoms are not seen until people are in their thirties and forties? Because none of the previous childhood cancer studies monitored survivors longitudinally through childhood and into their thirties and forties, there is no definite answer to this question. It is possible that this and other cross-sectional studies are detecting a cohort effect. For example, newer, less-toxic treatments, less reliance on cranial radiotherapy for non–central nervous system tumors, and better supportive care may mean that younger survivors now are less traumatized and have fewer phys-

TABLE 5 Risk of PTSD Among Survivors, According to Diagnosis, in Comparison With Siblings

Type of Cancer	OR (95% CI)	*P*
Bone cancer	3.57 (1.56–8.21)	<.01
Central nervous system cancer	3.64 (1.54–8.63)	<.01
Hodgkin's lymphoma	4.64 (1.91–11.26)	<.001
Kidney cancer (Wilms' tumor)	2.41 (1.04–5.55)	.04
Leukemia	3.84 (1.74–8.46)	<.01
Non-Hodgkin's lymphoma	4.08 (1.74–9.54)	<.01
Neuroblastoma	2.89 (1.01–8.31)	.05
Soft-tissue sarcoma	3.24 (1.42–7.41)	<.01

Models were adjusted for demographic features, personal information, and intrafamily correlation.

ical and cognitive late effects than did the survivors in the past. This hypothesis seems to be supported by the higher risk of PTSD associated with older age at interview in this study. However, when findings were compared specifically with respect to year of treatment (which was not included as an independent variable in the general analytic model because of covariance with age at interview), there was no significant difference in risk for PTSD between survivors treated in the 1970s and those treated in the 1980s. The effects of newer treatments and supportive care in the 1990s and in the 21st century have yet to be explored.

Another potential explanation for the difference in prevalence of PTSD between children or adolescents and young adults is that the criteria for PTSD are more appropriate for adults than for younger individuals. However, many studies of adolescents exposed to a variety of traumatic events found that the PTSD criteria can be used with adolescents.[33] One study found a prevalence of PTSD symptoms among adolescent recipients of solid-organ transplants of 20%, much closer to that seen in the studies of young adult childhood cancer survivors than in the studies of younger cancer survivors.[34] This finding suggests that child and adolescent recipients of organ transplants are able to endorse symptoms of PTSD.

It may be that symptoms, clinical distress, and functional impairment emerge only among more-vulnerable childhood cancer survivors as they contend with the developmental tasks of young adulthood[35,36] and the added challenges of late effects of treatment.[29] The relative protection of the parental home is diminished as young adult survivors face the challenges of completing their education, finding a job, obtaining health insurance, establishing long-lasting intimate relationships, and starting a family. All of these tasks contain reminders that the survivors may be at a disadvantage, relative to their peers, as a result of the cancer and its treatment (eg, infertility, decreased height, or learning disabilities). Difficulties with developmental tasks may serve to remind the survivors of traumatic events, causing previously latent PTSD symptoms, clinical distress, or emotional impairment to surface. Developmentally expected but difficult stressors (eg, relationship difficulties, problems with schoolwork, peer pressures, and challenges in finding and retaining employment) may overwhelm coping skills and precipitate the emergence of clinically significant symptoms.

It is not surprising then that lower levels of income, employment, and marriage were associated with PTSD among both the survivors and their siblings. Directionality is unclear in this association. People without the social and economic supports of a job and partner are generally at greater risk for emotional distress. However, another interpretation is that PTSD is a cause or correlate of difficulty getting or keeping an education, job, or relationship. PTSD may indicate psychological vulnerability in the survivors. Therefore, it may be a marker for people who are prone to other adverse life events and represent a target population for mental health intervention.

Not all of those who were contacted for the baseline survey of this study chose to participate, and not all who were invited to participate in the psychosocial component completed those measures, which suggests that there might have been some self-selection among the respondents. Nonparticipants were younger at diagnosis, more likely to have had cancers of the central nervous system, more often male, younger, less well-educated, and less likely to be employed, married, or earning more than $20 000 a year. They also were more likely to have BSI-18 scores in the clinically significant range for depression, anxiety, somatization, and global severity of emotional distress. These findings suggest that subjects who seemed to be at higher risk for PTSD were less likely to participate in this study and that the observed prevalence of PTSD in this study reflects a conservative estimate of the true population affected.

CONCLUSIONS

Although the vast majority of adult survivors of childhood cancer do not report PTSD, significantly higher rates were reported by long-term survivors, compared with sibling control subjects. Treatment intensity seemed to be a significant predictor, and increased expectations for independent living for survivors as adults may exacerbate symptoms. Whatever the cause, there seems to be a group of adult survivors of childhood cancer with significant functional impairment or clinical distress and PTSD who might benefit

from intervention. The next step in this line of research is to identify potential protective factors and interventions that may be used to reduce the rate of PTSD in these very long-term survivors.

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APPENDIX 1 Criteria for Intensity of Treatment Variable

	Intensive Parameters
Diagnosis	
Acute lymphoblastic leukemia	Treatment: >2000 mg/m^2 cyclophosphamide, administered intravenously, plus >120 mg/m^2 anthracycline
Acute myeloid leukemia	All cases
Central nervous system tumors	Treatment: any combined-modality therapy
Ewing sarcoma family of tumors	Treatment: any combined-modality therapy
Hodgkin's lymphoma	Treatment: any combined-modality therapy
Non-Hodgkin's lymphoma	Treatment: any combined-modality therapy or >6500 mg/m^2 cyclophosphamide, administered intravenously, plus >300 mg/m^2 anthracycline
Neuroblastoma	Treatment: any combined-modality therapy
Osteosarcoma	Treatment: any combined-modality therapy
Rhabdomyosarcoma	Treatment: any combined-modality therapy
Wilms' tumor	Treatment: any combined-modality therapy
Chemotherapy	
Hematopoietic cell transplant (ICD-9-CM codes 41.00–41.09)	All cases
Recurrence	All cases
Anthracycline	Dose: >300 mg/m^2
Alkylating agent	Dose: 3rd tertile (summed score: >3)
Anthracycline plus alkylating agent	Anthracycline dose: 2nd tertile (209–359 mg/m^2); alkylating agent dose: 2nd tertile
Radiotherapy	
Craniospinal (brain and/or spine)	Any dose
Mantle/mediastinal (chest and/or neck)	Any dose
Whole lung (heart)	Any dose
Whole abdomen (abdomen)	Any dose
Pelvic (gonadal)	Any dose
Total nodal (total-body irradiation)	Any dose
Surgery	
Amputation (ICD-9-CM codes 84.00–84.19 and 84.91)	Any time after diagnosis
Bowel resection (ICD-9-CM codes 45.61–45.89)	Within 2 y after diagnosis
Cystectomy (ICD-9-CM codes 57.60–57.79)	Within 2 y after diagnosis
Hysterectomy (ICD-9-CM codes 68.30–68.99)	Within 2 y after diagnosis
Lysis of adhesions (ICD-9-CM codes 54.50–54.59)	Any time after diagnosis
Oophorectomy/orchidectomy (ICD-9-CM codes 65.50–65.69 and 62.40–62.49)	Bilateral, within 2 y after diagnosis
Ostomy (ICD-9-CM codes 46.10–46.39)	Within 2 y after diagnosis

ICD-9-CM indicates International Classification of Diseases, Ninth Revision, Clinical Modification.

APPENDIX 2 Comparison of CCSS Survivors Who Completed Psychosocial Survey and Those Who Completed Neither Baseline nor Psychosocial Survey

	n (%)		*P*
	Did Not Complete Baseline or Psychosocial Survey	Completed Psychosocial Survey	
Diagnosis			
Bone cancer	640 (8.3)	617 (8.8)	<.0001
Central nervous system cancer	1102 (14.2)	845 (12.0)	
Hodgkin's lymphoma	966 (12.5)	952 (13.5)	
Kidney cancer (Wilms' tumor)	625 (8.1)	665 (9.4)	
Leukemia	2558 (33.1)	2356 (33.5)	
Non-Hodgkin's lymphoma	600 (7.8)	529 (7.5)	
Neuroblastoma	553 (7.1)	447 (6.3)	
Soft-tissue sarcoma	695 (9.0)	629 (8.9)	
Age at diagnosis			
0–4 y	3249 (42.0)	2684 (38.1)	<.0001
5–9 y	1730 (22.4)	1582 (22.5)	
10–14 y	1527 (19.7)	1477 (21.0)	
15–20 y	1233 (15.9)	1297 (18.4)	
Gender			
Female	3099 (40.0)	3593 (51.0)	<.0001
Male	4640 (60.0)	3447 (49.0)	

APPENDIX 3 Comparison of CCSS Survivors Who Completed Psychosocial Survey and Those Who Did Not

	n (%)		*P*
	Did Not Complete Psychosocial Survey	Completed Psychosocial Survey	
Diagnosis			
Bone cancer	307 (6.8)	617 (8.8)	<.0001
Central nervous system cancer	591 (13.0)	845 (12.0)	
Hodgkin's lymphoma	522 (11.5)	952 (13.5)	
Kidney cancer (Wilms' tumor)	415 (9.2)	665 (9.4)	
Leukemia	1577 (34.8)	2356 (33.5)	
Non-Hodgkin's lymphoma	377 (8.3)	529 (7.5)	
Neuroblastoma	367 (8.1)	447 (6.3)	
Soft-tissue sarcoma	378 (8.3)	629 (8.9)	
Age at diagnosis			
0–4 y	2088 (46.1)	2684 (38.1)	<.0001
5–9 y	997 (22.0)	1582 (22.5)	
10–14 y	835 (18.4)	1477 (21.0)	
15–20 y	614 (13.5)	1297 (18.4)	
Radiotherapy			
Radiation to brain	1248 (33.4)	2046 (30.9)	.0011
Radiation but not to brain	1077 (28.8)	2130 (32.2)	
No radiotherapy	1282 (34.3)	2246 (34.0)	
Radiotherapy, site unknown	131 (3.5)	193 (2.9)	
Intensive therapy			
No	895 (23.9)	1402 (21.3)	.0018
Yes	2848 (76.1)	5193 (78.7)	
Gender			
Female	1876 (41.4)	3593 (51.0)	<.0001
Male	2658 (58.6)	3447 (49.0)	
Age at baseline			
0–9 y	33 (0.7)	32 (0.5)	<.0001
10–19 y	1743 (38.5)	2268 (32.2)	
20–29 y	1825 (40.3)	2975 (42.3)	
30–39 y	840 (18.5)	1584 (22.5)	
40–49 y	89 (2.0)	180 (2.6)	
Education at baseline			
High school graduate or less	1274 (42.8)	1303 (25.6)	<.0001
Some college	1053 (35.3)	1895 (37.3)	
College graduate or more	653 (21.9)	1886 (37.1)	
Employed at baseline			
No	521 (16.6)	560 (10.6)	<.0001
Yes	2623 (83.4)	4713 (89.4)	
Personal income at baseline			
Below $20 000	1934 (68.6)	3054 (61.5)	<.0001
$20 000–39 999	630 (22.3)	1320 (26.6)	
$40 000 or above	257 (9.1)	588 (11.9)	
Marital status at baseline			
Single	1633 (52.6)	2616 (50.1)	<.0001
Married or living as married	1157 (37.3)	2236 (42.9)	
Widowed, divorced, or separated	312 (10.1)	365 (7.0)	
BSI-18 global severity at baseline			
No	2657 (90.9)	4742 (92.9)	.0012
Yes	267 (9.1)	363 (7.1)	
BSI-18 depression at baseline			
No	2602 (88.9)	4627 (90.5)	.0159
Yes	326 (11.1)	483 (9.5)	
BSI-18 anxiety at baseline			
No	2696 (92.1)	4788 (93.7)	.0071
Yes	230 (7.9)	321(6.3	
BSI-18 somatization at baseline			
No	2671 (91.2)	4733 (92.6)	.0232
Yes	257 (8.8)	376 (7.4)	

Prevalence and Predictors of Posttraumatic Stress Disorder in Adult Survivors of Childhood Cancer

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