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Children's Psychological Distress During Pediatric HSCT: Parent and Child Perspectives

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Background. Hematopoietic stem cell transplantation (HSCT) can be challenging to pediatric recipients and their families. Little is known about the recipients' psychological status as they initiate treatment and in the year afterwards. The purpose of this study is to describe the psychological status of 107 pediatric HSCT recipients from their parents' perspective, and to compare reports from parents and children in a subset of 55 children. We hypothesized that there would be discrepancies between parent and child report of child distress. ***Procedure.*** Multi-site, prospective study of eligible child participants and their parents who completed selected modules from the Structured Clinical Interview for DSM-IV-TR, Childhood Version (KID-SCID) the month before and one year after HSCT. Diagnoses were threshold or subthreshold. ***Results.*** According to parents, nearly 30% of children had anxiety disorder both before and after HSCT; approximately half of these met threshold criteria. Agreement between parents and children for anxiety disorders was poor at baseline ($\kappa = -0.18$, 95%CI $= -0.33, -0.02$) and fair at 12 months ($\kappa = 0.31$, 95%CI $= -0.04, 0.66$). Agreement about mood disorders was fair at baseline (10% prevalence, $\kappa = 0.39$, 95%CI $= -0.02, 0.79$) and moderate at 12 months (14% prevalence, $\kappa = 0.41$, 95%CI $= 0.02, 0.80$). ***Conclusions.*** Anxiety (30%) and mood (10–14%) symptoms are common in children both before and after HSCT; parent and child reports of these symptoms do not agree. Input from parents and children is recommended to identify more accurately children who may need additional intervention during and following HSCT Pediatr Blood Cancer 2012;58:289–296. © 2011 Wiley Periodicals, Inc.

Key words: child; parent; psychological distress

INTRODUCTION

According to available data, hematopoietic stem cell transplantation (HSCT) was the second most frequent major organ transplant performed in the United States in 2008 [1,2]. An estimated 17% of HSCTs are performed in children under 20 years of age worldwide [3,4]. Once reserved for rare hematologic, metabolic, or immunologic disorders, therapeutic advances in pediatric HSCT and supportive care have resulted in its expanded application to children with malignancies and more chronic hematological conditions (e.g., bone marrow failure and hemoglobinopathies) [4].

Children undergoing HSCT may be at particular risk for psychological distress as they receive what is commonly acknowledged to be a challenging but potentially life-saving treatment. The prevalence of major depressive disorder, depressive symptoms, or anxiety in children with cancer (in general) has been estimated to be between 7 and 32% [5]. Children's reactions to HSCT have been an area of burgeoning inquiry principally because of the recognition that it is an intense treatment for all children and carries with it the risk of lasting psychological impact for at least some of these recipients.

Given the intensity of treatment, beginning typically with a one-week preparative regimen immediately prior to transplant, the feasibility of collecting in-depth information on children's psychological status from the children themselves remains a challenge. As such, proxy reporting has been used in the past to supplement direct reports from the child. Since parents are commonly the decision makers and care providers for their children, their perceptions of their children's psychological state are influential. A cross-sectional study of 82 pediatric HSCT survivors that compared parent and child assessments of child functioning after transplant found that, whereas there was excellent agreement between parental and child assessments for ''objective issues'' such as missed school days, there was little agreement in parental and child ratings of the child's mental health and quality of life [6]. A recent longitudinal study of 153 children undergoing HSCT concluded that these children appeared to enter the hospital with heightened distress (as characterized by high levels of self-reported somatic symptoms and mood disturbance, along with low levels of activity) that increased steadily until one week after transplantation and then declined to pre-transplant levels at 4–6 months. The trajectory, but not the extent of distress, as reported by the child, was confirmed by the parent [7].

While validated measures of adjustment, depression, anxiety, and other psychosocial indicators obtained by proxy or self-report have been used in studies thus far, this study used a structured diagnostic interview both with children undergoing transplant, and with their parents, in order to assess the prevalence of these

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problems in pediatric HSCT. Parents and children independently completed the interview in the month prior to transplant and then 1 year later. Results of the interviews are summarized and parent and child perspectives compared. We hypothesized that there would be discrepancies between parent and child reports about child disorders and symptoms.

METHODS

Participants

Subjects were drawn from a cohort of 165 child–parent dyads enrolled in the Journeys to Recovery Study (JTR), a multi-site, prospective study of pediatric HSCT including children and their parents [8]. All HSCT candidates at each of the participating sites were screened for potential eligibility by trained study staff. Eligibility included working knowledge of English (parent and child), child age of 5–18 years, and parent/legal guardian who was able to consent on behalf of the minor child. After consultation with clinical providers, all potentially eligible dyads were approached for recruitment. The recruitment period extended from 30 days prior to the planned HSCT to the date of HSCT (''Day 0''). All parents and those children ages 8 and older were invited to complete a structured psychiatric diagnostic interview at baseline (prior to transplant) and 12 months later as part of the JTR study. Informed consent was obtained by parents; age-appropriate assent was also obtained, as stipulated by the Institutional Review Board (IRB) at each institution. Both members of the parent–child dyad had to agree to participate in the study for either member to participate. The study was approved by the IRB at Tufts Medical Center and at each of the clinical sites.

The Interview

Selected modules of the Structured Clinical Interview for DSM-IV-TR, Childhood Version (KID-SCID) were used to evaluate the psychiatric status in the study. The KID-SCID assesses the intensity, duration, and pervasiveness of symptoms and relies on the clinical judgment of the interviewer to determine if diagnostic criteria are satisfied. The interview utilizes differential diagnosis to rule out potentially related disorders, such as those due to medications or the medical condition, or those that may be developmentally expected responses. Both the child and parent can be interviewed separately about the child's symptoms and impairment, using the interview's parallel forms for each rater, thereby allowing for a more precise evaluation of the agreement/disagreement between children and parents regarding the psychological health of the child. The KID-SCID has demonstrated excellent inter-rater reliability and very good test–retest reliability [9].

Procedures

The KID-SCID was administered by trained interviewers and was audiotaped. Parent and child interviews were conducted by different researchers for independent assessment; in the rare instances where this was not possible, the child's interview was conducted prior to the parent's interview. This design attempted to avoid influencing the interviewer with the parent's appraisal of the child. As part of required study staff training, each interviewer attended a didactic teaching session, followed by at least one practice interview, which was individually reviewed by the study psychiatrist (GC) exclusively for training purposes. Formal feedback was provided to the interviewer. After training, parents of children aged 5–18 years and children aged 8 years and older were administered the KID-SCID by the trained interviewers at baseline and 12 months; each interview required approximately 45–60 minutes to complete. Twelve-month interviews assessed psychological status over the past year only. Due to developmental considerations, children under the age of 8 years were not administered the KID-SCID.

The interviewer scored each module of the interview, which was then reviewed with the audiotape by the study psychiatrist (GC) to ensure that scoring was consistent with the available information. The product of this review was a ''Best Estimate'' (BE) of each KID-SCID interview [10], which was used for all analyses. This process for establishing a BE diagnosis, while time-consuming and costly, is considered to be most reflective of clinical decision-making [11].

Interview Content

The overview and selected mood, anxiety, and adjustment disorder modules from the KID-SCID were used with participating parents and children. Mood modules included major depressive episode (MDE); substance–induced mood disorder; mood disorder because of a general medical condition; and dysthymia. A mood diagnosis was considered present whenever the criteria for any one of these disorders were present. Anxiety modules included separation anxiety; specific phobia; obsessive–compulsive disorder (OCD); current panic disorder; agoraphobia; generalized anxiety disorder; social phobia; and post traumatic stress disorder (PTSD). An anxiety diagnosis was considered present whenever the criteria for any one of these disorders were satisfied. Adjustment disorder was a separate diagnostic category. Diagnoses for all of the disorders were threshold, subthreshold, or indeterminate, and are reported separately. Threshold diagnoses were those that met diagnostic criteria completely. Subthreshold diagnoses were those whereby diagnostic criteria were not completely satisfied, but were associated with clinical symptoms or distress. Indeterminate diagnoses were those where uncertainty at the time of the interview precluded a definitive clinical decision. Only diagnoses classified as current were included in this study.

Medical and Demographic Information

As part of the baseline assessment, parents also completed a demographics questionnaire about patient and family characteristics, as well as a validated, single item on the overall severity of the child's medical condition that utilized a 10-point scale in which higher scores reflected increased severity [12].

Medical information was collected on each patient by trained research staff via medical records review. These data included the child's causal diagnosis for transplant, disease stage, duration of illness, remission status, type of transplant, donor type and source, degree of match, and planned graft versus host disease prophylaxis.

Data Analysis

Demographic and clinical characteristics were described for the study population using means (standard deviations (SD)), medians (25th to 75th percentile), frequencies, and percentages. To determine if there was a difference in demographic and clinical

characteristics by whether or not the parent completed the KID-SCID, the Wilcoxon signed-rank (continuous variables) or Fisher's exact test (categorical variables) was used. Among those completing the KID-SCID, the aforementioned statistical tests were used to compare demographic and clinical characteristics among those with and without any baseline diagnosis.

Frequencies were reported for each diagnostic category: Mood, anxiety, and adjustment disorder at baseline and 12 months for each rater. Comparisons of the proportion meeting threshold versus subthreshold criteria were made using the binomial test. The Fisher's exact test was used to compare the number meeting threshold versus subthreshold criteria by time period. The McNemar test for paired binary data was used to determine the change in proportion of each diagnosis from baseline to 12-month follow-up among parents who completed the KID-SCID at both time points.

The weighted kappa coefficient (κ) with its 95% asymptotic confidence interval was calculated to measure the extent of agreement between child and parent report taking chance into account. The following guidelines have been suggested to interpret the strength of agreement for kappa values: $\kappa < 0.0$, poor; $\kappa = 0.0$–0.20, slight; $\kappa = 0.21$–0.40, fair; $\kappa = 0.41$–0.60, moderate; $\kappa = 0.61$–0.80, substantial; $\kappa = 0.81$–1.0, almost perfect [13]. The alpha level was set at 0.05, and was not adjusted for multiple comparisons. All statistical analyses were performed using SAS software (version 9.1; SAS Institute, Cary, NC).

RESULTS

Participants

The KID-SCID was completed by 107 parents and 59 children at baseline and 79 parents and 59 children at 12 months. Sixty-nine parents and 38 children completed the interview at both time points. Among those who completed the interviews at both times were 35 parent–child pairs. Baseline demographic and clinical characteristics of the children and their parents are summarized in Table I. Most of the 107 participating parents were female (86.0%) with an average age of 39.0 years (SD = 6.8). The children had an average age of 11.1 years (SD = 4.1) and approximately half were female. For most, malignancy was the causal diagnosis for HSCT. Dyads completing the interview at baseline were significantly more likely to have been recruited

TABLE I. Demographic and Clinical Characteristics of Study Participants Based on Parental Completion of the KID-SCID at Baseline

Characteristics	Total (n = 165)	Declined (n = 58)	Completed (n = 107)	*P*-value
Parent				
Female	84.2%	81.0%	86.0%	0.50
Age, mean years (SD[a])	38.9 (6.9)	38.7 (7.1)	39.0 (6.8)	0.76
Race/ethnicity				
White	80.6%	70.7%	86.0%	<0.01
Black	4.2%	12.1%	0.0%	
Asian	2.4%	3.5%	1.9%	
Other	12.7%	13.8%	12.2%	
Education, mean years (SD)	13.9 (2.3)	13.1 (2.4)	14.3 (2.1)	<0.01
Annual income[b]				
<$20 k	11.3%	16.4%	8.6%	0.34
$20–40 k	22.5%	27.3%	20.0%	
$>40–60 k	22.5%	21.8%	22.9%	
>$60–80 k	12.5%	10.9%	13.3%	
>$80 k	31.3%	23.6%	35.2%	
Child				
Female	49.7%	46.6%	51.4%	0.63
Age, mean years (SD)	10.8 (3.9)	10.2 (3.3)	11.1 (4.1)	0.17
Baseline timing, median days (25th and 75th percentile)	5.0 (2.0−8.0)	2.0 (1.0−5.0)	7.0 (3.0−14.0)	<0.01
Mean illness severity (SD)	8.5 (1.8)	8.4 (2.0)	8.6 (1.7)	0.82
Location of prior treatment				
Local	40.6%	48.3%	36.5%	<0.05
Referred	49.7%	36.2%	57.0%	
Unknown	9.7%	15.5%	6.5%	
HSCT Type				
Autologous	19.4%	6.9%	26.2%	<0.01
Allogeneic, related	30.9%	37.9%	27.1%	
Allogeneic, unrelated	49.7%	55.2%	46.7%	
Site				
MA	39.4%	13.8%	53.3%	<0.01
WS	12.7%	20.7%	8.4%	
TX	17.6%	39.7%	5.6%	
CA	17.0%	15.5%	17.8%	
PA	2.4%	6.9%	0.0%	
WA	10.9%	3.5%	15.0%	

[a]SD, standard deviation; [b]Five parents declined to provide information about their annual income.

prior to the child's hospitalization and the initiation of the child's preparative regimen for HSCT (7 or more days before the HSCT) than if they were recruited during the preparative regimen (6 days or fewer before the HSCT, baseline timing, $P < 0.001$). Completers (n = 107) and non-completers (n = 58) also differed by recruitment site, reflecting different rates of recruitment and local practices with respect to pre-transplant work up, and geographic relocation (location of prior treatment). Compared to non-completers, parental completers were more highly educated (mean 14.3 years (SD = 2.1) vs. 13.1 years (SD = 2.4, $P < 0.01$) and were more likely to be Caucasian (86% versus 71%, $P < 0.01$). Moreover, a significantly higher proportion of parents whose children were scheduled to receive autologous HSCT completed the interview (87.5%) compared to parents of allogeneic HSCT recipients (56.9% for related and 61.0% for unrelated, $P < 0.01$). However, there was no difference in overall childhood severity of illness between the parents who participated and those who did not (8.6 (SD = 1.7) vs. 8.4 (SD = 2.0), $P = 0.82$).

Parent Reports of Children's Diagnoses at Baseline and 12 Months

Overall, 45 of 107 (42%) children were identified from the parental BE as having met criteria for one or more diagnoses at baseline; threshold diagnoses (n = 27) were more common than subthreshold (n = 18) ones (60% versus 40%, $P < 0.01$). While mothers were more likely to endorse a diagnosis than fathers ($P < 0.01$), there were no differences in rates of diagnosis by parental education, race/ethnicity, family income, child gender, or study site. These results are summarized in Table II.

Table III summarizes the rates of threshold and subthreshold psychiatric diagnoses within each diagnostic group, based on parent and child report by time. According to parents at baseline, anxiety was the most prevalent diagnosis (29.0%), followed by adjustment disorder (11.2%) and mood (10.3%). Anxiety was also at the most prevalent diagnosis at 12 months (27.8%), followed by adjustment disorder (13.9%), and mood (13.9%).

TABLE II. Demographic and Clinical Characteristics of Study Participants by Any Diagnosis as Reported by the Parental KID-SCID

	Any baseline diagnosis			
Characteristics	No/indeterminate (n = 62)[a]	Subthreshold (n = 18)	Threshold (n = 27)	*P*-value
Parent				
Female	77.4%	100.0%	96.3%	<0.01
Age, mean years (SD)[b]	39.0 (6.3)	38.7 (7.7)	39.2 (7.5)	0.95
Race/ethnicity				
White	82.3%	88.9%	92.6%	0.84
Black	0.0%	0.0%	0.0%	
Asian	3.2%	0.0%	0.0%	
Other	14.5%	11.1%	7.4%	
Education, mean years (SD)	14.5 (1.9)	14.0 (2.4)	14.1 (2.3)	0.77
Annual income[c]				
<$20 K	6.6%	11.1%	11.5%	0.23
$20–40 K	26.2%	11.1%	11.5%	
>$40–60 K	24.6%	11.1%	26.9%	
>$60–80 K	14.8%	22.2%	3.9%	
>$80 K	27.9%	44.4%	46.2%	
Child				
Female	53.2%	55.6%	46.2%	0.74
Age, mean years (SD)	11.2 (4.0)	10.4 (4.5)	11.2 (4.3)	0.76
Baseline timing, median days (25th-75th percentile)	7.0 (3.0−14.0)	5.5 (4.0−8.0)	8.0 (4.0−23.0)	0.32
Illness severity, mean (SD)	8.3 (1.8)	8.8 (1.4)	9.0	0.08
Prior treatment	72.6%	66.7%	77.8%	0.75
Local	32.3%	38.9%	44.4%	0.27
Referred	56.5%	61.1%	55.6%	
Unknown	11.3%	0.0%	0.0%	
HSCT type				
Autologous	17.7%	44.4%	33.3%	0.12
Allogeneic, related	32.3%	11.1%	25.9%	
Allogeneic, unrelated	50.0%	44.4%	40.7%	
Site				
MA	50.0%	55.6%	59.3%	0.52
WS	9.7%	11.1%	3.7%	
TX	6.5%	5.6%	3.7%	
CA	14.5%	27.8%	18.5%	
PA	0.0%	0.0%	0.0%	
WA	19.4%	0.0%	14.8%	

[a]Could not be determined with available information, n = 6; [b]Eight parents declined to disclose their ages, SD = standard deviation; [c]Two parents declined to disclose their annual income.

TABLE III. Threshold and Subthreshold Psychiatric Diagnosis Based on Parental and Child KID-SCID Report by Time

Diagnosis	Parent baseline (n = 107)	12-month F-U[a] (n = 79)	Child baseline (n = 59)	12-month F-U (n = 59)
Any current mood diagnosis, n (%)				
Threshold or subthreshold	11 (10.3%)	11 (13.9%)	4 (6.8%)	2 (3.4%)
Threshold	4 (3.7%)	8 (10.1%)	3 (5.1%)	2 (3.4%)
Subthreshold	7 (6.5%)	3 (3.8%)	1 (1.7%)	0 (0.0%)
Indeterminate	1 (0.9%)	1 (1.3%)	0 (0.0%)	2 (3.4%)
Any current anxiety diagnosis, n (%)				
Threshold or Subthreshold	31 (29.0%)	22 (27.8%)	10 (16.9%)	6 (10.2%)
Threshold	16 (15.0%)	13 (16.5%)	4 (6.8%)	3 (5.1%)
Subthreshold	15 (14.0%)	9 (11.4%)	6 (10.2%)	3 (5.1%)
Indeterminate	6 (5.6%)	3 (3.8%)	11 (18.6%)	5 (8.5%)
Adjustment disorder, n (%)				
Threshold or subthreshold	12 (11.2%)	11 (13.9%)	1 (1.7%)	4 (6.8%)
Threshold	9 (8.4%)	8 (10.1%)	1 (1.7%)	4 (6.8%)
Subthreshold	3 (2.8%)	3 (3.8%)	0 (0.0%)	2 (3.4%)
Indeterminate	1 (0.9%)	0 (0.0%)	4 (6.8%)	1 (1.7%)

[a]F-U, follow-up.

According to child report, anxiety was the most prevalent diagnosis at baseline (16.9%), followed by any current mood diagnosis (6.8%) and then by adjustment disorder (1.7%). While anxiety diagnoses continued to be the most prevalent (10.2%) condition at 12-month follow-up, adjustment disorder (6.8%) became more frequent than any current mood diagnosis (3.4%). While the proportion of threshold and subthreshold diagnoses varied both by time and diagnostic group (i.e., threshold vs. subthreshold), these differences were not statistically significant for either rater (Fisher exact test, P = NS).

Parent Reports of Children's Specific Disorders at Baseline and 12 Months

Table IV summarizes the prevalence of specific disorders by child age group at baseline and 12 months. There were no significant differences in mood or adjustment disorders by age group at either time point. However, this was not the case within the anxiety modules, where parents of younger children (i.e., ages 5–12 years) reported higher rates of separation anxiety (9.4% subthreshold and 6.3% threshold vs. 0.0% subthreshold and 2.3% threshold, $P < 0.05$) and specific phobia (6.6% subthreshold and 13.1% threshold vs. 4.7% subthreshold and 0.0% threshold, $P < 0.05$) at baseline than parents of children aged 13–18 years old. These differences were not observed at 12 months. Differences in the distribution of threshold and substhreshold diagnoses are also presented (Table IV).

Persistence of Parent Reports of Aggregate Diagnoses From Baseline to 12 Months

Sixty-nine parents completed the KID-SCID at both baseline and 12 months. The proportion of children with any of the diagnoses at either time period did not differ significantly. At baseline, 40 (58.0%) children had no diagnosis, while 39 (56.5%) had no diagnosis at 12 months. Of the 29 children with a diagnosis at baseline, 17 (58.6%) of the children's diagnoses persisted to 12-month follow-up. In addition to these 17 children, 13 children met criteria for a diagnosis at 12 months for a total of 30 (McNemar test, $P = 0.84$).

Parent/Child Agreement at Baseline and 12 Months

Table V summarizes the extent of agreement between parent and child report on the presence of psychiatric distress in the children at baseline and at 12 months for mood and/or anxiety diagnoses or adjustment disorder. Overall, the agreement between the child self-reports and parents' reports about their children varied by diagnosis and time. At baseline, the strength of agreement for mood diagnoses ($\kappa = 0.39$, 95%CI = −0.02, 0.79) and adjustment disorder ($\kappa = 0.31$, 95%CI = −0.16, 0.78) was fair, but poor for anxiety diagnosis ($\kappa = -0.18$, 95%CI = −0.33, −0.02). Discordance occurred in both directions. Eleven children endorsed an anxiety disorder when the parent did not and six parents endorsed an anxiety disorder when the child did not. Of note, these were evenly distributed across threshold and subthreshold diagnoses. At 12 months, parent–child agreement was moderate for mood ($\kappa = 0.41$, 95%CI = 0.02, 0.80) and fair for anxiety ($\kappa = 0.31$, 95%CI = −0.04, 0.66), but only slight for adjustment disorders ($\kappa = 0.03$, 95%CI = −0.17, 0.23).

DISCUSSION

This study reports on the rates of emotional and psychological symptoms meeting subthreshold and threshold diagnostic criteria in children undergoing HSCT from the perspective of both children and their parents (typically mothers). Whereas both older and younger children had similar rates of mood and adjustment disorders at both times, younger children had significantly higher rates of specific anxiety disorders before HSCT. This finding is especially noteworthy since anxiety in pre-adolescent children in general has been thought to be common, but relatively understudied and unappreciated [14]. Because of their developmental stage, younger children may have particular difficulty with separation anxiety [5]. The consequences of depression and anxiety in medically ill children include the disability and morbidity that is associated with psychiatric illness in any patient; but medically ill children constitute a special, high-risk group [15]. As such, recognition is important as psychiatric symptoms can affect quality of life and other treatment outcomes [16].

TABLE IV. Parent KID-SCI Report of Specific Psychiatric Disorders by Child Age Group and Time

	Total (n = 107)		Age 5–12 (n = 64)		Age 13–18 (n = 43)		
Baseline	Subthreshold	Threshold	Subthreshold	Threshold	Subthreshold	Threshold	*P*-value
Mood							
Major depressive episode	5.7%	0.9%	6.3%	0.0%	4.8%	2.4%	0.64
Dysthymia	0.9%	2.8%	1.6%	1.6%	0.0%	4.8%	0.74
Substance-induced mood	n/a	0.0%	n/a	0.0%	n/a	0.0%	n/a
Due to a Gen Med condition[a]	0.0%	0.0%	0.0%	0.0%	0.0%	0.0%	n/a
Anxiety							
Separation anxiety	5.6%	4.7%	9.4%	6.3%	0.0%	2.3%	<0.05
Specific phobia	5.8%	7.7%	6.6%	13.1%	4.7%	0.0%	<0.05
Obsessive compulsive	1.0%	1.0%	0.0%	0.0%	0.0%	2.4%	0.66
Panic disorder	0.0%	1.0%	1.6%	0.0%	2.3%	0.0%	1.00
Generalized anxiety	1.9%	0.0%	1.6%	0.0%	2.3%	0.0%	1.00
Social phobia	5.6%	1.9%	6.3%	1.6%	4.7%	2.3%	1.00
PTSD[b]	0.9%	1.9%	1.6%	1.6%	0.0%	2.3%	1.00
Agoraphobia	0.0%	0.0%	0.0%	0.0%	0.0%	0.0%	n/a
Adjustment disorder	2.8%	8.5%	4.8%	7.9%	0.0%	9.3%	0.48

	Total (n = 79)		Age 5–12 (n = 51)		Age 13–18 (n = 28)		
12 month follow-up	Subthreshold	Threshold	Subthreshold	Threshold	Subthreshold	Threshold	*P*-value
Mood							
Major depressive episode	1.3%	5.1%	2.0%	5.9%	0.0%	3.6%	1.00
Dysthymia	2.6%	3.9%	4.0%	2.0%	0.0%	7.1%	0.37
Substance-induced mood	n/a	1.3%	n/a	0.0%	n/a	3.6%	0.35
Due to a Gen Med condition	0.0%	0.0%	0.0%	0.0%	0.0%	0.0%	n/a
Anxiety							
Separation anxiety	5.2%	5.2%	6.0%	8.0%	3.7%	0.0%	0.50
Specific phobia	3.8%	8.9%	3.9%	9.8%	3.6%	7.1%	1.00
Obsessive compulsive	2.5%	1.3%	3.9%	0.0%	0.0%	3.6%	0.27
Panic disorder	0.0%	2.6%	0.0%	0.0%	0.0%	7.4%	0.12
Generalized anxiety	1.3%	0.0%	0.0%	0.0%	3.6%	0.0%	0.35
Social phobia	1.3%	1.3%	2.0%	2.0%	0.0%	0.0%	1.00
PTSD	2.6%	0.0%	0.0%	0.0%	7.1%	0.0%	0.13
Agoraphobia	0.0%	0.0%	0.0%	0.0%	0.0%	0.0%	n/a
Adjustment disorder	3.8%	10.1%	5.9%	9.8%	0.0%	10.7%	0.66

[a]Disorder due to a general medical condition; [b]PTSD, post-traumatic stress disorder.

TABLE V. Extent of Agreement between Child and Parent KID-SCID Report by Psychiatric Diagnosis by Time

	Child rating							
	Baseline				12-month follow-up			
Parent rating	None	S/T[a]	Threshold	κ (95%CI)	None	S/T	Threshold	κ (95% CI)
Any mood diagnosis				0.39 (−0.02, 0.79)				0.41 (0.02, 0.80)
None	47	0	2		43	0	0	
S/T	3	0	0		2	0	0	
Threshold	0	1	1		4	0	2	
Any anxiety diagnosis				−0.18 (−0.33, −0.02)				0.31 (−0.04, 0.66)
None	22	4	4		35	2	1	
S/T	5	0	0		3	1	0	
Threshold	6	1	0		4	0	2	
Adjustment disorder				0.31 (−0.16, 0.78)				0.03 (−0.17, 0.23)
None	47	0	0		43	1	2	
S/T	0	0	0		1	0	0	
Threshold	4	0	1		5	1	0	

[a]S/T, sub-threshold.

Our findings mirror other studies of children with cancer which have noted that there tends to be a substantial subset of children and adolescents (often estimated to be 15–30%) who exhibit psychological problems at one time or another and are in need of more intensive psychosocial intervention. They are distinct from the majority of children and families who are distressed, but also show signs of resilience [17].

When the children's reports were compared to their parents' reports, some interesting patterns were observed. First, although parents and children had the highest rates of agreement with respect to mood and adjustment disorders experienced by the children before HSCT, the strength of agreement was only fair when chance was taken into account. Parents and children had even less agreement for anxiety disorders before HSCT. After HSCT, parents and children had the least agreement on the presence of adjustment disorders.

The discordance between child and parent reporters is consistent with other studies, but the explanation remains speculative [18,19]. Parents and children may have access to different information with which to formulate their reports (information variance) and/or may interpret the information differently (criterion variance). Another possible explanation includes the parent's own emotional state, which we and others have shown to be related to ratings of the child's well-being [8,20,21]. For example, a parent's perception of anxiety in his/her child may reflect his/her own anxiety.

There is no ready method to remedy the discrepancies between child and parent report about the child's symptoms. If we assume that the children are in many instances accurate reporters of their own situation, it is then important that parents not be the sole informants about the child's emotional state. At the same time, parents may well be more aware than the child of distress in some of the children, underscoring the need to include their evaluations. Hence, multiple perspectives are desirable when evaluating children undergoing HSCT so that those most at risk for current or later problems are identified and offered preventive psychological interventions.

The apparent necessity of such multiple perspectives, however, does complicate evaluation of the psychological consequences of HSCT. If both parent and child reports are accurate and valid representations of their different experiences, then assessment efforts need to focus on understanding these perspectives and the important information they contain rather than trying to determine which one is the most accurate. By providing a window into the different experiences of children and parents, understanding more about the differences in parent and child reports may be useful information for understanding how parents and children adapt to the highly stressful demands of HSCT and recovery. Reliance on one informant alone may result in missed opportunities for providers to intervene [22].

A major strength of this study is the use of structured diagnostic interviews to obtain responses directly from the children themselves, as well as from their parents. As such, it was possible to evaluate the comparative significance of the psychiatric symptoms using diagnostic criteria. Given the importance of clinical judgment in the conduct and interpretation of the interviews, we required formal training of interviewers and the oversight and review of *all* interviews by a senior psychiatrist. These steps both contributed to achieving the highest possible accuracy in reporting.

Subthreshold and threshold diagnoses were both reported to more accurately reflect the distress in this cohort. Subthreshold diagnoses were included because extensive research in other patient groups has confirmed their clinical significance [23]. For example, subthreshold depression in older adults, women, and those receiving primary care has been significantly associated with decreased quality of life, increased risk of subsequent depression meeting diagnostic criteria, increased morbidity, and other impairments of clinical importance [24–29]. The increased risk of subsequent depression among those with subthreshold disease was likewise confirmed in a population study of 8,622 people aged 20–64 [24]. Similarly, the association between subthreshold anxiety disorders and subsequent anxiety problems reaching diagnostic criteria has been described [24]. While approximately 40% of the identified cases did not meet DSM criteria for threshold diagnosis in our study, principally due to subclinical levels of impairment, they do represent substantial emotional distress within the population, warranting close monitoring and possible intervention. In addition, we encountered cases in which the disorder could not be ruled in or out with sufficient certitude in the course of the interview. In clinical application, both the indeterminate and subthreshold cases would be monitored over time to ensure that the children were receiving the kind of care they may need.

Potential limitations to the generalizability of study findings include several characteristics of the sample. While more than half of participants were recruited from the Boston site, which had the highest overall enrollment in the study, endorsement of psychiatric disorders did not vary by site. In addition, although participating parents were better educated than those who declined to participate, the endorsement of diagnosis did not differ by parent educational level. The interview was presented as an optional assessment; 35% declined to participate. It appeared that a higher proportion of parents whose children were scheduled to receive allogeneic HSCT declined to participate when compared to those parents associated with the autologous procedure. Possible explanations include the common perception that allogeneic procedures are more difficult and so parents did not want to undertake an additional obligation. Finally, changes in frequency of diagnoses are described in the aggregate. Hence, individual differences for understanding the meaning of these changes are not available.

Future studies are needed to address the long-term impact of HSCT on pediatric survivors to determine both the proportion of survivors with emotional distress who could be identified from the initiation of the transplant and the role of interventions to mitigate that distress. While a growing body of research in pediatric cancer (see reviews by References [30–32]) has indicated the lack of serious psychopathology in many survivors, and in some children even evidence of growth and resiliency, several studies have indicated that a small but important minority of children and adolescents have continued psychological distress and other symptoms beyond the period of active treatment [33–35]. The exploration of these findings and their possible confirmation within the HSCT population would be extremely important to determine who is at risk for emotional distress and how best to care for them.

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