Prevalence and predictors of symptoms of anxiety and depression, and comorbid symptoms of distress in parents of childhood cancer survivors and bereaved parents five years after end of treatment or a child’s death

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ABSTRACT

Background: Symptoms of anxiety and depression and their comorbidity in parents of children diagnosed with cancer, particularly later in the cancer trajectory, need further study. The aim was to investigate the prevalence and predictors of symptoms of anxiety and depression in parents of childhood cancer survivors and bereaved parents, five years after end of treatment or a child’s death and to investigate comorbidity between symptoms of anxiety, depression and posttraumatic stress.

Material and methods: Participants were 132 parents (68 mothers, 64 fathers) of survivors and 37 bereaved parents (20 mothers, 17 fathers). Chi-square test and t-test were used to explore differences in symptoms of anxiety and depression. Comorbidity was explored using Pearson’s correlations and Chi-square test. Multivariable hierarchical linear regressions were used to identify predictors of symptoms of anxiety and depression.

Results: In parents of survivors, 20% reported anxiety and 14% reported depression. Corresponding figures among bereaved parents were 30% and 35%. Among parents of survivors reporting clinically relevant anxiety and depression, a larger proportion were mothers than fathers. No such difference was found among bereaved parents. Symptoms of anxiety, depression and posttraumatic stress were highly correlated (all r ≥ 0.65, p < .001). Comorbid symptoms were reported by 7–11% of parents of survivors and 14–24% of bereaved parents. In multivariable analyses, more severe symptoms of depression were associated with anxiety, posttraumatic stress and distress related to previous stressful life events. Being a mother, symptoms of depression and posttraumatic stress were associated with more severe symptoms of anxiety.

Conclusion: A subset of parents report clinically elevated symptoms of anxiety and depression, comorbid anxiety, depression and posttraumatic stress. Experiencing distress related to previous stressful life events as well as concurrent comorbidity were associated with more severe psychological distress at five years after end of treatment/a child’s death. These results deserve further attention in research and clinical care.

Introduction

In recent decades, the prognosis of childhood cancer has improved significantly in developed countries, with the overall five-year survival rate reaching 80% [1,2]. Although the increased survival rate reflects ongoing treatment successes for a variety of pediatric cancers, there is an increasing prevalence of morbidity in those ≥5 years after diagnosis, including impaired health status and neurocognitive dysfunction [3]. Further, attention has been directed towards the link between parental factors and children’s long-term outcomes as recent studies suggest that parental distress is associated with negative effects on children’s psychological adjustment and quality of life [4–6].

The literature on parental distress demonstrate elevated levels, relative to norms and controls, at the time of diagnosis and that parental distress decline over time [7–12]. Yet, studies have highlighted persisting long-term distress in a subgroup of parents of pediatric cancer survivors [8,9,12–14]. Following a pediatric cancer diagnosis, studies have shown that parents experience symptoms of distress including anxiety, concentration difficulties, feelings of guilt, pessimism, posttraumatic stress symptoms (PTSS), sadness and sleep disorders [15,16]. The completion of cancer treatment is a significant milestone for families [15]. For parents, the off-treatment phase includes celebrations [17] as well as positive changes in self, relationships with others and plans for the future [18]. However, elevated levels of distress including disease-related thoughts and feelings, fatigue, fear of recurrence, loneliness, marital strain and worry have been described [8,15]. Risk factors for distress in parents include disease severity, treatment intensity, being a mother, negative affectivity and poor personal resources and family stressors or weaknesses before the diagnosis [6].
In pediatric oncology, PTSS and posttraumatic stress disorder (PTSD) have received significant attention [19]. Studies indicate that parents report a higher level of PTSS than the children themselves at the time of the diagnosis [20]. In a previous study we found that 19% and 8% of mothers and fathers of survivors and 20% and 35% of bereaved mothers and fathers, reported at least partial PTSD, five years after the end of treatment or a child’s death [12]. Although there is a growing body of research on parental distress such as PTSS following pediatric cancer, the prevalence and predictors of symptoms of anxiety and depression in the long-term among parents are less well understood. Moreover, although the comorbidity between anxiety and mood disorders is well known, the comorbidity between anxiety and depression has, to our knowledge, not been clarified in parents of long-term survivors of childhood cancer and bereaved parents. Comorbidity is associated with worse health outcomes and greater demands of clinical management, making early recognition of comorbidity important. In addition, the general literature on depression, parenting practices and child development indicates worse outcomes in children of parents who have comorbid psychiatric conditions [21]. The aim of the present study was to examine the prevalence and predictors of symptoms of anxiety and depression in mothers and fathers of childhood cancer survivors and in bereaved parents five years after the end of treatment or a child’s death and to explore comorbidity between symptoms of anxiety and depression and partial PTSD.

Methods

Participants and procedure

Data from a Swedish prospective longitudinal study aiming at investigating psychological and economic consequences of childhood cancer for parents were used in the present study. Participants were parents of children diagnosed with cancer during an 18-month period between 2002 and 2004 with follow-up until 2013. In this multicenter study, children were treated at four of the six pediatric oncology centers in Sweden and parents were included via each hospital according to the following criteria: Swedish and/or English-speaking parent of a child (0–18 years at study-start), with a primary cancer diagnosis (<14 days), scheduled for chemotherapy and/or radiotherapy (not applicable to CNS tumors) and with access to a telephone. Parents who met the inclusion criteria were provided with written and oral information about the study by a coordinating nurse at the respective center within the first two weeks after the child’s diagnosis. The same nurse asked parents for oral informed consent to participate and permission to be contacted over the telephone by a research assistant. The project included seven assessments: ≤14 days (T1), two months (T2) and four months (T3) post diagnosis, one week after end of treatment (at the time considered successful by the responsible oncologist) or six months after end of stem cell transplantation (T4), three months following end of treatment or nine months after end of stem cell transplantation or the child’s death (T5), one year after end of treatment or 18 months after stem cell transplantation or the child’s death (T6), five years after end of treatment, stem cell transplantation or the child’s death (T7). Data were collected via telephone.

Two hundred and fifty-nine of 352 eligible parents participated at T1. Data on symptoms of anxiety and depression were collected at T7 only. One hundred and sixty-nine parents who participated at T1 and T7 (65%) were included for the purposes of the present analyses. Non-responders at T7 were more likely to report lower educational level at T1 (χ² = 10.8, p = .005) and had no other children at T1 than the child diagnosed with cancer (χ² = 8.6, p = .014). There were no differences between non-responders and responders at T7 on age, sex, marital status or child’s diagnosis at T1. A detailed description of study enrollment has been presented previously [12]. Ethical approval was obtained from the local research ethics committees in 2002 (DNR: 2002-006) and from the Regional Ethical Review Board in Uppsala in 2008 (DNR: 2008/109). Oral informed consent was obtained from all participants.

Measures

Sociodemographic and clinical variables

Information on parents age at T1 and T7 (categorized as <30, 30–39 and ≥40) and education level at T1 (defined as nine years, upper secondary and university) and the child’s age at T1 and T7 (categorized as 0–3, 4–7, 8–12 and 13–18), sex (defined as girl, boy) and number of siblings at T1 (categorized as 0, 1–2 and ≥3) were obtained via telephone. Clinical information on the child’s diagnosis (categorized as ‘leukemia’, ‘CNS tumor’ or ‘other solid tumor’) was gathered from medical charts. Information on parents marital status (defined as married, single, non-cohabitating partner) were obtained via telephone at T7.

Psychological variables

Anxiety was assessed using the Beck Anxiety Inventory (BAI) [22]. The instrument includes 21 items. Each item has four statements, which describe symptom severity along an ordinal scale from absent or mild (a score of 0) to severe (a score of 3). The total score ranges from 0–63. According to the scoring manual, scores of 0–7 indicate minimal, 8–15 mild, 16–23 moderate and 24–63 severe anxiety. Scores ≥8 were used as cut-off in the present analyses to indicate clinically relevant anxiety [23]. In addition, the BAI was analyzed as a continuous variable. The BAI has shown good test-retest reliability and convergent validity [22].

Depression was assessed using the 21-item Beck Depression Inventory-Second Edition (BDI-II) [24]. Each item has four statements describing symptom severity along an ordinal scale from absent or mild (a score of 0) to severe (a score of 3). The total score ranges from 0–63. According to the scoring manual, scores of 0–13 indicate minimal symptoms of depression, 14–19 mild, 20–28 moderate and 29–63 severe depression. Scores ≥14 were used as cut-off in the present analyses to indicate clinically relevant depression [24,25]. In addition, the BDI-II was analyzed as a continuous variable.
The BDI-II has shown good test-retest reliability [25] and convergent validity [26]. The PTSD Checklist Civilian Version (PCL-C) [27] was used to assess PTSS and the prevalence of partial PTSD. Partial PTSD is an important diagnostic entity in populations exposed to serious illness, associated with comorbid psychiatric symptoms almost to the same extent as full PTSD [28]. The PCL-C consists of 17 items corresponding to the B (reexperiencing), C (avoidance/numbing) and D (hyper-arousal) criteria in the DSM-IV. Items are scored on a five-point scale, ranging from 1 (not at all) to 5 (extremely), with a total score ranging from 17–85. Items are designed to indicate how much the respondent has been bothered by each symptom during the last month. Partial PTSD was defined by a score of ≥3 on at least one symptom of reexperiencing, avoidance and hyper-arousal [29]. The PCL-C was also analyzed as a continuous variable. The PCL-C has shown good test-retest reliability and convergent validity in populations with mixed civilian trauma exposure [30] as well as among nonclinical samples [31].

Information on previous stressful life event/s and whether parents were currently experiencing distress in relation to this/those event/s was gathered via telephone at T7 using the questions; ‘Have you previously experienced one or more stressful life event/s, unrelated to your child’s cancer disease’ (no or yes) and ‘Are you presently affected by this/these previous event/s?’ (no or yes).

### Statistical analyses

Standard descriptive statistics were calculated to present parent and child characteristics. Parents responses to the BAI, BDI-II and PCL-C are reported as means and standard deviations (SD) for total scores on each scale and as numbers (n) and proportions (%) of parents responding above cutoff on each measure. Potential differences in anxiety, depression, PTSS and partial PTSD between mothers and fathers were analyzed using independent samples t-test or Chi-square test for parents of survivors and bereaved parents, respectively. Pearson’s correlations were carried out to explore comorbidity. Chi-square test was used to explore differences in clinically relevant comorbid symptoms, that is, the proportion of parents responding above cut-off on two or more measures. Two multivariable hierarchical linear regressions were conducted to identify independent predictors of symptoms of anxiety and depression at T7. Two models were tested. Model 1 included parent sex and age at diagnosis, child age at diagnosis, whether parents were bereaved or parents of a survivor and previous stressful life events. In Model 2, parent sex and age at diagnosis, child age at diagnosis, whether parents were bereaved or parents of a survivor and previous stressful life events were entered at step 1 and psychological factors (i.e., currently experiencing distress related to previous stressful life events, concurrent PTSS and symptoms of anxiety or depression) at step 2, to account for comorbid symptoms and distress on symptoms of anxiety and depression, respectively. $R^2$, $\Delta R^2$ and standardized regression coefficients ($\beta$) with standard errors (SE) are also presented.

### Results

#### Descriptive statistics

Among 169 parents of 96 children, 132 (78.1%) were parents of survivors and 37 (21.9%) were bereaved. At T7, 74 (77.0%) children were alive and 22 (23.0%) were deceased. Parent and child characteristics are presented in Table 1. Among parents of survivors, 86 (65.2%) reported previous stressful life event/s unrelated to the child’s cancer disease and 43 (32.6%) reported currently experiencing distress in relation to this/these event/s. Among bereaved parents, 30 (81.1%) had experienced previous stressful life event/s unrelated to the child’s cancer disease and 11 (29.7%) reported currently experiencing distress in relation to this/these event/s.

### Prevalence of symptoms of anxiety and depression and comorbid symptoms

#### Anxiety

The mean anxiety score was 4.6 (SD = 6.1) among parents of survivors. Mothers of survivors reported more symptoms (mean = 6.2, SD = 6.8) than did fathers of survivors (mean = 2.9, SD = 4.8) ($t_{130} = -3.115$, $p < .05$). The majority reported no symptoms of anxiety ($n = 106, 80.3\%$) whereas one fifth ($n = 26, 19.7\%$) reported symptoms above cut-off (Table 2). Among those reporting symptoms above cut-off ($n = 26$), a larger proportion were mothers (69.2%) than fathers (30.8\%); $\chi^2 = 4.1, p < .05$.

The mean anxiety score among bereaved parents was 6.7 (SD = 7.8). Although the majority of bereaved parents reported no anxiety ($n = 24, 64.9\%$), more than one-third reported symptoms of anxiety above cut-off ($n = 13, 35.1\%$; Table 2). There was no difference between bereaved mothers (mean = 6.8, SD = 5.9) and bereaved fathers (mean = 6.6, SD = 9.7) ($t_{135} = -0.059$, $p > .05$) or in the proportion of mothers (61.5%) and fathers (38.5%) reporting symptoms above clinical cut-off among those ($n = 13$) reporting scores above cut-off ($\chi^2 = 0.5, p > .05$).

#### Depression

The mean score on the BDI-II was 6.0 (SD 6.9) for parents of survivors. Mothers of survivors (mean = 7.3, SD = 7.9) reported more symptoms of depression than fathers of survivors (mean = 4.5, SD = 5.2) ($t_{130} = -2.4, p < .05$). The majority reported no symptoms of depression ($n = 113, 85.6\%$) whereas 14.4% ($n = 19$) reported symptoms of depression above cut-off (Table 2). Among parents of survivors who reported symptoms above cut-off ($n = 19$) a greater proportion were mothers (78.9%) than fathers (21.1%) ($\chi^2 = 6.7, p < .05$).

Among bereaved parents, the mean score on the BDI-II was 9.7 (SD 9.9). Nearly 30% ($n = 11, 29.7\%$) reported symptoms of depression above cut-off and 70.3% ($n = 26$) reported no symptoms of depression (Table 2). There was no difference between bereaved mothers (mean = 8.7, SD = 7.4) and bereaved fathers (mean = 10.9, SD = 12.3) at T7 ($t_{375} = .666, p > .05$), nor in the proportion of mothers...
and fathers (45.5%) reporting symptoms above cut-off among the 11 bereaved parents with scores above cut-off ($\chi^2 = 0.002$, $p > .05$).

**Comorbid symptoms**

Symptoms of anxiety, depression and PTSS were highly correlated at T7. The correlation between symptoms of anxiety and depression was 0.67 ($p < .001$), anxiety and PTSS was 0.71 ($p < .001$) and depression and PTSS was 0.76 ($p < .001$), among parents of survivors. In bereaved parents, the correlation between anxiety and depression was 0.79 ($p < .001$), anxiety and PTSS was 0.73 ($p < .001$) and depression and PTSS was 0.65 ($p < .001$).

In parents of survivors, 15 (11.4%) reported symptoms of anxiety and depression above cut-off, 10 (7.6%) reported symptoms of anxiety above cut-off and partial PTSD, and nine (6.8%) reported symptoms of depression above cut-off and partial PTSD. Nine parents reported symptoms of anxiety and depression above cut-off and partial PTSD (6.8%) (Table 2). Mothers of survivors were more likely to report comorbid symptoms above cut-off than were fathers of survivors (all $p < .05$).

Among bereaved parents, nine (24.3%) reported symptoms of anxiety and depression above cut-off, five (13.5%) reported symptoms of depression above cut-off and partial PTSD and seven (18.9%) reported symptoms of anxiety above cut-off and partial PTSD. Five (13.5%) parents reported symptoms of anxiety and depression above cut-off and partial PTSD (Table 2). There were no differences in the proportion of bereaved mothers and fathers reporting comorbid symptoms.

**Predictors of psychological distress**

The hierarchical multivariable regression analysis revealed that after controlling for parent and child age at diagnosis and bereavement, symptoms of anxiety at T7 were predicted by parental age and marital status at T7. It was found that age at diagnosis of the child and number of siblings were also significant predictors of psychological distress.

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**Table 1. Sample characteristics.**

| Parent characteristics | Parents of survivors | Bereaved parents |
|------------------------|----------------------|-----------------|
| Parents, total         | 132 (78.1)           | 37 (21.9)       |
| Mothers                | 68 (51.5)            | 20 (54.1)       |
| Fathers                | 64 (48.5)            | 17 (45.9)       |
| Age (years), T1        | 38.9 (6.6)           | 37.1 (7.5)      |
| <30                    | 12 (9.1)             | 5 (13.5)        |
| 33–39                  | 67 (50.8)            | 20 (54.1)       |
| ≥40                    | 53 (40.2)            | 12 (32.4)       |
| Age (years), T7a       | 45.3 (6.4)           | 43.3 (7.6)      |
| <30                    | –                    | 1 (2.7)         |
| 33–39                  | 23 (18.2)            | 11 (29.7)       |
| ≥40                    | 105 (79.5)           | 20 (54.1)       |
| Marital status, T7     |                      |                 |
| Married/cohabitating   | 112 (84.8)           | 33 (89.2)       |
| Single                 | 11 (3.0)             | 3 (8.1)         |
| Non-cohabitating partner | 9 (6.8)             | 1 (2.7)         |
| Education level, T1    |                      |                 |
| Nine years             | 16 (12.1)            | 4 (10.8)        |
| Upper secondary        | 64 (48.5)            | 18 (48.6)       |
| University             | 50 (37.9)            | 14 (37.8)       |
| Not stated             | 2 (1.5)              | 1 (2.7)         |

| Child characteristics | Survivors | Deceased children |
|----------------------|-----------|--------------------|
| Children, total      | 74 (77.0) | 22 (23.0)         |
| Girl                 | 35 (47.3) | 10 (45.5)         |
| Boy                  | 39 (52.7) | 12 (54.5)         |
| Age (years), T1      | 7.8 (5.1) |                    |
| 0–3                  | 20 (27.0) | 7 (31.8)          |
| 4–7                  | 23 (31.1) | 5 (22.7)          |
| 8–12                 | 17 (23.0) | 6 (27.3)          |
| 13–18                | 14 (18.9) | 4 (18.2)          |
| Age (years), T7b     | 14.2 (5.0) |                 |
| 4–7                  | 8 (10.8)  | –                 |
| 8–12                 | 25 (33.8) | –                 |
| 13–18                | 40 (54.0) | –                 |
| Number of siblings, T1 |         |                   |
| 0                    | 6 (8.1)   | 2 (9.1)           |
| 1–2                  | 55 (74.3) | 17 (77.3)         |
| ≥ 3                  | 13 (17.6) | 3 (13.6)          |
| Diagnosis            |           |                   |
| Leukemia             | 27 (36.5) | 7 (31.8)         |
| CNS tumor            | 6 (8.1)   | 5 (22.7)          |
| Other solid tumor    | 41 (55.4) | 10 (45.5)         |

*Missing: parents of survivors $n = 3$, bereaved parents $n = 5$.

*Missing: survivors $n = 1$.

$n$: number; SD: standard deviation.
by female sex ($\beta = 0.166$, $p = 0.042$) and previous stressful life event/s ($\beta = 0.162$, $p = 0.038$; Table 3, Model 1), the model accounting for 8.5% of the variance ($R^2 = 0.085$, $F(5,161) = 2.999$, $p = 0.013$). The psychological factors (Model 2, Step 2) accounted for an additional 52% of the variance ($\Delta R^2 = 0.520$) and the complete model explained 60.5% of the variance in symptoms of anxiety ($R^2 = 0.605$, $F(8,158) = 30.210$, $p < 0.001$). Symptoms of depression ($\beta = 0.393$, $p = 0.001$) and PTSS ($\beta = 0.421$, $p = 0.001$) predicted symptoms of anxiety at T7. Female sex remained a significant predictor of symptoms of anxiety ($\beta = 0.115$, $p = 0.035$).

After controlling for parent age and sex and child age at diagnosis, symptoms of depression at T7 were predicted by previous stressful life event/s ($\beta = 0.244$, $p = 0.002$) and bereavement ($\beta = 0.159$, $p = 0.036$), the model accounting for 11.8% of the variance ($R^2 = 0.118$, $F(5,161) = 4.313$, $p = 0.001$, Table 4, Model 1). The psychological factors (Model 2, Step 2) accounted for an additional 52.3% of the variance ($\Delta R^2 = 0.523$), and the complete model explained 64.1% of the variance in symptoms of depression at T7 ($R^2 = 0.641$, $F(8,158) = 35.325$, $p < 0.001$). Symptoms of anxiety ($\beta = 0.357$, $p = 0.001$), PTSS ($\beta = 0.387$, $p = 0.001$) and currently experiencing distress in relation to previous stressful life event/s ($\beta = 0.170$, $p = 0.005$) predicted symptoms of depression at T7.

### Discussion

This study investigated the prevalence and predictors of psychological distress in parents of children treated for cancer five years after end of treatment or a child’s death. A noteworthy proportion of parents reported a clinically relevant level of symptoms of anxiety and/or depression. Results support previous studies showing that a subset of parents report psychological distress in the long-term [8,9,32].

Around one-third of bereaved parents reported clinically relevant symptoms of anxiety and depression. The proportion appears to be higher than observed in the Swedish general population [33], whereas the corresponding proportion in parents of survivors appears similar to that of the Swedish population [34].
Among parents of survivors, mothers were more likely than fathers to report clinically relevant symptoms of anxiety and/or depression. This difference is in line with findings showing that mothers, more than fathers, are at risk for psychological distress following treatment completion [15,35], but in contrast to findings showing that differences between fathers and mothers level out over time [6]. Affective disorders and subclinical symptoms of anxiety and depression are reportedly more common in women than men in the general population [36,37] and may account for the differences found in this study between fathers and mothers of survivors. Another explanation may be that mothers tend to take more responsibility for childcare compared to fathers [38] and thus mothers are more exposed to the stressors associated with caring for the child. Alternatively, it may be that fathers, to a greater extent, remain connected to employment [39,40] and thus more easily reengage with employment once the child is well enough to be at home or following a child’s death. Connections to social networks and the respite that work allows may contribute to fathers experiencing lower levels of anxiety and depression than mothers [19,41]. However, in a previous study on the same sample, we did not observe any differences between mothers and fathers of survivors or between bereaved mothers and fathers with regard to work situation and sick leave at five years after end of treatment or a child’s death. Results did however show that the number of bereaved mothers who reported sick leave decreased between eighteen months and five years after a child’s death whereas there was an opposite trend observed for bereaved fathers [42].

When comparing the outcomes in mothers and fathers it is also important to bear in mind that self-reports of symptoms of anxiety and depression may reflect gender differences in reporting style and manner of expression than actual differences with regard to experienced distress [43,44]. Due to social and gender norms, it has been suggested that some men have greater difficulty in identifying and communicating their emotions [45]. In addition, the way distress was measured may be biased towards detecting symptoms that are more common in women than men, which can result in an increased likelihood of men’s mental health problems not being recognized [43]. This could at least partly explain the difference in distress between mothers and fathers of survivors. Further, it is interesting that no differences in symptoms of anxiety and depression were observed between bereaved mothers and fathers. In light of previous studies [43–45], it is conceivable that the similar proportions of clinically relevant symptoms of anxiety and depression in bereaved mothers and fathers in fact signifies more distress among bereaved fathers than bereaved mothers. Taken together, the similar level of distress among bereaved fathers and bereaved mothers deserves careful consideration and further exploration. Future studies need to consider how distress experienced by fathers should be conceptualized and measured.

A minority of parents reported comorbid symptoms of clinically relevant anxiety, depression and PTSS. Comorbid symptoms were more prevalent in mothers than in fathers of survivors. No such difference was found among bereaved parents. In both research and clinical practice, it is important to take comorbidity of symptoms into account as it has implications on the individual as well as on clinical management, being associated with higher symptom severity and poorer quality of life and distinct treatment challenges [33]. Although no statistical analyses were performed, the proportion of parents of survivors reporting comorbid symptoms of clinically relevant anxiety and depression appear similar to that in the Swedish general population (8.3%) [33], whereas the proportion reporting comorbid symptoms appear higher among bereaved parents than in the general population. The fact that a substantial proportion of bereaved parents report overlapping symptoms of distress calls for further efforts regarding prevention and treatment.

A recent review synthesized the current knowledge on factors predicting parental distress related to childhood cancer [6]. The most probable factors identified included disease severity, treatment intensity, being a mother, negative affectivity, poor personal resources and family stressors or weaknesses before the diagnosis. In this study, clinically relevant symptoms of depression was predicted by bereavement and previous stressful life event/s whereas being a mother and previous stressful life event/s predicted clinically relevant symptoms of anxiety. These results are in line with previous research, which has shown a link between stressful life events and psychological vulnerability when faced with a child’s cancer [46,47]. However, in this study previous stressful event/s did not remain as an independent predictor after the

Table 4. Multivariable predictors of symptoms of depression five years after end of treatment or a child’s death.

| Predictor                                      | Model 1 (Standardized regression coefficient (SE) | p value | Model 2 (Standardized regression coefficient (SE) | p value |
|------------------------------------------------|--------------------------------------------------|--------|--------------------------------------------------|--------|
| Parent sex (male/female)                       | 0.037 (0.079)                                    | .640   | −0.061 (0.052)                                   | .240   |
| Parent age at diagnosis                        | −0.095 (0.105)                                   | .366   | −0.091 (0.068)                                   | .184   |
| Child age at diagnosis                         | −0.018 (0.102)                                   | .861   | 0.037 (0.066)                                    | .577   |
| Bereaved (no/yes)                              | 0.159 (0.075)                                    | .036   | 0.055 (0.051)                                    | .284   |
| Previous stressful life events (no/yes)        | 0.244 (0.076)                                    | .002   | 0.017 (0.055)                                    | .757   |
| Current distress in relation to previous stressful life events (no/yes) | 0.118 | | 0.170 (0.060) | .005 |
| Anxiety at T7                                  | 0.061 (0.052)                                    | .240   | 0.357 (0.070)                                    | .284   |
| PTSS at T7                                     | 0.159 (0.075)                                    | .036   | 0.055 (0.051)                                    | .284   |
| Parent sex (male/female)                       | 0.037 (0.079)                                    | .640   | −0.061 (0.052)                                   | .240   |
| Parent age at diagnosis                        | −0.095 (0.105)                                   | .366   | −0.091 (0.068)                                   | .184   |
| Child age at diagnosis                         | −0.018 (0.102)                                   | .861   | 0.037 (0.066)                                    | .577   |
| Bereaved (no/yes)                              | 0.159 (0.075)                                    | .036   | 0.055 (0.051)                                    | .284   |
| Previous stressful life events (no/yes)        | 0.244 (0.076)                                    | .002   | 0.017 (0.055)                                    | .757   |
| Current distress in relation to previous stressful life events (no/yes) | 0.118 | | 0.170 (0.060) | .005 |
| Anxiety at T7                                  | 0.061 (0.052)                                    | .240   | 0.357 (0.070)                                    | .284   |
| PTSS at T7                                     | 0.159 (0.075)                                    | .036   | 0.055 (0.051)                                    | .284   |
| R²                                             | .095 (0.068)                                     | .184   | .061 (0.052)                                     | .240   |

PTSS: posttraumatic stress symptoms; SE: standard error; T7: five years after end of treatment or a child’s death.
psychological variables were entered into the models. Concurrent symptoms of anxiety and PTSS were most strongly associated with symptoms of depression at T7. Similarly, concurrent symptoms of depression and PTSS were most strongly associated with symptoms of anxiety at T7. These findings are not surprising, considering the comorbidity between symptoms of anxiety, depression and PTSS in the sample.

The strengths of this study include the long-term follow-up, the homogenous sample with regard to time since end of treatment/child's death as it allows conclusions with regard to parental distress at a specific time-point and the inclusion of both mothers and fathers of survivors and bereaved mothers and father. However, the results for bereaved parents must be interpreted with caution as the number of bereaved parents is relatively small.

Some potential limitations should be mentioned. Despite the study's longitudinal design most investigated potential predictors of distress were measured at the same time as the outcomes which of course limits the possibility to draw firm conclusions regarding prediction. Data on symptoms of anxiety and depression were collected only five years after end of treatment/the child's death which precludes a comparison with symptoms of anxiety and depression at previous time points. Such a comparison would have clarified if it is the same subset of parents who continue to report clinically relevant distress over time or if some parents report clinically relevant levels only five years after end of treatment or the child's death, respectively. The fact that distress was assessed with self-reports and not clinically assessed should be considered. Clinical interviews might have allowed a more valid assessment of symptoms of anxiety, depression and PTSS and could potentially more accurately have captured distress experienced by fathers considering gender differences in distress it should be considered that the cut-offs used include mild symptoms, with only few parents reporting severe symptoms. However, results from a Norwegian study indicated that a cut-off at ≥12 on the BDI-II showed the best sensitivity and specificity for clinically relevant symptoms [48]. Lastly, we would like to mention that it could have been valuable to report parental distress in relation to the child's health status. Previous research has shown that, at five years after diagnosis, parents of children having experienced a cancer relapse reported more severe anxiety and general distress than did parents of disease-free survivors or bereaved parents [16]. In an additional analysis we addressed this issue among parents of survivors by including the child's current health status (by parent self-report, ranging from very poor to very good) in the multivariable model. The results did not show that the child's current health status was related to parental symptoms of anxiety and depression (data not shown). Though it is worth mentioning that the majority (89%) of parents reported their child's current health status as good or very good.

Long-term psychological distress is a problem for a subset of parents of survivors of childhood cancer and bereaved parents. Approximately a third of bereaved parents reported a clinically relevant level of distress. Clinically relevant distress was more prevalent among mothers than fathers of survivors, whereas no such difference was found between bereaved fathers and mothers. Experiencing distress related to previous stressful life events as well as comorbid symptoms of distress were associated with more severe psychological distress five years after end of treatment or a child's death. These results deserve further attention in research and could potentially be important in terms of addressing ways to reduce parental distress. The present findings are also worth considering in light of the growing body of evidence highlighting the negative effects of parental distress on children's psychological adjustment and cognitive performance [6]. In addition, future studies would be strengthened by also addressing the interpersonal processes that may influence distress levels and adaptation over time. For example, partner-oriented self-regulation in bereaved parents, defined as the avoidance of talking about loss while remaining apparently strong in each other's presence in order to protect one's partner, has been shown to increase grief not only in the parent themselves, but also in their partner, over time [49].

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