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Posttraumatic stress, depression and anxiety among adult long-term survivors of cancer in adolescence

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ABSTRACT

Background: To determine the prevalence of posttraumatic stress, depression and anxiety in adults who have survived cancer (⩾5 years) diagnosed in adolescence, as compared to healthy controls.

Patients and methods: Survivors ($n = 820$) of cancer during adolescence (age $M = 30.4 \pm 6.0$ years; $M = 13.7 \pm 6.0$ years since diagnosis) and 1027 matched controls without history of cancer (age $M = 31.5 \pm 6.9$ years) completed standardised questionnaires measuring posttraumatic stress, depression and anxiety. Additionally, sub-groups of 202 survivors and 140 controls with elevated scores received structured interviews to ascertain DSM-IV-diagnoses.

Results: A total of 22.4% of the survivors reported clinically relevant symptoms of posttraumatic stress, anxiety and/or depression compared to 14.0% of the controls (odds ratios [ORs] 1.77; 95% confidence interval [CI] 1.39–2.26). The odds of posttraumatic stress symptoms in male (OR 3.92, 95% CI 1.80–8.51) and female (OR 3.83, 95% CI 2.54–5.76) survivors were more than three times those in the controls. However, only female survivors reported symptoms of depression and anxiety significantly more often (respectively: OR 2.12, 95% CI 1.16–3.85; and OR 1.86, 95% CI 1.33–2.59) than the controls. A relevant subgroup of 24.3% of the survivors met DSM-IV criteria for at least one mental disorder compared to 15.3% of the controls.

Conclusion: Survivors of cancer during adolescence show an elevated risk of presenting symptoms of posttraumatic stress, anxiety and/or depression during adulthood which is also reflected in a greater number of DSM-IV diagnoses when compared to controls. Comprehensive follow-up assessments should include the examination of possible psychological late effects of a cancer diagnosis in adolescence in order to identify survivors needing psychosocial interventions even years after the completion of successful medical treatment.

1. Introduction

In the past years the overall 5-year survival rate for adolescents with cancer has steadily improved and is now roughly at 73–78%.[1,2] Nevertheless, malignant neoplasm are still ranked as the fourth leading cause of death in children and adolescents up to the age of 19.[3] Therefore, a diagnosis of cancer can be expected to cause considerable stress and

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may lead to acute or prolonged maladaptive psychological reactions.

1.1. Psychological reactions in survivors of paediatric cancer

There are several studies which demonstrate that most survivors of paediatric cancer are resilient and function well psychosocially.[4–8] Other studies, however, suggest that a large proportion of survivors of childhood cancer experiences clinically relevant mental health problems.[9] Especially posttraumatic stress disorder (PTSD) is found in a considerable number of the short- and long-term survivors of paediatric cancer.[10–13] With respect to other mental health problems, there is still an insufficient knowledge base, but there are also findings which describe a greater amount of depression and anxiety in paediatric cancer patients after completion of medical treatment, when compared to healthy controls.[14] However, the currently available data are limited to the assessment of both children and adolescents with cancer, and are narrowed to the time of acute treatment or shortly afterwards. Only one study investigated the presence of anxiety and depression in survivors of adolescent cancer but within 5 years of the diagnosis.[15] This study described a steady decrease in symptoms, resulting in lower levels of depression and anxiety 18 months after diagnosis when compared to the general population. Another study revealed that young adult survivors (>18 years) experienced a greater amount of posttraumatic stress symptoms than survivors who were not yet grown up.[13] On the other hand, Rourke and colleagues found no evidence that age at diagnosis is a significant predictor for PTSD symptomatology in young adult survivors of childhood cancer.[16] Therefore the effect of age remains non-distinctive and up to now no study has investigated the possible long-term impact of a cancer diagnosis received during adolescence. This seems an important issue considering that adolescence is a delicate and vulnerable phase of development.

1.2. Impact of a cancer diagnosis during the vulnerable phase of adolescence

Establishing a sense of self and sex-role identity, a focus on appearance and self-image, morality development, setting future goals as well as a growing independence, and an increasing importance of peer-relationship are typical developmental tasks of this period[17,18] which may be impacted upon by a cancer diagnosis and the subsequent treatment.[19] Due to frequent and prolonged hospital stays, aggressive multimodal therapies and impairing side-effects, the adolescents are often extremely dependent on their parents and therefore isolated from their peers, although autonomy development and peer relationship are important milestones of this phase. Moreover, certain treatment side-effects, such as hair loss, diarrhoea, nausea, skin changes, pain and insomnia,[20,21] can be extremely challenging and may, for example, affect the development of body image and sexual identity[22] and cause low self-esteem and social anxiety.[23] Even years after successful completion of medical treatment, numerous survivors of adolescent cancer have to deal with multiple sequelae, such as cognitive impairment, infertility, alterations in development and growth or damages of the organ system.[24] Those persisting stressors may be tremendously challenging and overwhelming. Furthermore, the vulnerability to emotional stress might be seriously worsened by the cancer experience and cause prolonged psychological adjustment problems.

Considering this developmental background, this study aims to investigate the psychological long-term impact of a cancer diagnosis and treatment during adolescence and to determine the degree of mental health problems in the survivors who have since become adults. At this point we hypothesised that the former patients would be experiencing a greater amount of symptoms of posttraumatic stress, depression and/or anxiety when compared to non-cancer controls.

2. Patients and methods

2.1. Procedure

Data were collected between January 2008 and February 2009 in a two-stage procedure.

First stage: In a first step, adult long-term survivors as well as healthy controls were asked to fill in self-report questionnaires to assess symptoms of posttraumatic stress, depression and anxiety. Eligible long-term survivors were invited by the German Childhood Cancer Registry (GCCR) to participate in the study and supplied with written information and a set of questionnaires. In addition, all survivors were asked to invite three of their friends to participate in the study as controls by handing out brochures to gain a group of controls with a similar educational and socioeconomic background. To maximise the amount of controls, we also invited persons to participate in the same comparison group via an email snowball-system as well as leaflets which were distributed in several local organisations. If four weeks passed without the questionnaire being returned, a reminder letter was mailed to both survivors and controls.

A second control group was used to compare the obtained anxiety and depression scores with a normative reference group by deriving an age-matched sub-sample from a study which was conducted at the University of Leipzig.[25] In this project, which took place in 1998, a representative sample of the German general population ($N = 2037$) completed the same questionnaire (HADS) as used in our present study.

Second stage: In a second step, telephone-based interviews were conducted in order to estimate the prevalence of DSM-IV (Diagnostic and Statistical Manual of Mental Disorders, 4th edition) diagnoses in our study population. All persons who gave informed consent to be interviewed and who showed at least one subclinically suspicious (see measures) set of questionnaire scores were contacted by trained interviewers in the subsequent weeks after returning the questionnaires.

The study was approved by the Ethics Committee of the University of Ulm, all participants gave written informed consent.

2.2. Participants

From the population of the GCCR, 1876 cancer survivors were invited to participate. The inclusion criteria were aged between 15 and 18 years at first cancer diagnosis with an onset

Table 1 – Medical characteristics of the cancer survivors.

	Responders (*n* = 820)	Non-responders (*n* = 1056)
Age at diagnosis in years (*M* ± *SD*)	15.78 ± 0.89	15.86 ± 0.90
Time since diagnosis in years	13.68 ± 6.02	13.23 ± 6.04
Duration of treatment in months (*M* ± *SD*)	19.61 ± 25.02	n.a.
Oncology treatment		
Surgery	589 (71.8%)	n.a.
Chemotherapy	742 (90.5%)	n.a.
Radiation	474 (57.8%)	n.a.
Other	70 (8.5%)	n.a.
ICCC3 classification		
Leukaemia	158 (19.3%)	211 (20.0%)
Lymphoma	250 (30.5%)	297 (28.1%)
CNS	78 (9.5%)	139 (13.2%)
Neuroblastoma	4 (0.5%)	7 (0.7%)
Retinoblastoma	n.a.	n.a.
Renal tumours	7 (0.9%)	8 (0.8%)
Hepatic tumours	0 (0.0%)	2 (0.2%)
Malignant bone tumours	174 (21.2%)	195 (18.5%)
Soft tissue and other extra-osseous sarcomas	75 (9.2%)	96 (9.1%)
Germ cell tumours	54 (6.6%)	69 (6.5%)
Other malignant epithelial neoplasms and malignant melanomas	20 (2.4%)	30 (2.8%)
Other and unspecified malignant neoplasms	0 (0%)	2 (0.2%)
Relapse (⩾1)	96 (11.8%)	n.a.
Second malignancy (⩾1)	33 (4.1%)	n.a.

Abbreviations: *M*, mean; *SD*, standard deviation; n.a., not applicable; ICCC3, International Classification of Childhood Cancer.

at least 5 years earlier than the beginning of this study. The GCCR systematically ascertains all malignant neoplasm and benign brain tumours in children under the age of 15 years at diagnosis with a completeness of more than 95% since 1980. In addition, it also administers a large data set of patients older than 15. For those patients however, there is no information regarding the completeness of registration available and the sample is therefore not population-based. The medical characteristics of the persons included in the final data set and the 'non-responders' can be retrieved from Table 1. A flow chart with the description of the study population is shown in Fig. 1. The inclusion criteria for the control group were aged in the same range of the cancer survivor group at study entry, i.e. 20–46 years, and no history of cancer.

Since only persons who had given informed consent to be interviewed and who had elevated questionnaire scores were contacted by telephone, interview data were obtained from 202 survivors and 140 controls (see Fig. 1).

2.3. *Measures*

Posttraumatic Stress Diagnostic Scale (PDS): In order to assess symptoms of posttraumatic stress we used an authorised German version[26] of the PDS.[27] The scale is a 49-item self-report questionnaire, which reflects DSM-IV criteria of PTSD. A clinically relevant questionnaire score was achieved when all six DSM-IV diagnosis criteria (A–F) were met. Additionally, participants who also experienced a traumatic event and reported at least one symptom per criterion B, C, and D as well as any impairment were considered as showing a subclinically relevant symptomatology. The PDS also allows a quantification of symptom severity. The symptom scale consists of 17 items (4-point Likert scale) and comprises the subscales 'Intrusions', 'Avoidance' and 'Hyperarousal'. The scale has a good internal consistency (*Cronbach*'s $\alpha = 0.92$) and convergence with other measures of PTSD.

Hospital Anxiety and Depression Scale (HADS): We used the HADS which was originally developed by Zigmond and Snaith[28] to detect states of depression and anxiety in physically ill patients. However, the HADS is also known to be a useful measure in the general population.[29] The questionnaire consists of 14 questions, seven for each subscale. The possible scores range from 0 to 21 for anxiety as well as for depression. A score of 0–7 can be regarded as being in the normal range, a score of 8–10 is considered as subclinically relevant and a score of 11 or higher indicates a probable presence of an anxiety or mood disorder and is thus clinically relevant. The HADS shows good internal consistency (depression scale: $\alpha = 0.81$; anxiety scale: $\alpha = 0.80$). The convergent validity has been documented by correlations with other commonly used questionnaires.

The lower thresholds (subclinically relevant scores) were used as a precondition of being interviewed by telephone. The reported amount of symptoms of depression, anxiety and PTSD is based on the higher threshold indicating clinically relevant symptoms (PDS all DSM-IV Clusters (A–F) are fulfilled and HADS $\geqslant 11$ for each scale).

Expert System for Diagnosing Mental Disorders DIA-X/M-CIDI: Mental disorders were diagnosed according to DSM-IV criteria using the computer-assisted version of the DIA-X Interview.[30] The DIA-X is a fully structured interview which is based on the Composite International Diagnostic Interview (CIDI).[31] Both interviews have a high inter-rater reliability and satisfactory test-retest reliability for most diagnostic categories. Their

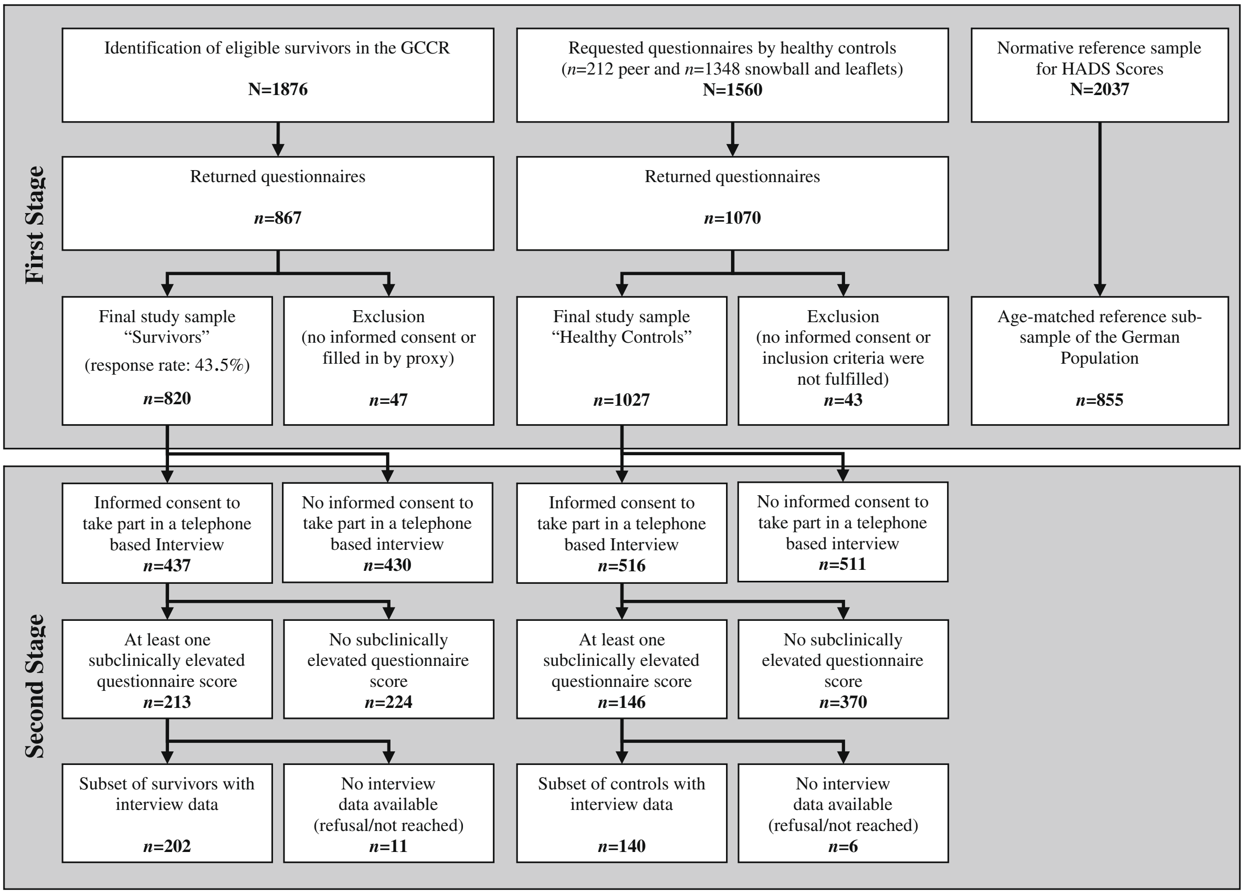


Fig. 1 – Flow chart describing the study population.

validity has also been proven to be acceptable. We established the 12-month prevalence of psychiatric diagnoses by the use of the following three sections: Section D 'Anxiety Disorders' (generalised anxiety disorder, panic disorder, agoraphobia, social phobia and specific phobia), section E 'Mood Disorders' (major depressive episode and dysthymia) and section N 'PTSD'.

Demographic and clinical variables: Items concerning the socioeconomic background were taken from the German Socioeconomic Panel (SOEP[32]) and included in the set of questionnaires. Medical information on the former cancer patients was partly abstracted from the medical records saved in the GCCR (cancer site, age at cancer onset) and partly obtained by self-developed items in the questionnaires (oncology treatment, second malignancies or cancer relapse).

2.4. *Data analysis*

Descriptive statistics were conducted to present the overall characteristics of the study sample. Pearson's χ^2-tests were applied for categorical variables as well as odds ratios (ORs) and 95% confidence intervals (CIs). For continuous variables we calculated independent-sample *t*-tests and *Cohen*'s *d* effect sizes. Moreover, logistic regression analyses were performed to investigate the effect of group on the amount of clinically relevant questionnaire scores after statistical control for sex, age and education The comparisons of the study population with the normative anxiety and depression scores were tested by the use of a three-factorial ANOVA.

3. Results

3.1. *Demographic and clinical factors of the study population*

The final sample consisted of 820 adult long-term survivors (response rate: 43.7%) and 1027 non-cancer controls. A flow chart describing the origin of the study population is presented in Fig. 1. The socio-demographic sample characteristics are shown in Table 2. Comparisons of cancer survivors and controls revealed significant differences with respect to sex, age, marital status, educational level and employment status. However, the difference of age was only marginal. The medical characteristics of the cancer survivors are displayed in Table 1. The cancer survivors suffered from a variety of different neoplasia, the most common being lymphoma, bone tumours and leukaemia.

Concerning the comparison of anxiety and depression scores with the normative reference sample, the sub-set of data available from the general population consisted of 855 persons (*M* = 34.7 years, *SD* = 7.1 years, 41% male).

Interview data were available from 202 (*M* = 30.7 years, *SD* = 5.9, 44% male) survivors and 140 (*M* = 31.9 years, *SD* = 6.6, 21% male) controls (see Fig. 1). Concerning the

Table 2 – Socio-demographic sample characteristics.

	Survivors ($n = 820$)	Controls ($n = 1027$)
Age in years (M ± SD)*	30.44 ± 6.05	31.52 ± 7.00
Sex (m:f)*	402:418 (49.0%:51.0%)	278:749 (27.1%:72.9%)
*Marital status**		
Not married	576 (70.5%)	601 (58.8%)
Married	223 (27.3%)	389 (38.1%)
separated/divorced/widowed	18 (2.2%)	32 (3.1%)
*Educational level**		
Low (mandatory basic school with 9 years of schooling)	104 (12.8%)	42 (4.1%)
Middle (intermediate type of advanced school with 10 years of schooling)	256 (31.6%)	266 (26.1%)
High (advanced school with 12–13 years of schooling)	423 (52.3%)	701 (68.8%)
Other/none	27 (3.3%)	9 (0.9%)
*Employment status**		
Full-time	442 (54.6%)	531 (52.0%)
Part-time	101 (12.5%)	191 (18.7%)
Still in education	30 (3.7%)	46 (4.5%)
Marginal part-time	70 (8.7%)	97 (9.5%)
Not employed	165 (20.4%)	152 (14.9%)
Other	1 (0.1%)	4 (0.4%)

Abbreviations: *M*, mean; *SD*, standard deviation; m, male; f, female.

* $p < 0.05$.

amount of clinically relevant symptoms of posttraumatic stress, depression and anxiety in the questionnaires, there were no significant differences between persons willing to be interviewed versus refusers, neither for survivors nor for controls.

3.2. *Total amount of clinical relevant symptoms based on the questionnaires*

Of the former cancer patients, 13.9% ($n = 114$) had clinically relevant scores (HADS$\geqslant$11 or PDS Cluster A–F fulfilled) for either symptoms of posttraumatic stress, depression or anxiety, 5.9% ($n = 48$) showed clinically relevant scores in two and 2.7% ($n = 22$) in all three conditions (posttraumatic stress, depression and anxiety) at the same time. Of the controls, 10.6% ($n = 109$) showed one, 3.1% ($n = 32$) two and 0.3% ($n = 3$) three clinically relevant questionnaire scores in terms of the investigated three conditions (see Fig. 2). Altogether we found evidence for at least one clinically relevant symptom in 22.4% ($n = 184$) of the survivors compared to 14.0% ($n = 144$) in the healthy controls ($\chi^2[1, n = 1847] = 22.1$, $p < 0.001$; OR 1.77; 95% CI 1.39–2.26). The difference in the total amount of distress remained significant when males ($p = 0.007$) and females ($p < 0.001$) were investigated separately.

3.3. *Posttraumatic stress symptoms, depression and anxiety based on the questionnaires*

Concerning posttraumatic stress, both male and female survivors were more often in the range of a possible PTSD than healthy controls: 10.5% of the male survivors reported clinically relevant symptoms of PTSD compared to 2.9% in the controls ($\chi^2[1, n = 656] = 13.6$, $p < 0.001$; OR 3.92; 95% CI 1.80–8.51). For females the discrepancy is also striking and significant ($\chi^2[1, n = 1134] = 46.2$, $p < 0.001$; OR 3.83; 95% CI 2.54–5.76) (see Fig. 3). Moreover we found that cancer patients reported more symptoms of re-experiencing, avoidance and hyperarousal (symptom severity index $M = 6.6$, $SD = 8.1$) than those healthy controls ($M = 4.4$, $SD = 6.8$) who had been confronted with a traumatic event other than cancer ($t[1331] = 5.4$, $p < 0.001$; $d = 0.30$).

For symptoms of depression ($\chi^2[1, n = 1163] = 6.3$, $p = 0.012$; OR 2.12; 95% CI 1.16–3.85) and anxiety ($\chi^2[1, n = 1164] = 13.6$, $p < 0.001$; OR 1.86; 95% CI 1.33–2.59) we observed that female survivors experienced significantly more often clinically relevant symptoms than the female controls. Male survivors, however, did not report more symptoms in the clinically relevant range for depression and anxiety than their same sex controls. The prevalences of posttraumatic stress, depression and anxiety according to the questionnaires are displayed in Fig. 3.

In a logistic regression the effect of group (survivors versus control) remained significant for symptoms of PTSD (OR 3.26, 95% CI 2.25–4.74, $p < .001$), depression (OR 1.69, 95% CI 1.01–2.81, $p = 0.045$) and anxiety (OR 1.657, 95% CI 1.16–2.12, $p = 0.004$) after statistical control for sex, age and education.

3.4. *Depression and anxiety scores in comparison with normative reference scores*

The three-factorial ANOVA revealed a significant difference between the former patients and the additional comparison sample from the general population concerning anxiety ($F[1, 1651] = 66.4$, $p < 0.001$; $d = 0.39$), with constantly higher anxiety scores in the long-term survivors of adolescent cancer (see Fig. 4). We also found a main effect of sex for anxiety scores with females reporting significantly higher scores than males ($F[1, 1651] = 35.4$, $p < 0.001$; $d = 0.28$). For symptoms of depression, no effects of group or sex could be revealed. However, we found an additional effect of age for both depression

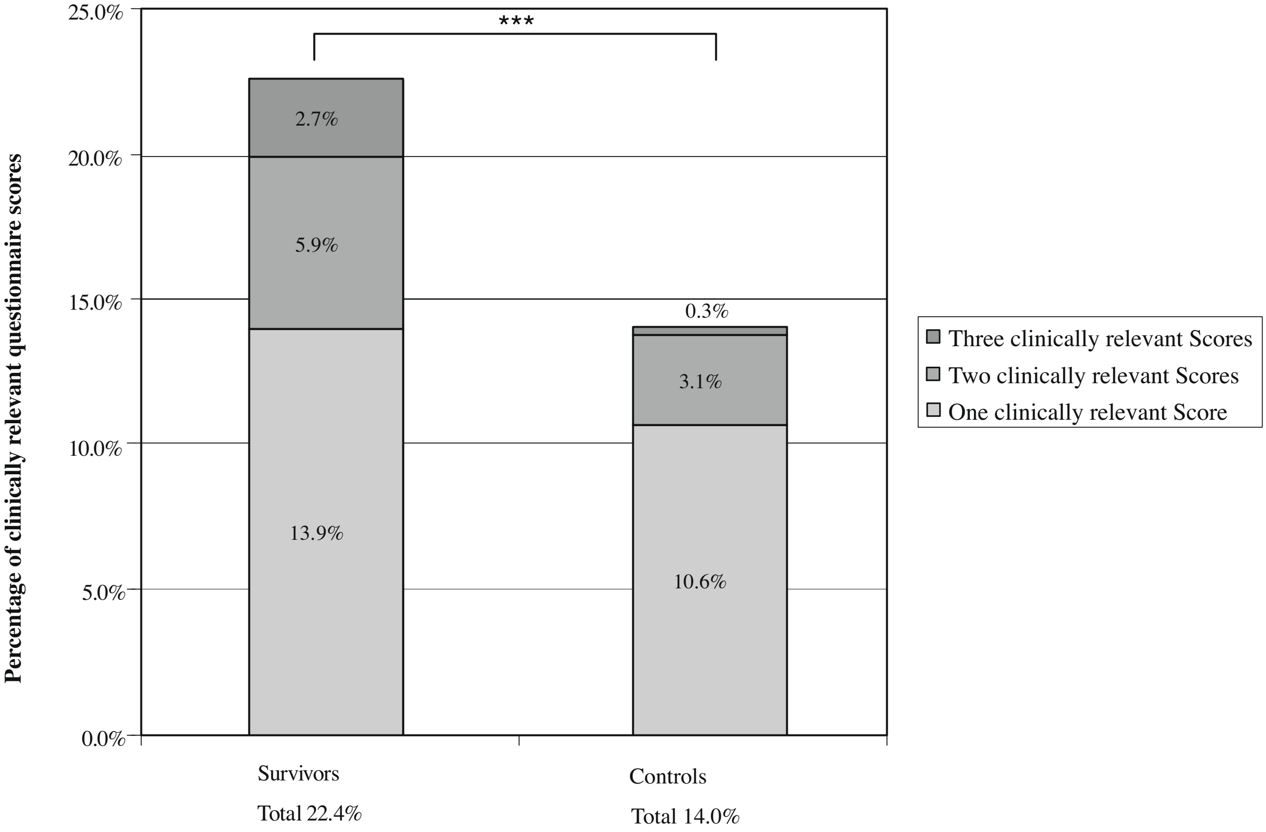
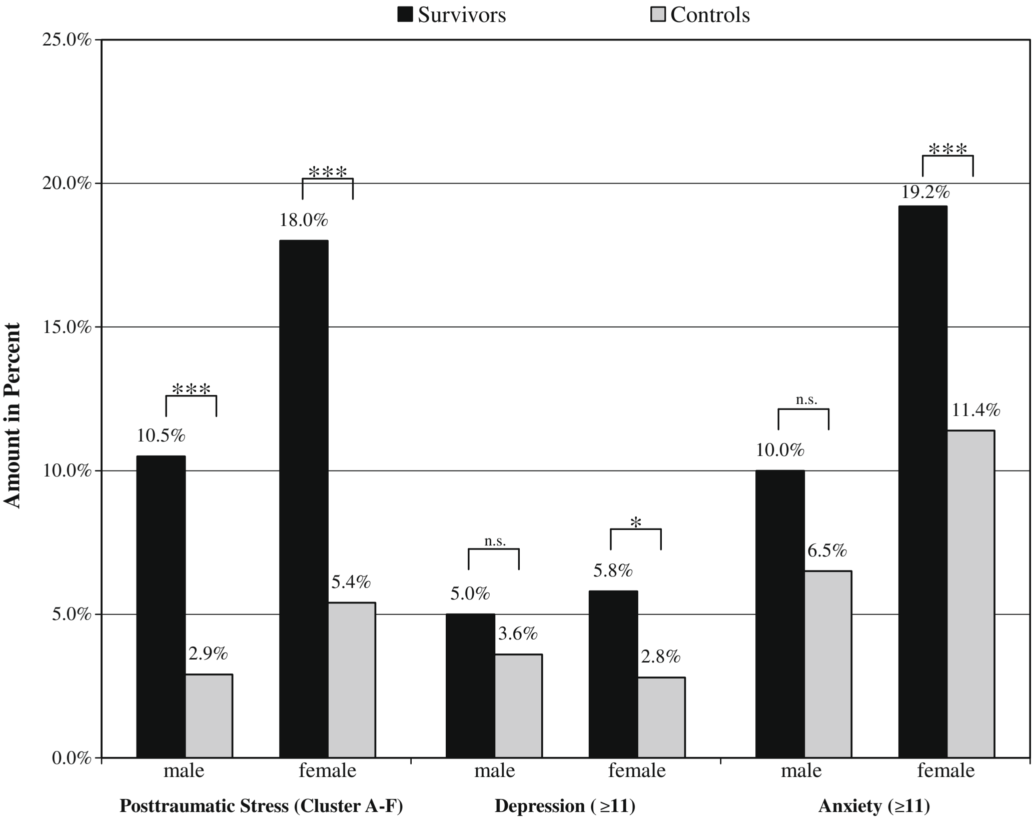


Fig. 2 – Amount of clinically relevant questionnaire scores in survivors and controls.



Abbreviations: n.s., no significant difference; * $p<0.05$; ** $p<0.01$; *** $p<0.001$

Fig. 3 – Proportion of subjects with psychological symptoms according to the questionnaires.

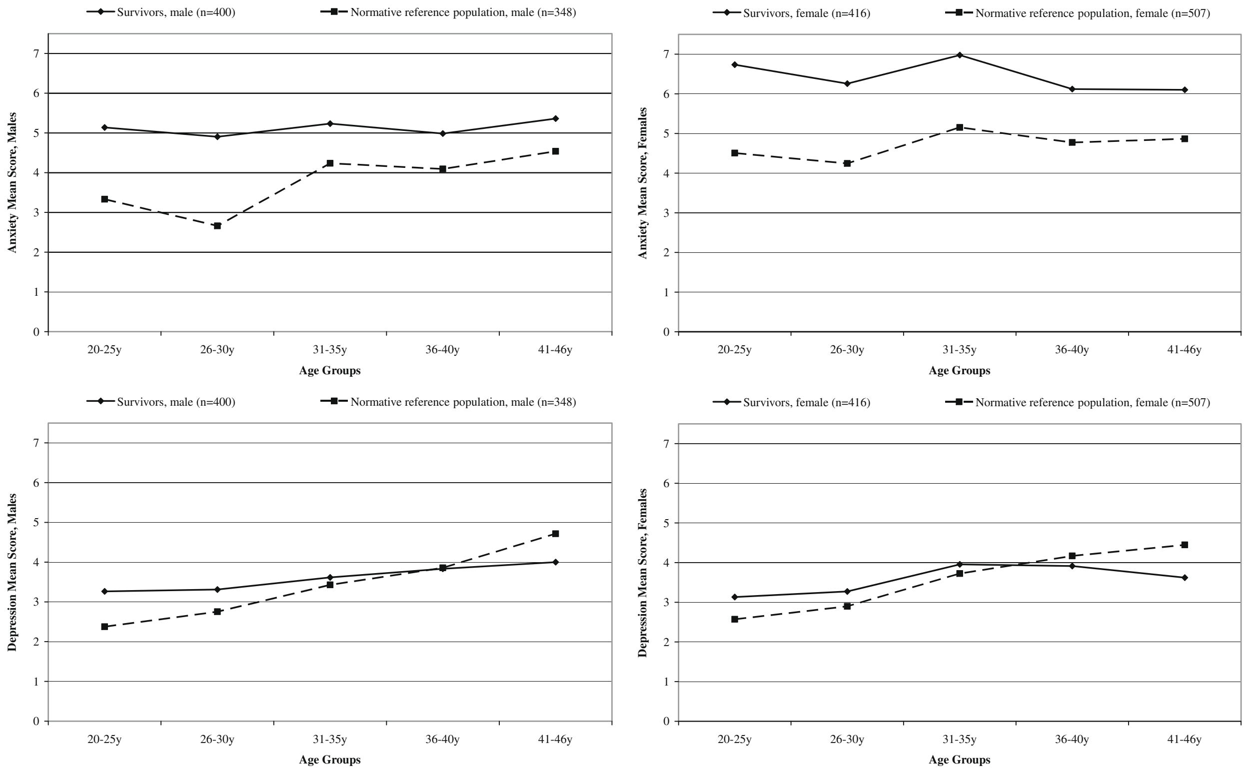
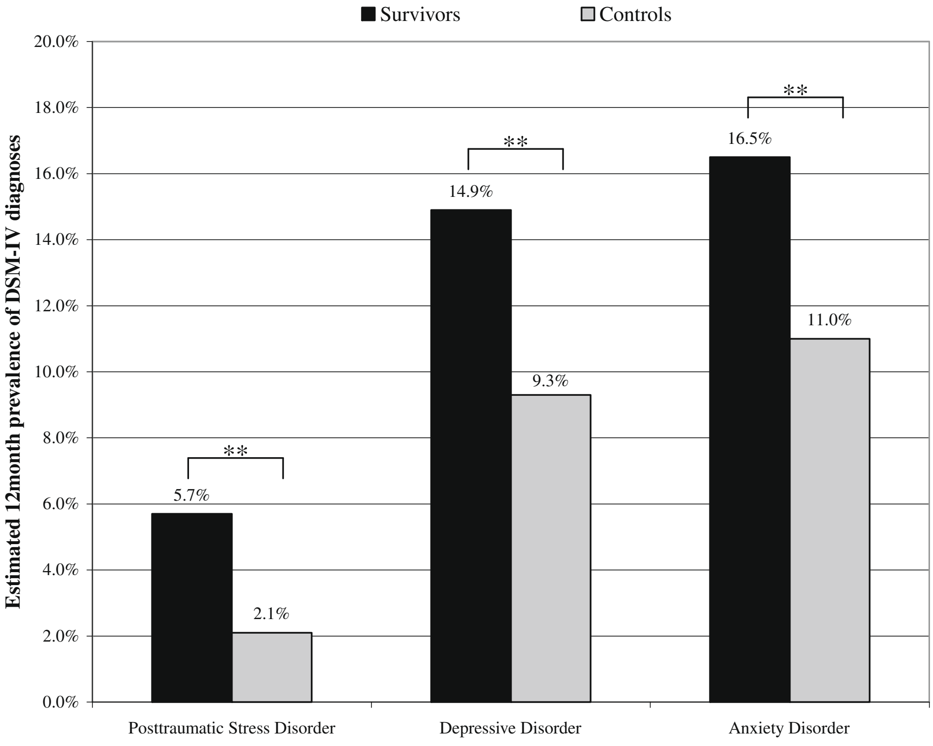


Fig. 4 – Mean anxiety and depression scores (HADS) by age group, sex and population.



** $p<0.01$

Fig. 5 – Prevalence of DSM-IV diagnoses based on the structured clinical interview.

($F[4, 1651] = 7.7$, $p < 0.001$) and anxiety ($F[4, 1651] = 3.0$, $p = 0.019$) indicating higher scores in older persons. The mean anxiety and depression scores for males and females in each age group are shown in Fig. 4.

3.5. *Prevalence of PTSD, mood and anxiety disorders based on clinical interviews*

According to the structured telephone interviews, survivors were in general more distressed than the healthy controls: 24.3% (*n* = 106) of all survivors willing to be interviewed fulfilled the diagnostic criteria for at least one DSM-IV diagnosis involving posttraumatic stress, depression and/or anxiety, whereas only 15.3% (*n* = 79) of the controls showed at least one psychiatric disorder of the previously mentioned domains (χ^2[1, *n* = 953] = 12.1, *p* = 0.001; OR 1.77; 95% CI 1.28–2.45).

The estimated 12-month prevalence of the three diagnosis groups is also shown in Fig. 5. The most frequent diagnoses were anxiety disorders, which were found in 16.5% (*n* = 72) of the survivors and thus were significantly more common than in the healthy controls 11.0% (*n* = 57) (χ^2[1, *n* = 953] = 6.0, *p* = 0.015; OR 1.59; 95% CI 1.09–2.31). In both survivors (11.9%) and controls (8.3%) panic attacks (with or without agoraphobia) were the most common anxiety disorders. Among the survivors, the second most prevalent anxiety disorder was social phobia (4.6%), which was only diagnosed in 1.4% of the controls. Moreover, 2.3% of the survivors fulfilled the diagnostic criteria of a specific phobia of the blood-injection type whereas only 0.8% of the controls were diagnosed with this type of anxiety disorder.

Of the survivors, 14.9% (*n* = 65) cases of depression were identified, whereas in the controls only 9.3% (*n* = 48) fulfilled the diagnostic criteria for a depressive mood disorder, indicating a significant difference as well (χ^2[1, *n* = 953] = 7.0, *p* = 0.008; OR 1.70; 95% CI 1.15-2.53). PTSD was found to be less frequent, but nevertheless still more often diagnosed in the long-term survivors (5.7% (*n* = 25) versus 2.1% (*n* = 11)) than in the non-cancer controls (χ^2[1,*n* = 953] = 8.4, *p* = 0.004; OR 2.79; 95% CI 1.36-5.73).

The false negative rate of PDS was 6.0%, which means 20 persons were diagnosed with a PTSD but showed no clinically relevant questionnaire score in the PDS. The false negative rate of the HADS anxiety scale was 26.1% (*n* = 89) and that of the depression scale was 22.9% (*n* = 78) (both cut-off $\geqslant$ 11).

4. Discussion

This study constitutes the first epidemiological survey of the impact of a cancer diagnosis during adolescence on the long-term psychological adjustment ($\geqslant$5 years since diagnosis). Our findings are in line with the results of long-term survivors of paediatric cancer as a whole[14,33] and demonstrate that survivors who have been diagnosed with cancer during adolescence experience a greater amount of psychological distress when compared to same-age controls who have not faced a malignant diagnosis.

We identified a large proportion of survivors reporting clinically relevant symptoms of posttraumatic stress, although the cancer diagnosis had been made more than 5 years previously ago. This is extremely striking since there are reports that most of the survivors are adjusting well to the malignant disease as time goes by.[15]

For symptoms of depression and anxiety, our questionnaire findings were not as unambiguous as for the symptoms of PTSD. On the one hand, we found higher levels of symptoms of anxiety in both male and female survivors when compared to the reference data from the general population. On the other hand, we identified more symptoms of depression and anxiety in female survivors when compared to our self-recruited control group. It might be that the lower level of depression in our own control group and thus the significant difference to the group of survivors was partly due to the educational level of our own group of controls, which was higher than in the general population. From studies with the general population there is some evidence that persons with less than 12 years of schooling are at higher risk for developing a major depression.[34] Due to a lack of financial resources, we used an innovative recruitment strategy with several modes to invite potential participants (email-snowball system as well as leaflets which have been distributed in several local organisations and to the healthy peers of the participating survivors) in order to gain a large control group with a widespread educational and socioeconomic background. However, it has to be noted that we were not able to establish a representative sample of controls and a larger proportion of females as well as persons with a higher educational background were willing to participate. Nevertheless, the results are strengthened by the use of an additional control group which derived from a representative sample of the German population.

The findings based on our standardised psychiatric interviews clearly demonstrate that there are significantly more posttraumatic stress, anxiety and depressive disorders in the former patients when compared to controls. However, the amount of PTSD is significantly lower than in a study with young adult survivors of childhood cancer[35] and more in line with findings on very young survivors, which show current PTSD diagnoses to be in the order of 4.7%.[36] When compared to the questionnaire results, the preponderance of PTSD based on the interviews was also unexpectedly low, although the PDS is also based on DSM-IV criteria. This difference might be partly due to the different methodologies used. While the response format of the PTSD Clusters ‘Intrusion’, ‘Avoidance’ and ‘Hyperarousal’ in the PDS Questionnaire is a 4-point-likert scale, the participants had to specify the corresponding symptom merely as present or absent when being interviewed. It is possible indeed that the forced choice format may have led to a neglect of symptoms, since they are not perceived as present all the time; on the other hand it is also conceivable that the likert-scaled items may have caused an error of central tendency. In addition subjects are not as anonymous during the interview situation as when answering a paper–pencil questionnaire and might therefore be not as likely to express clinical relevant symptoms of posttraumatic stress. It might be that in terms of social desirability or avoidance – one of the core symptoms of PTSD – the participants might have missed detailing their symptoms when interviewed, particularly immediately after being asked to recall their traumatic event.[37–39]

However, in comparison with representative data of the German population, the PTSD prevalence found in our study is still considerably elevated. Epidemiological studies on the prevalence of PTSD in Germany are rare, but there are two studies – one with a sample of 14–24-year-old[40] and one with 18–64-year-olds[41] – which both used the same diagnostic interview as in our present study and reported a 12-month prevalence of 0.7%. In terms of depression and anxiety the prevalences of the present survivor study are also slightly higher as in a representative sample, where unipolar depressions were found in 11.0% and anxiety disorders (including obsessive-compulsive disorder) in 14.5% of the 18–65-year-olds.[42]

All together the findings indicate that the impact of a cancer diagnosis on mental health during adolescence does not end with the termination of medical treatment but rather needs a long-term follow-up and monitoring. In the long-term, it might be difficult to distinguish which problems derive from the cancer diagnosis during the vulnerable phase of adolescence and which have emerged due to ordinary stressful life-events. However, the specificity of the symptoms and the comparison with prevalence rates in the general population lend weight to the interpretation that the morbidity is at least partly due to the cancer-experience or the 'Damocles' syndrome'[43] of an incalculable risk of having a cancer relapse or developing secondary malignancies.

4.1. *Limitations*

Although the GCCR also administers a large data set of patients older than 15 years, it has to be noted that this population is not representative. The registration is voluntary and might therefore be biased. The response rate of 43.7% is acceptable. However, in our study sample there is a higher proportion of females and fewer survivors of CNS tumours among the responders than in the non-responders and we do not know which additional selection bias might have occurred. In comparison with our own group of controls, survivors were less married, poorly educated and differed poorly in terms of their employment status. However, it has to be noted that the survivors are still higher educated and more gainfully employed than a representative sample (G-SOEP[32]) of the German population. This finding fits in line with an international study, which indicates that a cancer diagnosis among older paediatric cancer patients has no negative impact on their level of education.[44] The effect of surviving cancer on the marital status is also consistent with international findings and occurred especially among older survivors.[45] However, besides this possible selection bias, we also do not know, whether the refusers were not willing to participate as a consequence of avoidance and are therefore experiencing an even higher level of PTSD, depression or anxiety or whether they adapted well and did not consider their cancer experience anymore as a relevant part of their lives. Moreover, there are also other possible factors beyond the cancer experience, which may influence PTSD or depression and anxiety (e.g. history of other stressful experiences, subjective perception of life threat, family functioning and social support).[46,47] Although not object of the current study, they should be considered and investigated in future research.

As demonstrated in the sample description, our self-recruited group of controls was biased in terms of sex and educational background. Any generalisations of the findings should therefore be made cautiously. However, even after statistical control for those possibly biasing variables the effect of surviving cancer remained statistically significant. In addition, the use of a second group of controls as well as the comparison to representative prevalence rates strengthens the study and indicates that there are clinically relevant differences between long-term survivors of adolescent cancer in Germany and the general population.

4.2. *Future implications*

These findings support the need for a comprehensive long-term follow-up of cancer survivors which includes the possibility of psychological late effects in order to identify survivors needing psychosocial assistance even years after the end of successful medical treatment.[48] In this respect, the transition from paediatric care to adult care is crucial to assure long-term follow-up of the former adolescent patients.[49] To ensure that survivors with long-term adjustment problems are adequately identified, psychological screening instruments should be routinely and repeatedly administered in the long-term follow-up. Moreover, there is a need for brief psychosocial interventions which address the specific concerns of adolescent cancer patients and survivors[50] to deal with and prevent long-term adjustment problems as well as to maintain and restore quality of life.

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Conflict of interest statement

None declared.

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