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Impact of a mental training program for pediatric cancer patients after allogeneic hematopoietic stem cell transplantation or high-dose chemotherapy – Results of a randomized controlled trial

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Abstract

Objectives. Hematopoietic stem cell transplantation (HSCT) or intensive chemotherapy for the treatment of malignant diseases is a highly distressing experience. The affected person's resilience is crucial to coping with this challenging experience. Experience with resilience-enhancing interventions in children and young adults during cancer therapy is scarce. The major objective of this work was developing and evaluating an effective psycho-oncological mental training that complements the standard psychosocial care.

Methods. In this prospective, randomized single-center study, a total of 30 patients (12 to 22 years of age) who underwent HSCT or high-dose chemotherapy received either the standard psychosocial care (control group [CG]) or additionally underwent a novel and specifically developed resilience-enhancing 14-session mental training (therapy group [TG]). The patients were observed over an 8-month period and were screened for distress, thyroid, and immune function parameters, as well as generalized anxiety, affect, and sports orientation.

Results. Patients of the TG showed significantly greater improvements in all assessed mental aspects, including anxiety, affect, competitiveness, win orientation, goal orientation, self-optimization, self-blocking, and loss of focus, as well as cortisol levels within 8 months, as opposed to patients of the CG (effect size range ξ: 0.74–1.00).

Significance of results. Patients who underwent the mental training displayed less anxiety, better affect, and improved mental performance with less self-blocking. This resulted in improved goal orientation, competitiveness, self-optimization, and focus when compared to the CG patients. However, larger prospective trials are necessary to substantiate these findings.

Introduction

Hematopoietic stem cell transplantation (HSCT) or intensive chemotherapy for the treatment of malignant disease is a highly distressing, potentially traumatic, and life-threatening experience – not only physically but also psychologically – that can have dramatic impacts on a patient's individual concept of life. This especially applies to pediatric, adolescent, or young adult patients who, instead of following their natural maturation and growing experiences and developing their individual characteristics and life goals, have to face severe sickness and an acute and persistent threat to life. This not only affects their mental health but also their personal relationships, the identity of their family, and their family members, all of whom experience severe distress (Guilcher 2016; Linder and Hooke 2019; Packman et al. 2010; West et al. 2020). Pediatric alloHSCT patients are at high risk for anxiety (16–37% of patients) and depression (7–25% higher than age-matched population) (Di Giuseppe et al. 2020) and are likely to develop symptoms of post-traumatic stress (Kronenberger et al. 1996; Stuber et al. 1991). The psychological effects of oncological diseases and their treatment can occur before, during, or a long time after the situation and, depending on the underlying disease, its prognosis, or the patient's age and gender, may significantly impair the patients' overall mental health and quality of life (Bergerot et al. 2015; Chan et al. 2018; Linden et al. 2012; Luo et al. 2019; Rodin et al. 2009). Especially,

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the first year after HSCT in children and adolescents presents significant challenges for the survivors, including difficulties with social competence, self-esteem, and emotional well-being (Luo et al. 2019; Phipps et al. 1995).

The affected person's resilience, which can be defined as their ability to use personal resources to maintain their psychological and physical stability and ability to function while being exposed to major stress or threat (Sisto et al. 2019), is crucial to coping with such a challenging journey. Previous research has shown that personality-related variables such as optimism, hope, self-esteem, positive emotions, and personal control are important factors to build resilience, increase the quality of life, and reduce distress in patients with cancer. Resilience interventions that include stress management, redirection of perceptions, focus on growth and adjustment, or meaning-making can reduce distress, increase the quality of life, and improve optimism and self-efficacy in pediatric, adolescent, and adult cancer patients (Chung et al. 2021; Greup et al. 2018; Kazak et al. 2003; Molina et al. 2014; Rosenberg et al. 2018; Seiler and Jenewein 2019). The German national S3 Guideline "*Psychosocial care in childhood and adolescent oncology*" recommends basic psychosocial care in pediatric hemato-oncology patients that can be complemented with intensified psychosocial care if indicated. (Leiss et al. 2012; Schröder et al. 2019).

The hypothalamus–pituitary–thyroid axis and the hypothalamus–pituitary–adrenal (HPA) axis are important neuroendocrine axes that are key regulators of the endocrine, neurological, neuroendocrine, psychological, and immune systems (Ortiga-Carvalho et al. 2016). These axes can be significantly altered due to stress disorders, cancer, or inflammation (De Luca et al. 2021; Mazzoccoli et al. 2012; Olff et al. 2006; Wong et al. 2008). Psychoneuroimmunology research has clearly shown that the stress-dependent constitutive activation of the HPA axis in cancer patients is likely to undermine therapy success. In particular, several mechanisms of the impact of psychological distress and upregulated glucocorticoid secretion in cancer patients have been proposed, potentially subverting therapeutic tumor control via blocking of type I interferon responses in dendritic cells and interferon gamma (IFNγ) T cell activation (Ma et al. 2020; Yang et al. 2019).

In this prospective randomized controlled single-center study, a total of 30 adolescent and young adult patients aged between 12 and 22 years who underwent allogeneic HSCT or high-dose chemotherapy for the treatment of a malignant or nonmalignant oncologic or hematologic disease, received either the standard psychosocial care during and after their treatment (control group [CG]) or additionally underwent a novel and specifically developed mental training program consisting of 14 one-hour training sessions that include elements of sports psychology, resource activation, motivational training, and resilience enhancement (therapy group [TG]). The study was created following the CONSORT 2010 guidelines for randomized controlled trials (Schulz et al. 2010). The major objectives of this study were to develop and evaluate an effective psycho-oncological training program that complements the standard psychosocial care and that focuses on the major strategies, influencing anxiety, especially reducing recurrence anxiety, increasing motivation, clearing goal orientation by stopping negative thoughts, increasing self-confidence, and making one's own decisions, to prepare the patients and facilitate their transformation from a sick and fighting patient to a survivor who is strong and motivated to create their own, self-determined future.

We hypothesize that this training will therefore lessen anxiety and negative affect, as well as increase positive affect to a significantly greater extent than the standard care protocol in the CG. As a secondary hypothesis, we predict that through the training, heightened achievement motivation, goal orientation, as well as volition will be induced in participants, while there will be no enhancement of these traits following standard protocol in the CG. As an exploratory analysis, we will moreover analyze if these psychological changes further translate into biological changes in thyroid and immune function parameters. Due to the small sample size, no additional exploratory subgroup analyses will be computed.

Material and methods

Study design and patients

In this prospective randomized controlled intervention study (CentraXX study registration number UKT-2018-KI3-2685), adolescent and young adult patients of the University Children's Hospital Tübingen between the ages of 12 and 22 who underwent an allogeneic HSCT or intensive chemotherapy between 2018 and 2020 were consecutively offered study participation and were subsequently recruited at the time of inpatient admission before the commencement of HSCT/chemotherapy. The exclusion criteria were psychoactive substance abuse and diagnosis of a mental disorder according to the International Classification of Disease-11 (Khoury et al. 2017). In total, 30 patients were recruited and randomized to the CG or the TG. The urn randomization was done by hand via random draw from a physical urn without replacement. Due to the limited capacity for training sessions in the TG, participants were recruited successively over the study period so that a maximum of 6 to 7 patients were simultaneously in the training phase. Specifically, this means that initially suitable subjects were invited to participate in the study consecutively at the beginning of the study period and, after consent, were randomized via urn randomization to the study groups until capacity in the TG was reached. Recruitment continued as soon as at least 3 places in the therapy group could be filled. Patients of the CG received the standard psychosocial care and patients of the TG additionally received a mental training program (see below). The observation period started on the day of inpatient admission and ended 8 months after study enrollment. The check-up days on which the patients were screened for laboratory markers and answered questionnaires were the day of study enrollment before starting chemotherapy (baseline/at study enrollment), 3 months (after session 6), 6 months (after session 14), and 8 months (6–8 weeks after session 14) after enrollment. All 30 patients completed all assessments, and every patient from the TG completed the full 14-session program. The study was carried out as an open-label study.

Psycho-oncological care and novel mental training

The patients of both the TG and the CG were offered the standard psycho-oncological care that includes social or psychological counseling with social workers, systemic therapists, or other professionals (e.g., art therapists). In addition, the patients of the TG received a novel and specifically developed mental training program consisting of 14 one-hour training sessions that include elements of sports psychology, resource activation, motivational training, and resilience enhancement. The training program focuses on the major strategies: influencing anxiety, especially reducing recurrence anxiety, increasing motivation, a clear goal orientation by

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stopping negative thoughts, increasing self-confidence, and making one's own decisions. In the first session, medical history and personal goals of the patients are assessed. In the following sessions, patients learn several techniques to strengthen their concentration, attentiveness, stress management, and emotional control and regulation. Negative and anxious thoughts are analyzed and reframed, and personal abilities and strengths are explored. Then, the comprehensive concept of mental strength is introduced and linked to previously learned techniques using a currently existing problem of the patients, for which an individual mental training cycle is established. The last sessions focus on motivation for further development and reflection on the progress the patients made during the program. The description of the concept with a further summary of each session is provided in Supplementary data 1.

Applied questionnaires

On the observation days at baseline (at study enrollment), 3 months (after session 6), 6 months (after session 14), and 8 months (6–8 weeks after session 14), the patients of both cohorts were screened for generalized anxiety (generalized anxiety questionnaire [GAD-7]) (Spitzer et al. 2006), affectivity (Positive and Negative Affect Schedule [PANAS]) (Krohne et al. 1996), sports orientation (Sports Orientation Questionnaire [SOQ]) (Elbe et al. 2008), and volition (volitional components in sports [VKS]) (Wenhold et al. 2008) using standardized questionnaires. The data sets were analyzed between the observation days (baseline, 3 months, 6 months, and 8 months) within the study groups.

The GAD-7 is a screening tool to detect generalized anxiety disorders (Löwe et al. 2008; Spitzer et al. 2006). Since anxiety may represent a normal reaction to a malignant disease, we chose a questionnaire that has been used in this context to assess pathological levels of anxiety in adult cancer patients (Esser et al. 2018). The recommended cutoff score for cancer patients is ≥ 7 (Esser et al. 2018).

The German version (Krohne et al. 1996) of the PANAS (Watson et al. 1988) was applied to assess the positive and negative affect of the patients. The German PANAS is a 20-item questionnaire. Higher scores represent higher affect.

The SOQ was developed as an instrument designed to measure individual achievement motivation in sport situations and was validated for high school and university students. For this study, a validated German version was applied (Elbe et al. 2008). For young athletes (teens to adolescents; performance level 1 [participation in national or international competitions]), standard scores (ranges) for mean competitiveness, win orientation, and goal orientation were defined as 54 (range 48–59), 24 (range 20–27), and 26 (range 24–30), respectively.

The questionnaire for the assessment of VKS was designed to assess skills and deficits in self-direction or volition specifically for sport (Wenhold et al. 2008).

Laboratory analyses

Blood levels of cortisol and thyroid function parameters thyroid-stimulating hormone (TSH), free triiodothyronine (fT_3), and free thyroxine (fT_4) of the immune cells CD3+ T cells, CD4+ T cells, CD8+ T cells, and the CD4+/CD8+ ratio were assessed starting at baseline as well as 3 and 6 months thereafter. Blood collection was performed between 7.00 and 9.00 a.m. Cortisol measurements were not included during corticosteroid treatment. Likewise, thyroid function parameters (TSH, fT3, and fT4) were not included in the analyses during thyroxine treatment.

Statistical analysis

Questionnaire results were calculated in accordance with the individual analysis manuals and then averaged across participants for each time and group combination. Laboratory measurements were determined as mean (M) and standard deviation (SD) of the results of all patients of the respective observation day and study cohort. There was neither missing data from the laboratory analyses nor from the questionnaires. Due to frequent non-normality of data sets as tested by the Shapiro–Wilk normality test, as well as a generally small sample size, robust, nonparametric statistical tests were applied (Feys 2016; Mair and Wilcox 2020). Distributions of patient characteristics were compared between both groups using a Fisher's exact test. To assess the primary psychological outcomes, as well as the secondary explorative laboratory analyses, robust mixed 2×4 analysis of variances (ANOVAs) with between-subject factor group (control and therapy) and within-subject factor time (baseline, 3, 6, and 8 months after HSCT) as independent variables were conducted using the WRS2 R Package. The robust mixed ANOVA uses the 20% trimmed means and returns the test statistic Q, which is approximately F-distributed; however, it does not return an effect size. Significant interactions were therefore followed up by carrying out simple effects analyses with robust t-tests, which compute a robust explanatory measure of effect size ξ (Wilcox and Tian 2011). 0.10, 0.30, and 0.50 correspond to small, medium, and large effect sizes, respectively.

Graphs and statistical tests were created with GraphPad Prism version 8.4.3 (686) for Windows (GraphPad Software. Inc., La Jolla, CA, USA) and R version 4.1.1 (2021-08-10, Copyright 2021, The R Foundation for Statistical Computing). All statistical tests were 2-sided. p-Values <0.05 (*), <0.01 (**), and <0.001 (***) were defined as statistically significant.

Results

Patient characteristics and observation period

A total of 30 pediatric patients with a median age of 16.1 years (range 12.6–22.2 years) were enrolled in this analysis. The TG comprised a significantly higher percentage of female patients when compared to the CG (11 vs. 3 patients; $p = 0.0092$). Since the participants were randomized, this is considered to be coincidental. No other patient characteristic differed significantly between groups. In each group, one patient died of multi-organ failure ($n = 2$; 7%) after study completion. None of the patients were lost to follow-up. Detailed patient characteristics are summarized in Table 1.

Primary and secondary analyses of psychological measures

Means and standard deviations of the psychological measures for the respective observation day and study cohort, as well as the 2 main and the interaction effects examined by the robust 2-way mixed ANOVAs are summarized in Table 2. For the primary outcomes anxiety, positive affect and negative affect, the robust ANOVA revealed significant main effects for group, time, and importantly significant interaction effects (each $p < 0.001$), signifying that the change in the primary psychological measures differed between groups.

To assess the interaction further, post hoc robust t-tests between groups were performed. For self-reported anxiety, the robust t-test showed no significant difference between groups at baseline measurement, $t(11.05) = 0.58$, $p = 0.576$, while there was a significant difference at 3, $t(13.3) = 5.62$, $p < 0.001$, $\xi = 0.86$; 6, $t(13.26) = 7.88$, $p < 0.001$, $\xi = 0.91$; and 8, $t(16) = 9.72$, $p < 0.001$,

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Table 1. Patient characteristics

	Control group		Therapy group		
	n	(%)	*n*	(%)	*p*
Total	15	(100.0)	15	(100.0)	>0.9999
Age					
Median (range)	16.3 (12.6–18.2)		15.8 (13.6–20.2)		
Sex					
Male	12	(80.0)	4	(26.7)	0.0092
Female	3	(20.0)	11	(73.3)	
Diagnosis					
Acute lymphoblastic leukemia	4	(26.7)	3	(20.0)	>0.9999
Acute myeloid leukemia	2	(13.3)	1	(6.7)	>0.9999
Hodgkin's lymphoma	2	(13.3)	2	(13.3)	>0.9999
Medulloblastoma	0	(0.0)	2	(13.3)	0.4828
Osteosarcoma	1	(6.7)	1	(6.7)	>0.9999
Sickle cell anemia	0	(0.0)	2	(13.3)	0.4828
Other	6	(40.0)	4	(26.7)	0.6999
Therapy					
Chemotherapy	8	(53.3)	7	(46.7)	>0.9999
Allogeneic HSCT	7	(46.7)	8	(53.3)	
HSCT donor					
Matched unrelated donor	3	(20.0)	5	(33.3)	0.6817
Matched family/sibling donor	2	(13.3)	2	(13.3)	>0.9999
Mismatched family donor	2	(13.3)	1	(6.7)	>0.9999
Graft-versus-host disease					
Grade I	0	(0.0)	1	(6.7)	>0.9999
Grade II	1	(6.7)	0	(0.0)	>0.9999
Grade III	0	(0.0)	1	(6.7)	>0.9999
Grade IV	2	(13.3)	0	(0.0)	0.4828
Other complications					
Veno-occlusive disease	2	(13.3)	1	(6.7)	>0.9999
Viremia	7	(46.7)	6	(40.0)	>0.9999
Sepsis/SIRS	6	(40.0)	3	(20.0)	0.4270
Invasive fungal infection	1	(6.7)	0	(0.0)	>0.9999
GvHD prophylaxis/Immunosuppression					
ATG-Grafalon	5	(33.3)	6	(40.0)	>0.9999
Thymoglobulin	0	(0.0)	2	(13.3)	0.4828
MMF	2	(13.3)	1	(6.7)	0.5977
CsA	5	(33.3)	7	(46.7)	0.5977
Without	8	(53.3)	7	(46.7)	>0.9999
Death					
Multi-organ failure	1	(6.7)	1	(6.7)	>0.9999

CsA = cyclosporine A, HSCT = hematopoietic stem cell transplantation, MMF = mycophenolate mofetil, *n* = sample size, *p* = probability value.

$\xi = 0.94$, months after HSCT, with the TG reporting significantly less anxiety than the CG. For positive affect, there was a significant difference at baseline level, with the CG reporting significantly more positive affect than the TG, $t(8.94) = 2.35$, $p = 0.044$, $\xi = 0.61$. For months 3, $t(10.65) = 11.01$, $p < 0.001$, $\xi = 0.98$; 6, $t(15) = 23.49$, $p < 0.001$, $\xi = 0.96$; and 8, $t(14.1) = 16.16$, $p < 0.001$, $\xi = 0.93$, the difference between groups was again significant; however, the direction of the effect changed. For the months after the therapy program was started and then completed, participants in the TG reported significantly more positive affect than CG participants. For negative affect, no significant difference between groups was found at baseline, $t(13.17) = 0.79$, $p = 0.442$. However, at 3, $t(14.12) = 15.43$, $p < 0.001$, $\xi = 0.97$; 6, $t(15.98) = 25.84$, $p < 0.001$, $\xi = 0.95$; and 8, $t(12.07) = 17.21$, $p < 0.001$, $\xi = 0.94$, months after HSCT, the robust *t*-test revealed that the CG reported significantly more negative affect than the TG.

For the secondary outcomes sports orientation and volition, the subscale competitiveness, win orientation, goal orientation, self-optimization, self-blocking, lack of activation, and loss of focus were assessed. Again, the robust 2-way mixed ANOVAs showed significant main effects of time and group for all subscales, as well as significant interaction effects (competitiveness, win orientation, goal orientation, and self-optimization with $p < 0.001$ self-blocking and lack of activation with $p < 0.010$ and loss of focus with $p = 0.010$). To specify the interaction, post hoc robust *t*-tests between groups for every level of the time factor were performed. For competitiveness, win orientation, goal orientation, self-optimization, and loss of focus, the robust *t*-test at baseline showed no significant difference, while the *t*-tests performed for month 3, 6, and 8 showed significant differences between groups (all $p < 0.001$, except loss of focus on month 3 comparison at $p = 0.005$, ξ-Range: 0.86–1). For each subscale, TG participants reported on average significantly higher scores after starting and completing the program than CG participants receiving standard care. For the subscales, self-blocking and lack of activation on both the baseline and the 3-month comparison between groups were nonsignificant. At months 6 and 8, a significant difference between groups was shown (all $p < 0.010$, ξ-Range: 0.79–0.94). Therapy group participants reported significantly lower self-blocking tendencies and lack of activation than control participants.

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Table 2. Questionnaire analyses

Months after HSCT	Control group, *M* (SD)				Therapy group, *M* (SD)				*Q*, *p*-value		
	Baseline	3	6	8	Baseline	3	6	8	Group	Time	Interaction
GAD anxiety	19.87 (2.50)	20.73 (1.67)	18.67 (4.05)	18.07 (1.94)	20.00 (5.18)	16.40 (2.35)	11.67 (3.81)	9.73 (1.44)	$Q = 69.00$, $p < 0.001^{***}$	$Q = 29.77$, $p < 0.001^{***}$	$Q = 11.35$, $p < 0.001^{***}$
PANAS positive affect	1.74 (0.15)	1.81 (0.21)	1.79 (0.22)	1.91 (0.27)	1.57 (0.31)	3.02 (0.28)	3.98 (0.34)	4.13 (0.35)	$Q = 507.37$, $p < 0.001^{***}$	$Q = 99.48$, $p < 0.001^{***}$	$Q = 87.37$, $p < 0.001^{***}$
PANAS negative affect	4.10 (0.21)	3.93 (0.28)	3.79 (0.27)	3.67 (0.30)	3.91 (0.48)	2.46 (0.24)	1.69 (0.20)	1.57 (0.21)	$Q = 409.30$, $p < 0.001^{***}$	$Q = 87.69$, $p < 0.001^{***}$	$Q = 51.52$, $p < 0.001^{***}$
Competitiveness	33.40 (3.42)	34.33 (2.99)	34.00 (2.85)	33.13 (2.59)	33.93 (5.23)	46.87 (4.29)	53.07 (4.51)	53.87 (3.11)	$Q = 161.68$, $p < 0.001^{***}$	$Q = 36.03$, $p < 0.001^{***}$	$Q = 31.85$, $p < 0.001^{***}$
Win orientation	14.73 (2.37)	14.60 (1.99)	15.47 (2.39)	15.07 (2.05)	15.40 (1.76)	22.67 (1.29)	24.67 (1.35)	24.33 (1.40)	$Q = 145.52$, $p < 0.001^{***}$	$Q = 47.74$, $p < 0.001^{***}$	$Q = 29.81$, $p < 0.001^{***}$
Goal orientation	15.60 (2.77)	16.53 (2.42)	15.27 (3.28)	15.87 (1.13)	16.20 (4.81)	21.53 (2.90)	24.53 (2.56)	25.87 (1.60)	$Q = 69.94$, $p < 0.001^{***}$	$Q = 6.25$, $p = 0.008^{**}$	$Q = 145.52$, $p < 0.001^{***}$
Self-optimization	36.87 (3.68)	41.13 (2.33)	40.80 (3.08)	41.27 (3.08)	33.20 (15.19)	52.60 (8.89)	61.53 (9.35)	69.13 (5.07)	$Q = 82.26$, $p < 0.001^{***}$	$Q = 40.74$, $p < 0.001^{***}$	$Q = 33.04$, $p < 0.001^{***}$
Self-blocking	18.00 (2.59)	16.73 (2.02)	17.27 (2.05)	17.67 (2.35)	17.27 (4.89)	16.47 (2.95)	14.13 (2.42)	11.13 (3.00)	$Q = 9.63$, $p = 0.010^{*}$	$Q = 4.68$, $p = 0.022^{*}$	$Q = 6.54$, $p = 0.007^{**}$
Lack of activation	28.67 (2.97)	26.27 (3.20)	27.20 (2.51)	25.60 (3.29)	28.80 (4.57)	23.87 (2.29)	20.27 (4.28)	16.53 (5.62)	$Q = 22.73$, $p < 0.001^{***}$	$Q = 13.21$, $p < 0.001^{***}$	$Q = 7.72$, $p = 0.003^{**}$
Loss of focus	18.07 (2.28)	17.60 (1.55)	18.33 (2.16)	17.53 (1.51)	17.33 (2.47)	14.73 (2.09)	12.27 (2.76)	12.27 (2.55)	$Q = 51.75$, $p < 0.001^{***}$	$Q = 4.76$, $p = 0.021^{*}$	$Q = 5.86$, $p = 0.010^{*}$

Means and standard deviations in the control and TG for psychological questionnaire measurements at baseline and 3, 6, and 8 months after hematopoietic stem cell transplantation (HSCT). The last 3 columns show the results of the statistical analysis, using a robust 2-way mixed ANOVA design with group and time/months after HSCT as factors.
*p<0.05, **p<0.01, ***p<0.001, ****p<0.0001.

Exploratory laboratory analyses

Normal values, means, and standard deviations of the laboratory measures for the respective observation day and study cohort, as well as the 2 main and the interaction effect examined by a robust 2-way mixed ANOVAs, are summarized in Table 3. We found significant main effects of group for TSH ($p < 0.001$), FT4 ($p < 0.01$), cortisol, CD8+ T cells, and the CD4+/CD8+ ratio ($p < 0.05$). A significant main effect of time was found in the analysis of CD3+ T cells ($p < 0.05$), and CD8+ T cells ($p < 0.001$). CD8+ T cells furthermore showed a significant interaction effect ($p < 0.05$). No other interaction effect was significant. Therefore, for cortisol, CD8+ cells, and the CD4+/CD8+ ratio, it can be said that there was a significant difference between groups, independent from the time of measurement. The significant main effects of time for CD3+ cells, on the other hand, signify that there is a difference between the different times of measurement, independent from group affiliation. For CD8+ T cells, the significant interaction shows that the change in cell concentration differed between groups. To explore this interaction further, post hoc robust *t*-tests were performed. Neither the difference in CD8+ T cell concentration at baseline, $t(15.26) = 0.58$, $p = 0.867$, nor at month 3, $t(15.92) = 1.13$, $p = 0.276$, was significant. However, at month 6, the TG had significantly more CD8+ T cells than the CG, $t(15.91) = 3.74$, $p = 0.002$, $\xi = 0.74$.

Discussion

The incidence of anxiety and post-traumatic stress disorder is significantly and relevantly higher in survivors of pediatric alloHSCT than in the normal population (Sanders et al. 2010; Taskıran et al. 2016). During the acute and intensive treatment of their life-threatening disease, pediatric HSCT patients are requested to focus on the moment and to invest their whole energy and mind in every single day, one day at a time. In our own clinical experience, we noticed that as soon as the acute existential threat declines, that is, when the success of a disease treatment becomes increasingly evident, and the patients face the inpatient discharge after intensive chemotherapy or HSCT, they begin to focus on the journey that lies ahead of them. During this time, the patients, especially those aged 12 and older, frequently ask about how to find their way back to their past lives and how to create a future that they want to live in. This process is often accompanied by great anxiety and self-blockage. Based on this experience, we developed our mental training. The present study is the first study to investigate a psycho-oncological intervention program based on sport psychology elements and adapted to pediatric and young adult HSCT patients, focusing on methods to reduce anxiety, increase motivation and goal orientation, and to implement this in the form of mental training in 15 pediatric patients. The major objective of this intervention study was to show that our mental training over 14 sessions alleviates anxiety and its negative effects and promotes positive developments, compared to standard care. This could be confirmed. Thus, it was shown that the mental training led to decreased generalized anxiety and negative affect reported by patients significantly more than standard care. Furthermore, the increase of positive affect was significantly greater in the TG than in the CG.

There are only few comparable studies examining psycho-oncology intervention programs in children, adolescents, or young

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Table 3. Laboratory analyses

Months after HSCT	Normal values	Control group, *M* (SD)			Therapy group, *M* (SD)			*Q*, *p*-value		
		Baseline	3	6	Baseline	3	6	Group	Time	Interaction
Cortisol (nmol/L)	125–400	283.53 (141.18)	403.33 (217.45)	463.13 (146.77)	294.20 (157.94)	311.40 (118.92)	287.60 (84.69)	$Q = 7.69$, $p = 0.015$*	$Q = 3.28$, *n.s.*	$Q = 3.11$, *n.s.*
TSH (mU/L)	1.1–8.2	3.32 (1.90)	2.16 (1.29)	2.04 (1.22)	3.51 (1.04)	3.93 (0.85)	3.84 (1.09)	$Q = 19.16$, $p = < 0.001$***	$Q = 0.53$, *n.s.*	$Q = 2.11$, *n.s.*
FT4 (pmol/L)	3.5–6.5	14.53 (3.11)	14.80 (4.44)	13.73 (1.53)	16.67 (1.91)	16.00 (2.39)	16.93 (1.49)	$Q = 12.93$, $p = 0.003$**	$Q = 0.70$, *n.s.*	$Q = 1.16$, *n.s.*
FT3 (pmol/L)	13–26	5.18 (1.26)	4.90 (1.47)	4.12 (1.24)	4.52 (0.80)	4.69 (0.59)	4.59 (0.77)	$Q = 1.79$, *n.s.*	$Q = 1.29$, *n.s.*	$Q = 1.24$, *n.s.*
CD3+ (cells/μL)	>800	290.00 (289.97)	341.47 (221.71)	459.93 (225.73)	649.07 (813.84)	387.73 (255.03)	606.60 (274.46)	$Q = 2.23$, *n.s.*	$Q = 6.06$, $p = .017$*	$Q = 1.08$, *n.s.*
CD4+ (cells/μL)	>400	169.40 (189.94)	164.53 (105.44)	151.07 (102.19)	344.13 (404.76)	158.33 (108.75)	252.67 (161.08)	$Q = 1.28$, *n.s.*	$Q = 0.49$, *n.s.*	$Q = 2.33$, *n.s.*
CD8+ (cells/μL)	>500	178.40 (135.28)	205.40 (131.86)	308.87 (229.79)	197.07 (152.23)	288.07 (156.60)	498.40 (191.96)	$Q = 5.74$, $p = 0.030$*	$Q = 12.28$, $p < 0.001$***	$Q = 4.28$, $p = 0.035$*
CD4+/CD8+ ratio	1.0–1.36	0.81 (0.59)	0.72 (0.31)	0.76 (0.65)	0.68 (0.37)	1.10 (0.37)	1.16 (0.29)	$Q = 7.57$, $p = 0.020$*	$Q = 2.89$, *n.s.*	$Q = 3.65$, *n.s.*

n.s. = not significant. Normal values, means, and standard deviations in the control and TG for laboratory measurements at baseline and 3 and 6 months after hematopoietic stem cell transplantation (HSCT). The last 3 columns show the results of the statistical analysis, using a robust 2-way mixed ANOVA design with group and time/months after HSCT as factors.
*p<0.05, **p<0.01, ***p<0.001, ****p<0.0001.

adults in the setting of HSCT. In a multicenter study of 171 patients and their parents, patients and parents in the TG received an intervention program with massage and humor therapy compared with the CG with standard care. The intervention began at hospital admission and lasted until week 3 after HSCT. Participants completed outcome measures at admission and 24 weeks after HSCT. Across the sample, significant improvements were seen in all outcomes from admission to week 24. Benefits were high at admission and increased at week +24. However, there were no statistically significant differences between intervention arms for any of the measures (Phipps et al. 2012). Another phase 2 randomized controlled trial assigned English-speaking adolescent and young adult patients (AYA; 12–25 years old) with cancer to the *Promoting Resilience in Stress Management* intervention or to usual care. The study suggests that brief, skills-based interventions could provide benefit for this patient population (Rosenberg et al. 2018).

In a study of 66 children and adolescents between 8 and 16 years of age with depressive or anxiety disorders, it was shown that patients who already had high positive and low negative affect prior to 8 weeks of cognitive behavioral therapy (with and without the use of serotonin reuptake inhibitors) responded significantly better to therapy (lower expression of symptoms of depression and anxiety) (Forbes et al. 2012). It has been demonstrated in 50 adult patients with generalized anxiety disorder that positive affect contributes relevantly to quality of life in these patients, and strategies to improve positive affect are a useful starting point in improving the quality of life in these patients (Das et al. 2020). Positive affect was further described as a buffer against chronic stress by ameliorating symptoms of emotional disorders (Sewart et al. 2019). In this sense, the patients of the TG might have benefited both in terms of a reduction of anxiety and increased affect functioning, thereby potentially facilitating their overall treatment response to therapeutic interventions and alleviating stress levels. Research has demonstrated that the individual mental resources and resilience of cancer patients greatly influence their psychological health, post-traumatic growth (i.e., a positive change of life that results from major health or life crises), and quality of life during and after therapy (Rosenberg et al. 2018). In a systematic review, Seiler and Jenewein described personality-related variables such as optimism, hope, self-esteem, positive emotions, and personal control as important factors to build resilience and report an increased quality of life and less distress in patients with effective coping strategies (Seiler and Jenewein 2019). Symptoms of post-traumatic stress and anxiety decreased in patients and their families with the help of family group interventions that combines cognitive behavioral and family therapy approaches (Kazak et al. 2004, 1999).

The hypothesis that the training induced an increased goal orientation and achievement motivation as well as an increased willpower in the participants, while there was no improvement in these characteristics in the CG according to the standard protocol, was confirmed. Analyses of the sports orientation and volitional components showed a significantly greater improvement of competitiveness, win orientation, goal orientation, and self-optimization scores in the TG than in the CG, as well as a significantly greater reduction in self-blocking and a significantly more reduced loss of focus and lack of activation than in patients receiving standard care. The role of goal orientation and competitiveness in achieving academic goals has been thoroughly investigated. Several studies indicated that goal setting in adults is associated with increased use of health activities that promote rehabilitation and recovery (Hurn et al. 2006). The future orientation of adolescents is proposed to have a close relationship to their development outcomes and their individual physical and mental health (Johnson et al. 2014). The determinations of the stress biomarker were only punctual measurements of a dynamic endocrine system that follows circadian variations; however, it is notable that the cortisol levels of the CG patients were significantly higher ($p = 0.0030$) at 6 months when compared to the baseline levels. Although a more

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dynamic development of thyroid function parameters was seen in the CG, monitoring for effects of the mental training on inflammatory signals and thyroid function should be a component in larger clinical trials, further investigating these observations. In our experiment, we observed significant main effects of group for cortisol, TSH, and FT4, signifying the levels of these measurements are significantly different between groups. However, there was neither a significant main effect of time nor a significant interaction effect, meaning the measurements remained relatively stable across time.

The CD4+/CD8+ ratio is decisive for a normal immune function (Robinson et al. 1996). The CD8+ T cell levels increased significantly more in patients of the TG in contrast to patients of the CG. This effect might be based on several influencing factors such as the chemotherapy or immunosuppressive regime. In view of the diversity of the applied medication, we consider it likely that these were the major influencing effects on the T cell regeneration. These observations should be analyzed in larger cohorts.

The limitations of this analysis are the small cohort size and the unequal gender distribution, potentially biasing an inter-group comparison. Nevertheless, the results of this study indicate the importance and efficacy of a supportive and motivation-enhancing mental training. Taken together, the presented data indicate that the adolescent and young adult patients who underwent our mental training displayed less anxiety, better affect, and improved mental performance with less self-blocking. This resulted in improved goal orientation, competitiveness, self-optimization, and focus when compared to the CG patients. Moreover, the data suggest a favorable development of immune and stress function parameters in patients undergoing our mental training program. However, these effects and their interdependent relationships need to be further investigated to facilitate valid conclusions. Additional research questions to explore in this regard could be extensive subgroup analyses such as gender or age subgroups in bigger cohort studies. In this study, patients from the age of 12 to 22 were assessed. As this age range is rather large and spans from the beginning of puberty to early adulthood, it would be beneficial to examine whether certain age groups may benefit more from such a mental training. Similarly, gender is an important moderator for therapy success to explore. Furthermore, this study showed that the improvement of several psychological measurements remained stable at least up until 2 months after completion of the mental training. A long-term experiment could explore further how long the effects of this training last. Lastly, as the whole family is impacted by pediatric cancer, it could be beneficial to the family system to include siblings and parents in therapeutic interventions. A future study could examine whether this mental training program could be extended to contain sessions for other family members and whether this would further strengthen the perceived positive effects.

Supplementary material. The supplementary material for this article can be found at https://doi.org/10.1017/S1478951523000986.

Authors' contributions. All authors made substantial contributions to the conception or design of the work or the acquisition, analysis, or interpretation of data. All authors drafted the work or revised it critically for important intellectual content. MD created the mental training program. MD, KMCS, and JX collected and analyzed the data and wrote the manuscript. DW, MS, ST, VS, and SM analyzed the data. MD and KMCS were head of the study and responsible for the study design. DW and JS contributed to the study conception and design. DW, SM, MS, JS, VS, and PL reviewed the manuscript. All authors read and approved the final manuscript and agreed to be accountable for all aspects of the work.

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Competing interests. The authors declare that they have no conflict of interest.

Ethical approval. This analysis was performed in accordance with the Helsinki declaration adopted by the 18th WMA General Assembly, Helsinki, Finland, June 1964, and amended by the 64th WMA General Assembly, Fortaleza, Brazil, October 2013. The legal basis for the data processing is Art. 6, 7, 9, 89 of the general data protection regulation (EU) 2016/679 of the EU in combination with §§ 4, 5, 6, 8, 9, 12, 13 of the Landesdatenschutzgesetz Baden-Württemberg in its current form of May 25, 2018. Formal written consent for participation and publication of the data was obtained from the patients and/or their legal representatives. Approval for this analysis was granted by the Ethics Committee of the University Hospital Tübingen and the Eberhard Karls University of Tübingen (ID# 317/2018BO1).

References

Bergerot CD, Clark KL, Nonino A, *et al.* (2015) Course of distress, anxiety, and depression in hematological cancer patients: Association between gender and grade of neoplasm. *Palliative & Supportive Care* **13**(2), 115–123. doi:10.1017/S1478951513000849

Chan CMH, Ng CG, Taib NA, *et al.* (2018) Course and predictors of posttraumatic stress disorder in a cohort of psychologically distressed patients with cancer: A 4-year follow-up study. *Cancer* **124**(2), 406–416. doi:10.1002/cncr.30980

Chung JOK, Li WHC, Cheung AT, *et al.* (2021) Relationships among resilience, depressive symptoms, self-esteem, and quality of life in children with cancer. *Psychooncology* **30**(2), 194–201. doi:10.1002/pon.5548

Das A, Clerkin EM, Tolin DF, *et al.* (2020) Moving beyond the negative: Contributions of positive and negative affect on quality of life in patients with generalized anxiety disorder. *Journal of Nervous & Mental Disease* **208**(11), 843–847. doi:10.1097/NMD.0000000000001228

De Luca R, Davis PJ, Lin HY, *et al.* (2021) Thyroid hormones interaction with immune response, inflammation and non-thyroidal illness syndrome. *Frontiers in Cell and Developmental Biology* **8**, 614030. doi:10.3389/fcell.2020.614030

Di Giuseppe G, Thacker N, Schechter T, *et al.* (2020) Anxiety, depression, and mental health-related quality of life in survivors of pediatric allogeneic hematopoietic stem cell transplantation: A systematic review. *Bone Marrow Transplantation* **55**(7), 1240–1254. doi:10.1038/s41409-020-0782-z

Elbe A-M, Wenhold F and Beckmann J (2008) SOQ: Fragebogen zur Erfassung der Leistungsorientierung im Sport. www.bisp.de (accessed 17 July 2023).

Esser P, Hartung TJ, Friedrich M, *et al.* (2018) The Generalized Anxiety Disorder Screener (GAD-7) and the anxiety module of the Hospital and Depression Scale (HADS-A) as screening tools for generalized anxiety disorder among cancer patients. *Psychooncology* **27**(6), 1509–1516. doi:10.1002/pon.4681

Feys J (2016) Nonparametric tests for the interaction in two-way factorial designs using R. *The R Journal* **8**, 367–378. doi:10.32614/RJ-2016-027

Forbes EE, Stepp SD, Dahl RE, *et al.* (2012) Real-world affect and social context as predictors of treatment response in child and adolescent depression and anxiety: An ecological momentary assessment study. *Journal of Child and Adolescent Psychopharmacology* **22**(1), 37–47. doi:10.1089/cap.2011.0085

Greup SR, Kaal SEJ, Jansen R, *et al.* (2018) Post-traumatic growth and resilience in adolescent and young adult cancer patients: An overview. *Journal of Adolescent and Young Adult Oncology* **7**(1), 1–14. doi:10.1089/jayao.2017.0040

Guilcher GM (2016) Hematopoietic stem cell transplantation in children and adolescents. *Pediatrics in Review* **37**(4), 135–144; quiz 145. doi:10.1542/pir.2015-0044

Hurn J, Kneebone I and Cropley M (2006) Goal setting as an outcome measure: A systematic review. *Clinical Rehabilitation* **20**(9), 756–772. doi:10.1177/0269215506070793

Johnson SR, Blum RW and Cheng TL (2014) Future orientation: A construct with implications for adolescent health and wellbeing. *International Journal*

of Adolescent Medicine and Health **26**(4), 459–468. doi:10.1515/ijamh-2013-0333

Kazak AE, Alderfer MA, Streisand R, *et al.* (2004) Treatment of posttraumatic stress symptoms in adolescent survivors of childhood cancer and their families: A randomized clinical trial. *Journal of Family Psychology* **18**(3), 493–504. doi:10.1037/0893-3200.18.3.493

Kazak AE, Cant MC, Jensen MM, *et al.* (2003) Identifying psychosocial risk indicative of subsequent resource use in families of newly diagnosed pediatric oncology patients. *Journal of Clinical Oncology* **21**(17), 3220–3225. doi:10.1200/JCO.2003.12.156

Kazak AE, Simms S, Barakat L, *et al.* (1999) Surviving cancer competently intervention program (SCCIP): A cognitive-behavioral and family therapy intervention for adolescent survivors of childhood cancer and their families. *Family Process* **38**(2), 175–191. doi:10.1111/j.1545-5300.1999.00176.x

Khoury B, Kogan C and Daouk S (2017) International Classification of Diseases 11th Edition (ICD-11). In Zeigler-Hill V and Shackelford TK (eds), *Encyclopedia of Personality and Individual Differences*. Cham: Springer International Publishing, 1–6.

Krohne HW, Egloff B, Kohlmann C, *et al.* (1996) Untersuchungen mit einer deutschen version der "Positive and Negative Affect Schedule" (PANAS) [investigations with a German version of the Positive and Negative Affect Schedule (PANAS)]. *Diagnostica* **42**. doi:10.1037/t49650-000

Kronenberger WG, Carter BD, Stewart J, *et al.* (1996) Psychological adjustment of children in the pretransplant phase of bone marrow transplantation: Relationships with parent distress, parent stress, and child coping. *Journal of Clinical Psychology in Medical Settings* **3**(4), 319–335. doi:10.1007/BF01994017

Leiss U, Griessmeier B, Minetzke-Gruner A-C, *et al.* (2012) Psychosoziale Basisversorgung in der pädiatrischen Onkologie und Hämatologie. In: Projektgruppe Qualitätssicherung der PSAPOH.

Linden W, Vodermaier A, Mackenzie R, *et al.* (2012) Anxiety and depression after cancer diagnosis: Prevalence rates by cancer type, gender, and age. *Journal of Affective Disorders* **141**(2-3), 343–351. doi:10.1016/j.jad.2012.03.025

Linder LA and Hooke MC (2019) Symptoms in children receiving treatment for cancer-part II: Pain, sadness, and symptom clusters. *Journal of Pediatric Oncology Nursing* **36**(4), 262–279. doi:10.1177/1043454219849578

Löwe B, Decker O, Müller S, *et al.* (2008) Validation and standardization of the Generalized Anxiety Disorder Screener (GAD-7) in the general population. *Medical Care* **46**(3), 266–274. doi:10.1097/MLR.0b013e318160d093

Luo Y, Yang P, Yang Y, *et al.* (2019) Cognitive and psychological outcomes of pediatric allogeneic hematopoietic stem cell transplantation survivors in a single center in China. *Medicine (Baltimore)* **98**(39), e17307. doi:10.1097/MD.0000000000017307

Mair P and Wilcox R (2020) Robust statistical methods in R using the WRS2 package. *Behavior Research Methods* **52**(2), 464–488. doi:10.3758/s13428-019-01246-w

Ma Y, Yang H and Kroemer G (2020) Endogenous and exogenous glucocorticoids abolish the efficacy of immune-dependent cancer therapies. *Oncoimmunology* **9**(1), 1673635. doi:10.1080/2162402X.2019.1673635

Mazzoccoli G, Pazienza V, Piepoli A, *et al.* (2012) Alteration of hypothalamic-pituitary-thyroid axis function in non-small-cell lung cancer patients. *Integrative Cancer Therapies* **11**(4), 327–336. doi:10.1177/1534735411413269

Molina Y, Yi JC, Martinez-Gutierrez J, *et al.* (2014) Resilience among patients across the cancer continuum: Diverse perspectives. *Clinical Journal of Oncology Nursing* **18**(1), 93–101. doi:10.1188/14.CJON.93-101

Olff M, Güzelcan Y, de Vries GJ, *et al.* (2006) HPA- and HPT-axis alterations in chronic posttraumatic stress disorder. *Psychoneuroendocrinology* **31**(10), 1220–1230. doi:10.1016/j.psyneuen.2006.09.003

Ortiga-Carvalho TM, Chiamolera MI, Pazos-Moura CC, *et al.* (2016) Hypothalamus-pituitary-thyroid axis. *Comprehensive Physiology* **6**(3), 1387–1428.

Packman W, Weber S, Wallace J, *et al.* (2010) Psychological effects of hematopoietic SCT on pediatric patients, siblings and parents: A review. *Bone Marrow Transplantation* **45**(7), 1134–1146. doi:10.1038/bmt.2010.74

Phipps S, Brenner M, Heslop H, *et al.* (1995) Psychological effects of bone marrow transplantation on children and adolescents: Preliminary report of a longitudinal study. *Bone Marrow Transplantation* **15**(6), 829–835.

Phipps S, Peasant C, Barrera M, *et al.* (2012) Resilience in children undergoing stem cell transplantation: Results of a complementary intervention trial. *Pediatrics* **129**(3), e762–70. doi:10.1542/peds.2011-1816

Robinson M, O'Donohoe J, Dadian G, *et al.* (1996) An analysis of the normal ranges of lymphocyte subpopulations in children aged 5-13 years. *European Journal of Pediatrics* **155**(7), 535–539. doi:10.1007/s004310050437

Rodin G, Lo C, Mikulincer M, *et al.* (2009) Pathways to distress: The multiple determinants of depression, hopelessness, and the desire for hastened death in metastatic cancer patients. *Social Science & Medicine* **68**(3), 562–569. doi:10.1016/j.socscimed.2008.10.037

Rosenberg AR, Bradford MC, McCauley E, *et al.* (2018) Promoting resilience in adolescents and young adults with cancer: Results from the PRISM randomized controlled trial. *Cancer* **124**(19), 3909–3917. doi:10.1002/cncr.31666

Sanders JE, Hoffmeister PA, Storer BE, *et al.* (2010) The quality of life of adult survivors of childhood hematopoietic cell transplant. *Bone Marrow Transplantation* **45**(4), 746–754. doi:10.1038/bmt.2009.224

Schröder HM, Lilienthal S, Schreiber-Gollwitzer BM, *et al.* (2019) Psychosocial care in paediatric oncology and hematology https://www.gpoh.de/kinderkrebsinfo/content/sites/kinderkrebsinfo/content/e1676/e176475/e176588/e176595/PSAPOHS3-Guideline_025_002_englisch2019_ger.pdf.

Schulz KF, Altman DG and Moher D (2010) CONSORT 2010 statement: Updated guidelines for reporting parallel group randomised trials. *Journal of Pharmacology & Pharmacotherapeutics* **1**(2), 100–107. doi:10.4103/0976-500X.72352

Seiler A and Jenewein J (2019) Resilience in cancer patients. *Frontiers in Psychiatry* **10**, 208. doi:10.3389/fpsyt.2019.00208

Sewart AR, Zbozinek TD, Hammen C, *et al.* (2019) Positive affect as a buffer between chronic stress and symptom severity of emotional disorders. *Clinical Psychological Science* **7**(5), 914–927. doi:10.1177/2167702619834576

Sisto A, Vicinanza F, Campanozzi LL, *et al.* (2019) Towards a transversal definition of psychological resilience: A literature review. *Medicina (Kaunas)* **55**(11), 745. doi:10.3390/medicina55110745

Spitzer RL, Kroenke K, Williams JB, *et al.* (2006) A brief measure for assessing generalized anxiety disorder: The GAD-7. *Archives of Internal Medicine* **166**(10), 1092–1097. doi:10.1001/archinte.166.10.1092

Stuber ML, Nader K, Yasuda P, *et al.* (1991) Stress responses after pediatric bone marrow transplantation: Preliminary results of a prospective longitudinal study. *Journal of the American Academy of Child and Adolescent Psychiatry* **30**(6), 952–957. doi:10.1097/00004583-199111000-00013

Taskıran G, Sürer Adanır A and Özatalay E (2016) Living with the unknown: Posttraumatic stress disorder in pediatric bone marrow transplantation survivors and their mothers. *Pediatric Hematology and Oncology* **33**(3), 209–218. doi:10.3109/08880018.2016.1149749

Watson D, Clark LA and Tellegen A (1988) Development and validation of brief measures of positive and negative affect: The PANAS scales. *Journal of Personality and Social Psychology* **54**(6), 1063–1070. doi:10.1037/0022-3514.54.6.1063

Wenhold F, Elbe A-M and Beckmann J (2008) VKS: Fragebogen zur Erfassung Volitionaler Komponenten im Sport. [Online]. www.bisp.de (accessed 17 July 2023).

West CH, Dusome DL, Winsor J, *et al.* (2020) Falling down the rabbit hole: Child and family experiences of pediatric hematopoietic stem cell transplant. *Qualitative Health Research* **30**(7), 1125–1138. doi:10.1177/1049732320912410

Wilcox R and Tian S (2011) Measuring effect size: A robust heteroscedastic approach for two or more groups. *Journal of Applied Statistics* **38**(7), 1359–1368. doi:10.1080/02664763.2010.498507

Wong ML, Dong C, Maestre-Mesa J, *et al.* (2008) Polymorphisms in inflammation-related genes are associated with susceptibility to major depression and antidepressant response. *Molecular Psychiatry* **13**(8), 800–812. doi:10.1038/mp.2008.59

Yang H, Xia L, Chen J, *et al.* (2019) Stress-glucocorticoid-TSC22D3 axis compromises therapy-induced antitumor immunity. *Nature Medicine* **25**(9), 1428–1441. doi:10.1038/s41591-019-0566-4

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