



ORIGINAL ARTICLE OPEN ACCESS

Risk and Protective Factors of Psychosocial Functioning in Survivors of Childhood Cancer: Results of the DCCSS-LATER Study

Anne Maas¹  | Heleen Maurice-Stam¹  | E. A. M (Lieke) Feijen¹ | Jop C. Teepen¹ | Alied M. van der Aa-van Delden¹ | Nina Streefkerk¹ | Eline van Dulmen-den Broeder² | Wim J. E. Tissing^{1,3} | Jacqueline J. Loonen⁴ | Helena J. H. van der Pal¹ | Andrica C. H. de Vries^{1,5} | Marry M. van den Heuvel-Eibrink^{1,5,6} | Cécile Ronckers^{1,7} | Sebastian Neggers^{1,8} | Dorine Bresters^{1,9} | Marloes Louwerens¹⁰ | Birgitta A. B. Versluys^{1,6} | Margriet van der Heiden-van der Loo¹ | Leontien C. M. Kremer^{1,6,11} | Martha Grootenhuis¹ | on behalf of the DCCSS-LATER Study Group

¹Princess Máxima Center for Pediatric Oncology, Utrecht, The Netherlands | ²Department of Pediatric Oncology/Hematology, Amsterdam University Medical Center, Amsterdam, The Netherlands | ³Beatrix Children's Hospital, University of Groningen, University Medical Center Groningen, Groningen, The Netherlands | ⁴Center of Expertise for Cancer Survivorship, Department of Hematology, Radboud University Medical Center, Nijmegen, The Netherlands | ⁵Sophia Children's Hospital, Erasmus Medical Center, Rotterdam, The Netherlands | ⁶Wilhelmina Children's Hospital, University Medical Center Utrecht, Utrecht, The Netherlands | ⁷Division of Childhood Cancer Epidemiology, Institute of Medical Biostatistics Informatics and Epidemiology, University Medical Center of the Johannes Gutenberg University, Mainz, Germany | ⁸Department of Medicine, Section Endocrinology, Erasmus Medical Center, Rotterdam, The Netherlands | ⁹Willem Alexander Children's Hospital, Leiden University Medical Center, Leiden, The Netherlands | ¹⁰Department of Internal Medicine, Leiden University Medical Center, Leiden, The Netherlands | ¹¹Department of Pediatrics, Emma Children's Hospital, Amsterdam UMC, University of Amsterdam, Amsterdam, The Netherlands

Correspondence: Anne Maas (a.maas-9@prinsesmaximacentrum.nl)

Received: 19 January 2024 | **Revised:** 26 June 2024 | **Accepted:** 31 August 2024

Funding: Funding for this study was provided by KiKa.

Keywords: childhood cancer survivors | health-related quality of life | illness cognitions | illness perceptions | psycho-oncology | psychosocial functioning | self-esteem | social support

ABSTRACT

Objective: This study examines the association between psychosocial risk and protective factors and a wide range of psychosocial outcomes including emotional, social, cognitive, and physical domains in childhood cancer survivors (CCS).

Methods: CCS from the Dutch Childhood Cancer Survivor Study (DCCSS)-LATER cohort (diagnosed 1963–2001) part 2 (age ≥ 18 years, diagnosed < 18 years, ≥ 5 years since diagnosis) completed questionnaires on psychosocial risk and protective factors (Benefit and Burden Scale, Illness Cognition Questionnaire, Rosenberg Self-Esteem Scale, and Impact of Cancer Scale), and psychosocial outcomes (Hospital Anxiety and Depression Scale, Self-Rating Scale for Post-Traumatic Stress Disorder, TNO-AZL Questionnaire for Adult Health-Related Quality of Life, and Short Form-36). Associations were assessed with regression analysis, adjusting for attained age, sex, number of health conditions, and time since diagnosis, while correcting for multiple testing ($p < 0.004$).

Results: A total of 1382 CCS participated, all diagnosed ≥ 15 years ago. The mean age of participating CCS was 36 years, and 51% were female. Perceived benefit and burden, acceptance, and helplessness, self-esteem and social support were associated with the psychosocial outcomes. In the models including all psychosocial factors, most associations with psychosocial outcomes

A list of non-author study group members appears in the Acknowledgments.

This is an open access article under the terms of the [Creative Commons Attribution](https://creativecommons.org/licenses/by/4.0/) License, which permits use, distribution and reproduction in any medium, provided the original work is properly cited.

© 2024 The Author(s). *Psycho-Oncology* published by John Wiley & Sons Ltd.

were seen for self-esteem (10×), and perceived burden (9×). Self-esteem (all $\beta \leq 0.47$) and perceived burden (all $\beta \leq 0.38$) demonstrated strongest associations of medium/large size.

Conclusions: Perceptions of childhood cancer, illness cognitions, self-esteem, and social support play a role in explaining psychosocial functioning in CCS, outweighing the influence of socio-demographic and medical variables. Addressing negative perceptions and reducing feelings of helplessness, while promoting acceptance, self-esteem, and social support, could provide intervention targets for CCS who encounter psychosocial challenges.

1 | Introduction

With the growing number of childhood cancer survivors (CCS) reaching adulthood due to improved survival rates, understanding their psychosocial outcomes has become crucial [1]. CCS can encounter physical and psychosocial late effects in adulthood stemming from cancer and its treatment [2, 3]. Encouragingly, the majority of CCS adapt well and score within normal ranges on measures of health related quality of life (HRQOL) and mental well-being. However, certain subgroups report worse HRQOL compared to general population norms, and experience symptoms like anxiety, depression, and post-traumatic stress [4, 5].

Recently, we studied psychosocial outcomes, and socio-demographic and cancer-related medical determinants in a large cohort of Dutch adult CCS [6, 7]. Our findings confirmed that, on average, CCS have psychosocial outcomes comparable to the general population. In line with other studies, we found that CCS with certain socio-demographic characteristics, including female sex, lower educational attainment, and unemployment, along with cancer-related medical characteristics, such as a CNS tumor diagnosis, reported poorer psychosocial outcomes [4, 8]. Additionally, we found that specific health conditions were associated with psychosocial problems [9]. However, these characteristics explained merely a small proportion of the variability in CCS' psychosocial outcomes.

The limited explained variance of socio-demographic and medical characteristics suggests that other factors play a more prominent role in explaining psychosocial functioning in CCS. Although the literature in this domain mostly stems from comparatively small-sized studies, results indeed highlighted that subjective appraisals regarding the cancer experience and its aftermath are stronger predictors of psychosocial functioning than objective medical data [10–12]. Notably, the literature emphasizes the importance of subjective factors including perceptions regarding childhood cancer [11, 13], coping strategies to manage the cancer experience and its long-term effects [12, 14], self-esteem [15], and social support [16]. Unlike medical histories, these psychosocial factors could be modified and addressed through targeted interventions. Consequently, further research on this subject is vital to inform and develop tailored care for CCS.

The present study is the first large nationwide cohort study to examine the association between psychosocial risk and protective factors (perceived benefit and burden, illness cognitions, self-esteem and social support) and a wide range of psychosocial outcomes (emotional, social, cognitive, physical) in CCS.

2 | Methods

2.1 | Design and Population

This study is part of the Dutch Childhood Cancer Survivor Study (DCCSS)-LATER, a nationwide cohort study including all CCS diagnosed between 1963 and 2001 at age ≤ 18 , and ≥ 5 years since diagnosis. The participants were treated at one of the seven former Dutch pediatric oncology centers. The medical ethics board of all participating centers approved the study, and all participants provided informed consent.

The study consists of two cross-sectional studies conducted within the DCCSS-LATER cohort. First, the DCCSS-LATER 1 study (2013–2014) in which, among others, data on health conditions were collected using a questionnaire [17]. Second, the DCCSS-LATER 2 study (2017–2020), which included the LATER Psycho-oncology sub-study, in which data on psychosocial outcomes were collected using questionnaires [7, 18]. This sub-study included CCS aged ≥ 18 years at outcome assessment. From their homes, participants completed online or paper/pencil-based questionnaires on health conditions and potential psychosocial risk and protective factors.

2.2 | Measures

We addressed emotional, social, cognitive, and physical domains as outcomes. We operationalized these outcome domains using the most relevant scales of various questionnaires administered in the DCCSS-LATER 2 study (Table S1), which have adequate to good psychometric properties [15, 19–25]. Higher scores on the measures indicate higher levels of the concepts. Additional information on the questionnaires below can be found in Table S1.

2.2.1 | Psychosocial Outcomes

- *Hospital Anxiety and Depression Scale (HADS)* [19] consists of the scales anxiety, and depression (range: 0–21).
- *Self-Rating Scale for Post-Traumatic Stress Disorder (SRS-PTSD)* [20, 21] measures PTSD symptoms in three domains: re-experiencing, avoidance, and hyper-arousal. A total scale score was calculated (range: 0–17).
- *TNO-AZL Questionnaire for Adult Health-Related Quality of Life (TAAQOL)* [26] measures various HRQOL domains, of which we used the following scales: positive emotions, social functioning, cognitive functioning, gross motor

functioning, sleep, pain, daily activities, and vitality (range 0–100).

- *Short Form 36 (SF-36)* [22] of which the scale general health perceptions was used (range 0–100).

2.2.2 | Psychosocial Risk and Protective Factors

- *Rosenberg Self-Esteem Scale (RSE)* [27] consists of one scale: self-esteem (range 10–40).
- *Benefit and Burden Scale (BBSC)* [24] consists of two scales: perceived benefit and burden of childhood cancer (range 10–50).
- *Illness Cognition Questionnaire (ICQ)* [25] of which the scales childhood cancer-related helplessness and acceptance were used (range 6–24).
- *Impact of Cancer Scale—Childhood Cancer (IOC-CS), Social Support Item* [28] measures social support with a single item: “I receive love and support from my friends” (range 1–5).

2.2.3 | Background Characteristics

Included socio-demographic characteristics were sex (obtained in a questionnaires in the DCCSS-LATER 2 study) and attained age at time of questionnaire completion (birth month and year obtained from the DCCSS-LATER registry). Included medical characteristics were time since childhood cancer diagnosis (obtained from the DCCSS-LATER registry) and number of clinically relevant health conditions, defined as health conditions that exhibited symptoms and/or required medical intervention [3]. Health conditions were assessed in the DCCSS-LATER 1 study, and validated through self-reported medication use or review of medical records, as reported previously [3]. We adjusted for these background characteristics in the analysis to mitigate potential confounding effects, as these characteristics have been associated with various psychosocial determinants and outcomes in prior research [5, 7, 9, 29].

2.3 | Statistical Analysis

We used Independent *t*-tests and Chi-square tests to examine differences between participants and non-participants on socio-demographic and medical characteristics, with Cohen's *d* and Cramer's *V* as effect sizes.

The impact of background characteristics and psychosocial risk and protective factors on the psychosocial outcomes was examined with multiple linear regression analyses. In the first step, we constructed a model for each psychosocial outcome with background characteristics solely, including sex, time since diagnosis, and number of health conditions. In the second step, we explored psychosocial factors (benefit and burden, illness cognitions, self-esteem, and social support) in relation to the psychosocial outcomes in four separate models in order to gain insight into alterations of the explained variance. In the third and final step, all psychosocial factors from step 2 were included

together in a model for each psychosocial outcome in order to identify the strongest factors. In both step 2 and 3 we adjusted for background characteristics (step 1).

Following Cohen [30], for mean differences between two groups and for regression coefficients of dichotomous independent variables, we considered effect sizes of 0.2, 0.5, and 0.8 respectively small, medium and large. For regression coefficients of continuous independent variables and for Cramer's *V*, 0.1, 0.3, and 0.5 were considered small, medium and large, respectively. Effect sizes falling below these thresholds (regression coefficients <0.2 for dichotomous variables or <0.1 for continuous variables) were not considered relevant, and these results are therefore not discussed.

We used a significance level of 0.004 for the regression analyses to address multiple testing, which corresponds to 0.05 divided by the number of 12 outcome measures.

3 | Results

3.1 | Participants

The DCCSS-LATER cohort comprised 6165 CCS of which 5455 were alive at time of the DCCSS-LATER 2 study. For the DCCSS-LATER 2 study, a total of 4671 adult CCS were invited of whom 2485 participated (53.5%) (Figure 1). Of these 2485 CCS, 1382 (55.6%) CCS had both completed the questionnaire on health outcomes in LATER 1 as well as at least one questionnaire on psychosocial risk and protective factors, and at least one psychosocial outcomes questionnaire in LATER 2.

Participating CCS had a mean age of 36.3 years (SD 9.5, range 18–70), 51% were female and mean time since diagnosis was 29.4 years (SD 8.5, range 15–55). Participants were compared to the 2569 (of the 3289) non-participants who did not decline the use of their medical data. Only small ($V \leq 0.12$) differences were found between participants and non-participants on some socio-demographic and medical characteristics (Table 1).

3.2 | Background Characteristics (Step 1)

Tables 2 and 3 present the regression models of the association of background characteristics and the psychosocial factors with the psychosocial outcomes. Overall, attained age, sex, time since diagnosis, and number of health conditions accounted for 1%–13% of variance in psychosocial outcomes.

3.3 | Psychosocial Factors Analyzed Separately, Adjusted for Background Characteristics (Step 2)

3.3.1 | Benefit and Burden (BBSC) Model

More perceived benefit was associated with better emotional outcomes (anxiety, depression, positive emotions), social functioning, cognitive functioning, and some of the evaluated physical outcomes (daily activities, vitality). The effect sizes

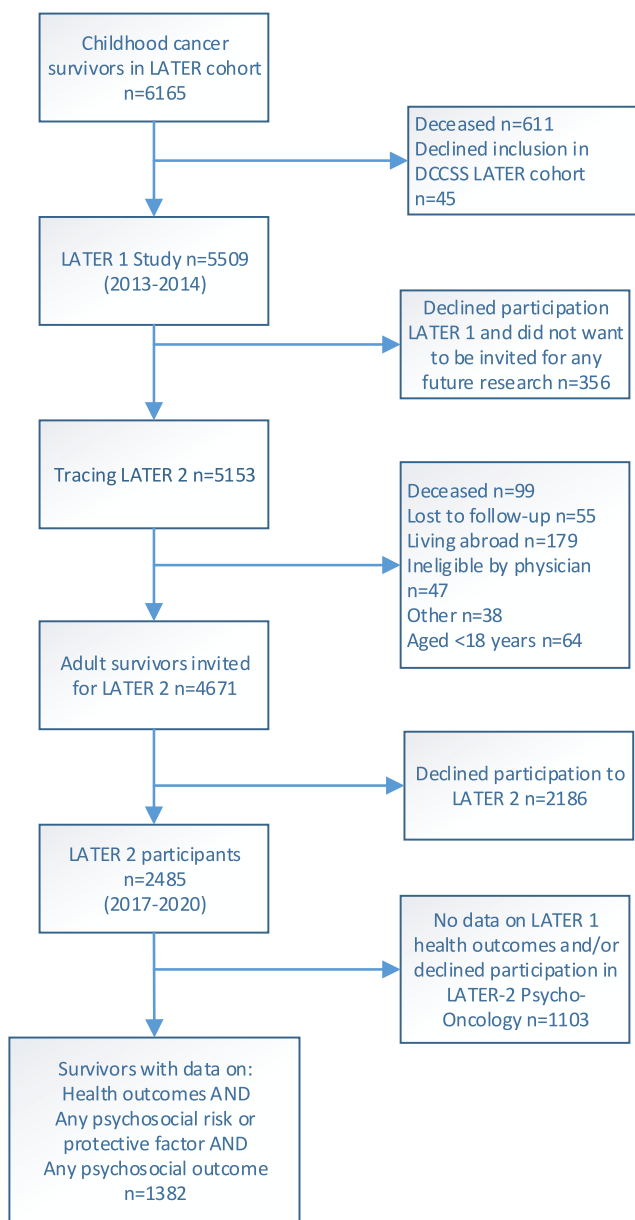


FIGURE 1 | Flowchart of participants.

ranged from small to medium. Perceived burden was associated with worse outcomes across all domains, with effect sizes ranging from medium to large. The models including perceived benefit and burden explained 17.0%–38.9% of variance in psychosocial outcomes.

3.3.2 | Illness Cognitions: Acceptance and Helplessness (ICQ) Model

Higher levels of acceptance were associated with better outcomes across all domains, except gross motor function. The effect sizes ranged from small to medium/large. More helplessness was associated with worse outcomes across all domains, with medium to large effect sizes. The model including helplessness and acceptance explained 13.6%–34.8% of variance in psychosocial outcomes.

3.3.3 | Self-Esteem (RSE) Model

More self-esteem was associated with better outcomes across all domains, with small/medium to large effect sizes. The model including self-esteem explained 15.5%–40.2% of variance in psychosocial outcomes.

3.3.4 | Social Support (Separate Item IOC-CS) Model

More social support was associated with better outcomes across all domains, with small/medium effect sizes. The model including social support explained 6.7%–14.8% of variance in psychosocial outcomes.

3.4 | Psychosocial Risk and Protective Factors Analyzed Together Adjusted for Background Characteristics (Step 3)

In the 12 outcome models that included all psychosocial risk and protective factors while adjusting for background characteristics, most associations were seen for perceived burden (9×), and self-esteem (10×). Self-esteem (all $\beta \leq 0.47$) and perceived burden (all $\beta \leq 0.38$) also demonstrated the strongest associations of medium/large size. Perceived burden appeared stronger associated with emotional domains compared to physical domains, while helplessness appeared stronger associated with physical domains compared to emotional domains. In the models for emotional and social outcomes, acceptance and social support remained significant for three out of five outcomes, albeit with smaller effect sizes compared to the step-2 models.

Overall, the models including all psychosocial risk and protective factors explained 41.3%–49.7% of variance in the emotional domain, 33.2% in the social domain, 29.6% in the cognitive domain and 19.4%–38.0% in the physical domain.

4 | Discussion

This is the first study on psychosocial risk and protective factors of a range of psychosocial outcomes in a large, nationwide cohort of adult CCS. Our findings underscore the importance of psychosocial factors such as perceptions, illness cognitions, self-esteem, and social support in explaining psychosocial functioning in CCS. These factors surpassed the influence of socio-demographic and cancer-related medical characteristics. These results are in line with previous studies demonstrating the importance of subjective appraisals and social support in predicting CCS' psychosocial outcomes [10–13].

We found that the illness cognitions helplessness and acceptance were associated to respectively poorer and better psychosocial outcomes. Although these concepts have not been extensively studied in CCS, similar results were found in studies among patients with chronic health problems [25], and among adolescent and young adult cancer survivors [14]. Furthermore, we found that both perceived benefit and burden were associated with respectively better and poorer psychosocial outcomes,

TABLE 1 | Demographic and medical characteristics CCS: Participants versus non-participants.

	Participants (N = 1382)			Non-participants (N = 2569)			Cohen's <i>d</i>
	<i>M</i>	<i>SD</i>	Range	<i>M</i>	<i>SD</i>	Range	
Age at study (years)	36.27	9.53	18.29–70.88	35.12	9.15	18.02–70.52	−0.12***
Age at first diagnosis (years)	6.85	4.77	0.00–17.96	6.59	4.69	0.00–17.95	−0.06
Time since first diagnosis (years)	29.42	8.53	15.34–55.01	28.53	8.25	15.44–56.18	−0.11**
	% (N)			% (N)			Cramer's V
Socio-demographic characteristics							
Sex							0.10***
Male	49.1 (679)			59.8 (1537)			
Female	50.9 (703)			40.2 (1032)			
Partnered	71.0 (981)						
Educational attainment							
Low	12.2 (166)						
Middle	41.0 (560)						
High	46.8 (639)						
Employed	83.9 (1159)						
Medical characteristics							
Clinically relevant health conditions (number)							
0	55.4 (766)						
1	27.0 (373)						
2	10.6 (147)						
3	4.6 (63)						
≥ 4	2.4 (33)						
Age at first diagnosis (years)							
0–5	52.7 (729)			53.9 (1384)			0.03
6–11	27.4 (378)			28.5 (733)			
12–17	19.9 (275)			17.6 (452)			
Time since first diagnosis (years)							0.05*
10–19	15.2 (210)			17.1 (440)			
20–29	41.0 (566)			42.9 (1101)			
30–39	31.1 (430)			29.2 (751)			
40–49	11.1 (154)			10.0 (258)			
50–59	1.6 (22)			0.7 (19)			
Recurrence (yes)	13.6 (188)			11.9 (305)			0.03
Diagnosis							
Hematologic	52.2 (712)			59.8 (199)			0.06*
Central nervous system	9.2 (126)			8.7 (29)			0.01
Solid	38.5 (525)			31.5 (105)			0.06*
Treatment							
Surgery (yes)	51.1 (705)			50.7 (1295)			0.00
Chemotherapy (yes)	87.6 (1211)			82.2 (2110)			0.07***
Radiotherapy (yes)	40.3 (557)			31.5 (807)			0.09***

Note: Significant differences ($p < 0.05$) are presented in bold. Because of missing values, *N* varies slightly across variables. Data were missing for non-participating survivors who declined the use of their data in the DCCSS-LATER registry ($N = 720$).

* $p < 0.05$, ** $p < 0.01$, *** $p < 0.001$.

TABLE 2 | Psychosocial risk and protective factors in relation to psychosocial outcomes—Domain *emotional, social, and cognitive*.

Outcome domains	Emotional			Social	Cognitive	
	Anxiety β (95% CI)	Depression β (95% CI)	PTSS β (95% CI)	Positive emotions β (95% CI)	Social functioning β (95% CI)	Cognitive functioning β (95% CI)
Step 1: Background characteristics						
<i>N</i>	1366	1363	1204	1413	1413	1419
Attained age	0.03 (−0.08; 0.13)	0.05 (−0.05; 0.16)	0.06 (−0.05; 0.17)	−0.05 (−0.15; 0.05)	−0.06 (−0.16; −0.04)	−0.07 (−0.17; 0.04)
Female sex	0.27*** (0.16; 0.37)	0.05 (−0.05; 0.16)	0.20*** (0.09; 31)	0.03 (−0.07; 0.14)	−0.06 (−0.16; 0.04)	−0.34*** (−0.44; −0.24)
Time since diagnosis	−0.05 (−0.15; 0.06)	−0.04 (−0.15; 0.06)	−0.03 (−0.15; 0.08)	−0.00 (−0.10; 0.10)	−0.02 (−0.13; 0.08)	0.06 (−0.04; 0.17)
Number of health conditions	0.02 (−0.03; 0.08)	0.13*** (0.08; 0.18)	0.11*** (0.05; 0.17)	−0.07* (−0.12; −0.01)	−0.12*** (−0.17; −0.07)	−0.06* (−0.11; −0.01)
<i>R</i> ²	0.02***	0.02***	0.02***	0.01**	0.03***	0.03***
Step 2: Psychosocial factors in separate models, adjusted for background characteristics (step 1) ^a						
a. Model BBSC						
<i>N</i>	1321	1320	1171	1327	1327	1330
Benefit	−0.15*** (−0.19; −0.10)	−0.21*** (−0.26; −0.17)	−0.05* (−0.10; −0.00)	0.26*** (0.21; 31)	0.14*** (0.18; 0.93)	0.12*** (0.07; 0.17)
Burden	0.56*** (0.51; 0.61)	0.61*** (0.56; 0.65)	0.62*** (0.57; 0.67)	−0.44*** (−0.49; −0.40)	−0.48*** (−0.53; −0.43)	−0.46*** (−0.51; −0.42)
<i>R</i> ²	0.32***	0.39***	0.37***	0.23***	0.25***	0.24***
b. Model ICQ						
<i>N</i>	1323	1322	1169	1336	1335	1339
Acceptance	−0.27*** (−0.32; −0.21)	−0.25*** (−0.30; −0.20)	−0.22*** (−0.27; −0.17)	0.29*** (0.24; 0.34)	0.15*** (0.10; 0.20)	0.17*** (0.11; 0.22)
Helplessness	0.30*** (0.25; 0.35)	0.40*** (0.35; 0.45)	0.43*** (0.37; 0.48)	−0.23*** (−0.28; −0.17)	−0.34*** (−0.40; −0.29)	−0.28*** (−0.34; −0.23)
<i>R</i> ²	0.24***	0.32***	0.32***	0.20***	0.21***	0.17***
c. Model RSE						
<i>N</i>	1353	1351	1193	1365	1364	1368
Self-esteem	−0.59*** (−0.64; −0.55)	−0.64*** (−0.68; −0.59)	−0.51*** (−0.56; −0.46)	0.61*** (0.57; 0.66)	0.48*** (0.43; 0.52)	0.49*** (0.45; 0.54)
<i>R</i> ²	0.35***	0.40***	0.26***	0.36***	0.24***	0.26***
d. Model social support IOC-CS						
<i>N</i>	1320	1318	1164	1318	1317	1321
Social support	−0.23*** (−0.28; −0.18)	−0.34*** (−0.40; −0.29)	−0.24*** (−0.30; −0.19)	0.35*** (0.30; 0.40)	0.35*** (0.30; 0.97)	0.17*** (0.12; 0.23)
<i>R</i> ²	0.07***	0.13***	0.08***	0.12***	0.15***	0.06***
Step 3: Models including all psychosocial factors (step 2), adjusted for background characteristics (step 1) ^a						
Model psychosocial factors						
<i>N</i>	1269	1268	1128	1266	1266	1269
Benefit	−0.01 (−0.06; −0.04)	−0.08*** (−0.12; −0.03)	0.04 (−0.01; 0.09)	0.08** (0.03; 0.13)	0.02 (−0.04; 0.07)	0.02 (−0.03; 0.07)
Burden	−0.31*** (0.24; 0.38)	0.26*** (0.20; 0.33)	0.38*** (0.30; 0.46)	−0.07* (−0.14; −0.00)	−0.19*** (−0.26; −0.11)	−0.24*** (−0.32; −0.16)

(Continues)

TABLE 2 | (Continued)

Outcome domains	Emotional			Social	Cognitive	
	Anxiety β (95% CI)	Depression β (95% CI)	PTSS β (95% CI)	Positive emotions β (95% CI)	Social functioning β (95% CI)	Cognitive functioning β (95% CI)
Acceptance	-0.12*** (-0.17; -0.07)	-0.08** (-0.12; -0.03)	-0.11*** (-0.16; -0.05)	0.12*** (0.07; 0.17)	0.03 (-0.03; 0.08)	0.04 (-0.02; 0.10)
Helplessness	-0.04 (-0.11; 0.02)	0.10** (0.04; 0.16)	0.11** (0.03; 0.18)	0.00 (-0.07; 0.07)	-0.12** (-0.19; -0.05)	-0.02 (-0.09; 0.06)
Self-esteem	-0.38*** (-0.44; -0.33)	-0.35*** (-0.40; -0.29)	-0.19*** (-0.25; -0.13)	0.47*** (0.41; 0.53)	0.23*** (0.17; 0.29)	0.33*** (0.27; 0.39)
Social support	-0.01 (-0.06; 0.03)	-0.11*** (-0.15; -0.07)	-0.05* (-0.10; -0.00)	0.13*** (0.08; 0.17)	0.20*** (0.15; 0.25)	-0.01 (-0.06; 0.04)
R^2	0.42***	0.50***	0.43***	0.41***	0.33***	0.30***

Note: Regression coefficients of ≥ 0.20 for dichotomous independent variables, and ≥ 0.10 for continuous independent variables, with a p -value of < 0.004 are presented in bold.

Abbreviations: BBSC = Benefit and Burden Scale, ICQ = Illness Cognition Questionnaire, IOC-CS = Impact of Cancer Scale, RSE = Rosenberg Self-Esteem Scale.

^aNot presented.

* $p < 0.05$, ** $p < 0.01$, *** $p < 0.001$.

although perceived benefit had weaker associations with the psychosocial outcomes than the other risk and protective factors and appeared no longer statistically significant in the model including all these factors. In line with a previous study in underage CCS, perceived burden was more strongly associated to the outcomes than perceived benefit [23], in the same way helplessness was more strongly associated to the outcomes than acceptance. These findings imply that negative cognitions and perceptions are better predictors of psychosocial outcomes than positive cognitions and perceptions. In the literature benefit finding is described as conceptually distinct from general emotional adjustment, with no clear associations between benefit finding and psychosocial distress [31]. Consequently, positive experiences can coexist with psychosocial challenges and are, therefore, not strongly associated to these outcomes.

It has been acknowledged that the social context of cancer survivors is crucial in understanding their psychosocial outcomes [14, 16]. Our findings indeed reveal an association between social support and psychosocial outcomes. CCS receiving greater social support from family and friends may have more resources to cope with stressors, resulting in fewer psychosocial problems [32].

Finally, most associations with the psychosocial outcomes were seen for perceived burden and self-esteem. We studied these relevant constructs for CCS previously [7, 29]. Encouragingly, we observed that only a minority (3.5%–12.1%) reported much burden because of childhood cancer, and CCS did not differ from the general population on generic self-esteem. However, for CCS experiencing psychosocial challenges, these factors may be compromised, and for this subgroup interventions to enhance perceptions and self-esteem could be beneficial. Although most and strongest associations were seen between self-esteem and psychosocial outcomes in the present study, there is a scarcity of research examining this relationship in CCS. A study among young adult cancer survivors also identified self-esteem as an important predictor of the social aspect of HRQOL [15], and self-esteem difficulties have been found to be

associated to worse psychosocial outcomes in the general population [33].

These findings can be interpreted in the light of the disability-stress-coping model proposed by Wallander and Varni [34]. This model suggests that the link between stressors related to illness and subsequent adjustments is influenced by individual appraisals and coping strategies. These factors are in turn shaped by a range of personal and social risk and protective factors. In this context, our results underscore the significance of negative appraisals and coping mechanisms characterized by helplessness as important determinants of psychosocial outcomes. This study also revealed the protective effect of acceptance, social support, and especially self-esteem. While this study focused on direct relationships, future research could look into stress-processing, personal and social-ecological factors that might moderate observed associations.

4.1 | Clinical Implications

Our findings suggest that illness cognitions (helplessness, acceptance), perceptions (perceived burden), self-esteem, and social support could be a target for interventions. Given that most and strongest associations were seen between self-esteem and psychosocial outcomes, for CCS encountering psychosocial problems, fostering a healthy self-esteem could be an important initial step as early on in the trajectory as possible. Cognitive Behavioral Therapy (CBT) and Acceptance and Commitment Therapy (ACT) are examples of evidence-based interventions addressing these factors and improving psychosocial outcomes [35–38]. CBT involves identifying and replacing unhelpful thoughts, while ACT focuses on reducing the impact of negative thoughts through acceptance and defusion techniques [39]. Given the positive association between social support and psychosocial outcomes, offering group interventions to CCS may be an effective way to support CCS. A recent example of a psychosocial group intervention is “Op Koers” which aims

TABLE 3 | Psychosocial risk and protective factors in relation to psychosocial outcomes—Domain *physical*.

	Gross motor function β (95% CI)	Daily activities β (95% CI)	Sleep β (95% CI)	Pain β (95% CI)	Vitality β (95% CI)	General health perceptions β (95% CI)
Step 1: Background characteristics						
<i>N</i>	1418	1413	1417	1414	1415	1381
Attained age	-0.22*** (-0.32; -0.12)	-0.03 (-0.13; 0.07)	-0.05 (-0.15; 0.05)	-0.10* (-0.20; -0.01)	-0.04 (-0.14; 0.06)	-0.04 (-0.14; 0.06)
Female sex	-0.40*** (-0.50; -0.31)	-0.34*** (-0.44; -0.23)	-0.41*** (-0.51; -0.31)	-0.50*** (-0.60; -0.40)	-0.41*** (-0.51; -0.32)	-0.29*** (-0.39; 0.19)
Time since diagnosis	0.08 (-0.02; 0.18)	0.02 (-0.08; 0.12)	-0.01 (-0.10; 0.10)	-0.02 (-0.12; 0.08)	0.01 (-0.09; 0.11)	-0.00 (-0.10; 0.09)
Number of health conditions	-0.20*** (-0.25; -0.15)	-0.11*** (-0.16; -0.06)	-0.04 (-0.09; 0.01)	-0.09*** (-0.14; -0.04)	-0.19*** (-0.23; -0.14)	-0.28*** (-0.33; -0.23)
<i>R</i> ²	0.13***	0.04***	0.05***	0.09***	0.09***	0.11***
Step 2: Psychosocial factors in separate models, adjusted for background characteristics (step 1) ^a						
Model BBSC						
<i>N</i>	1329	1328	1328	1327	1328	1324
Benefit	-0.01 (-0.06; 0.04)	0.11*** (0.06; 0.16)	0.07** (0.02; 0.12)	0.04 (-0.01; 0.09)	0.11*** (0.06; 0.15)	0.06* (0.01; 0.10)
Burden	-0.33*** (-0.38; -0.28)	-0.47*** (-0.52; -0.42)	-0.37*** (-0.42; -0.32)	-0.31*** (-0.36; -0.26)	-0.42*** (-0.47; -0.38)	-0.47*** (-0.52; -0.42)
<i>R</i> ²	0.22***	0.25***	0.17***	0.17***	0.25***	0.31***
Model ICQ						
<i>N</i>	1339	1337	1337	1336	1337	1332
Acceptance	0.07* (0.01; 0.12)	0.15*** (0.10; 0.20)	0.16*** (0.11; 0.22)	0.13*** (0.08; 0.18)	0.18*** (0.13; 0.23)	0.15*** (0.10; 0.20)
Helplessness	-0.35*** (-0.41; -0.30)	-0.38*** (-0.43; -0.33)	-0.20*** (-0.25; -0.14)	-0.21*** (-0.26; -0.15)	-0.33*** (-0.39; -0.28)	-0.42*** (-0.47; -0.37)
<i>R</i> ²	0.26***	0.25***	0.14***	0.17***	0.27***	0.35***
Model RSE						
<i>N</i>	1367	1366	1366	1365	1366	1358
Self-esteem	0.26*** (0.21; 0.31)	0.45*** (0.40; 0.50)	0.37*** (0.32; 0.42)	0.26*** (0.21; 0.31)	0.48*** (0.44; 0.53)	0.43*** (0.38; 0.47)
<i>R</i> ²	0.19***	0.23***	0.18***	0.16***	0.31***	0.28***
Model social support IOC-CS						
<i>N</i>	1321	1319	1319	1318	1319	1314
Social support	0.10*** (0.04; 0.15)	0.17*** (0.12; 0.23)	0.15*** (0.10; 0.21)	0.14*** (0.09; 0.20)	0.22*** (0.17; 0.27)	0.18*** (0.13; 0.24)
<i>R</i> ²	0.14***	0.07***	0.07***	0.12***	0.13***	0.15***
Step 3: Models including all psychosocial factors (step 2), adjusted for background characteristics (step 1) ^a						
Model psychosocial factors						
<i>N</i>	1269	1267	1267	1266	1267	1266
Benefit	-0.05 (-0.11; 0.00)	0.02 (-0.03; 0.07)	-0.02 (-0.07; 0.04)	-0.03 (-0.09; 0.03)	-0.02 (-0.07; 0.04)	-0.04 (-0.09; 0.01)
Burden	-0.03 (-0.11; 0.06)	-0.14*** (-0.22; -0.06)	-0.21*** (-0.30; -0.13)	-0.12** (-0.21; -0.04)	-0.04 (-0.11; 0.04)	-0.11** (-0.19; -0.04)

(Continues)

TABLE 3 | (Continued)

	Gross motor function β (95% CI)	Daily activities β (95% CI)	Sleep β (95% CI)	Pain β (95% CI)	Vitality β (95% CI)	General health perceptions β (95% CI)
Acceptance	0.04 (-0.02; 0.10)	0.06* (0.01; 0.12)	0.06* (0.00; 0.12)	0.08* (0.02; 0.14)	0.07* (0.02; 0.12)	0.08** (0.03; 0.13)
Helplessness	-0.32*** (-0.39; -0.24)	-0.23*** (-0.30; -0.16)	0.01 (-0.06; 0.09)	-0.11** (-0.18; -0.03)	-0.20*** (-0.27; -0.13)	-0.27*** (-0.34; -0.20)
Self-esteem	0.08* (0.02; 0.15)	0.23*** (0.17; 0.29)	0.23*** (0.16; 0.30)	0.08* (0.01; 0.14)	0.31*** (0.25; 0.37)	0.19*** (0.13; 0.25)
Social support	0.01 (-0.05; 0.06)	-0.00 (-0.05; 0.05)	0.02 (-0.03; 0.08)	0.06* (0.01; 0.12)	0.05* (0.01; 0.10)	0.03 (-0.02; 0.08)
R^2	0.27***	0.31***	0.21***	0.19***	0.35***	0.38***

Note: Regression coefficients of ≥ 0.20 for dichotomous independent variables, and ≥ 0.10 for continuous independent variables, with a p -value of < 0.004 are presented in bold.

Abbreviations: BBSC = Benefit and Burden Scale, ICQ = Illness Cognition Questionnaire, IOC-CS = Impact of Cancer Scale, RSE = Rosenberg Self-Esteem Scale.

^aNot presented.

* $p < 0.05$, ** $p < 0.01$, *** $p < 0.001$.

to teach CCS active coping skills using CBT and ACT to prevent psychosocial problems. Initial findings from a pilot study were promising, showing a decrease in feelings of helplessness and an improvement in self-efficacy [40].

4.2 | Study Limitations

This is the first cohort study comprehensively examining the association between psychosocial risk and protective factors and a wide range of psychosocial outcomes in CCS. Major strengths are the unselected nationwide cohort, the detailed and reliable data regarding health conditions, and the comprehensive range of psychosocial risk and protective factors as well as outcomes. Nevertheless, there are some limitations to consider. First, because of the cross-sectional nature of this study we could not distinguish between cause and effect within the identified associations. For instance, it is possible that the association between psychosocial risk and protective factors and psychosocial outcomes is bidirectional, and that factors such as self-esteem, helplessness, and negative perceptions could both contribute to and result from psychosocial challenges. Second, social support was assessed using a single item rather than a validated scale, with the item specifically focusing on receiving love and support from friends. Research has highlighted the importance of family as a vital source of social support in addition to support from peers [16]. Finally, this study included over half of the CCS invited for the LATER 2 study which may introduce selection bias. However, we have not found important differences between participants and non-participants by diagnosis and treatment characteristics.

5 | Conclusion

Perceptions, illness cognitions, self-esteem, and social support play a role in explaining psychosocial functioning in CCS, outweighing the influence of socio-demographic and medical

variables. Addressing negative perceptions and feelings of helplessness, while promoting acceptance, self-esteem, and social support, could provide intervention targets for CCS encountering psychosocial problems.

Acknowledgments

We thank the other members of the Dutch LATER study group (Flora van Leeuwen, Lideke van der Steeg, Geert Janssens, Hanneke van Santen, Margreet Veening, Jaap den Hartogh, Saskia Pluijm, Lilian Batenburg, Hanneke de Ridder, Nynke Hollema, Lennart Teunissen, Anke Schellekens) and all physicians, research nurses, data managers, and participating CCS for their contribution. Funding for this study was provided by KiKa (Stichting Kinderen Kankervrij).

Conflicts of Interest

The authors declare no conflicts of interest.

Data Availability Statement

The data that support the study findings are available upon reasonable request from the corresponding author.

References

1. R. L. Siegel, K. D. Miller, and A. Jemal, "Cancer Statistics, 2019," *CA: A Cancer Journal for Clinicians* 69, no. 1 (2019): 7–34, <https://doi.org/10.3322/caac.21551>.
2. M. M. Hudson, K. K. Ness, J. G. Gurney, et al., "Clinical Ascertainment of Health Outcomes Among Adults Treated for Childhood Cancer," *JAMA* 309, no. 22 (2013): 2371–2381, <https://doi.org/10.1001/jama.2013.6296>.
3. N. Streefkerk, J. C. Teepe, E. A. M. Feijen, et al., "The Cumulative Burden of Self-Reported, Clinically Relevant Outcomes in Long-Term Childhood Cancer Survivors and Implications for Survivorship Care: A DCCSS LATER Study," *Cancer* 130, no. 8 (2023): 1349–1358, <https://doi.org/10.1002/cncr.35148>.
4. G. Michel, T. M. Brinkman, C. E. Wakefield, and M. Grootenhuys, "Psychological Outcomes, Health-Related Quality of Life, and

- Neurocognitive Functioning in Survivors of Childhood Cancer and Their Parents,” *Pediatric Clinics of North America* 67, no. 6 (2020): 1103–1134, <https://doi.org/10.1016/j.pcl.2020.07.005>.
5. J. McDougall and M. Tsonis, “Quality of Life in Survivors of Childhood Cancer: A Systematic Review of the Literature (2001–2008),” *Supportive Care in Cancer* 17, no. 10 (2009): 1231–1246, <https://doi.org/10.1007/s00520-009-0660-0>.
6. M. van Gorp, L. M. E. van Erp, A. Maas, et al., “Increased Health-Related Quality of Life Impairments of Male and Female Survivors of Childhood Cancer: DCCSS LATER 2 Psycho-Oncology Study,” *Cancer* 128, no. 5 (2022): 1074–1084, <https://doi.org/10.1002/cncr.34003>.
7. A. Maas, H. Maurice-Stam, L. C. M. Kremer, et al., “Psychosocial Outcomes in Long-Term Dutch Adult Survivors of Childhood Cancer: The DCCSS-LATER 2 Psycho-Oncology Study,” *Cancer* 129, no. 16 (2023): 2553–2567, <https://doi.org/10.1002/cncr.34795>.
8. M. J. Bitsko, D. Cohen, R. Dillon, J. Harvey, K. Krull, and J. L. Klosky, “Psychosocial Late Effects in Pediatric Cancer Survivors: A Report From the Children’s Oncology Group,” *Pediatric Blood and Cancer* 63, no. 2 (2016): 337–343, <https://doi.org/10.1002/pbc.25773>.
9. A. Maas, H. Maurice-Stam, E. A. M. Feijen, et al., “The Impact of Clinically Relevant Health Conditions on Psychosocial Outcomes in Survivors of Childhood Cancer: Results of the DCCSS-LATER Study,” *Journal of Cancer Survivorship* (2024): 1–11, <https://doi.org/10.1007/s11764-024-01617-z>.
10. W. L. Hobbie, M. Stuber, K. Meeske, et al., “Symptoms of Post-traumatic Stress in Young Adult Survivors of Childhood Cancer,” *Journal of Clinical Oncology* 18, no. 24 (2000): 4060–4066, <https://doi.org/10.1200/jco.2000.18.24.4060>.
11. O. Taieb, M. R. Moro, T. Baubet, A. Revah-Lévy, and M. F. Flament, “Posttraumatic Stress Symptoms After Childhood Cancer,” *European Child & Adolescent Psychiatry* 12, no. 6 (2003): 255–264, <https://doi.org/10.1007/s00787-003-0352-0>.
12. K. Wenninger, A. Helmes, J. Bengel, M. Lauten, S. Völkel, and C. M. Niemeyer, “Coping in Long-Term Survivors of Childhood Cancer: Relations to Psychological Distress,” *Psycho-Oncology* 22, no. 4 (2013): 854–861, <https://doi.org/10.1002/pon.3073>.
13. J. Fleer, D. Sleijfer, H. Hoekstra, M. Tuinman, E. Klip, and J. Hoekstra-Weebers, “Objective and Subjective Predictors of Cancer-Related Stress Symptoms in Testicular Cancer Survivors,” *Patient Education and Counseling* 64, no. 1-3 (2006): 142–150, <https://doi.org/10.1016/j.pec.2005.12.009>.
14. J. van Dijk, M. A. Grootenhuys, S. M. Imhof, P. T. Cohen-Kettenis, A. C. Moll, and J. Huisman, “Coping Strategies of Retinoblastoma Survivors in Relation to Behavioural Problems,” *Psycho-Oncology* 18, no. 12 (2009): 1281–1289, <https://doi.org/10.1002/pon.1507>.
15. N. E. Langeveld, M. Grootenhuys, P. Voûte, R. de Haan, and C. van den Bos, “Quality of Life, Self-Esteem and Worries in Young Adult Survivors of Childhood Cancer,” *Psycho-Oncology* 13, no. 12 (2004): 867–881, <https://doi.org/10.1002/pon.800>.
16. A. Deegan, C. Brennan, P. Gallagher, V. Lambert, and S. Dunne, “Social Support and Childhood Cancer Survivors: A Systematic Review (2006–2022),” *Psycho-Oncology* 32, no. 6 (2023): 819–833, <https://doi.org/10.1002/pon.6128>.
17. J. C. Teepen, J. L. Kok, E. A. M. Feijen, et al., “Questionnaire- and Linkage-Based Outcomes in Dutch Childhood Cancer Survivors: Methodology of the DCCSS LATER Study Part 1,” *Cancer Medicine* 12, no. 6 (2023): 7588–7602, <https://doi.org/10.1002/cam4.5519>.
18. E. A. M. Feijen, J. C. Teepen, E. van Dulmen-den Broeder, et al., “Clinical Evaluation of Late Outcomes in Dutch Childhood Cancer Survivors: Methodology of the DCCSS LATER 2 Study,” *Pediatric Blood and Cancer* 70, no. 5 (2023): e30212, <https://doi.org/10.1002/pbc.30212>.
19. P. Spinhoven, J. Ormel, P. P. A. Sloekers, G. I. J. M. Kempen, A. E. M. Speckens, and A. M. V. Hemert, “A Validation Study of the Hospital Anxiety and Depression Scale (HADS) in Different Groups of Dutch Subjects,” *Psychological Medicine* 27, no. 2 (1997): 363–370, <https://doi.org/10.1017/s0033291796004382>.
20. A. P. Association, *Diagnostic and Statistical Manual of Mental Disorders (DSM-IV-TR)* (Washington DC: American Psychiatric Association, 2000).
21. M. B. Bronner, N. Peek, H. Knoester, A. P. Bos, B. F. Last, and M. A. Grootenhuys, “Course and Predictors of Posttraumatic Stress Disorder in Parents After Pediatric Intensive Care Treatment of Their Child,” *Journal of Pediatric Psychology* 35, no. 9 (2010): 966–974, <https://doi.org/10.1093/jpepsy/jsq004>.
22. N. K. Aaronson, M. Muller, P. D. Cohen, et al., “Translation, Validation, and Norming of the Dutch Language Version of the SF-36 Health Survey in Community and Chronic Disease Populations,” *Journal of Clinical Epidemiology* 51, no. 11 (1998): 1055–1068, [https://doi.org/10.1016/s0895-4356\(98\)00097-3](https://doi.org/10.1016/s0895-4356(98)00097-3).
23. H. Maurice-Stam, A. Broek, A. M. M. Kolk, et al., “Measuring Perceived Benefit and Disease-Related Burden in Young Cancer Survivors: Validation of the Benefit and Burden Scale for Children (BBSC) in The Netherlands,” *Supportive Care in Cancer* 19, no. 8 (2011): 1249–1253, <https://doi.org/10.1007/s00520-011-1206-9>.
24. J. M. Currier, S. Hermes, and S. Phipps, “Brief Report: Children’s Response to Serious Illness: Perceptions of Benefit and Burden in a Pediatric Cancer Population,” *Journal of Pediatric Psychology* 34, no. 10 (2009): 1129–1134, <https://doi.org/10.1093/jpepsy/jsp021>.
25. A. W. Evers, F. W. Kraaimaat, W. van Lankveld, P. J. H. Jongen, J. W. G. Jacobs, and J. W. J. Bijlsma, “Beyond Unfavorable Thinking: The Illness Cognition Questionnaire for Chronic Diseases,” *Journal of Consulting and Clinical Psychology* 69, no. 6 (2001): 1026–1036, <https://doi.org/10.1037/0022-006x.69.6.1026>.
26. J. Bruil, M. Fekkes, T. Vogels, and G. H. W. Verrrips, *TAAQOL Manual* (Leiden, the Netherlands: Leiden Center for Child Health and Pediatrics, 2004).
27. M. Rosenberg, *Society and the Adolescent Self-Image* (New Jersey: Princeton University Press, 1995).
28. B. J. Zebrack, J. E. Donohue, J. G. Gurney, M. A. Chesler, S. Bhatia, and W. Landier, “Psychometric Evaluation of the Impact of Cancer (IOC-CS) Scale for Young Adult Survivors of Childhood Cancer,” *Quality of Life Research* 19, no. 2 (2010): 207–218, <https://doi.org/10.1007/s11136-009-9576-x>.
29. A. Maas, H. Maurice-Stam, A. M. van der Aa-van Delden, et al., “Positive and Negative Survivor-Specific Psychosocial Consequences of Childhood Cancer: The DCCSS-LATER 2 Psycho-Oncology Study,” *J Cancer Surviv* (2023): 1–12, <https://doi.org/10.1007/s11764-023-01394-1>.
30. J. Cohen, *Statistical Power Analysis for the Behavioral Sciences* (New York: Academy Press, 1988).
31. R. G. Tedeschi and L. G. Calhoun, “Posttraumatic Growth: Conceptual Foundation and Empirical Evidence,” *Psychological Inquiry* 15, no. 1 (2004): 1–18, https://doi.org/10.1207/s15327965pli1501_01.
32. C. J. Holahan, R. H. Moos, and L. Bonin, “Social Support, Coping, and Psychological Adjustment: A Resource Model,” in *Sourcebook of Social Support and Personality*, eds. G. R. Pierce, B. Lakey, I. G. Sarason, and B. R. Sarason (Boston, MA: Plenum Press, 1997), 169–186.
33. J. Arsandaux, C. Galera, and R. Salamon, “The Association of Self-Esteem and Psychosocial Outcomes in Young Adults: A 10-Year Prospective Study,” *Child and Adolescent Mental Health* 26, no. 2 (2021): 106–113, <https://doi.org/10.1111/camh.12392>.
34. J. L. Wallander and J. W. Varni, “Effects of Pediatric Chronic Physical Disorders on Child and Family Adjustment,” *Journal of Child*

Psychology and Psychiatry 39, no. 1 (1998): 29–46, <https://doi.org/10.1111/1469-7610.00302>.

35. A. C. Butler, J. Chapman, E. Forman, and A. Beck, “The Empirical Status of Cognitive-Behavioral Therapy: A Review of Meta-Analyses,” *Clinical Psychology Review* 26, no. 1 (2006): 17–31, <https://doi.org/10.1016/j.cpr.2005.07.003>.

36. S. G. Hofmann, A. T. Sawyer, and A. Fang, “The Empirical Status of the ‘New Wave’ of Cognitive Behavioral Therapy,” *Psychiatric Clinics of North America* 33, no. 3 (2010): 701–710, <https://doi.org/10.1016/j.psc.2010.04.006>.

37. D. C. Seitz, C. Knaevelsrud, G. Duran, S. Waadt, S. Loos, and L. Goldbeck, “Efficacy of an Internet-Based Cognitive-Behavioral Intervention for Long-Term Survivors of Pediatric Cancer: A Pilot Study,” *Supportive Care in Cancer* 22, no. 8 (2014): 2075–2083, <https://doi.org/10.1007/s00520-014-2193-4>.

38. G. Poggi, M. Liscio, V. Pastore, et al., “Psychological Intervention in Young Brain Tumor Survivors: The Efficacy of the Cognitive Behavioural Approach,” *Disability & Rehabilitation* 31, no. 13 (2009): 1066–1073, <https://doi.org/10.1080/09638280802509546>.

39. S. C. Hayes, J. B. Luoma, F. W. Bond, A. Masuda, and J. Lillis, “Acceptance and Commitment Therapy: Model, Processes and Outcomes,” *Behaviour Research and Therapy* 44, no. 1 (2006): 1–25, <https://doi.org/10.1016/j.brat.2005.06.006>.

40. L. M. E. van Erp, H. Maurice-Stam, L. R. Beek, et al., “Online Cognitive-Behavioral Group Intervention for Young Adult Survivors of Childhood Cancer: A Pilot Study,” *Journal of Psychosocial Oncology* 41, no. 5 (2022): 1–21, <https://doi.org/10.1080/07347332.2022.2150110>.

Supporting Information

Additional supporting information can be found online in the Supporting Information section.