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Original Research

Sexual dysfunction in young adult survivors of childhood cancer – A population-based study

Emma Hovén [a,*], Kristina Fagerkvist [a,e], Kirsi Jahnukainen [b,c], Lisa Ljungman [a,f], Päivi M. Lähteenmäki [a,g], Ove Axelsson [e,f], Claudia Lampic [a,d,1], Lena Wettergren [a,d,1]

[a] *Department of Women's and Children's Health, Karolinska Institutet, Sweden*
[b] *Division of Haematology-Oncology and Stem Cell Transplantation, Children's Hospital, University of Helsinki, Helsinki University Central Hospital, Helsinki, Finland*
[c] *NORDFERTIL Research Lab Stockholm, Childhood Cancer Research Unit, Department of Women's and Children's Health, Karolinska Institutet and University Hospital Karolinska Institutet, Stockholm, Sweden*
[d] *Department of Public Health and Caring Sciences, Uppsala University, Sweden*
[e] *Centre for Clinical Research Sörmland, Uppsala University, Eskilstuna, Sweden*
[f] *Department of Women's and Children's Health, Uppsala University, Sweden*
[g] *Department of Pediatric and Adolescent Medicine, Turku University Hospital, FICANWEST, University of Turku, Finland*

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Abstract ***Objective:*** To determine the prevalence of sexual dysfunction and to identify the factors associated with sexual dysfunction in young adult childhood cancer survivors.
Methods: All survivors of childhood cancer (aged 19–40 years) in Sweden were invited to this population-based study, and 2546 men and women (59%) participated. Sexual function was examined with the PROMIS Sexual Function and Satisfaction Measure. Logistic regression was used to assess the differences between survivors and a general population sample (n = 819) and to identify the factors associated with sexual dysfunction in survivors.
Results: Sexual dysfunction in at least one domain was reported by 57% of female and 35% of male survivors. Among females, dysfunction was most common for Sexual interest (36%), Orgasm – ability (32%) and Vulvar discomfort – labial (19%). Among males, dysfunction was most common for the domains satisfaction with sex life (20%), Sexual interest (14%) and Erectile function (9%). Compared with the general population, male survivors more frequently reported sexual dysfunction in ≥2 domains (OR = 1.67, 95% CI: 1.03–2.71), with an increased likelihood of dysfunction regarding Orgasm – ability (OR = 1.82; 95% CI: 1.01–3.28) and Erectile function (OR = 2.30; 95% CI: 1.18–4.49). Female survivors reported

* *Corresponding author*:
E-mail address: emma.hoven@ki.se (E. Hovén).
[1] Dr. Lampic and Dr. Wettergren contributed equally as co-last authors.

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more dysfunction regarding Orgasm – pleasure (9% versus 5%, OR = 1.86; 95% CI: 1.11–3.13). A more intensive cancer treatment, emotional distress and body image disturbance were associated with sexual dysfunction in survivors.

Conclusions: The findings underscore the need for routine assessment of sexual health in follow-up care of childhood cancer survivors and highlight that those treated with more intensive cancer treatment and who experience concurrent psychological concerns may benefit from targeted screening and interventions.

1. Introduction

With an increased 5-year survival rate approaching 80%, the population of long-term childhood cancer survivors is growing [1]. Only in Europe, there are about 500,000 people living with a childhood cancer experience [2]. This is a group known to be at risk of physical and psychological late effects [3,4], and many survivors suffer from chronic health conditions [4]. Despite being acknowledged as an integral part of health and quality of life [5,6], data on the effect of childhood cancer on sexual health in young adult survivors are limited.

Sexual dysfunction in childhood cancer survivors can be secondary to physical, psychological and social implications related to the cancer experience [7,8]. Abdominal/pelvic or total body irradiation as well as certain types of chemotherapy can result in delayed or arrested puberty, premature menopause and testicular dysfunction [3]. Previous studies suggest that both male [9–12] and female [13,14] survivors experience more sexual dysfunction than siblings and peers in similar ages.

Sexual dysfunction has been reported for 20–52% of female and 20–32% of male survivors of childhood cancer [6,13,15]. Reported problems include low interest, erectile dysfunction, vaginal dryness, vaginal pain/discomfort and difficulties enjoying sex [6,13,15–17]. Risk factors for sexual dysfunction among survivors include female sex, older age at study, health problems and low income [8]. In addition, a negative body image [16–20] and depressive symptoms [9,12,15] have been linked to sexual problems. How treatment and illness-related factors affect survivors' sexual function is not clear. Some studies suggest that survivors of certain types of cancer are at higher risk for sexual dysfunction [12–14], but other studies show no such associations [15].

The evidence concerning sexual dysfunction among childhood cancer survivors is hampered by methodological limitations regarding sampling and measures [6,15,21]. Large-scale, methodologically rigorous studies using representative samples and validated measures are, thus, needed to gain better knowledge about the extent of sexual problems in survivors and how these are associated with sociodemographic, psychological and clinical factors. Such knowledge can be used to develop targeted screening and interventions for this population. The aim of this study was, therefore, to determine the prevalence of sexual dysfunction and to identify factors associated with sexual dysfunction in young adult childhood cancer survivors.

2. Methods

2.1. Design

The study is part of the Fex-Can Childhood project, whose methods are described in a study protocol [22]. This nationwide, population-based study combines registry and survey data for cancer survivors and includes a general population sample described in detail elsewhere [23].

2.2. Participants

Survivors were identified through the National Quality Registry for Childhood Cancer (NQRCC), which includes all individuals diagnosed with paediatric cancers in Sweden. Eligible participants were diagnosed between ages 0 and 17 and were 19–40 years of age and residents in Sweden at the time of enrolment. Exclusion criteria were as follows: unable to read/write in Swedish, self-reported poor health and/or cognitive impairment that prevented survey completion.

For the comparison group, a random sample (1000 women; 1000 men) from the general population aged 19–40 was identified by the Swedish population registry and invited to the study [23]. The same exclusion criteria as for survivors were used. Additionally, individuals who reported treatment for cancer were excluded.

2.3. Procedure

The survey was sent to potential participants together with a letter describing the study. Participants could complete the survey via paper or Web, and non-responders received two reminders. Data for survivors were collected from August 2019 to February 2020 and

for the comparison group from April to June 2018. Ethical approval was granted by the Regional Ethical Review Board in Stockholm, Sweden (approval number: 2015/1609-31; 2018/2688-32; 2019/01066; 2019/04603).

2.4. Measures

Participants completed established self-report instruments together with study-specific items on use of antidepressants, sexual orientation and sociodemographic factors.

Sexual function was measured by the Patient-Reported Outcomes Measurement Information System (PROMIS) Sexual Function and Satisfaction Measure (SexFS) version 2.0 [24]. The following domains were answered by females: Vaginal lubrication, Vaginal discomfort, Vulvar discomfort − clitoral and Vulvar discomfort − labial. The Erectile function domain was answered by males. Four gender-neutral domains were used: Satisfaction with sex life, Interest in sexual activity, Orgasm − ability and Orgasm − pleasure. All respondents completed items related to Interest in sexual activity, whereas remaining domains were completed only by respondents who had been sexually active. In the questionnaire, sexual activity was defined as sex with a partner and/or solo sex including masturbation, oral sex and intercourse. Domain scores were transformed to a T-score metric, where 50 represents the mean for the American general population (standard deviation [SD] = 10) [24]. As recommended by the PROMIS network (http://www.nihpromis.org/), a cut-off of 1 SD from mean was used to define sexual dysfunction. The SexFS has shown adequate construct, content and known-groups validity and test-retest reliability [24–26]. The items were translated into Swedish and linguistically validated in accordance with FACITrans and PROMIS procedures [27].

Body image disturbance was assessed using the Swedish version of the Body Image Scale (BIS). BIS assesses body image discomfort in general (five items) and in relation to cancer and its treatment (five items) [28]. In line with previous research on non-cancer populations [29], the comparison group responded only to the five general items. The total sum score was used in this study, with higher scores indicating more disturbance. BIS has shown clinical validity, high test-retest reliability and satisfactory internal consistency [28,30].

Emotional distress was assessed using the Swedish version of The Hospital Anxiety and Depression scale (HADS) [31]. HADS has shown satisfactory internal consistency and concurrent validity [32,33]. In this study, the two subscales assessing symptoms of anxiety and depression were combined in one overall score (range 0–42), with higher scores indicating greater emotional distress.

Clinical data were retrieved from the NQRCC including cancer diagnosis, date of diagnosis, age at diagnosis and treatment. Diagnoses were classified according to the International Classification of Childhood Cancer, 3rd revision [34]. Each child's treatment was categorised by a paediatric oncologist using the Intensity of Treatment Rating scale (ITR-3.0), a psychometrically validated measure of treatment intensity of current treatment protocols in paediatric oncology [35]. Different disease and/or treatment modalities were classified according to one of the four intensity levels, from level 1 (minimally intensive) to level 4 (most intensive).

2.5. Analyses

Clinical and sociodemographic characteristics of groups were compared by gender using Student's t-tests and chi-square tests. Prevalence of sexual dysfunction was compared between survivors and the comparison group using logistic regression, adjusted for sociodemographics (age at study, education, relationship status, having children and country of birth). To identify the factors associated with dysfunction in survivors, logistic regression models were conducted for each SexFS domain and for dysfunction in two or more domains. The following potential factors were selected a priori based on the literature: age at diagnosis, time since diagnosis, age at study, education, country of birth, relationship status, sexual orientation, use of antidepressants, having children, type of cancer, treatment intensity, body image disturbance and emotional distress. First, each factor was examined in bivariate analyses, using simple logistic regression and chi-square tests as appropriate. Factors associated with dysfunction in the respective domain ($P < 0.10$) were thereafter analysed using multivariable logistic regression.

All tests were two-tailed with $P < 0.05$ denoting statistical significance. Analyses were performed using SPSS Statistics version 25 (IBM Corp., Armonk, N.Y., USA).

3. Results

3.1. Study participants

Of the 4328 survivors approached, 90 survivors were excluded due to unknown address (n = 49), living outside Sweden (n = 3), cognitive dysfunction (n = 32) and administrative failure (n = 6). Study participants were 2546 survivors (59% response rate), of which 1333 females (67% response) and 1213 males (52% response). Table 1 shows the characteristics of the participants. Among survivors with leukaemia (most common diagnosis), 65% of females and 56% of males had received moderately intensive treatment, whereas 35% and 44%, respectively, had undergone very/most intensive treatment. More detailed information on intensity of

Table 1
Sociodemographic, psychological and clinical characteristics of the study sample.

	Survivors		The comparison group	
	Female (n = 1333)	Male (n = 1213)	Female (n = 493)	Male (n = 326)
	No. (%)	No. (%)	No. (%)	No. (%)
Sociodemographics				
Age at study, years				
Mean (SD)	28.8 (6.1)*	29.2 (6.1)	29.7 (6.1)	29.3 (6.4)
Country of birth				
Sweden	1272 (95.8)***	1157 (95.9)***	422 (85.6)	271 (83.4)
Other	56 (4.2)	50 (4.1)	71 (14.4)	54 (16.6)
Highest education				
University	745 (56.1)	523 (43.3)	283 (57.8)	150 (46.3)
Upper secondary	479 (36.1)	589 (48.8)	179 (36.5)	153 (47.2)
Elementary	47 (3.5)	51 (4.2)	18 (3.7)	13 (4.0)
Other	56 (4.2)	45 (3.7)	10 (2.0)	8 (2.5)
In a relationship				
Yes	940 (70.8)***	728 (60.4)***	394 (80.6)	231 (71.5)
Have children				
Yes	495 (37.3)***	368 (30.7)**	230 (46.8)	127 (39.2)
Sexual orientation				
Heterosexual	1178 (89.2)	1137 (94.4)	454 (92.7)	307 (94.8)
Homosexual	20 (1.5)	20 (1.7)	6 (1.2)	7 (2.2)
Bisexual	83 (6.3)	23 (1.9)	26 (5.3)	7 (2.2)
Other[a]	27 (2.0)	11 (0.9)	3 (0.6)	3 (0.9)
Prefer not to answer	13 (1.0)	13 (1.1)	1 (0.2)	–
Psychological outcomes				
Emotional distress, HADS				
Mean (SD)	12.6 (7.6)	9.96 (6.7)	11.99 (7.4)	9.51 (5.9)
Body image, BIS				
Mean (SD)	8.6 (7.3)***	5.8 (6.0)	5.2 (3.6)	3.2 (2.7)
Clinical characteristics				
Age at diagnosis, years				
Mean (SD)	7.4 (5.4)	7.8 (5.4)		
0–5 years of age	615 (46.1)	496 (40.9)		
6–12 years of age	383 (28.7)	404 (33.3)		
13–17 years of age	335 (25.1)	313 (25.8)		
Time from diagnosis, years				
Mean (SD)	20.9 (7.8)	20.9 (7.8)		
Range	1–38	1–37		
Type of cancer[b]				
Haematological cancers	603 (45.3)	615 (50.7)		
Leukaemia (I)	418 (31.4)	377 (31.1)		
Lymphoma (II)	185 (13.9)	238 (19.6)		
CNS tumours (III)	310 (23.3)	267 (22.0)		
Solid tumours	417 (31.4)	331 (27.3)		
Neuroblastomas and other peripheral nervous cell tumours (IV)	55 (4.1)	39 (3.2)		
Retinoblastomas (V)	32 (2.4)	20 (1.6)		
Renal tumours (VI)	84 (6.3)	62 (5.1)		
Hepatic tumours (VII)	11 (0.8)	14 (1.2)		
Malignant bone tumours (VIII)	58 (4.4)	57 (4.7)		
Soft-tissue sarcomas (IX)	66 (5.0)	76 (6.3)		
Germ-cell, trophoblastic, and other gonadal tumours (X)	68 (5.1)	44 (3.6)		
Carcinomas and other malignant epithelial neoplasms (XI)	43 (3.2)	19 (1.6)		
Other and unspecified malignant neoplasms (XII)	3 (0.2)	0 (0.0)		
Treatment modality				
Chemotherapy	945 (70.9)	887 (73.1)		
Surgery	504 (37.8)	412 (34.0)		
Radiotherapy	282 (21.2)	262 (21.6)		
Cranial irradiation	155 (11.6)	142 (11.7)		

Table 1 (*continued*)

	Survivors		The comparison group	
	Female (n = 1333)	Male (n = 1213)	Female (n = 493)	Male (n = 326)
	No. (%)	No. (%)	No. (%)	No. (%)
Hematopoietic stem cell transplantation	83 (6.3)	99 (8.2)		
Intensity of treatment[c]				
Least intensive	156 (11.7)	119 (9.8)		
Moderately intensive	669 (50.2)	613 (50.6)		
Very intensive	330 (24.8)	312 (25.8)		
Most intensive	178 (13.4)	169 (13.9)		
Relapse/second malignant neoplasm				
Yes	148 (11.1)	124 (10.2)		

CNS, central nervous system; BIS, Body Image Scale; HADS, Hospital Anxiety and Depression scale.
*, **, *** Difference in comparison with females/males in the comparison group at $^{*}P < 0.05$ $^{**}P < 0.01$ $^{***}P < 0.001$.
[a] Includes individuals who reported not knowing, being pansexual, queer or asexual.
[b] According to the International Classification of Childhood Cancer, third edition (ICCC-3) [34].
[c] According to the Intensity of Treatment Rating (ITR-3.0) [35].

treatment by diagnosis is provided in Suppl. Table 1. For survivors, female responders and non-responders did not differ in demographic or clinical characteristics. Among males, responders were older (mean = 29 and 28 years, respectively; $P < 0.05$), and time since diagnosis was longer than for non-responders (mean = 21 and 20 years, respectively: $P < 0.05$).

Sociodemographic characteristics were compared between survivors and the comparison group (n = 819, 42% response rate). Compared with survivors, more females and males in the comparison group were born outside Sweden, were partnered and had children (Table 1). Moreover, females in the comparison group were older at the time of study.

3.2. Prevalence of sexual dysfunction

More than half of female (57%) and one-third of male (35%) survivors reported a dysfunction in at least one domain during the last month, and about one-fifth (22%) of females and one-tenth of males (13%) reported dysfunction in at least two domains (Table 2). Among females, sexual dysfunction was most common in the domains of Interest in sexual activity, Orgasm – ability and Vulvar discomfort – labial. The most commonly reported sexual dysfunction in male survivors concerned Satisfaction with sex life, Interest in sexual activity and Erectile dysfunction. For prevalence of dysfunction by ICCC-3 group diagnosis, see Suppl. Table 2.

Female survivors were more likely to report dysfunction in Orgasm – pleasure than females in the comparison group (OR = 1.86, 95% CI: 1.11–3.13) (Table 2). Male survivors were more likely than males in the comparison group to report dysfunction in two or more domains (OR = 1.67, 95% CI: 1.03–2.71) (Table 2). Specifically, male survivors were more likely to report dysfunction in Orgasm – ability (OR = 1.82, 95% CI: 1.01–3.38) and Erectile function (OR = 2.30, 95% CI: 1.18–4.49).

3.3. Factors associated with sexual dysfunction in survivors

Female survivors who were partnered and with a higher education were less likely to report dysfunction in certain domains (Table 3). Females with children and who were born outside Sweden were more likely to report dysfunction regarding Interest in sexual activity, whereas females who reported a sexual orientation other than heterosexual were less likely to report dysfunction in this domain. Females who had received more intensive treatment and with greater body image disturbance were more likely to report dysfunction in two or more domains. Furthermore, female survivors with greater emotional distress were more likely to report dysfunction in all outcomes.

Males in a relationship were less likely to report dysfunction in two or more domains, and males with a more intensive treatment were more likely to report dysfunction related to Orgasm – pleasure (Table 4). Male survivors with a higher educational attainment were less likely to report dysfunction in the domain Interest in sexual activity. Moreover, male survivors with greater emotional distress and greater body image disturbance were more likely to report dysfunction in two or more domains.

4. Discussion

This is one of the most comprehensive studies to date on sexual dysfunction in young adult survivors of childhood cancer. About half of the female and one-third of the male survivors reported at least one current sexual dysfunction. Among female survivors, dysfunction was most common in the domains Sexual interest,

Table 2
Prevalence of sexual dysfunction[a] by sex in survivors and comparison group; differences between groups were adjusted for sociodemographics (age at study, education, relationship status, having children and country of birth).

	Survivors	Comparison group	[Adj]*P*-value (95% CI)
	No. (%)	No. (%)	
Females	n = 1333	n = 493	
Satisfaction with sex life	146 (13)	51 (12)	0.742 (0.74–1.52)
Interest in sexual activity	474 (36)	156 (32)	0.115 (0.96-1-52)
Orgasm – ability	331 (32)	117 (28)	0.318 (0.88–1.48)
Orgasm – pleasure	91 (9)	21 (5)	**0.019 (1.11–3.13)**
Vaginal lubrication	94 (9)	30 (7)	0.114 (0.92–2.25)
Vaginal discomfort	92 (9)	35 (8)	0.860 (0.68–1.59)
Vulvar discomfort – clitoral	184 (17)	66 (16)	0.325 (0.85–1.63)
Vulvar discomfort – labial	199 (19)	80 (19)	0.995 (0.74–1.35)
Dysfunction ≥1 domain[b]	750 (57)	263 (54)	0.263 (0.91–1.40)
Dysfunction ≥2 domains[b]	239 (22)	77 (18)	0.057 (0.99–1.80)
Males	n = 1213	n = 326	
Satisfaction with sex life	217 (20)	52 (17)	0.788 (0.66–1.37)
Interest in sexual activity	163 (14)	32 (10)	0.095 (0.94–2.24)
Orgasm – ability	89 (8)	16 (5)	**0.045 (1.01–3.28)**
Orgasm – pleasure	73 (7)	17 (56)	0.776 (0.61–1.93)
Erectile function	95 (9)	11 (4)	**0.015 (1.18–4.49)**
Dysfunction ≥1 domain[b]	418 (35)	98 (31)	0.528 (0.82–1.47)
Dysfunction ≥2 domains[b]	145 (13)	24 (8)	**0.038 (1.03–2.71)**

CI, confidence interval; CNS, central nervous system.
Valid percentages.
Statistically significant ($P < 0.05$) differences in the logistic regression multivariable models indicated in bold.
[a] Self-reported dysfunction defined as cut-off = 1 SD above/below the t-score mean of the norm population [24].
[b] Based on reports for the domains: Satisfaction with sex life, Interest in sexual activity, Orgasm – ability, Orgasm – pleasure, Vaginal lubrication (females only) and Erectile function (males only).

Orgasm – ability and Vulvar discomfort. Among male survivors, sexual dysfunction was most frequently reported in the domains Satisfaction with sex life, Interest in sexual activity and Erectile function. While the prevalence of sexual dysfunction among female survivors was similar to that of women in the comparison group, male survivors reported a higher prevalence of dysfunction for two domains compared to men in the general population sample. Corresponding to what has been reported for the comparison group [23], increased likelihood of sexual dysfunction in one or more domains in survivors was associated with not having a partner, low education, as well as concurrent emotional distress and body image disturbance. Our results furthermore show an increased likelihood of sexual dysfunction in survivors subjected to a more intensive treatment.

In comparison with our general population sample, both female and male survivors were significantly less likely to have a partner and to have children. When controlling for sociodemographic variables, we found few differences in prevalence of sexual dysfunction between female survivors and women in the general population. This is in contrast to studies from the United States (US), indicating that female survivors are at risk for impaired sexual functioning across domains [13,14] but corresponds with results of a Swedish study [11]. Future studies are needed to determine if the differing results between our study and the US studies can be explained by differences in sampling, measures, definitions and/or cultural differences between the countries. For example, the definition of sexual dysfunction in one of the US studies [13] was based on the reports of the controls, making the definition sensitive to selection bias of the controls. The definition used in this study was, instead, based on standard scores with thresholds to identify clinically meaningful sexual dysfunction [25]. Moreover, the estimates of dysfunction in our comparison group corresponds with previous results for general population samples [29,36,37], highlighting that problems with sexual function are common, in particular among women.

In contrast to our findings for females, male survivors were at increased risk of sexual dysfunction compared with men in the general population, with a higher prevalence of dysfunction related to Orgasm – ability and Erectile function. Thus, in line with a previous study [11], our results indicate that childhood cancer can have adverse effects on certain domains of sexual functioning, and that this is more evident in male survivors. It is well known that men and women differ in perceived sexual function and that sexual dysfunction is more prevalent in women [23,36]. Therefore, analyses of survivors' sex life should be performed by gender and include appropriate non-cancer comparison data, as in the present study.

Previous studies have shown conflicting results regarding risk of erectile dysfunction in childhood cancer survivors [9,10]. Erectile dysfunction can be caused by a variety of reasons relating to psychological, endocrine, vascular and neurological factors [38]. The increased risk of erectile dysfunction that we observed might be related to both physical and psychological impact of the cancer. Body image disturbance was associated with sexual dysfunction in several domains for male as well as female survivors, highlighting this issue as a target for interventions aiming at

Table 3
Results of the multivariable logistic regression models for sexual dysfunction in female survivors. The model for each SexFs domain included only the factors that were associated with sexual dysfunction in the specific domain in bivariate analysis.

Factors	Satisfaction with sex life		Interest in sexual activity		Orgasm – ability		Orgasm – pleasure		Vaginal lubrication		≥2 domains above cut-off	
	OR	95%CI	OR	95%CI	OR	95%CI	OR	95%CI	OR	95% CI	OR	95%CI
Age at study			1.02	1.00–1.05								
Education												
University degree versus no university degree (ref)			**0.65**	**0.50–0.83**	**0.76**	**0.57–0.99**	**0.61**	**0.39–0.97**	0.77	0.49–1.20	**0.70**	**0.51–0.96**
Relationship status												
Partner versus no partner (ref)	**0.38**	**0.25–0.58**	**0.54**	**0.41–0.72**			0.67	0.41–1.08			0.77	0.55–1.09
Having children												
Yes versus no (ref)	0.93	0.60–1.44	**1.71**	**1.25–2.36**								
Treatment intensity												
Very/most intensive versus least/ moderately intensive (ref)			**1.63**	**1.27–2.10**	1.18	0.89–1.56	**1.97**	**1.25–3.13**	**1.59**	**1.02–2.49**	**1.62**	**1.18–2.22**
Type of cancer												
CNS tumours versus haematological cancer (ref)									0.70	0.38–1.28		
Solid tumours versus haematological cancer (ref)									0.88	0.54–1.46		
Use of antidepressants – no (ref)												
Yes versus no (ref)	0.83	0.51–1.34	0.94	0.68–1.31	1.08	0.76–1.56	0.92	0.52–1.62			0.90	0.60–1.34
Sexual orientation												
Other versus heterosexual (ref)	1.67	0.98–2.83	**0.63**	**0.41–0.97**								
Country of birth												
Other versus Sweden (ref)			**1.96**	**1.09–3.52**								
Emotional distress (HADS)	**1.08**	**1.05–1.11**	**1.05**	**1.03–1.07**	**1.03**	**1.01–1.05**	**1.08**	**1.04–1.12**	**1.05**	**1.02–1.09**	**1.08**	**1.06–1.11**
Body image disturbance (BIS)	1.03	1.00–1.06	1.01	0.99–1.03	**1.02**	**1.00–1.05**	1.01	0.97–1.04	**1.05**	**1.01–1.08**	**1.03**	**1.00–1.05**

BIS, Body Image Scale; CI, confidence interval; CNS, central nervous system; HADS, Hospital Anxiety and Depression Scale; OR, odds ratio; Ref, reference category.
Statistically significant ($P < 0.05$) factors in the multivariable model indicated in bold.

improving sexual health. Results of an interview study with adult survivors indicate that a negative body image as a result of the cancer experience hinders physical intimacy [39], which can explain our findings. Furthermore, consistent with previous reports [9,13,15], we found emotional distress to be linked to sexual dysfunction. The associations between sexual dysfunction and body image disturbance and emotional distress, respectively, may be bidirectional and underscore that sexual health interventions should consider combining psychological (e.g. counselling) and medical (e.g. hormones) treatment.

Conflicting results have been presented as to how specific cancer treatments are associated with sexual dysfunction [12–15]. Our findings demonstrate that the very or most intensive cancer treatments put survivors, particularly females, at increased risk for later sexual dysfunction. Patients treated with the very or most intensive treatments according to ITR-3.0 include those treated with hematopoietic stem cell transplantation (HSCT) and with relapse protocols, those treated for osteosarcoma, Ewing sarcoma and higher stages of other solid tumours, as well as those treated for acute myeloid leukaemia, acute lymphoblastic leukaemia with high-risk/T-cell lymphoma protocols and brain tumours with two or more modalities [35]. Risk of gonadotoxicity is not specifically measured in the ITR-3.0 rating system. However, cancer types in very or most intensive treatments groups are treated with high cumulative doses of alkylating chemotherapy, cranial or abdominal irradiation or HSCT, which are associated with increased risk of premature menopause, testicular dysfunction and deficiency of sexual hormones. Intensive treatment as a risk factor is an important

Table 4
Results of the logistic regression models for sexual dysfunction in male survivors. The model for each SexFs domain included only the factors that were associated with sexual dysfunction in the specific domain in bivariate analysis.

Factors	Satisfaction with sex life		Interest in sexual activity		Orgasm – ability		Orgasm – pleasure		Erectile function		≥2 domains above cut-off	
	OR	95%CI	OR	95%CI	OR	95%CI	OR	95%CI	OR	95%CI	OR	95%CI
Time since diagnosis	1.01	0.98–1.03	1.00	0.97–1.02								
Education												
University degree versus no university degree (ref)			**0.38**	**0.25–0.57**			0.60	0.35–1.05	0.71	0.44–1.15	0.69	0.46–1.02
Relationship status												
Partner versus no partner (ref)	**0.17**	**0.11–0.26**	**0.43**	**0.28–0.65**	0.77	0.49–1.20	**0.54**	**0.30–0.95**	**0.43**	**0.25–0.72**	**0.30**	**0.19–0.46**
Having children												
Yes versus no (ref)	1.25	0.75–2.08	0.84	0.49–1.43			0.78	0.38–1.62	0.93	0.49–1.77	1.14	0.67–1.94
Treatment intensity												
Very/most intensive versus least/ moderately intensive (ref)	1.17	0.82–1.67			1.42	0.90–2.23	**1.95**	**1.14–3.32**	1.32	0.82–2.12	1.46	0.99–2.17
Type of cancer												
CNS tumours versus haematological cancer (ref)									1.52	0.88–2.64		
Solid tumours versus haematological cancer (ref)									0.82	0.46–1.48		
Use of antidepressants												
Yes versus no (ref)	1.42	0.78–2.57	1.17	0.64–2.15	1.48	0.71–3.10	1.94	0.93–4.06	1.59	0.77–3.30	1.19	0.62–2.29
Sexual orientation												
Other versus heterosexual (ref)			1.18	0.54–2.54			1.36	0.51–3.64	1.18	0.47–2.97		
Emotional distress (HADS)	**1.07**	**1.04–1.10**	**1.04**	**1.01–1.07**	1.01	0.98–1.05	**1.08**	**1.04–1.12**	1.03	0.99–1.07	**1.05**	**1.01–1.08**
Body image disturbance (BIS)	**1.06**	**1.03–1.09**	1.03	1.00–1.06	**1.07**	**1.03–1.11**	**1.05**	**1.01–1.10**	**1.08**	**1.04–1.13**	**1.08**	**1.04–1.11**

BIS, Body Image Scale; CI, confidence interval; CNS, central nervous system; HADS, Hospital Anxiety and Depression Scale; OR, odds ratio; Ref, reference category.
Statistically significant ($P < 0.05$) factors in the multivariable model indicated in bold.

observation that warrants further investigation to elucidate factors underpinning the higher risk observed among these survivors.

The strengths of the present study include the large population-based cohort, use of treatment information from a national quality registry (NQRCC) with good coverage, use of standardised measures and inclusion of a randomly selected comparison group. Nevertheless, some limitations should be recognised. Our estimates of dysfunction rely on self-reports and were not validated against, for example, structured interviews by professionals experienced in diagnosing sexual disorders. Furthermore, the definition of sexual dysfunction was based on American norms; however, aspects of sexual function and activity are similar between the countries [36,40], including age for sexual debut. Moreover, women and men in our comparison group report similar rates of dysfunction as the US general population [36]. While our response rates are similar to Ref. [13] or higher [14] than other survey studies on this topic, there is still a risk of participation bias. Non-sexually active individuals might be less likely to participate in studies on sexuality, leading to sexual problems being underreported. Among male survivors, non-responders were older than responders, but we do not believe that the 1-year difference resulted in an overestimation of dysfunction in this group. Finally, as the comparison group differed from survivors in some sociodemographic characteristics the analyses between these groups were adjusted accordingly.

5. Conclusions

Overall, young adult survivors of childhood cancer report sexual functioning in line with peers, but male survivors have more problems related to erectile function and orgasm. Furthermore, survivors are partnered and have children to a lesser extent, indicating difficulties in building intimate relationships. This underscores the need for routine assessment of sexual health in follow-up care of survivors. Survivors subjected to a more intensive cancer treatment and who

experience concurrent psychological concerns are high-risk subgroups who may benefit from targeted screening and interventions.

Author contributions

Conceptualisation: Hovén, Fagerkvist, Lampic, Wettergren; Data curation: Hovén, Fagerkvist, Lähteenmäki, Jahnukainen, Lampic, Wettergren; Formal analysis: Hovén; Funding acquisition: Lampic, Wettergren; Investigation: Fagerkvist, Lampic, Wettergren; Methodology: Hovén, Fagerkvist, Jahnukainen, Lampic, Wettergren; Project administration: Fagerkvist, Lampic, Wettergren; Resources: Lampic, Wettergren; Software: N/A; Supervision: Lampic, Wettergren; Validation: Hovén, Fagerkvist, Lampic, Wettergren; Visualisation: Axelsson, Hovén, Fagerkvist, Jahnukainen, Lampic, Wettergren; Roles/Writing – original draft: Hovén; Writing – review and editing: All authors.

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Conflict of interest statement

The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

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Appendix A. Supplementary data

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