

Employment status and occupational positions of childhood cancer survivors from Denmark, Finland and Sweden: A Nordic register-based cohort study from the SALiCCS research programme

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Summary

Background A childhood cancer diagnosis and late effects of treatment may affect survivors' possibilities of employment or highly skilled occupations later in life. In this study, we compared the employment and occupational status of childhood cancer survivors with population comparisons and siblings.

Methods In a cohort study based on Nordic registers, we identified 10 461 survivors of childhood cancer diagnosed before age 20 years in Denmark, Finland and Sweden since 1971. Survivors were compared with 48 928 population comparisons matched to survivors by age, sex and geographical region and 12 605 siblings of survivors. Annual outcome information on employment, unemployment, health-related unemployment and occupational position was obtained from the statistical institutes between 1980-2017 and assessed in multivariate logistic regression analyses from age 30 onwards.

Findings By 30 years of age, 9.2% (95% CI, 8.6-9.9%) of survivors were unemployed for health reasons. Childhood cancer survivors had considerably higher odds of health-related unemployment at ages 30, 40 and 50 than population comparisons (OR_{age30}, 2.57; 95% CI, 2.35-2.81) and siblings (OR_{age30}, 2.50; 95% CI, 2.15-2.90). We observed no large difference in unemployment unrelated to health or in occupational position. Health-related unemployment was particularly pronounced among survivors of central nervous system tumours and survivors diagnosed below 15 years of age.

Interpretation Survivors at risk of health-related unemployment should be offered comprehensive survivorship care and interventions for obtaining and maintaining suitable employment.

Funding NordForsk [76111], the Danish Childhood Cancer Foundation [2016-0293], Aarhus University [43239402], the Swedish Childhood Cancer Foundation [PR2020-0130] and [OB2019-0003], T½mrmester J½rgen Holm og Hustru Elisa F. Hansens Mindelegat [20088] and the Swiss National Science Foundation to LM [P2LUP3_175288].

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The Lancet Regional Health - Europe 2022;12: 100258

Published online xxx
<https://doi.org/10.1016/j.lanepe.2021.100258>

Key words: Childhood cancer; Survivorship; Employment status; Occupation; Population-based cohort study; Nordic register study; Denmark; Finland; Sweden

Research in context

Evidence before this study

In an extensive systematic review based on literature search in Pubmed, EMBASE and PsycINFO for studies published between 2000 and 2017, we showed previously that findings from 11 studies assessing employment and occupation among childhood cancer survivors were inconsistent. Two meta-analyses have reported pooled estimates indicating a 1.5-2 times higher risk of unemployment among survivors than their peers. All three reviews, however, report geographical variations, with studies in Europe reporting inconsistent findings, and methodological heterogeneity of studies, including self-reported information, short follow-up or loss to follow-up, and lack of information on reasons for unemployment.

Added value of this study

Based on unique and high-quality register data from three Nordic countries with similar welfare and health-care systems, this study represents the most comprehensive population-based study of employment and occupation among childhood cancer survivors to date. We provide the novel finding that adult survivors of childhood cancer, especially those diagnosed before 15 years of age and/or with a CNS tumour, have a substantial burden of health-related unemployment later in life in comparison to the general population and their siblings. We found no notable differences in unemployment for reasons unrelated to health, and survivors obtained similar occupational positions as comparisons. The refined and novel contribution that this study adds to the existing literature include the annual measurements of employment and occupation during several ages of adulthood with virtually no loss to follow-up, the stratification by reasons for unemployment, the use of an international framework for occupational position, and the inclusion of somatic and psychiatric morbidities as important determinants.

Implications of all the available evidence

Particular vulnerable survivors at high risk of health-related unemployment might benefit from early, comprehensive support to address potential health problems that could interfere with their later employment situation.

Introduction

Survival after childhood cancer has improved substantially over the past decades, with 5-year survival now

exceeding 80% in most of Europe and North America¹. As a result, the population of childhood cancer survivors is steadily growing, and thorough understanding of the long-term consequences they may face in adult life is of substantial public health relevance.^{2,3} Survivors are at increased risk of a broad range of somatic⁴⁻⁷ and mental morbidities⁸⁻¹⁰ later in life. Moreover, the diagnosis of childhood cancer and treatment-induced late effects may affect socioeconomic achievements.¹¹ In an extensive systematic review, we showed previously that specific groups of childhood cancer survivors are at higher risk of lower educational achievement, lower income and greater uptake of social security benefits than their peers; however, the findings for employment and occupation were less conclusive.¹¹ Two systematic reviews and meta-analyses have reported that about one in six survivors of childhood cancer is unemployed in adulthood, pooled estimates indicating a 1.5-2 times higher risk of unemployment among survivors than in the general population.^{12,13} All three systematic reviews indicate, however, geographical variations with studies in Europe reporting inconsistent findings.¹¹⁻¹³ Methodological weaknesses in many previous studies exploring similar associations include use of self-reported information, short follow-up or loss to follow-up, and lack of information on reasons for unemployment, such as health-related inability or reduced ability to work.

To overcome the limitations of previous studies, we conducted the largest and most comprehensive population-based study, assessing whether the employment status and occupational positions of childhood cancer survivors differ from those in the general population and in their siblings. Based on unique register data from three Nordic countries, this is the first study to include reasons for unemployment and internationally recognised occupational positions with a long-term assessment, while taking into consideration somatic and psychiatric morbidities as important determinants. Further, we identified groups of childhood cancer survivors at particular risk of unemployment later in life.

Materials and methods

Design, study population and setting

This study is nested within the Nordic collaborative research programme Socioeconomic Consequences in Adult Life after Childhood Cancer (SALiCCS, www.saliccs.org).

We conducted a population-based matched cohort study based on the unique Nordic registers. The size of the cohort was pre-defined by the data availability and

time period of the registers in the three countries. We identified survivors of cancers diagnosed before the age of 20 years in Denmark, Finland and Sweden in the national cancer registries since 1971.^{14–19} From these registries, we obtained information on date of diagnosis (i.e. index date) and cancer type, which we classified into 12 main diagnostic groups according to the International Classification of Childhood Cancer (ICCC).^{20,21}

We compared childhood cancer survivors with individuals randomly selected from the general population who were individually matched by year of birth, sex and country of residence (in Sweden also by municipality), in a ratio of 1:5. As a second comparison group, we identified siblings (biological or adopted) of childhood cancer survivors to account for unmeasured genetic and familial background of individuals. We allowed a maximum age difference of 10 years between sibling pairs to increase the comparability of the social and environmental background in which they grew up. Both population comparisons and sibling comparisons were identified from the national population registries and were eligible as comparisons only if they were cancer-free until 20 years of age.^{22–24}

The unique personal identification numbers assigned to all residents of Denmark, Finland and Sweden, and legislation that permits register-based research enabled us to link individual-level information for our study population among the various nationwide registries.^{25–27} We obtained information on demographics and vital status from the national population registries,^{22–24} information on somatic and psychiatric diseases from the national hospital discharge registries^{28–31} and information on the educational level of the parents (using the educational level of the parent, who had achieved highest level) from the respective statistical institutes.^{25,32–36} We classified educational level according to the International Standard Classification of Education (ISCED).³⁷

We defined the index date as the date of cancer diagnosis for the survivors and the equivalent calendar date for population comparisons; for siblings, the index date was defined as the date on which they were of the same age as the survivor at the time of diagnosis of cancer. To avoid potential confounding, we excluded individuals with the following cancer predisposing syndromes: Down syndrome, neurofibromatosis and tuberous sclerosis. We excluded individuals who were under 31 years of age at the end of follow-up to enable complete annual assessment of employment and occupation, starting from the calendar year in which individuals turned 30 years of age (Figure 1).

Employment status and occupational position

We obtained annual information on employment status and occupational position from the statistical institutes of the respective countries.

Annual information on employment status was available in Denmark for the years 1980–2017 from the Integrated Database for Labour Market Research (IDA register),³³ in Finland for 1987–2015 from Statistics Finland³⁶ and in Sweden for 1990–2015 from the Longitudinal Integrated Database for Health Insurance and Labour Market Studies (LISA register).³⁴ We categorised the employment status of individuals into three groups: employed, unemployed (i.e. individuals receiving unemployment benefits and not receiving any health-related social security benefits during the calendar year) and unemployed for health-related reasons (i.e. individuals receiving sickness or disability benefits, social assistance or rehabilitation benefits or early health-related retirement during the calendar year). The groups who were unemployed or unemployed for health-related reasons were mutually exclusive within the same calendar year. Moreover, registration of an employment during the calendar year took precedence over any unemployment or health-related unemployment during the same calendar year. Individuals enrolled in any educational programme during the calendar year were excluded from the assessment of employment status for that year.

Annual information on occupational position was obtained from the Danish Employment Classification Module register for 1993–2017,³³ from Statistics Finland for 2004–2015³⁶ and from the Swedish LISA register for 2001–2015.³⁴ We categorised occupational positions according to the International Standard Classification of Occupation (ISCO-08),³⁸ into the 10 major groups: 1) managers, 2) professionals, 3) technicians and associate professionals, 4) clerical support workers, 5) services and sales workers, 6) skilled agricultural, forestry and fishery workers, 7) craft and related trades workers, 8) plant and machine operators and assemblers, 9) elementary occupations, 0) armed forces occupations.

Additionally, we grouped occupational position according to ISCO skill level (i.e. the ability to carry out the tasks and duties of a given occupation defined by the complexity and range of tasks) with highly skilled occupations defined by ISCO group 1, 2 or 3.³⁸

Statistical analyses

We assessed the employment status and occupational positions of childhood cancer survivors, population comparisons and siblings from attained age 30 years onwards.

For visual presentation of employment status, we plotted the annual prevalence of individuals who were employed, unemployed, or unemployed for health reasons between ages 30 and 50 years, stratified by sex and calendar period of index date (< 1990 vs ≥ 1990).

We assessed the odds of unemployment and of health-related unemployment among childhood cancer survivors as compared with the general population and with siblings of childhood cancer survivors at ages 30,

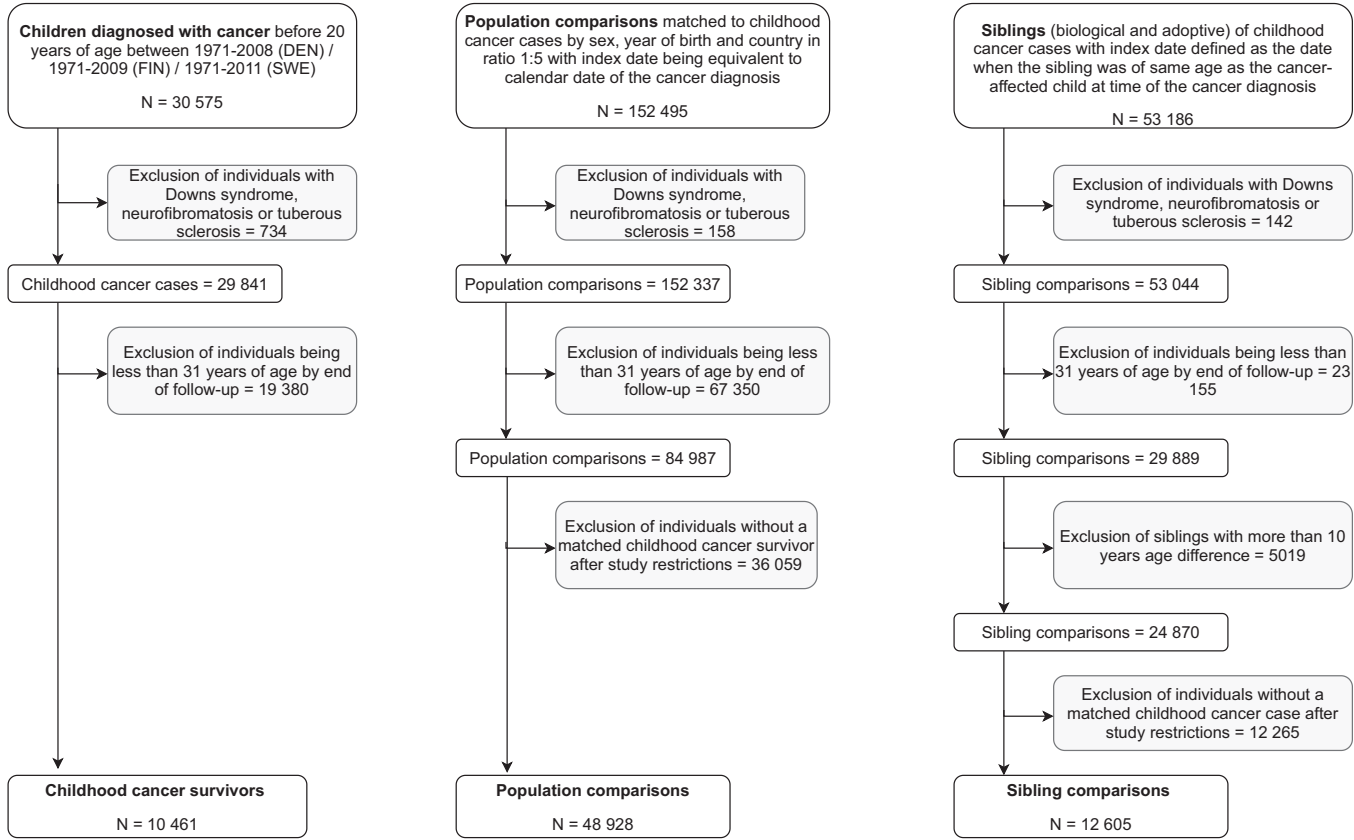


Figure 1. Flow chart of the sampling of the study population.

40 and 50 years by fitting multivariate logistic regression models and estimating odds ratios (ORs) with 95% confidence intervals (CIs). For comparison with the general population, we performed unconditional multivariate logistic regression analyses. When using siblings as the comparison group, we performed conditional multivariate logistic regression analyses to take into consideration the matched sibling pairs and their shared genetic and familial background. According to the conceptual framework of directed acyclic graphs (Figure S1),³⁹ we decided *a priori* to adjust our models for potential confounding by calendar period of index date (< 1990 vs ≥ 1990), sex and highest obtained parental education (assessed for the year closest to the index date and grouped into: low, intermediate and high). Additionally, we performed multivariate logistic regression analyses of unemployment and health-related unemployment at age 30 years, stratified by calendar period of index date (< 1990 vs ≥ 1990).

To identify subgroups of childhood cancer survivors at particular risk of unemployment and health-related unemployment at age 30 years, we performed multivariate logistic regression analyses comparing childhood cancer survivors with population comparisons and sibling comparisons, respectively, stratified by the following risk factors: Cancer type (12 diagnostic groups according to ICCC²⁰), age at diagnosis/corresponding index date (< 5, 5-14, 15-19 years), psychiatric in- and outpatient hospital contacts between 25 and 29 years of age (none vs any; see list of disorders in Table S2), and somatic in- and outpatient hospital contacts between 25 and 29 years of age (none vs any; see list of disorders in Table S1). The group of “any somatic hospital contacts” was subdivided into cancer-related hospital contacts (group 2) and hospital contacts for other somatic diseases (groups 1, 3-10; Table S1).

To assess differences in occupational position attained by age 30 years, we fitted multivariate unconditional (for population comparisons) and conditional (for sibling comparisons) logistic regression models for each of the 10 major ISCO groups,³⁸ adjusted by calendar period, sex and highest parental education. We fitted similar models to investigate the odds of achieving a highly skilled occupation, defined as ISCO group 1, 2 or 3, by ages 30, 40 and 50 years.

All analyses were performed with Stata® version 14.2.

The SALiCCS research programme has been approved by Statistics Denmark, The Regional Ethical Review Board in Stockholm, Sweden (dnr 2016/25-31/5, 2016/1561-32, 2017/1656-32, 2017/1990-32, 2017/2340-32, 2018/1165-32), Findata (Dnro THL/5543/14.06.00/2020) prolonging the former approvals by the National Institute for Health and Welfare and Social Insurance (KELA) and Statistics Finland (TK-53-394-17).

The funding sources had no role in study design, data collection, data analysis, data interpretation, or writing of the report.

Results

Our study population comprised 10 461 childhood cancer survivors, 48 928 population comparisons and 12 605 sibling comparisons (Figure 1), with an overall median attained age of 41.6 years (range, 31-66 years) by the end of follow-up (Table 1). The most common cancer diagnoses among the childhood cancer survivors were CNS tumours (22.8%), lymphomas (17.9%), and leukaemias (16.2%) (Table 1).

Figure 2 shows the proportions of employment, unemployment and health-related unemployment at each attained age between 30 and 50 years. Childhood cancer survivors were less often employed than population comparisons or siblings. While we did not observe any large differences in unemployment for reasons unrelated to health, survivors had a higher proportion of health-related unemployment than either comparison group at all attained ages. We observed similar patterns by sex and calendar period of index date, although the differences in employment and health-related unemployment between survivors and comparisons were slightly less pronounced in the more recent calendar period (Figure 2). In the calendar period 1971-1989, 9.5% of survivors, 3.6% of population comparisons and 4.0% of siblings were unemployed for health reasons by 30 years of age. In the calendar period 1990-2006, the respective proportions were 8.7% of survivor, 4.2% of population comparisons and 4.8% of siblings (Figure 2; Table 2).

The results of the multivariate analyses showed that childhood cancer survivors had higher odds of health-related unemployment at ages 30, 40 and 50 years than population comparisons (OR_{age 30} 2.57, 95% CI: 2.35-2.81; OR_{age 40} 2.50, 95% CI: 2.26-2.78; OR_{age 50} 1.98, 95% CI: 1.68-2.34) and their siblings (OR_{age 30} 2.50, 95% CI: 2.15-2.90; OR_{age 40} 2.78, 95% CI: 2.32-3.33; OR_{age 50} 2.17, 95% CI: 1.63-2.89) (Table 2). The adjusted effect estimates did not differ considerably from the unadjusted effect estimates (data not shown). We found no differences between survivors, population comparisons and siblings in the odds of unemployment unrelated to health at ages 30 and 40 years (Table 2). The odds of unemployment were higher among survivors than siblings at age 50 years (OR_{age 50} 1.76; 95% CI: 1.07-2.87). Stratification by calendar period at age 30 years revealed attenuated odds for health-related unemployment in the more recent calendar period (i.e. index date ≥ 1990) with similar findings for the two comparison groups (Table 2).

Leukaemia survivors had higher odds of being unemployed for reasons unrelated to health at age 30 years than population comparisons (OR: 1.34, 95% CI: 1.10-1.63). We found no other statistically significant association with unemployment for reasons unrelated to health after stratification by other cancer diagnostic group or age at diagnosis (Table 3). The odds for health-related unemployment at age 30 were much

	Childhood cancer survivors	General population comparisons	Sibling comparisons
Characteristics	n (%)	n (%)	n (%)
Size of study cohorts	10,461	48,928	12,605
Country			
Denmark	2,941 (28.1%)	13,608 (27.8%)	3,433 (27.2%)
Finland	2,743 (26.2%)	13,193 (27.0%)	3,466 (27.5%)
Sweden	4,777 (45.7%)	22,127 (45.2%)	5,706 (45.3%)
Sex			
Male	5,547 (53.0%)	25,990 (53.1%)	6,400 (50.8%)
Female	4,914 (47.0%)	22,938 (46.9%)	6,205 (49.2%)
Decade of birth			
1951-1959	766 (7.3%)	3,617 (7.4%)	931 (7.4%)
1960-1969	2,350 (22.5%)	11,110 (22.7%)	3,614 (28.7%)
1970-1979	4,493 (43.0%)	20,982 (42.9%)	5,668 (45.0%)
1980-1986	2,852 (27.3%)	13,219 (27.0%)	2,392 (19.0%)
Age at cancer diagnosis/index date			
<5 year	1,798 (17.2%)	8,183 (16.7%)	1,844 (14.6%)
5-14 years	3,836 (36.7%)	17,833 (36.5%)	4,588 (36.4%)
≥15 years	4,827 (46.1%)	22,912 (46.8%)	6,173 (49.0%)
Attained age at end of follow-up			
Median/second quartile	41.0 years	41.5 years	42.9 years
Calendar period of cancer diagnosis/index date			
1971-1979	2,768 (26.5%)	12,848 (26.3%)	3,499 (27.8%)
1980-1989	4,133 (39.5%)	19,370 (39.6%)	5,349 (42.4%)
1990-1999	2,926 (28.0%)	13,751 (28.1%)	3,246 (25.8%)
2000-2006	634 (6.1%)	2,959 (6.1%)	511 (4.1%)
Cancer types, classified according to the International Classification of Childhood Cancer (ICCC)(20)			
Leukaemias	1,695 (16.2%)	-	-
Lymphomas	1,875 (17.9%)	-	-
CNS tumours	2,382 (22.8%)	-	-
Neuroblastomas	146 (1.4%)	-	-
Retinoblastoma	205 (2.0%)	-	-
Renal tumours	391 (3.7%)	-	-
Hepatic tumours	24 (0.2%)	-	-
Bone tumours	424 (4.1%)	-	-
Soft tissue sarcomas	510 (4.9%)	-	-
Germ-cell neoplasms	894 (8.6%)	-	-
Carcinomas	1,637 (15.7%)	-	-
Other and unspecified neoplasms	278 (2.7%)	-	-
Highest attained parental education the year closest before index date^{a, b, c}			
Low	2,834 (28.7%)	14,042 (30.6%)	3,979 (33.2%)
Intermediate	4,393 (44.5%)	20,086 (43.7%)	5,032 (41.9%)
High	2,640 (26.8%)	11,819 (25.7%)	2,993 (24.9%)
Somatic hospital contact (in- and outpatient) in the period between 25-29 years of age			
None	5,156 (49.3%)	34,738 (71.0%)	8,985 (71.3%)
Any ^d	5,305 (50.7%)	14,190 (29.0%)	3,620 (28.7%)
Cancer-related diseases ^e	2,513 (24.0%)	1,144 (2.3%)	343 (2.7%)
Other diseases ^e	2,792 (26.7%)	13,046 (26.7%)	3,277 (26.0%)
Psychiatric hospital contact (in- and outpatient) in the period between 25-29 years of age			
None	9,830 (94.0%)	46,646 (95.3%)	12,008 (95.3%)
Any ^f	631 (6.0%)	2,282 (4.7%)	597 (4.7%)

Table 1: Characteristics of the study population.

^a Educational level is classified according to the International Standard Classification of Education [37].

^b Low education, primary and lower secondary education or less (ISCED levels 0-2); medium education, upper secondary education (ISCED level 3); high education, postsecondary education or higher (ISCED levels 4-8). We used the educational level of the parent, who had achieved the highest level.

^c 6% missing, whereas all other variables had <5% missing.

^d See Table S1 for full list of ICD codes included.

^e These groups represent sub-groups of the 'Any' group. The groups are mutually exclusive; thus if an individual is hospitalised for both cancer (group 2 in Table S1) and other somatic diseases (groups 1, 3-10 in Table S1), the individual is counted only in the cancer-related group.

^f See Table S2 for full list of ICD codes included.

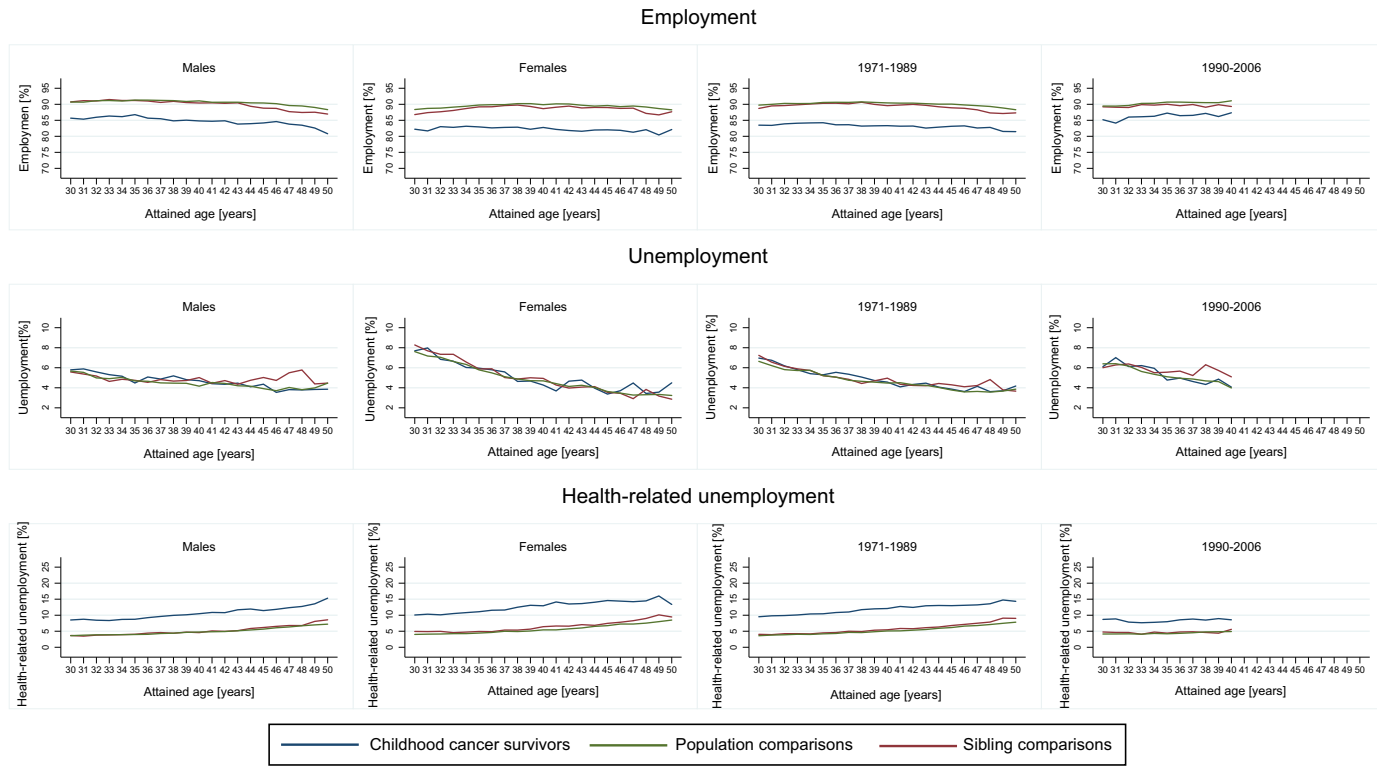


Figure 2. Employment, unemployment, and health-related unemployment by attained ages 30-50 years for childhood cancer survivors, sibling comparisons and population comparisons, stratified by sex and calendar period of cancer diagnosis/index date.

	Childhood cancer survivors	Population comparisons	Sibling comparisons	Childhood cancer survivors vs population comparisons	Childhood cancer survivors vs siblings comparisons
N	10,461	48,928	12,605		
Unemployment^b					
	N _{unemployed} (%)	N _{unemployed} (%)	N _{unemployed} (%)	OR ^a (95% CI)	OR ^a (95% CI)
Attained age 30	588 (6.7%)	2,709 (6.6%)	729 (6.9%)	1.04 (0.95-1.15)	0.99 (0.86-1.15)
1971-1989	394 (7.0%)	1,764 (6.6%)	530 (7.2%)	1.08 (0.95-1.21)	0.98 (0.81-1.18)
1990-2006	194 (6.1%)	945 (6.4%)	199 (6.0%)	0.98 (0.84-1.16)	0.94 (0.69-1.27)
Attained age 40	239 (4.5%)	1,130 (4.4%)	373 (5.0%)	1.08 (0.93-1.25)	1.06 (0.85-1.33)
Attained age 50	74 (4.2%)	352 (3.9%)	100 (3.7%)	1.15 (0.88-1.50)	1.76 (1.07-2.87)
Health-related unemployment^c					
	N _{unemployed for health reasons} (%)	N _{unemployed for health reasons} (%)	N _{unemployed for health reasons} (%)	OR ^a (95% CI)	OR ^a (95% CI)
Attained age 30	815 (9.2%)	1,572 (3.8%)	454 (4.3%)	2.57 (2.35-2.81)	2.50 (2.15-2.90)
1971-1989	539 (9.5%)	959 (3.6%)	296 (4.0%)	2.78 (2.48-3.11)	2.98 (2.43-3.65)
1990-2006	276 (8.7%)	613 (4.2%)	158 (4.8%)	2.25 (1.94-2.61)	1.65 (1.24-2.20)
Attained age 40	617 (11.6%)	1,299 (5.1%)	410 (5.5%)	2.50 (2.26-2.78)	2.78 (2.32-3.33)
Attained age 50	254 (14.3%)	714 (7.8%)	246 (9.0%)	1.98 (1.68-2.34)	2.17 (1.63-2.89)

Table 2: Multivariate logistic regression analyses for the odds of unemployment and health-related unemployment at age 30, 40 and 50 ? years.

^a Adjusted by sex, highest parental education (low (ISCED 0-2); intermediate (ISCED 3); high (ISCED 4-8)), and by calendar period of cancer diagnosis/reference (<1990 vs ≥1990)

^b Unemployment comprise individuals having received unemployment benefits during the calendar year and individuals not being registered with an employment and not having received any health-related social security benefits during the calendar year.

^c Health-related unemployment comprise individuals having received either sickness-, disability-, social assistance-, or rehabilitation benefits or early health-related retirement during the calendar year and not being registered with an unemployment.

more pronounced for CNS tumour survivors than for population comparisons (OR, 5.93; 95% CI, 5.23-6.73) or for siblings (OR, 6.96; 95% CI, 5.10-9.51). We also observed considerably higher odds for health-related unemployment among survivors of neuroblastoma and bone tumours, although the effect estimates were imprecise due to small samples of these diagnostic groups (Table 3). Moreover, survivors of cancers diagnosed at < 15 years of age had high odds for health-related unemployment at age 30 years (Table 3). The reported effect estimates for unemployment for reasons unrelated to health at age 30 years did not change appreciably within strata of individuals with and without somatic and psychiatric hospital contacts between 25 and 29 years of age, respectively. The reported effect estimates for health-related unemployment at age 30 years, however, were slightly stronger among survivors with somatic hospital contacts, and especially cancer-related hospital contacts, than population comparisons and sibling comparisons. In contrast, the higher odds of health-related unemployment among survivors than comparisons appeared to be strongest among individuals without a psychiatric hospital contact (Table 3).

Overall, we found similar distributions of the 10 groups of occupational positions at age 30 years in childhood cancer survivors, population comparisons and siblings (Table 4), although some differences were

noted. Survivors had slightly higher odds of being in an armed forces occupation than population comparisons (OR_{age30} 1.34; 95% CI, 1.12-1.60) and sibling comparisons (OR_{age30} 1.32; 95% CI, 1.00-1.74; Table 4). Moreover, survivors had slightly lower odds of being skilled agricultural, forestry and fishery workers than population comparisons (OR_{age30} 0.74; 95% CI, 0.54-1.02) and siblings (OR_{age30} 0.57; 95% CI, 0.31-1.07) and also lower odds for managerial occupations than siblings (OR_{age30} 0.74; 95% CI, 0.55-1.00; Table 4). The absolute differences were, however, minor, and the small samples for these specific occupations yielded imprecise effect estimates. Moreover, Table 4 shows that the odds of being in a high-skilled occupation were largely similar for survivors, population comparisons and siblings at ages 30, 40 and 50 years.

Discussion

Key findings

We observed that a considerable proportion of childhood cancer survivors were unemployed later in life for health-related reasons. By 30 years of age, 9.2% of survivors were unemployed for health reasons. Although this proportion was slightly smaller for survivors of cancers diagnosed in more recent decades, the risk of

	Childhood cancer survivors	Population comparisons	Sibling comparisons	Childhood cancer survivors vs population comparisons	Childhood cancer survivors vs siblings comparisons
N	10,461	48,928	12,605		
Unemployment at age 30 years^b					
	N _{unemployed} (%)	N _{unemployed} (%)	N _{unemployed} (%)	OR ^a (95% CI)	OR ^a (95% CI)
Childhood cancer type^b					
Leukaemias	121 (8.1%)			1.34 (1.10-1.63)	1.18 (0.83-1.68)
Lymphomas	112 (7.1%)			1.10 (0.90-1.36)	1.15 (0.81-1.64)
CNS tumours	108 (5.4%)			0.82 (0.67-1.01)	0.75 (0.54-1.03)
Neuroblastomas	8 (6.2%)			0.95 (0.44-2.05)	0.48 (0.17-1.38)
Retinoblastoma	12 (6.9%)			1.04 (0.55-1.98)	1.27 (0.43-3.72)
Renal tumours	19 (5.5%)			0.87 (0.53-1.42)	0.93 (0.43-2.00)
Hepatic tumours	-			-	-
Bone tumours	18 (5.2%)			0.84 (0.51-1.37)	0.70 (0.28-1.74)
Soft tissue sarcomas	33 (7.6%)			1.21 (0.84-1.77)	1.14 (0.60-2.16)
Germ-cell neoplasms	60 (7.8%)			1.30 (0.99-1.72)	1.16 (0.76-1.77)
Carcinomas	87 (6.7%)			0.96 (0.76-1.20)	1.00 (0.68-1.47)
Other and unspecified neoplasms	10 (4.6%)			0.75 (0.40-1.42)	0.51 (0.18-1.44)
Age at cancer diagnosis/corresponding index date					
<5 year	113 (7.1%)	439 (6.1%)	111 (6.8%)	1.25 (1.00-1.57)	1.09 (0.82-1.46)
5-14 years	226 (6.7%)	965 (6.2%)	782 (7.1%)	1.11 (0.95-1.30)	0.96 (0.79-1.16)
15-19 years	249 (6.4%)	1,305 (7.0%)	336 (6.7%)	0.92 (0.80-1.07)	0.98 (0.82-1.17)
Somatic hospital contacts in the period between 25-29 years of age					
None	295 (7.1%)	1,839 (6.4%)	520 (6.9%)	1.12 (0.98-1.29)	1.01 (0.87-1.18)
Any ^c	293 (6.3%)	870 (7.0%)	209 (6.7%)	0.94 (0.81-1.08)	1.02 (0.84-1.23)
Cancer-related diseases ^d	144 (6.6%)	56 (5.6%)	20 (6.9%)	1.13 (0.81-1.57)	1.08 (0.64-1.83)
Other diseases ^d	149 (6.0%)	814 (7.1%)	189 (6.7%)	0.88 (0.73-1.06)	0.95 (0.75-1.19)
Psychiatric hospital contacts in the period between 25-29 years of age					
None	521 (6.3%)	2,403 (6.1%)	661 (6.5%)	1.06 (0.95-1.17)	0.99 (0.87-1.12)
Any ^e	67 (12.5%)	306 (16.1%)	68 (13.7%)	0.77 (0.58-1.03)	0.93 (0.64-1.35)
Health-related unemployment at age 30 years^c					
N _{unemployed for health reasons} (%)	N _{unemployed for health reasons} (%)	N _{unemployed for health reasons} (%)	OR ^b (95% CI)	OR ^b (95% CI)	
Childhood cancer type^b					
Leukaemias	122 (8.2%)			2.35 (1.93-2.86)	1.90 (1.33-2.73)
Lymphomas	85 (5.4%)			1.45 (1.16-1.83)	1.63 (1.09-2.45)
CNS tumours	381 (18.9%)			5.93 (5.23-6.73)	6.96 (5.10-9.51)
Neuroblastomas	20 (15.5%)			4.76 (2.87-7.92)	13.26 (1.66-106.11)
Retinoblastoma	13 (7.5%)			2.01 (1.09-3.74)	2.74 (0.47-15.93)
Renal tumours	14 (4.0%)			1.08 (0.60-1.93)	0.72 (0.25-2.05)
Hepatic tumours	-			-	-
Bone tumours	31 (9.0%)			2.42 (1.65-3.56)	5.69 (2.11-15.34)
Soft tissue sarcomas	26 (6.0%)			1.66 (1.10-2.50)	1.11 (0.58-2.10)
Germ-cell neoplasms	46 (6.0%)			1.56 (1.15-2.13)	1.25 (0.71-2.20)
Carcinomas	65 (5.0%)			1.27 (0.97-1.63)	1.05 (0.67-1.63)
Other and unspecified neoplasms	11 (5.0%)			1.40 (0.76-2.59)	1.19 (0.45-3.15)
Age at cancer diagnosis					
<5 year	203 (12.8%)	266 (3.7%)	73 (4.5%)	3.71 (3.03-4.53)	3.38 (2.51-4.56)
5-14 years	365 (10.9%)	613 (3.9%)	169 (4.2%)	2.97 (2.58-3.41)	2.74 (2.26-3.33)

(continued)

Table 3 (Continued)

	Childhood cancer survivors	Population comparisons	Sibling comparisons	Childhood cancer survivors vs population comparisons	Childhood cancer survivors vs siblings comparisons
15-19 years	247 (6.4%)	693 (3.7%)	212 (4.2%)	1.81 (1.56-2.11)	1.59 (1.31-1.92)
Somatic hospital contacts in the period between 25-29 years of age					
None	233 (5.6%)	863 (3.0%)	254 (3.4%)	1.90 (1.63-2.21)	1.71 (1.42-2.06)
Any ^c	582 (12.5%)	709 (5.7%)	200 (6.4%)	2.39 (2.12-2.69)	2.23 (1.87-2.65)
Cancer-related diseases ^d	277 (12.7%)	44 (4.4%)	9 (3.1%)	3.29 (2.34-4.63)	4.71 (2.38-9.31)
Other diseases ^d	305 (12.4%)	665 (5.8%)	191 (6.8%)	2.31 (1.99-2.67)	2.07 (1.70-2.52)
Psychiatric hospital contacts in the period between 25-29 years of age					
None	642 (7.8%)	1,089 (2.8%)	318 (3.1%)	2.93 (2.64-3.24)	2.65 (2.30-3.06)
Any ^e	173 (32.2%)	483 (25.4%)	136 (27.3%)	1.41 (1.14-1.75)	1.32 (1.00-1.74)

Table 3: Multivariate logistic regression analyses for the odds of unemployment and health-related unemployment at age 30 ? years, stratified by childhood cancer type, age at cancer diagnosis, somatic hospital contacts and psychiatric hospital contacts.

- If less than five individuals with the event, data is not shown.

^a Adjusted by sex, highest parental education (low (ISCED 0-2); intermediate (ISCED 3); high (ISCED 4-8)), and by calendar period of cancer diagnosis/reference (<1990 vs ≥1990)

^b Childhood cancer type categorised according to the International Classification of Childhood Cancer (ICCC) [20,21]

^c See full list of somatic diseases included and their related International Classification of Diseases (ICD) codes in Table S1

^d These groups represent sub-groups of the 'Any' group. The reference group is no somatic hospital contacts. The groups are mutually exclusive; thus if an individual is hospitalised for both cancer (group 2 in Table S1) and other somatic diseases (groups 1, 3-10 in Table S1), the individual is counted only in the cancer-related group.

^e See full list of psychiatric disorders included and their related ICD codes in Table S2.

health-related unemployment was two times higher in childhood cancer survivors than in population or sibling comparisons at ages 30 and 40 years. We found no notable differences in the risk of being unemployed for reasons unrelated to health, and survivors obtained similar occupational positions and at similar skill levels as population comparisons and siblings.

Comparison of findings in light of the literature

The definitions of unemployment differ widely in previous studies of survivors of childhood cancer. To our knowledge, only three previous studies in France, Great Britain and North America⁴⁰⁻⁴² distinguished between reasons for unemployment, as we did, although the three studies were based on self-reported information on health-related unemployment assessed at one time point.⁴⁰⁻⁴² The studies found higher risks of health-related unemployment among survivors than peers,⁴⁰⁻⁴² in line with our findings. The reported risk estimates for health-related unemployment among survivors as compared with their peers varied from six times higher risk in the North American study,⁴⁰ five times higher risk in the British study⁴² and 60% higher risk in the study in France.⁴¹ In the British study, the risk was 15 times higher among CNS tumour survivors treated with cranial irradiation than in the general population,⁴² and the North American study found that survivors treated with cranial radiation at doses of ≥ 25 Gy

had a three times higher risk of health-related unemployment than survivors who had not been irradiated.⁴⁰ Similarly high risks among survivors of CNS tumours and survivors treated with cranial irradiation were reported in the French study.⁴¹ Although our study did not include information on treatment, we also found a particularly high risk of health-related unemployment among CNS tumour survivors, who had six to seven times higher odds than population comparisons and siblings.

Although our findings are in line with those of studies that also differentiated the reasons for unemployment, an international comparison is challenged by geographical variations in the organisation of, access to, and extent of welfare services, including social security benefits for unemployment or health problems.¹¹⁻¹³ We defined health-related unemployment as individuals receiving social security benefits for health problems. In Denmark, Finland and Sweden, there is universal access to such welfare services according to need and not to affiliation to the labour market, in order to reduce social inequality.⁴³ In the USA, employer-sponsored health insurance coverage plays an essential role.⁴⁴ Thus, any international comparison of findings outside the Nordic setting should be interpreted carefully in the light of such important differences in welfare systems, which may affect survivors' possibilities of obtaining and maintaining a job despite potential health problems.

	Childhood cancer survivors	Population comparisons	Sibling comparisons	Childhood cancer survivors vs population comparisons	Childhood cancer survivors vs siblings comparisons
N	10,461	48,928	12,605		
Occupational position at age 30, according to 10 major groups of the International Standard Classification of Occupation (ISCO-08) [38]					
	N (%)	N (%)	N (%)	OR ^a (95% CI)	OR ^a (95% CI)
ISCO group 1) Managers	132 (2.3%)	786 (2.8%)	204 (3.0%)	0.87 (0.71-1.05)	0.74 (0.55-1.00)
ISCO group 2) Professionals	1,238 (21.3%)	6,004 (21.1%)	1,345 (19.5%)	1.00 (0.93-1.07)	1.02 (0.91-1.16)
ISCO group 3) Technicians and associate professionals	1,085 (18.7%)	5,332 (18.7%)	1,301 (18.9%)	0.98 (0.91-1.06)	0.95 (0.84-1.07)
ISCO group 4) Clerical support workers	771 (13.3%)	3,599 (12.6%)	903 (13.1%)	1.08 (0.99-1.19)	1.13 (0.97-1.31)
ISCO group 5) Services and sales workers	1,094 (18.8%)	5,156 (18.1%)	1,249 (18.1%)	1.05 (0.97-1.14)	1.04 (0.91-1.18)
ISCO group 6) Skilled agricultural, forestry and fishery workers	46 (0.8%)	315 (1.1%)	77 (1.1%)	0.74 (0.54-1.02)	0.57 (0.31-1.07)
ISCO group 7) Craft and related trades workers	537 (9.2%)	2,850 (10.0%)	680 (9.9%)	0.92 (0.83-1.02)	0.91 (0.74-1.11)
ISCO group 8) Plant and machine operators, and assemblers	405 (7.0%)	2,163 (7.6%)	549 (8.0%)	0.91 (0.81-1.03)	0.94 (0.77-1.16)
ISCO group 9) Elementary occupations	339 (5.8%)	1,672 (5.9%)	405 (5.9%)	1.01 (0.90-1.14)	1.18 (0.96-1.44)
ISCO group 0) Armed forces occupation	164 (2.8%)	631 (2.2%)	178 (2.6%)	1.34 (1.12-1.60)	1.32 (1.00-1.74)
Odds of being in high-skilled occupation^b					
	N _{high-skilled occupation} (%)	N _{high-skilled occupation} (%)	N _{high-skilled occupation} (%)	OR ^a (95% CI)	OR ^a (95% CI)
Attained age 30	2,455 (42.3%)	12,122 (42.5%)	2,850 (41.4%)	0.97 (0.91-1.03)	0.93 (0.84-1.03)
Attained age 40	1,833 (49.1%)	9,584 (49.8%)	2,767 (49.0%)	0.95 (0.88-1.02)	0.87 (0.76-0.99)
Attained age 50	663 (48.6%)	3,505 (46.4%)	1,067 (47.3%)	1.06 (0.94-1.20)	0.86 (0.68-1.09)

Table 4: Occupational positions (defined according to the International Standard Classification of Occupation (ISCO-08)) at different attained ages of childhood cancer survivors, population comparisons and sibling comparisons.

^a Adjusted by sex, highest parental education (low (ISCED 0-2); intermediate (ISCED 3); high (ISCED 4-8)), and by calendar period of cancer diagnosis/reference (<1990 vs ≥1990).

^b High-skilled occupation defined by ISCO group 1 "Managers", 2 "Professionals" or 3 "Technicians and associate professors". Reference level is other occupations group (ISCO 0, 4, 5, 6, 7, 8, 9).

Our finding of no overall difference in the occupational positions attained by childhood cancer survivors are reassuring and concords to a certain extent with those of the very few previous studies assessing the occupations of childhood cancer survivors.^{41,42,45} A meaningful comparison of the occupational positions of survivors is, however, difficult because of the use of different occupational classifications and heterogeneous welfare systems.

Determinants of employment status among survivors

We found that survivors of a CNS tumour and/or diagnosed at a younger age had particularly high odds of health-related unemployment, which is probably explained by the intensive treatment and susceptibility to treatment-induced late effects. Surgical resection of a CNS tumour or cranial irradiation could lead to irreversible damage to healthy, developing brain tissue and result in CNS dysfunction and cognitive impairment. Additionally, we found that individuals who had somatic and psychiatric hospital contacts at ages 25-29 years had considerably higher odds of health-related unemployment by age 30. These findings provide a valuable indication of the risk-based need for timely support and interventions that address vulnerable survivors' possibilities of obtaining and maintaining a job later in life that is suitable for their health condition and needs.

Our findings indicate that survivors who are fit to work from a general health perspective are employed to the same degree as the general population and their siblings.

Strengths and limitations

With unique register data from three Nordic countries with similar welfare and health-care systems, we were able to assess annual measurements of employment status and occupational positions in the largest population-based cohort of childhood cancer survivors to be evaluated for these outcomes with a long follow-up period and virtually no loss to follow-up, thereby making selection bias very unlikely. In contrast to most previous studies, we were able to distinguish reasons for unemployment and we used an international scheme to define occupational position, thereby minimising the risk of outcome misclassification.³⁸ Further, registration of employment status and occupational position is linked to the administration of taxes and payment of social security benefits, which reduced the risk of information bias. We found largely similar effect estimates across our two comparison groups, which further strengthens the validity of our reported findings and reduced the risk of confounding by genetic and familial factors. Further, we were able to adjust for potential confounding by parental socioeconomic status using highest educational level of the parents of our study

population, and we investigated the effect of somatic and psychiatric morbidities on the risk of later unemployment.

By assessing employment status and occupational position from age 30 onwards, the diagnostic period reflected in this study ranged from 1971 to 2006. Consequently, many of the survivors of cancers diagnosed at young ages included in this study were diagnosed several decades ago, and our findings may not entirely represent the situation of survivors of cancers diagnosed more recently due to temporal changes in survival probability and treatment-induced late effects. Moreover, our definitions of annual unemployment and health-related unemployment, respectively, cover mixed groups of individuals who received such benefits 1-365 days during a calendar year and were not employed. Such potential misclassification would, however, probably be non-differential for survivors and comparisons and thereby result in bias towards the null. Lastly, some individuals may still be enrolled in educational programmes in their early 30s, which excluded them from the analyses at these ages. We overcame this potential limitation by assessing multiple measurements of employment and occupation at several ages, which is a refined and novel contribution to the existing literature.

Conclusion and implications

This is the most comprehensive population-based study of employment and occupation among childhood cancer survivors to date and based on high-quality register data from three Nordic countries. Although our study indicates that many survivors are employed and obtain highly skilled occupational positions to the same extent as the general population and their siblings, we provide the novel finding that adult survivors of childhood cancer, especially those diagnosed with cancer before 15 years of age and/or with a CNS tumour, have a substantial burden of health-related unemployment. These survivors might benefit from early, comprehensive support to address potential health problems and barriers that could interfere with their later possibilities for obtaining and maintaining a job. This may include comprehensive survivorship follow-up care focusing on potential socioeconomic challenges, where high-risk survivors would be offered support in educational programmes and obtaining jobs suitable for their health. The Perceived Barriers Scale was developed recently to address employment and vocational issues for survivors of childhood brain tumours with a focus on both internal (e.g. perceptions of physical, social and emotional challenges) and external barriers (e.g. access to education and support services and attitudes of families and employers), and such instrument would be essential to integrate into survivorship care.⁴⁶ An improved survivorship care for particularly vulnerable survivors would improve the quality of life of survivors and their families

and would be of particular societal value in light of the growing population of childhood cancer survivors.

Contributors

LEF, JFW and FE were responsible for the conceptualisation and investigation of the study. All authors contributed to the data curation and methodology. LEF conducted the formal analysis. LEF, JFW and FE drafted the original manuscript. All authors contributed to data interpretation and critically reviewed and edited the manuscript. All authors agreed to be accountable for all aspects of the work and approved the final manuscript before submission. LEF and JFW take responsibility for the integrity of the data and the accuracy of the data analysis.

Data availability statement

The data that support the information of this manuscript were accessed remotely on a secure platform at Statistics Denmark. Pseudonymised individual-level data were obtained from national registry holders after ethical approval (where applicable) and secrecy assessment. According to Danish, Finnish and Swedish laws and regulations, individual-level sensitive data can only be made available for researchers who fulfil legal requirements for access to personal sensitive data. Please contact Jeanette Falck Winther (jeanette@cancer.dk), the Principal Investigator of the SALiCCS research program, for further questions about data access.

Declaration of Interests

The authors report no conflicts of interest.

Acknowledgements

The authors are grateful to Thomas Tj $\frac{1}{2}$ rn $\frac{1}{2}$ nelund Nielsen and Anja Kr $\frac{1}{2}$ yer (Danish Cancer Society Research Center, Childhood Cancer Research Group) for their technical support with data acquisition and preparation of data and to Elisabeth Anne Wreford Andersen (Danish Cancer Society Research Center, Statistics and Data Analysis) for statistical advice.

Supplementary materials

Supplementary material associated with this article can be found in the online version at doi:[10.1016/j.lanepe.2021.100258](https://doi.org/10.1016/j.lanepe.2021.100258).

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