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Surviving childhood cancer: a systematic review of studies on risk and determinants of adverse socioeconomic outcomes

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Cancer Epidemiology

Substantial improvements in childhood cancer survival have resulted in a steadily increasing population of childhood cancer survivors. Whereas somatic late effects have been assessed in many studies, less is known about the impact of childhood cancer on socioeconomic outcomes in survivors. The aim of this article was to evaluate and summarise the evidence on the socioeconomic conditions of childhood cancer survivors and to identify survivors at particular risk of adverse socioeconomic outcomes. An extensive literature search of three electronic databases was conducted. Of 419 articles identified, 52 met the inclusion criteria. All the selected articles were appraised for quality, and findings were summarised in a narrative synthesis. Childhood cancer survivors were at higher risk of adverse socioeconomic outcomes with regard to educational achievement, income and social security benefits than the general population or a sibling comparison group. The risks for unemployment and a lower occupational position were significantly increased only for survivors of a central nervous system tumour. Notably, survivors of central nervous system tumours, survivors treated with cranial radiotherapy and those diagnosed at younger age independent of cancer type were determinants of particular adverse socioeconomic outcomes. Given the increasing population of childhood cancer survivors, targeted follow-up interventions and support strategies addressing not only the somatic and psychiatric late effects but also the socioeconomic difficulties that some childhood cancer survivors face is of high importance to reduce social inequity, and ensure a high quality of life after childhood cancer.

Introduction

Over the past decades, advances in diagnostics, treatment combinations and techniques, pharmacotherapy and better tailoring of treatment by risk grouping have led to substantial improvements in survival from childhood cancer.[1–5] As a result, the number of childhood cancer survivors is increasing continuously, raising awareness and concern about late effects of intensive cancer treatment that might affect the survivors in later life. Whereas there is a large body of evidence on somatic late effects,[6–10] less is known about the impact of

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What's new?

Increasing numbers of patients are surviving childhood cancers nowadays, raising new questions about their long-term health and socioeconomic life. In the present systematic review, survivors of all childhood cancer types were found to have an increased risk of various adverse socioeconomic outcomes during their life course. Notably, survivors of a central nervous system tumour, survivors treated with cranial radiation therapy and those diagnosed at younger age independent of cancer type, were at particular risk of adverse socioeconomic outcomes. Our findings may be used as the basis for future interventions and supportive strategies targeting particular vulnerable groups of childhood cancer survivors.

childhood cancer on socioeconomic outcomes in survivors. Moreover, there has been no comprehensive and systematic review of studies of the potential impact of a childhood cancer diagnosis and its treatment on various socioeconomic outcomes in long-term survivors.

Previous studies indicated that a childhood cancer diagnosis or its treatment may affect school performance,[11] educational achievement,[12] obtaining employment[13] or social life, including founding a family.[14–16] The current evidence is, however, inconsistent, with large geographical variations, and the underlying mechanisms and pathways are still poorly understood. Identification of groups of survivors who are at particular risk of adverse socioeconomic conditions is a first step to understand the pathways leading to differences in socioeconomic outcomes and could be the basis for future interventions to reduce such social inequity.[17]

The aim of this article was to critically evaluate and summarise the evidence from epidemiological studies published between January 2000 and November 2017 on educational achievements, working life, income, and uptake of social security benefits by childhood cancer survivors. The specific objectives were (i) to investigate adverse socioeconomic outcomes in long-term survivors of childhood cancer and (ii) to identify survivors who are at particular risk of adverse socioeconomic outcomes.

Methods

We followed the Preferred Reporting Items for Systematic review and Meta-Analysis (PRISMA) guidelines.[18] A systematic review protocol was designed, and the research group agreed on the search strategy and *a priori* defined inclusion and exclusion criteria (protocol not registered).

Search strategy

An extensive literature search of the three electronic databases MEDLINE (PubMed), EMBASE and PsycINFO was conducted in August 2017 to identify relevant research articles on the socioeconomic outcomes: Educational achievement, working life, income and uptake of social security benefits. The definitions and availability of social security benefits varies largely between countries and welfare systems. Our search strategy comprised social security benefits referring to unemployment, sickness, disability, rehabilitation and permanent invalidity (early retirement).[19]

Our search strategy consisted of four individual blocks combining cancer, survivorship, childhood and socioeconomic characteristics. The search strategy for the MEDLINE search is illustrated in Supporting Information Table S1. The reference lists of the included articles were examined manually to identify additional relevant articles. The search was updated in November 2017.

Study selection, inclusion and exclusion criteria

Criteria for inclusion and exclusion were defined *a priori* (Supporting Information Table S2). Articles published between January 2000 and November 2017 and written in English, Danish, Finnish, French, German, Norwegian or Swedish were eligible for inclusion. No geographical restrictions were applied. Only studies with quantitative methods, a cohort design and an external or internal comparison group were included. All studies including patients aged <20 years at diagnosis were eligible. We included survivors of all cancer types.

As an additional eligibility criterion for full-text screening, we restricted the follow-up period to patients who had survived at least 5 years since diagnosis of childhood cancer or patients who had survived at least 1 year after treatment. Use of a minimum length of follow-up avoided assessment of immediate effects of a childhood cancer diagnosis, such as absence from school for treatment requiring hospitalisation, rather than long-term impact of childhood cancer.

Relevant articles were selected by independent assessment of the title and abstract by two investigators (L.F. and F.E.). Full texts of potentially relevant articles were extracted and screened by the same investigators according to the eligibility criteria. Discrepancies between the investigators were resolved by consensus.

Data extraction

For each included article, we recorded the first author's name, year of publication, country, study design, cancer type, sample size, age at diagnosis, age at follow-up, diagnostic period, type of comparison group, follow-up period, loss to follow-up, outcome measurement, whether the study was population- or institution-based, variables for adjustment or stratification, main outcomes and results.

Quality assessment

All articles were appraised for quality by two independent researchers (LF, FE) using the Newcastle-Ottawa Quality

Assessment Scale (http://www.ohri.ca/programs/clinical_epidemiology/oxford.asp). The Scale is a tool for assessing risk of bias in observational studies on a star rating system, with a maximum of nine stars; it is recommended by the Cochrane Collaboration.[20] Risk for bias was assessed according to three criteria[1]: selection of study groups,[2] comparability of the study and the control group[3] and ascertainment of outcome.[20]

For the criteria 'selection of study groups', representativeness of the groups and ascertainment of exposure was assessed. For the assessment of 'comparability between groups', we defined parental socioeconomic background as a factor of particular relevance for adjustment, as it might have a substantial impact on the socioeconomic attainment in offspring in adult life. Decades of research on social capital and reproduction of social inequalities have suggested that parental socioeconomic background play an important role in the academic achievement of their children.[21] Other confounding factors that led to higher ratings when taken into consideration were sex, age at diagnosis or attained age at follow-up. Studies of somatic late effects of childhood cancer have found differences in effects related to sex and age at diagnosis,[6] which may be of importance for later socioeconomic outcomes. 'Ascertainment of outcome' was assessed by outcome measure, length of follow-up and follow-up rate. We defined *a priori* 70% as the threshold follow-up rate of cohorts when assessing potential selection bias caused by loss to follow-up. This threshold was based on the recommended threshold range of 60%–80% for follow-up in cohort studies by Kristman *et al.*[22]

Analytical approach

As we assumed that reported socioeconomic outcomes would differ by study, we decided to extract the definitions of outcomes reported in the studies. Given the heterogeneity in study methods, study period, outcomes, social welfare systems and cultural and societal aspects, *a priori* no quantitative meta-analysis was intended. We conducted a narrative synthesis of the study findings, with a focus on findings from studies including the most common childhood cancers and with higher quality ratings.

Results

We identified 419 articles published between 1 January 2000 and 15 November 2017 and included 52 articles that met the inclusion criteria (Fig. 1).

The characteristics of the included studies and their quality are summarised in Table 1. The studies varied widely by cancer type, age at diagnosis, diagnostic period and treatment era, sample size and study setting. Of the 52 studies included in this article, 27 (52%) were in European populations, 22 (42%) in North America and 3 (6%) in Asia (2 in Japan and 1 in Turkey). Thirty-one (60%) studies were institution-based and 21 (40%) were population-based. Self-reported outcomes were used in 39 (75%) studies, and outcomes in the remaining 13 (25%) were derived from registry data. The diagnostic period ranged from 1940 to 2010, but the most common diagnostic period was 1970–2000.

Thirty-seven (71%) of the studies explored educational outcomes, 29 (56%) reported on working life, 9 (17%) focused on income and 6 (12%) investigated the uptake of social security benefits by childhood cancer survivors.

Educational achievements

Table 2a summarises the studies that reported on educational achievements, including repeating grades, requirement for special education or learning disability programmes, school performance and highest attained educational level.

Repeating grades. Four studies investigated the likelihood that childhood cancer survivors repeated a grade during compulsory schooling, with inconsistent results.[23–26] A study of survivors of all childhood cancers in Canada showed that they were about twice as likely as the general population (21% *vs.* 9%, odds ratio (OR): 2.2, 99% confidence interval (CI): 1.4–3.3) to have repeated or failed a grade; the highest risks were those of survivors of central nervous system (CNS) tumours or leukaemia and treatment with cranial radiation therapy (CRT).[23] A study in British Columbia, however, showed no difference in the proportions of survivors and the general population who repeated a grade (21.5% *vs.* 22.0%).[25] In a study in France, only survivors who were attending high school at the time of diagnosis were significantly more likely than their siblings to repeat a grade (51% *vs.* 30%).[24]

Special education or learning disability programme. All studies reporting use of special education or learning disability programmes showed that survivors were more likely to be enrolled in these programmes than the general population or a sibling comparison group.[23,25,27–30] A report from the Childhood Cancer Survivor Study in North America indicated that 23% of survivors and 8% of siblings required special education.[30] A study in The Netherlands also reported that survivors were more likely than the general population to be enrolled in learning disability programmes (9% *vs.* 3% of boys and 6% *vs.* 2% of girls), although the proportions of enrolment were lower than in the North American study.[27]

The determinants of requiring a special education or learning disability programme were survival from a CNS tumour or leukaemia, diagnosis before the age of 6 years, female sex and higher doses of CRT for all childhood cancers.[23,25,30]

School performance. Seven of the studies reported on scholastic performance, as assessed from marks obtained during compulsory schooling.[11,23,25,26,31–33] Overall, survivors had lower school performance than the general population or a sibling comparison group.[11,23,31–33] In Denmark, survivors of all childhood cancers diagnosed at 0–6 years had lower marks in ninth grade than their classmates without cancer.[11] Lower grades were associated with a diagnosis of a CNS tumour, lymphoma,

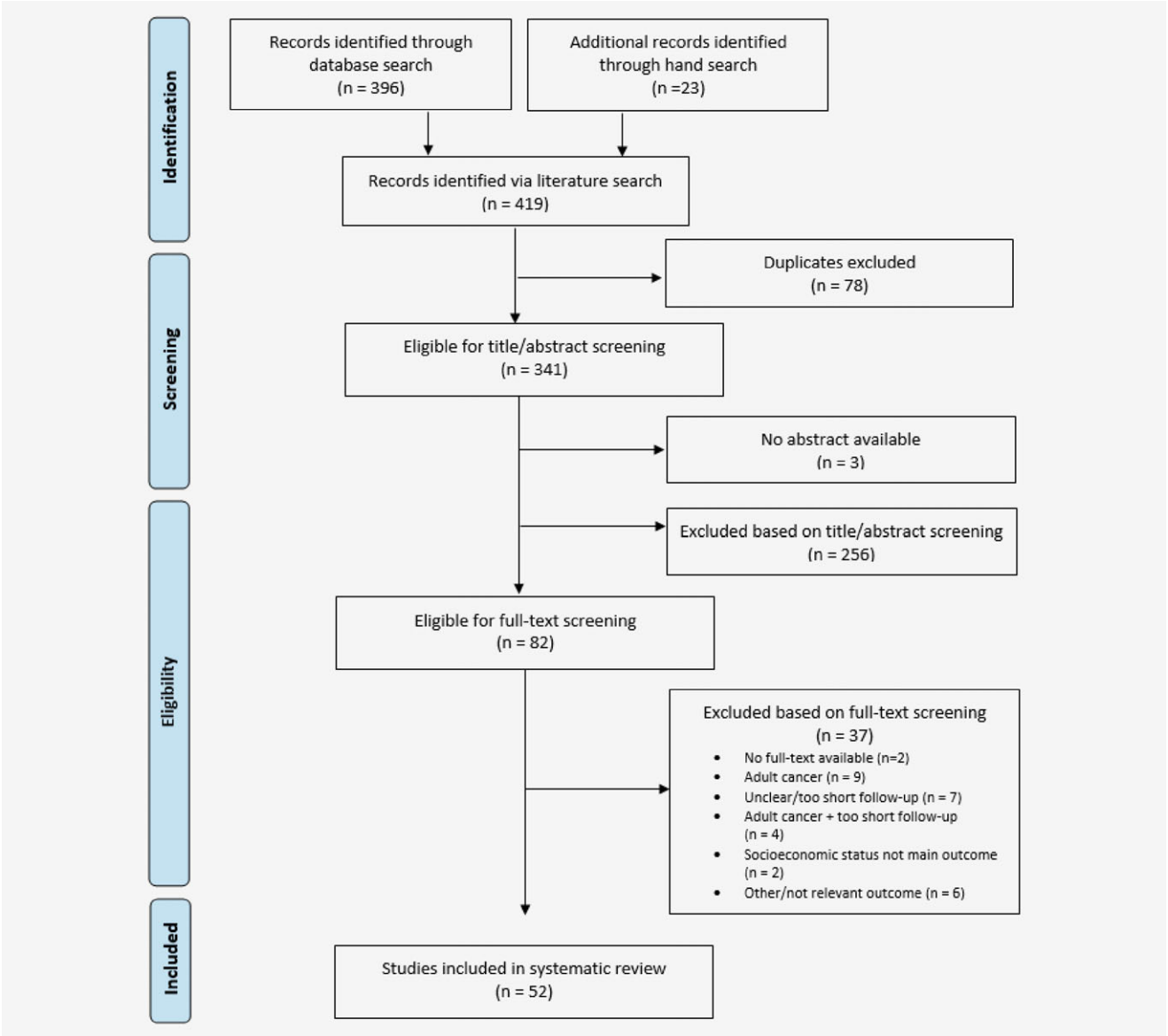

Figure 1. Flow chart of inclusion and exclusion of identified articles. [Color figure can be viewed at wileyonlinelibrary.com]

neuroblastoma or leukaemia; the marks of survivors of other solid tumours did not differ from those of other schoolchildren.[11] Similar findings were observed in Finland, where brain tumour survivors, leukaemia survivors treated with CRT and survivors of non-Hodgkin lymphoma, all diagnosed before 7 years of age, performed worse in ninth grade than the general population.[31–33]

Educational level. Most of the studies of attained education level among survivors of all childhood cancers found that they had lower educational qualifications than the general population or a sibling comparison group,[12,27,30,34–36] although some studies found no difference or even higher educational achievement among survivors.[37–40] In a population-based study in Great Britain, survivors of all childhood cancers had lower educational attainment than the general population (OR: 0.77, 99% CI: 0.68–0.87).[36] A population-based study in Switzerland obtained similar results, but found that when the population was restricted to survivors over 27 years of age, the differences largely disappeared, indicating only a delay in educational achievement.[35]

Many studies found that survivors of a CNS tumour achieved a much lower educational level than an external group without a history of childhood cancer or than survivors of other types of childhood cancer.[35,36,40–45] Additional determinants identified across the studies included treatment with radiation therapy (most frequently CRT) and younger age at diagnosis.[12,27,36,39–41,46]

Working life

Table 2b summarises the findings of 29 studies of the employment status and occupations of childhood cancer survivors.

Table 1. Characteristics and design of included articles

Reference	First author, publication year	Country	Cancer type	Sample size (no. of cases)	Age at diagnosis (years)	Period of diagnosis	Comparison group	Minimum follow-up	Source of the outcome measure	Population-or institution-based	Quality assessment (points)
All childhood cancers											
[11]	Andersen, 2017	Denmark	All cancers	857	<10	1982–1998	General population	5 Years post-diagnosis	Registry-based	Population-based	8
[42]	Boman, 2010	Sweden	All cancers	1,716	<16	1963–1991	General population	9 Years post-diagnosis	Registry-based	Population-based	9
[55]	Ghaderi, 2013	Norway	All cancers	2,489	<19	1965–1985	General population	5 Years post-diagnosis	Registry-based	Population-based	8
[12]	Ghaderi, 2016	Norway	All cancers	2,213	<19	1965–2004	General population	5 Years post-diagnosis	Registry-based	Population-based	9
[48]	Gunnes, 2016	Norway	All cancers	2,139	<15	1965–1999	General population	7 Years post-diagnosis	Registry-based	Population-based	9
[56]	Hjern, 2007	Sweden	All cancers	2,503	<16	1962–1996	General population	6 Years post-diagnosis	Registry-based	Population-based	9
[25]	Lorenzi, 2009	Canada	All cancers	782	<15	1975–1995	General population	5 Years post-diagnosis	Registry-based	Population-based	9
[39]	Maule, 2017	Italy	All cancers	520	<15	1971–2001	General population	5 Years post-diagnosis	Registry-based	Population-based	7
[37]	Dieluweit, 2011	Germany	All cancers	820	15–18	1980–2003	General population	5 Years post-diagnosis	Self-reported	Population-based	6
[47]	Frobisher, 2017	Great Britain	All cancers	10,488	<15	1940–1991	General population	5 Years post-diagnosis	Self-reported	Population-based	7
[35]	Kuehni, 2012	Switzerland	All cancers	961	<16	1976–2003	General population	5 Years post-diagnosis	Self-reported	Population-based	8
[36]	Lancashire, 2010	Great Britain	All cancers	10,183	<15	1940–1991	General population	5 Years post-diagnosis	Self-reported	Population-based	7
[23]	Barrera, 2005	Canada	All cancers	800	<18	1981–1990	General population	5 Years post-diagnosis	Self-reported	Institution-based	7
[34]	Boman, 2004	Sweden	All cancers	30	<15	N/A	1. Healthy controls 2. National averages	8 Years post-diagnosis	Self-reported	Institution-based	7
[24]	Bonneau, 2011	France	All cancers	148	<19	2001–2005	1. Siblings 2. General population	1 Year post-treatment	Self-reported	Institution-based	9
[93]	Crom, 2007	USA	All cancers	1,437	<21	1962–1992 (treated)	General population	10 Years post-diagnosis	Self-reported	Institution-based	7
[38]	Ishida, 2011	Japan	All cancers	184	<19	N/A	Siblings	5 Years post-diagnosis	Self-reported	Institution-based	6
[27]	Langeveld, 2003	Netherlands	All cancers	500	<19	N/A	General population	5 Years post-treatment	Self-reported	Institution-based	5
[50]	Pang, 2008	North America	All cancers except retinoblastoma, germ-cell tumours, other and unspecified cancers	10,399	<21	1970–1986	Siblings	5 Years post-diagnosis	Self-reported	Institution-based	7
[49]	Kirchhoff, 2010	North America	All cancers except retinoblastoma, germ-cell tumours, other and unspecified cancers	6,339	<21	1970–1986	Siblings	5 Years post-diagnosis	Self-reported	Institution-based	6

(Continues)

Table 1. Continued

Reference	First author, publication year	Country	Cancer type	Sample size (no. of cases)	Age at diagnosis (years)	Period of diagnosis	Comparison group	Minimum follow-up	Source of the outcome measure	Population-or institution-based	Quality assessment (points)
[53]	Kirchhoff, 2011a	North America	All cancers except retinoblastoma, germ-cell tumours, other and unspecified cancers	3,763 (occupation)/ 5,385 (employment)	<21	1970–1986	Internal comparison by psycho-social health	5 Years post-diagnosis	Self-reported	Institution-based	7
[52]	Kirchhoff, 2011b	North America	All cancers except retinoblastoma, germ-cell tumours, other and unspecified cancers	6,671	<21	1970–1986	Siblings	5 Years post-diagnosis	Self-reported	Institution-based	8
[57]	Kirchhoff, 2015	North America	All cancers except retinoblastoma, germ-cell tumours, other and unspecified cancers	698	<21	1970–1986	General population	5 Years post-diagnosis	Self-reported	Institution-based	6
[30]	Mitby, 2003	North America	All cancers except retinoblastoma, germ-cell tumours, other and unspecified cancers	11,425	<21	1970–1986	Siblings	5 Years post-diagnosis	Self-reported	Institution-based	7 points
[41]	Ahomaki, 2016	Finland	Brain tumours, solid tumours, leukaemia and non-Hodgkin lymphoma	2,132	<13	1964–2009	General population	5 Years post-diagnosis	Registry-based	Population-based	9
[54]	Wengenroth, 2016	Switzerland	Leukaemia, lymphoma, CNS tumours, malignant solid tumours, Langerhans cell histiocytosis	1,506	<21	1976–2005	Siblings	5 Years post-diagnosis	Self-reported	Population-based	7
[40]	Dumas, 2016	France	Solid malignant tumours, benign cerebral tumours, haematological malignancies	2,066	<19	1948–2000	General population	5 Years post-diagnosis	Self-reported	Institution-based	8
[58]	Johannesen, 2009	Norway	CNS tumours and haematological malignancies	1,144	<15	1970–1997	General population	5 Years post-diagnosis	Registry-based	Population-based	8
[51]	Mader, 2017	Switzerland	Leukaemia, lymphoma, CNS tumours, neuroblastoma, renal, hepatic and bone tumours, soft tissue sarcoma, germ cell tumours	160	16–25	1990–2005	General population	5 Years post-diagnosis	Self-reported	Population-based	6

(Continues)

Table 1. Continued

Reference	First author, publication year	Country	Cancer type	Sample size (no. of cases)	Age at diagnosis (years)	Period of diagnosis	Comparison group	Minimum follow-up	Source of the outcome measure	Population-or institution-based	Quality assessment (points)
Leukaemias											
[33]	Harila-Saari, 2007	Finland	Leukaemia	214	<7	1974–2001	General population	10 Years post-diagnosis	Registry-based	Population-based	9
[60]	Freycon, 2014	France	Leukaemia patients with a-HSCT and fTBI	59	<15	1987–2010	1. General population 2. Leukaemia patients with a-HSCT and chemotherapy	3 Years post-treatment	Self-reported	Population-based	8
[46]	Mody, 2008	North America	ALL	4,151	<21	1970–1986	1. General population 2. Siblings	5 Years post-diagnosis	Self-reported	Institution-based	7
[94]	Pillon, 2013	Italy	ALL	141	<16	1961–1990 (treated)	General population	14 Years off-therapy	Self-reported	Institution-based	7
[59]	Pui, 2003	USA	ALL	584	<21	1962–1992 (treated)	General population	9 Years post-therapy	Self-reported	Institution-based	6
[95]	Berbis, 2016	France	ALL and AML	845	<18	1980–2011 (treated)	General population	8 Years post-diagnosis	Self-reported	Institution-based	7
[96]	Mulrooney, 2008	North America	AML exposed to chemotherapy and/or radiotherapy	272	<21	1970–2002	Siblings	5 Years post-diagnosis	Self-reported	Institution-based	7
CNS tumours											
[45]	Armstrong, 2009	North America	CNS tumours	1,877	<21	1970–1986	Siblings	5 Years post-diagnosis	Self-reported	Institution-based	7
[97]	Brinkman, 2016	North America	CNS tumours	224	<21	1970–1986	Internal comparison by radiation treatment groups	10 Years post-diagnosis	Self-reported	Institution-based	6
[43]	Ellenberg, 2009	North America	CNS tumours	802	<21	1970–1985	1. Siblings 2. Non-CNS tumours	5 Years post-diagnosis	Self-reported	Institution-based	7
[31]	Lähteenmäki, 2007	Finland	Brain tumours	96	<7	1974–2001	General population	10 Years post-diagnosis	Registry-based	Population-based	9
[98]	Pfitzer, 2013	Germany	Brain tumours	203	<16	1980–2004	Internal comparison of irradiation *vs.* non-irradiation	5 Years post-diagnosis	Self-reported	Population-based	6
[99]	de Blank, 2016	North America	Astroglial tumours	587	<21	1970–1986	Internal comparison by vision impairment	5 Years post-diagnosis	Self-reported	Institution-based	6

(Continues)

Table 1. Continued

Reference	First author, publication year	Country	Cancer type	Sample size (no. of cases)	Age at diagnosis (years)	Period of diagnosis	Comparison group	Minimum follow-up	Source of the outcome measure	Population-or institution-based	Quality assessment (points)
Other solid tumours											
[44]	Yagci-Kupeli, 2013	Turkey	Solid tumours	201	<20	1972–2009 (treated)	General population	3 Years post-treatment	Self-reported	Institution-based	5
[100]	Nagarajan, 2011	North America	Osteosarcoma	733	<21	1970–1986	General population	5 Years post-diagnosis	Self-reported	Institution-based	7
[101]	Ottaviani, 2013	USA (Houston)	Osteosarcoma	38	<20	1980–2004	Internal comparison of limb salvage *vs.* amputation	19 Years post-diagnosis	Self-reported	Institution-based	6
[102]	Yonemoto, 2008	Japan	Osteosarcoma	41	<18	1976–1995 (treated)	Internal comparison of amputation *vs.* limb-sparing	9 Years post-treatment	Self-reported	Institution-based	5
[103]	Nagarajan, 2003	North America	Osteosarcoma or Ewing sarcoma of lower extremity or pelvis	694	<21	1970–1986	1. Siblings 2. Internal comparison of amputees *vs.* non-amputees	5 Years post-diagnosis	Self-reported	Institution-based	6
[104]	Termuhlen, 2011	North America	Wilms tumour	1,256	<21	1970–1986	Siblings	5 Years post-diagnosis	Self-reported	Institution-based	6
[29]	Punyko, 2007	North America	Rhabdomyosarcoma	417	<21	1970–1986 (treated)	Siblings	5 Years post-diagnosis	Self-reported	Institution-based	7
Miscellaneous cancer types											
[32]	Lähteenmäki, 2008	Finland	Lymphoma and Wilms tumour	32	<7	1974–2001	General population	10 Years post-diagnosis	Registry-based	Population-based	9
[26]	Buizer, 2006	Netherlands	ALL, Wilms tumour	64	<19	1985–1999	1. Siblings 2. Healthy schoolchildren	1 Year post-treatment	Self-reported	Institution-based	8
[28]	Ness, 2005	USA	Cancer treated with HCT	235	<21	1974–1998 (treated)	Siblings of another cohort of survivors	2 Years post-transplantation	Self-reported	Institution-based	5

Abbreviations: N/A, not available; CNS, central nervous system; ALL, acute lymphoblastic leukaemia; AML, acute myeloid leukaemia; HCT, haematopoietic cell transplantation; a-HSCT, allogeneic haematopoietic stem cell transplantation; fTBI, fractionated total body irradiation.

Table 2a Main findings for socioeconomic outcomes of childhood cancer survivors: educational achievements, by educational outcome and cancer type

Reference	First author, publication year	Country	Cancer type (*n*)	Comparison (*n*)	Main findings	Determinants
Repeating grades						
[23]	Barrera, 2005	Canada	All cancers (*n* = 800)	General population (*n* = 923)	Survivors more likely to have repeated or failed a grade (21% *vs.* 9%, OR: 2.2, 99% CI: 1.4–3.3).	CNS tumour survivors, leukaemia survivors and treatment only with CRT.
[24]	Bonneau, 2011	France	All cancers (*n* = 148)	Siblings (*n* = 194) and general population (expected)	No difference in rate of repeating a grade between survivors and the general population; however, rate of repeating a grade was higher for survivors who were attending high school at the time of diagnosis than in siblings (51% *vs.* 30%, $p = 0.02$).	Older age at diagnosis (attending secondary school at diagnosis) and low educational level of the father.
[25]	Lorenzi, 2009	Canada	All cancers (*n* = 782)	General population (*n* = 8,386)	Similar proportion of survivors repeated a grade (21.5% *vs.* 22.0%).	-
[26]	Buizer, 2006	Netherlands	ALL (*n* = 28) and Wilms tumour (*n* = 36)	Siblings (*n* = 37) and general population (*n* = 98)	ALL survivors were more likely to repeat a grade than the general population (30.8% *vs.* 9.4%, OR: 4.30, 95% CI: 1.46–12.64) but not more likely than siblings. No difference in rate of repeating a grade between Wilms tumour survivors and either comparison group.	-
Special education or learning disability programme						
[23]	Barrera, 2005	Canada	All cancers (*n* = 800)	General population (*n* = 923)	Survivors were more likely to attend learning disability programmes (19% *vs.* 7%, OR: 2.0, 99% CI: 1.3–3.2) and special education programmes (20% *vs.* 8%, OR: 2.4, 99% CI: 1.5–3.6)	CNS tumour survivors, leukaemia survivors and treatment only with CRT.
[27]	Langeveld, 2003	Netherlands	All cancers (*n* = 500)	General population (*n* = 1,092)	Survivors were more often enrolled in learning disability programmes (9% of male survivors *vs.* 3% of male comparisons; 6% of female survivors *vs.* 2% of female comparisons; $p < 0.001$).	-
[25]	Lorenzi, 2009	Canada	All cancers (*n* = 782)	General population (*n* = 8,386)	Survivors were more likely to require special education (32.5% *vs.* 14.1%, OR: 3.05, 95% CI: 2.6–3.6). No difference in rates of learning disability.	Survivors of CNS tumour, leukaemia and neuroblastoma. Female survivors were more likely to have a learning disability than females from the general population.

(Continues)

Table 2a. Continued

Reference	First author, publication year	Country	Cancer type (*n*)	Comparison (*n*)	Main findings	Determinants
[30]	Mitby, 2003	North America	All cancers except retinoblastoma, germ-cell tumours, other and unspecified cancers (*n* = 11,425)	Siblings (*n* = 3,410)	Survivors were more likely to require special education (23% *vs.* 8%). Use of special education increased significantly by treatment era (17%, 22% and 25% for diagnoses during 1970–1975, 1976–1980 and 1981–1986, respectively; no such information for siblings). Unclear whether the effect is attributable to changes in treatment or trends in use of educational services during this era.	CNS tumour survivors (OR: 18.8, 95% CI: 15.01–23.49), female sex (OR: 30.5, 95% CI: 21.40–43.50 compared with female siblings), diagnosis at age < 6 years and treatment with high levels of CRT.
[29]	Punyko, 2007	North America	Rhabdomyosarcoma (*n* = 417)	Siblings (*n* = 2,685)	Survivors were twice as likely to require special education (18.0% *vs.* 8.4%, $p < 0.01$).	-
[28]	Ness, 2005	USA	Cancer treated with HSCT (*n* = 235)	Siblings of another cohort of childhood cancer survivors (*n* = 705)	Survivors were more likely to require special education (24.4% *vs.* 9.4%, OR: 3.0, 95% CI: 1.5–6.0).	-
School performance						
[11]	Andersen, 2017	Denmark	All cancers (*n* = 857)	General population (*n* = 792,012)	Lower marks in 9th grade were observed in survivors diagnosed below the age of 6 ($p < 0.05$) before they attend school, but not in those survivors diagnosed in older age groups.	Young age at diagnosis, CNS tumour, lymphoma, neuroblastoma, leukaemia, germ-cell tumour and other (unspecified) malignant neoplasms.
[23]	Barrera, 2005	Canada	All cancers (*n* = 800)	General population (*n* = 923)	Survivors were more likely to have academic or other school problems (45.8% *vs.* 22.7%, OR: 2.2, 99% CI: 1.6–3.0)	CNS tumour survivors, leukaemia survivors, neuroblastoma survivors and treatment with CRT.
[25]	Lorenzi, 2009	Canada	All cancers (*n* = 782)	General population (*n* = 8,386)	Overall, no difference in school performance	CNS tumour survivors andsurvivors who received radiation therapy, particularly CRT. Female survivors generally fared worse than females from the general population.
[33]	Harila-Saari, 2007	Finland	Leukaemia (*n* = 214)	General population (*n* = 1,844)	Significantly lower overall average marks in 9th grade for survivors of leukaemia diagnosed at <7 years of age and treated with CRT (mean difference: −0.37, 95% CI: −0.46 to −0.25, $p < 0.001$).	Female survivors, regardless of treatment had lower average marks than female peers.
[31]	Lähteenmäki, 2007	Finland	Brain tumours (*n* = 96)	General population (*n* = 462)	Survivors of brain tumours diagnosed at <7 years had lower average marks in 9th grade than their matched controls, both males and females and irrespective of exposure to CRT.	Female survivors showed greater deficits in average marks than female peers.

(Continues)

Table 2a. Continued

Reference	First author, publication year	Country	Cancer type (*n*)	Comparison (*n*)	Main findings	Determinants
[32]	Lähteenmäki, 2008	Finland	Lymphoma or Wilms tumour (*n* = 32)	General population (*n* = 158)	NHL survivors had statistically significantly lower average marks in 9th grade; similar or better marks were observed for survivors of HL and Wilms tumour.	The decrease of average marks was greater among female survivors than female peers.
[26]	Buizer, 2006	Netherlands	ALL (*n* = 28) and Wilms tumour (*n* = 36)	Siblings (*n* = 37) and general population (*n* = 98)	Total school performance score of ALL survivors was lower than that of controls (score outside normal range: 82% *vs.* 17%, $p < 0.01$) but not of siblings. No differences were found for Wilms tumour survivors.	Exposure to intense treatment (higher cumulative systemic methotrexate dose than standard treatment).
Highest attained educational level						
[34]	Boman, 2004	Sweden	All cancers (*n* = 30)	Healthy controls (*n* = 30) and national population norms (expected)	Survivors entered university education less frequently than the general population (20% *vs.* 41%) and achieved an academic degree less frequently (24% *vs.* 7%). No difference between survivors and matched controls.	-
[42]	Boman, 2010	Sweden	All cancers (*n* = 1,716)	General population (*n* = 1,456,089)	Non-CNS tumour survivors had similar educational achievement	CNS tumour survivors more often had no more than basic education (≤ 9 years) (RR: 1.80, 95% CI: 1.45–2.23) and less often achieved post-secondary education (≥ 14 years) (RR: 0.69, 95% CI: 0.58–0.81)
[37]	Dieluweit, 2011	Germany	All cancers (*n* = 820)	General population (*n* = 820)	Survivors were more likely to have a high-school degree (52.4% *vs.* 38.3%, $p < 0.001$) and a college or university degree (24.7% *vs.* 17.0%, $p = 0.001$).	CNS tumour survivors, survivors with neuropsychological late effects and long duration of treatment.
[12]	Ghaderi, 2016	Norway	All cancers (*n* = 2,213)	General population (*n* = 1,212,623)	Survivors less frequently completed intermediate (67% *vs.* 70%), undergraduate (31% *vs.* 35%) and graduate education (7% *vs.* 9%).	Younger age at diagnosis, CNS tumour survivors and other survivors who were assumed to have received CNS-directed therapy.
[38]	Ishida, 2011	Japan	All cancers (*n* = 184)	Siblings (*n* = 72)	No difference in educational attainment ($p = 0.169$).	Survivors exposed to RT achieved were more likely to only achieve high-school level or lower compared to those unexposed to RT.

(Continues)

Table 2a. Continued

Reference	First author, publication year	Country	Cancer type (*n*)	Comparison (*n*)	Main findings	Determinants
[35]	Kuehni, 2012	Switzerland	All cancers (*n* = 961)	General population (*n* = 5,207)	Higher proportion of survivors achieved only compulsory schooling (8.7% *vs.* 5.2%, OR: 2.25, 95% CI: 1.65–3.07) and a lower proportion of survivors achieved a university degree (7.3% *vs.* 11%, OR: 0.75, 95% CI: 0.54–1.05). Educational achievement was similar when analyses were restricted to attained age ≥ 27 years.	CNS tumour survivors
[36]	Lancashire, 2010	Great Britain	All cancers (*n* = 10,183)	General population (expected)	Survivors had lower odds of obtaining a degree (OR: 0.77, 99% CI: 0.68–0.87) and generally performed worse at each level of educational attainment.	The lower educational attainment were restricted exclusively to survivors of CNS tumours (among both those exposed to RT and those not exposed to RT) and leukaemia (only those exposed to CRT). Diagnostic age between 1 and 4 years indicated lower achievement of an educational degree (OR: 0.68, 99% CI: 0.44–1.03).
[27]	Langeveld, 2003	Netherlands	All cancers (*n* = 500)	General population (*n* = 1,092)	Survivors had lower educational achievement (high educational level: male survivors 39% *vs.* 42% among male comparisons, female survivors 30% *vs.* 43% among female comparisons, $p = 0.003$))	Exposure to CRT dose of ≤25 Gy and female gender.
[39]	Maule, 2017	Italy	All cancers (*n* = 520)	General population (expected)	No statistically significant difference in attainment of higher education (OR: 0.81, 95% CI: 0.61–1.07)	Those diagnosed <5 years of age were less likely to achieve higher education (OR: 0.34, 95% CI: 0.16–0.72).
[30]	Mitby, 2003	North America	All cancers except retinoblastoma, germ-cell tumours, other and unspecified cancers (*n* = 11,425)	Siblings (*n* = 3,410)	All survivors, regardless of treatment type, were less likely to complete high school.	Survivors of leukaemia, CNS tumour, NHL and neuroblastoma.
[41]	Ahomaki, 2016	Finland	Brain tumours, solid tumours, leukaemia and NHL (*n* = 2,132)	General population (*n* = 16,215)	Survivors of brain tumours, solid tumours. Leukaemia and NHL were more likely to discontinue education after comprehensive school (brain tumour: 33.5% *vs.* 23.0%, solid tumours: 25.0% *vs.* 21.4%, leukaemia or NHL: 29.2% *vs.* 23.1%)	Diagnosis at <7 years of age (brain tumours), CRT (brain tumours) and latest treatment era (all three groups).

(Continues)

Table 2a. Continued

Reference	First author, publication year	Country	Cancer type (*n*)	Comparison (*n*)	Main findings	Determinants
[40]	Dumas, 2016	France	Solid malignant tumours, benign cerebral tumours and haematological malignancies (*n* = 2,066)	General population (expected)	Survivors were less likely to have no or little education (11.4% *vs.* 16.8%, $p = 0.001$) and more likely to have a college degree (38.9% *vs.* 33.5%, $p = 0.001$).	CNS tumour and leukaemia survivors. CRT independently reduced odds of attending college by 52% (OR: 0.48, 95% CI: 0.35–0.66). Male survivors were more likely to be college graduates than gender-matched expected (O/E: 1.3, 95% CI: 1.1–1.4), whereas female survivors were more likely to attend vocational schools than gender-matched expected (O/E: 1.2, 95% CI: 1.1–1.4)
[51]	Mader, 2017	Switzerland	Leukaemia, lymphoma, CNS tumours, neuroblastoma, renal, hepatic and bone tumours, soft tissue sarcoma, germ cell tumours (*n* = 160)	General population (*n* = 999)	Survivors were more likely to achieve only basic education (≤ 9 years compulsory schooling), but not statistically significantly (OR: 1.93, 95% CI 0.95–3.91). A higher proportion of survivors than controls reported upper secondary education (33% *vs.* 27%) and a lower proportion of survivors reported university education (12% *vs.* 21%).	-
[60]	Freycon, 2014	France	Leukaemia patients who underwent a-HSCT with fTBI (*n* = 59)	General population (expected) and leukaemia patients who underwent a-HSCT with chemotherapy (*n* = 19)	More survivors who underwent a-HSCT with fTBI had academic delay than the general population ($p < 0.001$). 23.7% of survivors and 4.5% of the general population were ≥ 2 years behind. No difference in academic delay was seen between a-HSCT with fTBI and a-HSCT with chemotherapy.	Male survivors with fTBI achieved a secondary school diploma at a lower rate as males from the general population (O/E = 0.48, 95% CI. 0.3–0.7).
[46]	Mody, 2008	North America	ALL (*n* = 4,151)	Siblings (*n* = 3,899)	Fewer survivors than siblings graduated from college ($p < 0.001$): 37.9% of male survivors *vs.* 48.5% of male siblings, and 43.3% of female survivors *vs.* 55.9% of female siblings.	Irradiated survivors.
[94]	Pillon, 2013	Italy	ALL (*n* = 141)	General population (expected)	No difference in educational level attained, regardless of attained age.	Survivors aged 25–34 years who received CRT at 24 Gy achieved lower educational level than those receiving CRT at 18 Gy ($p = 0.01$).
[96]	Mulrooney, 2008	North America	AML with chemotherapy and/or radiotherapy (*n* = 272)	Siblings (*n* = 3,899) and general population (expected)	Survivors were less likely to graduate from college than siblings (40% *vs.* 52%, $p = 0.01$) but more likely to graduate from college than the national average (40% *vs.* 34%, $p < 0.01$).	-

(Continues)

Table 2a. Continued

Reference	First author, publication year	Country	Cancer type (*n*)	Comparison (*n*)	Main findings	Determinants
[45]	Armstrong, 2009	North America	CNS tumours (*n* = 1,877)	Siblings (*n* = 3,899)	Siblings were more likely to graduate from college than survivors (RR: 1.4, 95% CI: 1.3–1.5)	Irradiation to the temporal lobe of ≥50 Gy slightly increased the risk of education below college graduate (RR: 1.2, 95% CI: 1.0–1.5)
[43]	Ellenberg, 2009	North America	CNS tumours (*n* = 802)	Siblings (*n* = 382) and non-CNS tumours (*n* = 5,937)	CNS tumour survivors were less educated than both siblings and non-CNS tumour survivors ($p < 0.001$).	Impaired task efficiency, emotional regulation and memory associated with lower educational attainment.
[97]	Brinkman, 2016	North America	CNS tumours (*n* = 224)	Internal comparison of no CRT (*n* = 63), FI (*n* = 71) and CSI (*n* = 83)	CNS tumour survivors who had received FI and CSI achieved less education than survivors without CRT treatment ($p = 0.005$). College graduation was achieved by 33.9% of those with no CRT, 20.3% with FI and 18.4% with CSI.	Survivors with neurocognitive impairment.
[98]	Pfitzer, 2013	Germanyy	CNS tumours (*n* = 203)	Internal comparison of irradiated (*n* = 151) and non-irradiated (*n* = 44)	Educational achievement was not statistically significantly different for irradiated and non-irradiated CNS tumour survivors.	Survivors diagnosed below 6 years of age achieved a lower educational level.
[99]	de Blank, 2016	North America	Astroglial tumours (*n* = 587)	Internal comparison by vision impairment	Survivors with bilateral blindness may be less likely to attend college than those without vision impairment (OR: 2.05, 95% CI: 0.99–4.23).	-
[44]	Yagci-Kupeli, 2013	Turkey	Solid tumours (*n* = 201)	General population (expected)	Survivors had higher rates of graduation from primary school, high school and university ($p < 0.001$).	CNS tumour survivors.
[101]	Ottaviani, 2013	USA	Osteosarcoma (*n* = 38)	Internal comparison of limb salvage (*n* = 19) and amputation (*n* = 19)	Survivors who underwent amputation were less likely to have a graduate degree than those with limb salvage (16% *vs.* 42%), although the result was not statistically significant.	-
[102]	Yonemoto, 2008	Japan	Osteosarcoma (*n* = 41)	Internal comparison of amputation (*n* = 18) and limb salvage (*n* = 9)	Limb-sparing osteosarcoma survivors were more likely to have a college or university degree than survivors treated by amputation ($p = 0.03$)	-
[103]	Nagarajan, 2003	North America	Osteosarcoma or Ewing sarcoma of the lower extremity or pelvis (*n* = 694)	Siblings (*n* = 2,667) and internal comparison of amputees (*n* = 471) and non-amputees (*n* = 223)	No overall difference in educational achievement was found between survivors and siblings. Amputees were less likely to have graduated from college than non-amputees (OR: 0.6, 95% CI: 0.44–0.96).	Amputees diagnosed at age > 12 years were less likely to graduate from high school (OR: 0.6, 95% CI: 0.34–0.95) and college (OR: 0.8, 95% CI: 0.59–0.99)
[104]	Termuhlen, 2011	North America	Wilms tumour (*n* = 1,256)	Siblings (*n* = 4,023)	Survivors of Wilms tumour were marginally but statistically significantly less likely to graduate from college ($p = 0.045$).	-

(Continues)

Table 2a. Continued

Reference	First author, publication year	Country	Cancer type (*n*)	Comparison (*n*)	Main findings	Determinants
[29]	Punyko, 2007	North America	Rhabdomyosarcoma (*n* = 417)	Siblings (*n* = 2,685)	Survivors were less likely to graduate from high school (91.7% *vs.* 94.7%, $p = 0.02$) and generally achieved lower educational levels ($p < 0.01$).	Survivors with performance limitations, health-related inability to work or attend school or moderate to high severity of cancer-related pain.
[28]	Ness, 2005	USA	Cancer treated with HSCT (*n* = 235)	Siblings of another cohort of childhood cancer survivors (*n* = 705)	No statistically significant differences.	-

Abbreviations: OR, odds ratio; CI, confidence interval; CNS, central nervous system; CRT, cranial radiation therapy; ALL, acute lymphoblastic leukaemia; NHL, non-Hodgkin lymphoma; HL, Hodgkin lymphoma; RR, relative risk; RT, radiation therapy; O/E, observed *vs.* expected; fTBI, fractionated total body irradiation; a-HSCT, allogeneic haematopoietic stem cell transplantation; AML, acute myeloid leukaemia; FI, focal irradiation; CSI, craniospinal irradiation; HSCT, haematopoietic stem cell transplantation.

Employment status. Studies of the employment status of survivors of a broad range of childhood cancers in comparison with the general population or sibling comparisons had inconsistent findings.[34,37,39–42,47–51] Seven studies observed higher unemployment rates among survivors,[27,38,39,47–50] whereas five studies found similar unemployment rates.[34,37,41,42,51] Studies with stratification by type of unemployment found that survivors were more likely to be unemployed due to illness or disability.[40,47,49,52] A study in North America reported that survivors were six times more likely to be unemployed for health reasons than their siblings (10.4% *vs.* 1.8%, relative risk (RR): 6.07, 95% CI. 4.32–8.53).[49]

Survivors of CNS tumours, especially those who had been treated with CRT, were at particular risk for a higher unemployment rate than the general population, a sibling comparison group or survivors of other types of childhood cancer.[39,40,42,43,45,47,50,53] Two studies found that younger age at diagnosis increased the risk for unemployment, independently of childhood cancer type.[37,50]

Occupation. Studies on occupation and occupational class in survivors of many different types of childhood cancer and in the general population gave conflicting results.[38,40,47,53] A French study indicated that survivors were more likely to be in higher occupational classes (managerial or professional jobs) as compared with national statistics (23.1% *vs.* 15.4%, $p < 0.001$),[40] whereas a study in Great Britain showed that survivors were less likely to hold higher skilled managerial or professional jobs than the general population (RR: 0.93, 95% CI: 0.89–0.98).[47] However, the odds of holding a managerial or professional occupation were negatively influenced by a diagnosis of a CNS tumour and by CRT in both studies,[40,47] in line with the findings of a North American study.[53]

Income

Table 2c summarises the findings of studies of the effect of childhood cancer on income. Most studies found that survivors of various childhood cancers had a lower income than the general population or a sibling comparison group.[41,48,54] CNS tumour survivors in particular had a lower income than the general population, a sibling comparison group and survivors of other childhood cancers.[41–43,45,54] Treatment with CRT was also associated with a lower income.[41,45,54] A study in Switzerland indicated that survivors were less likely than their siblings to have a high monthly net income (excluding social insurance and retirement insurance) (OR: 0.46, 95% CI: 0.33–0.64), even after adjustment for working hours. A CNS tumour diagnosis, treatment with CRT and a diagnosis at <5 years of age were related to a lower income.[54]

The studies varied widely in the definition of source of income; however, restriction to studies based on work-related income and studies in which students or income from social insurance, retirement insurance or other governmental

Table 2b Main findings for socioeconomic outcomes of childhood cancer survivors: work life, by employment status, occupation and cancer type

Ref. no.	First author, publication year	Country	Cancer type (*n*)	Comparisons (*n*)	Main findings	Determinants
Employment status						
[34]	Boman, 2004	Sweden	All cancers (*n* = 30)	Healthy controls (*n* = 30) and national population norms (expected)	Employment status and extent of employment similar between survivors and general population. 73% of survivors and 80% of matched controls were employed.	-
[42]	Boman, 2010	Sweden	All cancers (*n* = 1,716)	General population (*n* = 1,456,089)	No overall difference for non-CNS tumour survivors.	CNS tumour survivors were less often employed (RR: 0.85, 95% CI: 077–0.94), but no difference when those receiving economic compensation for disability were excluded (RR: 0.98, 95% CI: 0.88–1.09).
	Crom, 2007	USA	All cancers (*n* = 1,437)	General population (normative data)	Full-time employment was significant lower among survivors, except non-irradiated survivors of haematological malignancies whom had similar employment rates.	Irradiated CNS tumour survivors.
[37]	Dieluweit, 2011	Germany	All cancers (*n* = 820)	General population (*n* = 820)	Employment status did not differ (OR: 1.11, 95% CI: 0.83–1.47). Survivors were older when starting their first occupation (mean: 21.8 years *vs.* 19.9 years, $p < 0.001$), also after control for educational degrees.	Younger age at diagnosis, neuropsychological late effects.
[47]	Frobisher, 2017	Great Britain	All cancers (*n* = 10,257)	General population (*n* = 15,730)	Survivors were less likely to be employed (OR: 0.89, 99% CI: 0.81–0.98) and five times more likely to be unable to work due to illness or disability.	Irradiated CNS tumour survivors in whom the rate of health-related unemployment was 15 times that of the general population. Younger age at diagnosis (‹5 years).
[48]	Gunnes, 2016	Norway	All cancers (*n* = 1,138)	General population (*n* = 1,113,660)	Both female and male survivors of cancers diagnosed at ‹15 years were at increased risk for unemployment (male: RR: 1.38, 95% CI: 1.12–1.71 *vs.* male controls; female RR: 1.53, 95% CI: 1.16–2.01 *vs.* female controls).	

(Continues)

Table 2b. Continued

Ref. no.	First author, publication year	Country	Cancer type (*n*)	Comparisons (*n*)	Main findings	Determinants
[27]	Langeveld, 2003	Netherlands	All cancers (*n* = 500)	General population (*n* = 1,092)	More survivors were unemployed (male survivors 6% *vs.* male comparisons 2%, female survivors 3% *vs.* female comparisons 2%, *p* = 0.005).	Among employed groups, male survivors were less likely to be employed full-time (85% *vs.* 92%, *p* = 0.02) compared with males from the general population
[39]	Maule, 2017	Italy	All cancers (*n* = 117)	General population (*n* = 211,441)	Survivors were less likely to be employed (OR: 0.66, 95% CI: 0.45–0.98).	CNS tumour survivors (OR: 0.28, 95% CI: 0.13–0.58).
[38]	Ishida, 2011	Japan	All cancers (*n* = 184)	Siblings (*n* = 72)	Unemployment was more frequent among survivors (4% *vs.* 0%)	Survivors exposed to SCT and RT.
[49]	Kirchhoff, 2010	North America	All cancers except retinoblastoma, germ-cell tumours, other and unspecified cancers (*n* = 6,339)	Siblings (*n* = 2,280)	Survivors were more frequently unemployed due to health problems (10.4% *vs.* 1.8%, RR: 6.07, 95% CI: 4.32–8.53) and more likely to be unemployed but seeking for a job (5% *vs.* 2.7%, RR: 1.90, 95% CI: 1.43–2.54).	CNS tumour survivors had highest health-related unemployment rates (RR 14.84, 95% CI 10.42–21.14). CRT dose ≥25 Gy was associated with both types of unemployment.
[52]	Kirchhoff, 2011a	North America	All cancers except retinoblastoma, germ-cell tumours, other and unspecified cancers (*n* = 5,386)	Internal comparison by psychosocial health	Survivors in poor physical health had a higher risk for health-related unemployment than survivors with good physical health (RR: 7.83, 95% CI: 6.11–10.04) and were less likely to work full-time. Poor mental health also increased the likelihood of being unemployed but seeking work (RR: 2.08, 95% CI: 1.48–2.91)	-
[50]	Pang, 2008	North America	All cancers except retinoblastoma, germ-cell tumours, other and unspecified cancers (*n* = 10,399)	Siblings (*n* = 3,083)	Survivors were more likely to be unemployed (5.6% *vs.* 1.2%, OR: 3.7, 95% CI: 2.6–5.1).	Survivors of CNS tumours (OR: 1.5, 95% CI: 1.1–2.1) and bone tumours (OR: 1.5, 95% CI: 1.0–2.1), treatment with ≥30 Gy CRT (OR: 4.0, 95% CI: 2.9–5.5) and age < 4 years at diagnosis (OR: 1.4, 95% CI: 1.1–1.8)
[41]	Ahomaki, 2016	Finland	Brain tumours, solid tumours, leukaemia and NHL (*n* = 2,132)	General population (*n* = 16,215)	Rate of unemployment was not higher in survivors of brain tumours (OR: 1.2, 95% CI: 0.9–1.5), solid tumours (OR: 1.0, 95% CI: 0.8–1.3) or leukaemia or NHL (OR: 1.2, 95% CI: 0.9–1.5).	–

(Continues)

Table 2b. Continued

Ref. no.	First author, publication year	Country	Cancer type (*n*)	Comparisons (*n*)	Main findings	Determinants
40	Dumas, 2016	France	Solid malignant tumours, benign cerebral tumours and haematological malignancies (*n* = 2,066)	General population (expected)	Survivors were less frequently unemployed and seeking work (7.1% *vs.* 9.5%, O/E: 0.7, 95% CI: 0.6–0.9), but health-related unemployment was more frequent among survivors (6.5% *vs.* 4.2%, O/E: 1.6, 95% CI: 1.3–1.9).	Health-related unemployment was associated with CNS tumours and treatment with CRT. Both male and female survivors were more likely to be health-related unemployed than gender-matched expected, and female survivors were less likely to be unemployed and seeking work than gender-matched expected.
51	Mader, 2017	Switzerland	Leukaemia, lymphoma, CNS tumours, neuroblastoma, renal, hepatic and bone tumours, soft tissue sarcoma, germ cell tumours (*n* = 160)	General population (*n* = 999)	No difference in employment status between survivors and comparisons (OR: 0.82, 95% CI: 0.45–1.50)).	Having only basic education, having self-reported late effects, being married and being aged 16–20 years rather than 21–25 years at diagnosis.
95	Berbis, 2015	France	ALL and AML (*n* = 845)	General population (expected)	Survivors were more likely to be currently employed but also more likely to be in unstable employment (43.9% *vs.* 33.5%). Unemployed survivors were less likely to be seeking a job.	Younger attained age at the time of follow-up and more late effects were associated with unstable employment.
94	Pillon, 2013	Italy	ALL (*n* = 141)	General population (expected)	Survivors and comparisons had similar employment rates, regardless of attained age. Treatment with CRT did not change the employment rates.	–
46	Mody, 2008	North America	ALL (*n* = 4,151)	Siblings (*n* = 3,899)	Both female and male survivors were more unemployed, but the difference was only statistically significant for female survivors *vs.* female siblings ($p = 0.01$) and not for male survivors *vs.* male siblings ($p = 0.07$)	Relapsed female survivors.

(Continues)

Table 2b. Continued

Ref. no.	First author, publication year	Country	Cancer type (*n*)	Comparisons (*n*)	Main findings	Determinants
[59]	Pui, 2003	USA	ALL (*n* = 584)	General population (expected)	Non-irradiated male survivors had unemployment rates similar to those of the general population.	Irradiated survivors of both genders were significantly more likely to be unemployed than expected (males: 15.1% *vs.* 5.4%, females: 35.4% *vs.* 5.2%), and more non-irradiated female survivors were unemployed (22.4% *vs.* 7.6%).
[96]	Mulrooney, 2008	North America	AML who received chemotherapy and/or radiotherapy (*n* = 272)	Siblings (*n* = 3,899) and general population (expected)	Employment rates were similar for survivors, siblings and the general population (93%, 97.6%, 95.8%, respectively).	–
[45]	Armstrong, 2009	North America	CNS tumours (*n* = 1,877)	Siblings (*n* = 3,899)	Siblings were more likely to be employed than survivors (RR: 1.4, 95% CI: 1.3–1.5).	RT to the temporal or frontal lobe with ≥50 Gy.
[43]	Ellenberg, 2009	North America	CNS tumours (*n* = 802)	Siblings (*n* = 382) and non-CNS malignancies (*n* = 5,937)	CNS tumour survivors were significantly less likely to be employed full-time than either siblings or non-CNS tumour survivors ($p < 0.001$).	Impaired task efficiency, emotional regulation, organisation and memory.
[97]	Brinkman, 2016	North America	CNS tumours (*n* = 224)	Internal comparison of no CRT (*n* = 63), FI (*n* = 71) and CSI (*n* = 83)	Risk for unemployment did not differ by type of treatment ($p = 0.26$).	Neurocognitive impairment.
[99]	de Blank, 2016	North America	Astroglial tumours (*n* = 587)	Internal comparison of vision impairment	Survivors with bilateral blindness were more likely to be unemployed than those without vision impairment (OR: 2.17, 95% CI: 1.06–4.46).	–
[44]	Yagci-Kupeli, 2013	Turkey	Solid tumours (*n* = 201)	General population (expected)	Survivors were more likely to be unemployed (36.8% *vs.* 10.3%, $p < 0.001$).	–
[100]	Nagarajan, 2011	North America	Osteosarcoma (*n* = 733)	General population (*n* = 3,899)	Survivors were more likely to be unemployed (3.1% *vs.* 0.2%, OR: 17.2, 95% CI: 7.7–62.8).	–
[101]	Ottaviani, 2013	USA	Osteosarcoma (*n* = 38)	Internal comparison of limb salvage (*n* = 19) or amputation (*n* = 19)	No significant difference in employment status between the two groups of osteosarcoma survivors.	–
[103]	Nagarajan, 2003	North America	Osteosarcoma or Ewing sarcoma of the lower extremity or pelvis (*n* = 694)	Siblings (*n* = 2,667) and internal comparison of amputees (*n* = 471) and non-amputees (*n* = 223)	Survivors were less likely to ever have had a job than siblings (OR: 0.3, 95% CI: 0.17–0.51).	Amputees were less likely to ever have had a job, regardless of age at diagnosis.

(Continues)

Table 2b. Continued

Ref. no.	First author, publication year	Country	Cancer type (*n*)	Comparisons (*n*)	Main findings	Determinants
[104]	Termuhlen, 2011	North America	Wilms tumour (*n* = 1,256)	Siblings (*n* = 4,023)	Survivors of Wilms tumour were marginally but statistically significantly less likely to have ever held a job ($p = 0.046$).	–
[29]	Punyko, 2007	North America	Rhabdomyosarcoma (*n* = 417)	Siblings (*n* = 2,685)	Survivors were less likely to have ever had a job (96.9% *vs.* 98.7%, $p = 0.01$). No difference in whether they worked in the past year ($p = 0.77$).	–
Occupation						
[47]	Frobisher, 2017	Great Britain	All cancers (*n* = 10,257)	General population (*n* = 15,730)	Survivors were less likely to hold managerial or professional occupations (OR: 0.85, 99% CI: 0.77–0.94).	CNS tumour survivors and leukaemia survivors, especially CNS tumour survivors treated with CRT.
[38]	Ishida, 2011	Japan	All cancers (*n* = 184)	Siblings (*n* = 72)	Fewer survivors held white-collar occupations (15% *vs.* 25%), and more held blue-collar occupations (8% *vs.* 4%). A high proportion had medical jobs (11% *vs.* 0%).	–
[52]	Kirchhoff, 2011a	North America	All cancers except retinoblastoma, germ-cell tumours, other and unspecified cancers (*n* = 3,763)	Internal comparison of psycho-social health	Occupational categories did not differ significantly according to survivors' physical and mental health.	–
[53]	Kirchhoff, 2011b	North America	All cancers except retinoblastoma, germ-cell tumours, other and unspecified cancers (*n* = 6,671)	Siblings (*n* = 2,129)	Employed survivors were slightly less likely to have higher skilled managerial or professional occupations (RR: 0.93, 95% CI: 0.89–0.98) and more likely to be employed in non-physical occupations (RR: 1.15, 95% CI: 1.07–1.24).	CNS tumour, leukaemia and NHL survivors, diagnosis at young age (<5 years) and treatment with high-dose CRT. Female survivors likelihood of being in full-time professional occupations was lower than female siblings (27% *vs.* 41%).
[40]	Dumas, 2016	France	Solid malignant tumours, benign cerebral tumours, haematological malignancies (*n* = 2,066)	General population (expected)	Survivors were more likely to be in a higher occupational class (managerial or professional jobs) (23.1% *vs.* 15.4%).	CNS tumour survivors and treatment with CRT. Both male and female survivors were equally more likely to be professionals and managers than gender-matched expected (male O/E: 1.5, 95% CI: 1.3–1.7, female O/E: 1.5, 95% CI: 1.3–1.7)

(Continues)

Table 2b. Continued

Ref. no.	First author, publication year	Country	Cancer type (*n*)	Comparisons (*n*)	Main findings	Determinants
60	Freycon, 2014	France	Leukaemia patients who underwent a-HSCT with fTBI (*n* = 59)	General population (expected) and leukaemia patients who underwent a-HSCT with chemotherapy (*n* = 19)	The job distribution of survivors who underwent a-HSCT with fTBI or chemotherapy did not differ significantly from that of the general population.	More female survivors with fTBI were employed in intermediate-level professional positions such as nursing or teaching than expected in the female background population (O/E = 2.4, 95% CI: 1.2–2.4).
102	Yonemoto, 2008	Japan	Osteosarcoma (*n* = 41)	Internal comparison of amputation (*n* = 18) and limb-sparing (*n* = 9)	No difference between the two groups.	–

Abbreviations: CNS, central nervous system; RR, relative risk; CI, confidence interval; OR, odds ratio; SCT, stem cell transplantation; RT, radiation therapy; CRT, cranial radiation therapy; NHL, non-Hodgkin lymphoma; O/E, observed *vs.* expected; ALL, acute lymphoblastic leukaemia; AML, acute myeloid leukaemia; FI, focal irradiation; CSI, craniospinal irradiation; a-HSCT, allogeneic haematopoietic stem cell transplantation; fTBI, fractionated total body irradiation.

economic compensations were excluded did not change the overall finding.

Social Security Benefits

Table 2d summarises the findings on the uptake of social security benefits. Every study reported increased uptake of various social security benefits by survivors of childhood cancer.[41,48,55–57]

A Norwegian study observed that 39% of survivors diagnosed below 15 years of age, 25.9% of survivors diagnosed between 15 and 19 years of age and 10.8% of the general population received social security benefits (all combined).[55] Survivors diagnosed below 15 years of age were 5.4 times (95% CI: 4.9–5.8) more likely to receive social security benefits and survivors diagnosed between 15–19 years of age were 3.9 times (95% CI: 3.5–4.4) more likely to receive social security benefits. The highest risk was observed for the uptake of attendance benefits (age 0–14 at diagnosis: 20.5% (standardised incidence ratio (SIR): 18.3, 95% CI: 16.4–20.5), age 15–19 at diagnosis: 3.3% (SIR: 17.9, 95% CI: 12.4–25.0) *vs.* 1.1% among the general population), indicating financial compensation for the use of services (e.g., nursing or home care), but also basic benefits granted as a result of health problems (e.g., support bandages, transport, guide dog) and disability pension were significantly higher among survivors.[55] Similar results were reported in Sweden, where CNS tumour survivors had a 10 times higher risk than the general population for having received at least one social security benefit (handicap allowance, disability assistance or sickness pension) (RR: 10.7, 95% CI: 9.3–12.8).[56] Factors associated with a particular risk for receiving any social security benefit included a CNS tumour diagnosis, younger age at diagnosis and treatment with CRT.[41,55–58]

Dissimilarities in findings across studies

Geographical and demographical factors. The findings for educational achievements, income and use of social security benefits did not differ notably by region; however, the impact of a childhood cancer diagnosis on employment status in adulthood differed in studies in Europe and in North America. Some European studies found no difference in unemployment rates between survivors and the background population,[34,37,41,42,51] whereas other European studies indicated a slightly elevated risk of unemployment among survivors.[27,39,40,47,48] The two studies on employment conducted in North America on all childhood cancers found that survivors had substantially elevated risk for unemployment.[49,50]

Overall, larger proportions of both survivors and the background population in North American studies were enrolled in special education or learning disability programmes[23,25,30] than in a European study.[27] The number of studies in Asia was considered too small for any meaningful comparison.

Table 2c Main findings for socioeconomic outcomes of childhood cancer survivors: income, by cancer type

Ref. no.	First author, publication year	Country	Cancer type (*n*)	Comparisons (*n*)	Main findings	Determinants
[42]	Boman, 2010	Sweden	All cancers (*n* = 1,716)	General population (*n* = 1,456,089)	Income of non-CNS tumour survivors was similar to that of the general population (excluding students and individuals receiving economic compensation for disability).	CNS tumour survivors had a lower net salary (RR: 0.85, 95% CI: 0.77–0.94).
[48]	Gunnes, 2016	Norway	All cancers (*n* = 1,049)	General population (*n* = 1,052,076)	Survivors of cancers diagnosed at <15 years were at marginally increased risk for a low salary (men RR: 1.19, 95% CI: 1.03–1.38, and women RR: 1.18, 95% CI: 1.00–1.39).	Female survivors of all cancer types were less likely to achieve a high income when compared with females in the general population (RR: 0.76, 95% CI: 0.62–0.94).
[38]	Ishida, 2011	Japan	All cancers (*n* = 184)	Siblings (*n* = 72)	Survivors had a similar annual income level to siblings (students included).	Survivors receiving RT.
[41]	Ahomaki, 2016	Finland	Brain tumours, solid tumours, leukaemia and NHL (*n* = 2,132)	General population (*n* = 16,215)	Annual income of survivors of all three types of cancer was significantly lower than that of the general population.	Survivors of brain tumours, especially those who received irradiation.
[54]	Wengenroth, 2016	Switzerland	Leukaemia, lymphoma, CNS tumours, malignant solid tumours, Langerhals cell histiocytosis (*n* = 1,506)	Siblings (*n* = 598)	Survivors were less likely to have a high monthly net income (excluding social insurance and retirement insurance) (OR: 0.46, 95% CI: 0.33–0.64) than siblings, also after control for working hours.	CNS tumour survivors, survivors exposed to CRT, and those of cancers diagnosed at <5 years of age.
[45]	Armstrong, 2009	North America	CNS tumours (*n* = 1,877)	Siblings (*n* = 3,899)	Siblings were more likely to have an annual household income > US$20,000 than survivors (RR: 1.2, 95% CI: 1.1–1.3).	RT of ≥30 Gy to the temporal lobe, RT at ≥50 Gy to the posterior fossa and RT of <30 Gy and 30–49 Gy to the frontal lobe.
[43]	Ellenberg, 2009	North America	CNS tumours (*n* = 802)	Siblings (*n* = 382) and non-CNS tumours (*n* = 5,937)	CNS tumour survivors had lower household income than both siblings and non-CNS tumour survivors ($p < 0.001$).	Impaired task efficiency, emotional regulation, organisation and memory.
[99]	de Blank, 2016	North America	Astroglial tumours (*n* = 587)	Internal comparison of vision impairment	No difference in annual income between survivors with vision impairment and those without.	-
[101]	Ottaviani, 2013	USA	Osteosarcoma (*n* = 38)	Internal comparison of limb salvage (*n* = 19) or amputation (*n* = 19)	No significant difference in annual income between the two groups of osteosarcoma survivors.	-
[104]	Termuhlen, 2011	North America	Wilms tumour (*n* = 1,256)	Siblings (*n* = 4,023)	No difference in personal or household income ($p = 0.48$ and $p = 0.78$, respectively).	

Abbreviations: CNS, central nervous system; RR, relative risk; CI, confidence interval; RT, radiation therapy; NHL, non-Hodgkin lymphoma; OR, odds ratio; CRT, cranial radiation therapy.

Table 2d Main findings for socioeconomic outcomes of childhood cancer survivors: social security benefits, by cancer type

Ref. no.	First author, publication year	Country	Cancer type (*n*)	Comparisons (*n*)	Main findings	Determinants
[55]	Ghaderi, 2013	Norway	All cancers (*n* = 4,031)	General population (*n* = 1,194,198)	Survivors diagnosed below 15 years of age were 5.4 times (95% CI: 4.9–5.8) more likely to receive social security benefits. Survivors diagnosed between 15 and 19 years of age were 3.9 times (95% CI: 3.5–4.4) more likely to receive social security benefits..	Younger age at diagnosis (<15 years), more recent calendar year of diagnosis (1995–2004: SIR: 10.2, 95% CI: 9.2–11.3) and survivors of bone tumours and connective tissue, CNS tumours and haematological malignancies.
[48]	Gunnes, 2016	Norway	All cancers (*n* = 310)	General population (*n* = 239,996)	Marginally but statistically significantly higher uptake of government financial assistance by survivors *vs.* gender-matched controls (men: HR: 1.16, 95% CI: 1.00–1.36 and women: HR: 1.23, 95% CI: 1.05–1.45), including those receiving disability pension. No difference after exclusion of those receiving a disability pension (men: HR: 0.98, 95% CI: 0.81–1.18 and women HR: 1.09, 95% CI: 0.90–1.32)	-
[56]	Hjern, 2007	Sweden	All cancers (*n* = 2,503)	General population (*n* = 1,905,013)	Survivors were more likely to rely on social security benefits (handicap allowance, disability assistance or sickness pension). 13.8% of survivors and 2.7% of the general population had at least one disability.	CNS tumour survivors (RR: 10.7, 95% CI: 9.3–12.8) and younger age at diagnosis (<7 years) for survivors of leukaemia, lymphoma and solid tumours.
[57]	Kirchhoff, 2015	North America	All cancers except retinoblastoma, germ-cell tumours, other and unspecified cancers (*n* = 698)	Siblings (*n* = 210)	Survivors more frequently received supplemental security income and disability insurance ($p < 0.001$ and $p = 0.05$, respectively).	CRT at >25 Gy (supplemental security income: RR 3.93, 95% CI: 2.05–7.56; disability insurance: RR 3.65, 95% CI: 1.65–8.06) and age < 5 years at diagnosis (supplemental security income: RR: 7.56, 95% CI: 1.02–56.16).
[41]	Ahomaki, 2016	Finland	Brain tumours, solid tumours, leukaemia and NHL (*n* = 2,132)	General population (*n* = 16,215)	Survivors of all cancer types had a statistically significantly higher probability of early retirement.	Brain tumour survivors (OR: 14.8, 95% CI: 10.4–21.0), especially those who were irradiated and diagnosed at a younger age and in an earlier treatment era.
[58]	Johannesen, 2007	Norway	CNS tumours (*n* = 454) and haematological malignancies (*n* = 575)	Internal comparison of the two cancer groups	More CNS tumour survivors than haematological malignancy survivors received basic benefit, attendance benefit or disability pension ($p < 0.001$).	Irradiated survivors than non-irradiated survivors ($p < 0.001$).

Abbreviations: CI, confidence interval; SIR, standardised incidence ratio; CNS, central nervous system; HR, hazard ratio; RR, relative risk; CRT, cranial radiation therapy; NHL, non-Hodgkin lymphoma; OR, odds ratio.

Some studies have carried out gender-stratified analyses and suggested that female survivors might be at a particular increased risk of adverse socioeconomic outcomes compared with female controls.[25,27,30–33,40,46,48,53,59] Three studies with gender-stratified analyses suggested male survivors to be at an increased risk of some adverse socioeconomic outcomes compared to female survivors.[27,40,60] Finally, Dumas *et al.* observed both female and male survivors being equally likely to have professional and manager occupations compared to their gender-matched peers (male: observed/expected: 1.5, 95% CI: 1.3–1.7, female: observed/expected: 1.5, 95% CI: 1.3–1.7). Additionally, male survivors were more likely to be college graduates than the gender-matched comparisons (observed/expected: 1.3, 95% CI: 1.1–1.4).[40]

Quality assessment. On a quality scale with a maximum score of 9, the average for the 52 studies was 7.15. When the studies were divided into those of low quality (<7, n = 16, 30.8%) and high quality (>7, n = 18, 34.6%), no major difference was observed in the reported findings; including the intermediate quality category (7, n = 18, 34.6%) in this evaluation did not change the conclusion.

Overall, the quality ratings among studies of educational outcomes were similar and overall findings did not differ by quality ratings. Remarkably, 14 (39%) of the studies of work life had a quality rating of <7, and only seven (19%) were rated as of high quality (>7). However, the reported results on both employment and occupation did not differ by quality ratings. Three of the studies of income (30%) were of high quality and four (40%) of low quality; however, the findings were similar. All but one of the six studies of uptake of social security benefits were rated as of high quality, but the findings were similar to those of the study of lower quality.

Most of the high-quality studies were conducted in Europe (16 *vs.* 2 in North America). The three studies in Asia were all rated of low quality.

Discussion

Our systematic review of 52 published, peer-reviewed articles indicates that some childhood cancer survivors are at increased risk of adverse socioeconomic outcomes, requiring attendance at special education or learning disability programmes, poor school performance, lower attained educational level, lower income and greater uptake of social security benefits. The findings of studies including survivors of various types of childhood cancer with regard to repeating grades, employment status and occupation were inconsistent; however, survivors of CNS tumours, those who had been treated with CRT and those diagnosed at a younger age, independent of cancer type, were at particularly high risk for such adverse socioeconomic outcomes.

Determinants and underlying mechanisms

The identification of subgroups of childhood cancer survivors who are at particular risk for adverse socioeconomic outcomes is essential for elucidating the underlying mechanisms and pathways and for planning support strategies along the trajectory of cancer survivorship. Our systematic review points to tumour-, treatment- and patient-related determinants of socioeconomic outcomes: survivors of CNS tumours, treatment with CRT and diagnosis at a younger age were at particular risk for poor socioeconomic outcomes.

Radiation therapy plays an essential role in the treatment of children with CNS tumours.[61] Cranial irradiation has been associated with many, diverse late effects, including long-term neurocognitive impairment, such as fatigue, vision or hearing deficit, and problems in concentrating, learning and memory function.[62–66] Furthermore, cancer treatment at a younger age may profoundly influence growing tissues and development, with deformation of bones, development of tissue fibrosis and impaired organ function, which may result in a wide variety of morbidities and cognitive impairment.[62,66,67] Such somatic impairment may also cause educational and occupational difficulties and thereby constitute the underlying mechanism of the adverse socioeconomic outcomes we observed in some groups of childhood cancer survivors. As adverse socioeconomic outcomes were observed not only in survivors of a CNS tumour who were treated with CRT or diagnosed at a young age but also among other childhood cancer survivors, other pathways are also likely to play a role in the development of socioeconomic difficulties.

The role of treatment as a specific underlying mechanism of later socioeconomic difficulties is unclear, as treatment protocols and their toxicity have changed considerably during the past few decades.[68] While radiation therapy was used widely in earlier treatment eras, followed by incorporation of chemotherapy in the 1960s and 1970s, the main components of modern curative treatment are various chemotherapeutic agents, improved surgical techniques, direction of radiation only to target tissues to avoid damage to surrounding healthy tissue and personalised therapy.[69,70] A study in the USA, however, found that self-reported health status among survivors had not changed by treatment decade, indicating that survivors treated in the modern era may still have late effects.[71] When assessing the included studies, the findings generally did not show any changing pattern in survivors' socioeconomic attainment over time, and diagnostic period was therefore not considered a risk factor of specific adverse socioeconomic outcomes.

Another plausible underlying mechanism might be related not to childhood cancer treatment but to the psychosocial effects of a diagnosis of childhood cancer. This devastating experience, with management of the child's disease and treatment and everyday responsibilities, including work-related obligations, is highly challenging for caregivers and relatives and may have a substantial psychosocial impact on the child and the entire family, resulting in later socioeconomic difficulties. Such possible mechanisms are, however, poorly understood. Studies have shown that survivors are at increased risk

for mental disorders manifesting several years after a cancer diagnosis.[72,73] Further, the ability of survivors and their families to cope with a stressor such as a childhood cancer diagnosis and the availability of both internal and external resistance resources, such as cognitive skills, management of emotional distress and social support, may affect long-term socioeconomic outcomes.[74,75]

Finally, absence from school because of cancer and its treatment is likely to delay education or make it difficult for survivors to attain a similar educational level as their peers.[76] Both late effects and poor educational attainment may limit the ability to work or to attain a higher occupational position, and, as measures of income reflect employment and occupation, the possibility of earning a certain income or being independent of social security benefits may also be affected. Further research is needed to gain a deeper understanding of potential pathways of adverse socioeconomic outcomes in childhood cancer survivors.

Dissimilarities among studies and methodological heterogeneity

Differences in social welfare systems, including access to health care, family support and education, sociocultural aspects of a society and the availability of rehabilitation and follow-up interventions across studies make an international comparison challenging. The findings for educational achievements, income and use of social security benefits did not differ notably by region, indicating that survivors face difficulties independently of their welfare system. However, differences in coverage and access to health care and educational and occupational possibilities might have contributed to the geographical differences we observed in studies of employment, use of special education or learning disability programmes in Europe and in North America. Employer-sponsored health insurance coverage in the USA may play a role in the employment rejection rate of adult survivors of childhood cancer, because of the risk of late effects and thereby inability to work.[77,78] This might explain the difficulty of obtaining and maintaining employment seen in the studies in the USA.[49,50]

Societal tendencies often suggest that females are more likely to achieve higher grades and educational achievements than males,[79] whereas unemployment rates in the general population are higher among females compared to males.[80] Such general gender differences may also be expected among childhood cancer survivors. The included studies evaluated gender differences with inconsistent methodology. Studies analysing gender differences only among survivors are therefore considered less meaningful given the already existing difference in the background population, and those results have not been taken into account for our evaluation on determinants of adverse socioeconomic outcomes. Evidence from the studies reporting on gender differences in a meaningful way indicated a tendency of female survivors being at particular increased risk of adverse socioeconomic outcomes compared to gender-matched peers, suggesting that female survivors may be a more vulnerable group of survivors.

We included studies with wide methodological heterogeneity, with differences in cancer types, comparison groups, sample size, factors adjusted for, outcome of interest, measurement of outcome and whether the study was population-based or based on a selected group of survivors. This makes a meaningful comparison of effect estimates across studies challenging. Moreover, differences in attained age and length of follow-up in the studies allowed dissimilar assessment of socioeconomic achievements to occur, or important endpoints could potentially have been missed due to a delayed achievement rather than lack of achievement.

Strengths and limitations

To our knowledge, this is the first comprehensive systematic review of studies on long-term socioeconomic outcomes in childhood cancer survivors, being interested in survivors of all types of childhood cancers and understanding socioeconomic outcomes in a wide-ranging way including educational attainments and difficulties, employment and working life, income and the uptake of social security benefits. A major strength of this article is the scientifically rigorous methodological approach. Specifically, we searched three health-related, scientifically relevant databases, hand-searched the reference lists of the articles included and updated our search before drafting the manuscript so as not to miss any recently published article. We included articles from a broad range of languages published since 2000 to reduce any publication bias. Two researchers independently screened the articles and systematically assessed the quality of all the studies included. The effect size and statistical significance of the findings of each study are reported in this article, providing a comprehensive overview of the available evidence.

A major limitation of this article is the wide methodological heterogeneity of the studies, which limited meaningful comparison of effect estimates in our narrative synthesis. Moreover, in view of substantial improvements in treatment and survival after childhood cancer during the past few decades, studies of survivors of cancers diagnosed in earlier decades might have included less severe cases who survived even with the less effective treatment available at that time, whereas studies of children treated more recently presumably also included severe cases. Bearing in mind potential differences in cancer severity according to diagnostic period and treatment era among studies, the findings of this article should be interpreted with caution.

Further limitations are associated with specific studies. In a large number of studies, outcomes were self-reported, and they are thus prone to recall bias or reporting bias. A substantial loss to follow-up in several studies in North America could also have biased the results.

We found that a CNS tumour in childhood is a particular determinant of adverse socioeconomic outcomes. CNS

tumours are, however, some of the most common types of cancer in children, and a larger study population increases the chance of finding even small statistically significant effects. Many solid tumour types are very rare in childhood, and for solid tumours, there are often too few cases to draw meaningful conclusions.[81]

Another limitation of this article is that we had only one study from a middle-income country[44] and none from any low-income country. This limits the generalisability of the findings to high-income countries, for which late effects and adverse socioeconomic outcomes may also be of higher concern and public health relevance due to higher survival rates.[82]

The Newcastle-Ottawa Scale for appraising the quality of studies has some limitations, and it might be questioned how well the ranking reflects and differentiates the quality of the studies. First, the tool does not take into account sample size, which might affect the precision of the reported estimates, nor does it take into account the external generalisability of study findings. Additionally, by rewarding studies that accounted for parental socioeconomic background, matched siblings were unintentionally considered to be the ideal comparison group. The siblings of childhood cancer survivors may, however, also be affected psychosocially by the cancer diagnosis of their sibling, which could influence their socioeconomic achievement, thereby resulting in underestimation of any reported association.[83,84]

Conclusion, research implications and perspectives

This article indicates that late effects attributable to childhood cancer or its treatment are not limited to somatic and mental disorders, but that subgroups of survivors also face various socioeconomic difficulties in their life course. Particular risk factors for socioeconomic difficulties in later life appear to be survivors of a CNS tumour, treatment with cranial radiation therapy and diagnosis of cancer at a young age. Future research should address the underlying mechanisms of the socioeconomic difficulties observed in some childhood cancer survivors.

The methodological limitations of the studies included in this article indicate that registry-based cohort studies should be conducted, with adequate sample size, detailed clinical and treatment information, information on other potential risk factors to allow risk-stratified or adjusted analyses, and long follow-up and repeated measurements for assessment of socioeconomic conditions throughout the life course. Such a study design could eliminate bias due to selection, participation, loss to follow-up, reporting and recall.

The findings of this article could be used as a basis for future interventions and supportive strategies targeting vulnerable groups of survivors. A previous systematic review showed that long-term follow-up care for survivors resulted in better health and educational outcomes.[85] Given our findings, some vulnerable groups of survivors might therefore benefit from more careful follow-up to identify early signs of adverse educational or occupational progress, so that appropriate support strategies can be initiated, in line with guidelines for psychosocial care of children with cancer.[86] Increased awareness of survivors with particular adverse socioeconomic conditions is essential, as an unhealthy lifestyle and deleterious working conditions are usually more prevalent in such groups, making them even more vulnerable to comorbid conditions.[87–92] Thus, differences in the socioeconomic impact of childhood cancer, especially for CNS tumour survivors, may contribute to long-term social inequalities in health. Given the increasing population of survivors of childhood cancer, long-term follow-up and support strategies to address not only somatic and psychiatric late effects but also the socioeconomic difficulties of vulnerable groups of survivors will be of increasing importance to reduce social inequity, and ensure a high quality of life after childhood cancer.

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