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COHORT PROFILE

# Cohort Profile: The Swiss Childhood Cancer Survivor Study

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## How did the study come about?

Thanks to continuous improvements in therapy, 5-year survival of childhood cancer in developed countries now exceeds 80%,[1,2] leading to a growing population of long-term survivors. As the cancer and treatment can cause adverse effects long after the illness has been cured, assessment of long-term quality of life (QOL), somatic, psychological and social outcomes become increasingly important. Although cancer in children is rare, the population impact of late toxicities on disability-adjusted life years is considerable because of the young age at diagnosis.

Up to now, many single-centre studies or clinical trials have been published, but only few large representative long-term follow-up studies exist, including the Childhood Cancer Survivor Studies in the USA (CCSS),[3] Canada[4] and Great Britain (BCCSS).[5] These studies found increased risks of second malignant neoplasms (SMNs),[6] mortality[7,8] and chronic medical problems such as endocrine dysfunctions, cardiovascular problems, stroke or infertility.[9–11] Psychosocial problems such as depression, anxiety and post-traumatic symptoms have also been reported.[12,13] Life-long medical follow-up is thus recommended for high-risk patients.[14,15]

For these reasons, we created a national cohort study of all survivors of childhood and adolescent cancer in Switzerland, the Swiss Childhood Cancer Survivor Study (SCCSS).

### What does it cover?

The SCCSS is a nationwide population-based cohort study of all children diagnosed with cancer in Switzerland since 1976, which aims to study long-term consequences of childhood cancer, including mortality, SMNs, QOL, late somatic, psychological and social effects, health behaviours and health care.

In particular, the SCCSS aims to:

(i) determine the incidence of late effects of cancer and treatments, including overall and cause-specific mortality, SMNs, somatic toxicities (endocrine disorders, infertility and pregnancy complications, cardiovascular, pulmonary and orthopaedic problems), health-related QOL and psychosocial outcomes including psychological distress, educational and professional attainment;
(ii) study associations between adverse outcomes and prospectively collected risk factors, including tumour (exact diagnosis, histology, cytogenetics, tumour stage and clinical features at diagnosis), treatment modalities (chemotherapy, radiotherapy, surgery), participation in clinical trials, age, sex, nationality, geographic region and socio-economic position of parents;
(iii) describe the current health-care use and medical follow-up in survivors, including type of health care, frequency of visits and uptake of recommended screening procedures and
(iv) describe health-related behaviours and their determinants in survivors compared with the general population.

## Who is in the sample?

The Swiss Childhood Cancer Survivor Study is closely linked with the Swiss Childhood Cancer Registry (SCCR; www.childhoodcancerregistry.ch), including all children registered in the SCCR who survived ⩾5 years.



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The SCCR is the population-based cancer registry for all Swiss residents diagnosed <21 years of age with leukaemias, lymphomas, central nervous system (CNS) tumours, malignant solid tumours or Langerhans cell histiocytosis.[16–20] It was founded in 1976. Case ascertainment is excellent for children aged 0–15 years at diagnosis who are usually treated in one of the nine specialized paediatric cancer centres (Figure 1). Regular comparison of the SCCR with data sets from cantonal cancer registries, Swiss hospital statistics, major pathology laboratories and mortality statistics allows the integration of patients who had not been treated in paediatric cancer centres.

Adolescents aged 16–20 years at diagnosis are also registered in the SCCR. However, coverage of this age group is still unsatisfactory, because only a minority of adolescents in Switzerland are treated in paediatric cancer centres. Instead, care is shared between a large and heterogeneous group of specialists and hospitals, such that not all cases are reported.[21] The SCCR aims for a complete coverage of adolescents by the year 2015.

By 31 December 2010, the SCCR included information on 5553 Swiss residents with cancer diagnosed at the age of 0–15 years (Table 1). Of these, 2435 (44%) had been diagnosed at the age of 0–4 years, 1423 (26%) at age 5–9 years and 1695 (31%) at age 10–15 years; 3143 (57%) were males and 2410 (43%) females. The most common diagnosis was leukaemias (34%), followed by CNS tumours (18%), lymphomas (14%), neuroblastoma (7%), soft tissue sarcomas (6%) renal tumours (5%) and bone tumours (5%). In total, 1395 patients (25%) had died.

The SCCSS (Figure 2) is the long-term cohort study of all patients registered in the SCCR who survived $\geqslant 5$ years. For the questionnaire survey 2007–11, only children diagnosed from 1976 to 2003, in the age group of 0–15 years, were included ($N = 2738$). From 2011, the study will be extended to include adolescents diagnosed at the age of 16–20 years ($n \approx 1200$), children not treated in a paediatric cancer centre ($n \approx 500$), children diagnosed between 2003 and 2005 ($n = 463$) and children who had been registered in the SCCR after December 2003 although diagnosed earlier ($n = 160$, Figure 2).

## What has been measured?

The data collected for the SCCR and the SCCSS come from three sources:

(i) clinical data from medical records;
(ii) routine data on current address, vital status, SMNs and causes of death; and
(iii) questionnaire surveys and examinations.

These are briefly described below, with details given in Tables 2 and 3.

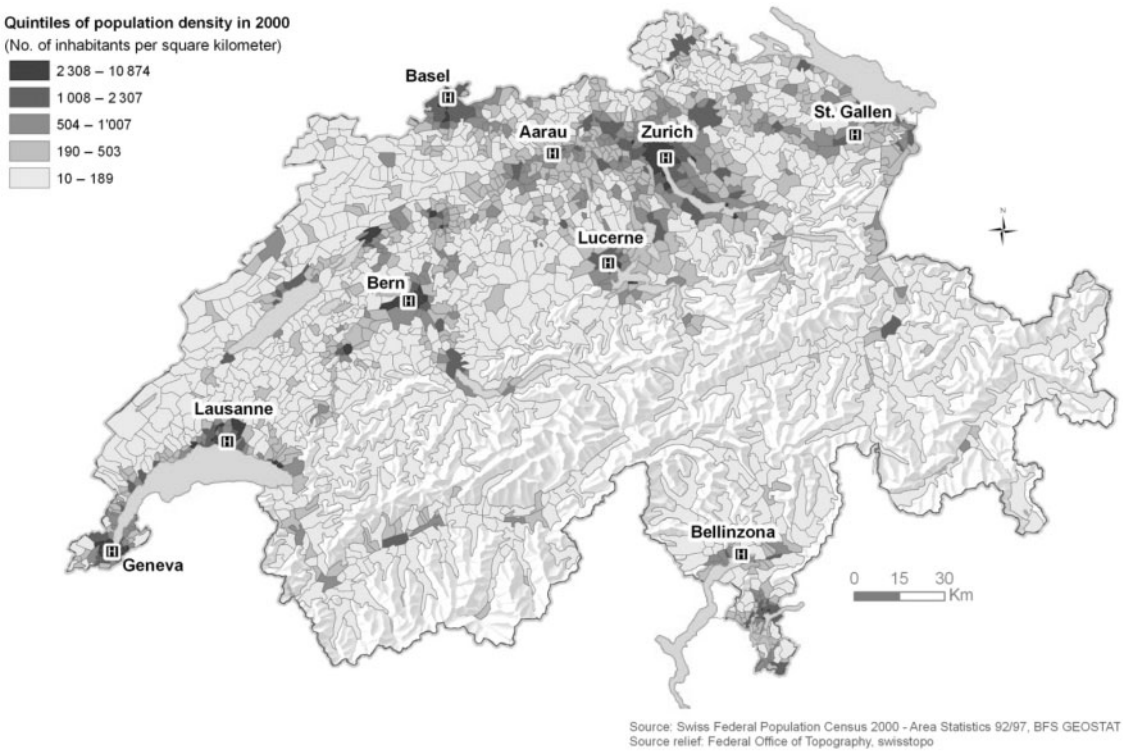


**Figure 1** Population density map of Switzerland showing the location of the nine paediatric cancer centres. Children living in the scarcely populated Alpine region (lower half of map) are treated in Bellinzona, St Gallen, Zurich, Bern or Lausanne

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**Table 1** Characteristics of the children registered in the Swiss Childhood Cancer Registry, by live status (diagnosed 1976–2010, aged 0–15 years at diagnosis, $N = 5553$)

| Characteristics | Survivors ($n = 4158$) $n$ (%)[a] | Deceased ($n = 1395$) $n$ (%)[a] | Total ($n = 5553$) $n$ (%)[a] |
|---|---|---|---|
| **Age at diagnosis (years)** | | | |
| 0–4.9 | 1830 (44.0) | 605 (43.4) | 2435 (43.9) |
| 5–9.9 | 1059 (25.5) | 364 (26.1) | 1423 (25.6) |
| ⩾10 | 1269 (30.5) | 426 (30.5) | 1695 (30.5) |
| **Sex** | | | |
| Male | 2315 (55.7) | 828 (59.4) | 3143 (56.6) |
| Female | 1843 (44.3) | 567 (40.7) | 2410 (43.4) |
| **Language region of Switzerland** | | | |
| German speaking | 2946 (71.5) | 953 (71.8) | 3899 (71.6) |
| French speaking | 1023 (24.8) | 307 (23.1) | 1330 (24.4) |
| Italian speaking | 152 (3.7) | 68 (5.1) | 220 (4.0) |
| **Diagnosis (ICCC-3 main groups)** | | | |
| (I) Leukaemias | 1380 (33.2) | 507 (36.3) | 1887 (34.0) |
| (II) Lymphomas | 664 (16.0) | 108 (7.7) | 772 (13.9) |
| (III) CNS tumours | 669 (16.1) | 349 (25.0) | 1018 (18.3) |
| (IV) Neuroblastoma | 239 (5.8) | 132 (9.5) | 371 (6.7) |
| (V) Retinoblastoma | 120 (2.9) | 13 (0.9) | 133 (2.4) |
| (VI) Renal tumours | 252 (6.1) | 39 (2.8) | 291 (5.2) |
| (VII) Hepatic tumours | 35 (0.8) | 21 (1.5) | 56 (1.0) |
| (VIII) Bone tumours | 173 (4.2) | 82 (5.9) | 255 (4.6) |
| (IX) Soft tissue sarcomas | 242 (5.8) | 101 (7.2) | 343 (6.2) |
| (X) Germ cell tumours | 132 (3.2) | 14 (1.0) | 146 (2.6) |
| (XI) Other malignant epithelial neoplasms | 63 (1.5) | 19 (1.4) | 82 (1.5) |
| (XII) Other and unspecified malignant neoplasms | 15 (0.4) | 3 (0.2) | 18 (0.3) |
| Langerhans cell histiocytosis | 174 (4.2) | 7 (0.5) | 181 (3.3) |
| **Treatment** | | | |
| Surgery only | 601 (15.7) | 66 (5.1) | 667 (13.0) |
| Chemotherapy[b] | 2030 (53.0) | 505 (38.9) | 2535 (49.4) |
| Radiotherapy[c] | 991 (25.8) | 568 (43.8) | 1559 (30.4) |
| BMT[d] | 211 (5.5) | 158 (12.2) | 369 (7.2) |

Adolescents aged 16–20 years at diagnosis are not included in this table, as their coverage in the SCCR is still incomplete. Percentages are based upon available data for each variable.
[a]Column percentages.
[b]Without radiotherapy, may have surgery.
[c]With or without chemotherapy or surgery.
[d]With or without chemotherapy, radiotherapy or surgery.
BMT, bone marrow transplantation; *n*, number; ICCC-3, International Classification of Childhood Cancer, third edition.

## Clinical data from medical records

### *Information at the time of diagnosis*

Children are usually registered in the SCCR within 3 months of diagnosis with standardized forms completed by local data managers of the paediatric cancer centres. In the SCCR, these forms are entered in the database after verification of missing or incorrect data. For cases not treated in paediatric cancer centres but identified via other sources [cantonal cancer registries, pathology laboratories, mortality statistics for death certificate only (DCO) cases], we migrate information into the SCCR in regular intervals. If not already available, an SCCR data manager extracts relevant information directly from hospital records.

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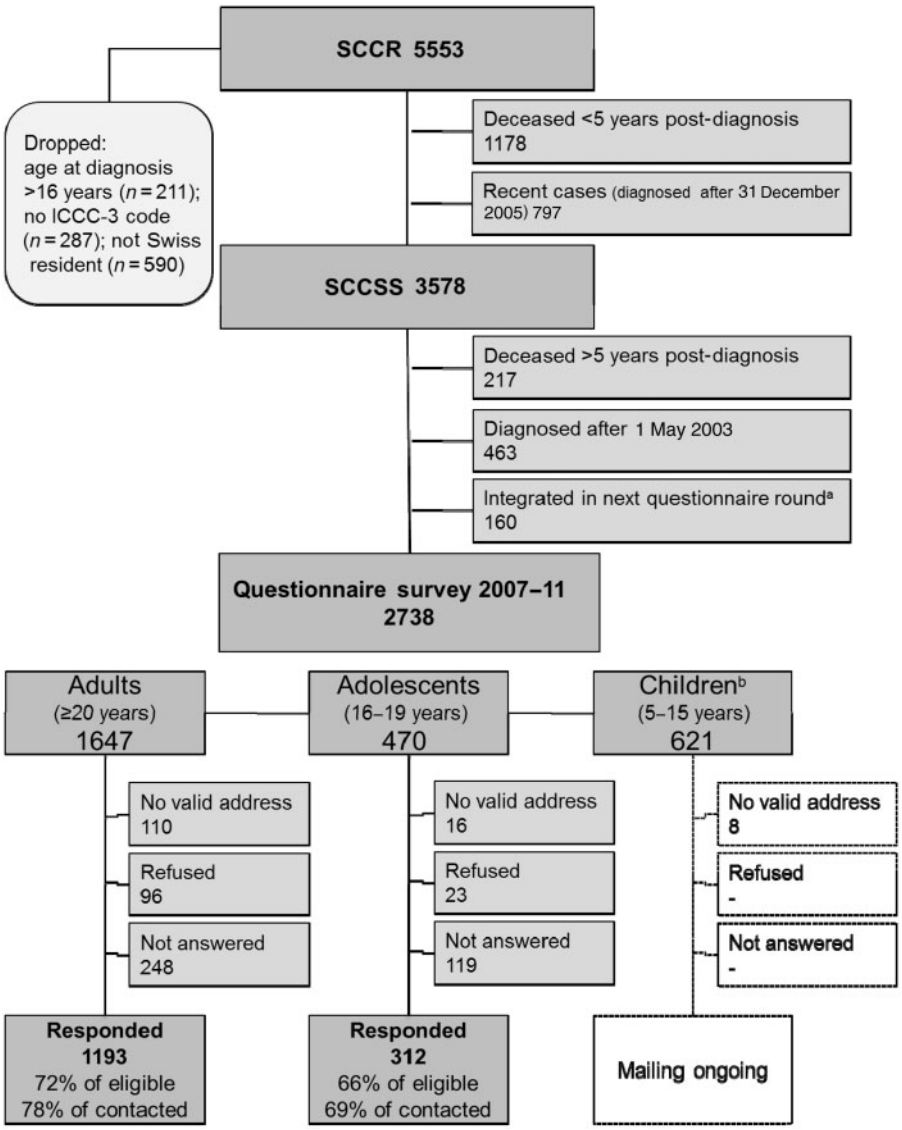


**Figure 2** Population of the Swiss Childhood Cancer Registry (SCCR) and the Swiss Childhood Cancer Survivor Study (SCCSS), showing the proportion deceased and response rates to the 2007–11 questionnaire survey. [a]Includes survivors diagnosed before 1 May 2003 who were included in the SCCR after 2003. [b]Mailing to families with survivors aged 5–15 years is performed from October 2010 to April 2011. ICCC-3, International Classification of Childhood Cancer, third edition

Information includes baseline demographic data and detailed medical information on the tumour, therapy and response to therapy.[16,17] Diagnoses are classified according to the International Statistical Classification of Diseases and Related Health Problems, 10th Revision (ICD-10), the International Classification of Diseases for Oncology, Third Edition (ICD-O3) and the International Classification of Childhood Cancer, third edition (ICCC-3).[22]

### *Clinical follow-up data*

As long as children are treated and followed up in paediatric cancer centres (usually 5–10 years from the time of diagnosis), follow-up information on remissions and relapses, changes in treatments and clinical study participation is extracted annually from patient records by local data managers. Similarly, late effects, SMNs or deaths occurring during this period are registered.

## Routine data and linkages

First, current address, vital status and date of death have been updated in a standardized way in 2005–10 for the whole cohort by contacting community registration offices.

Causes of death and death records are identified periodically from the Swiss mortality statistics in the Swiss Federal Statistical Office. The SCCR data are linked with the anonymous mortality statistics via

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**Table 2** Clinical data, routine data and survey data collected in the SCCSS: detailed description (number of participants with available data in Table 3)

| Time frame | Sample addressed | Description/measurements |
|---|---|---|
| **Clinical data from medical records** | | |
| Since 1976 | All children in the SCCR | **Report of new cases**: disease: prior disease, date of diagnosis, exact tumour diagnosis, localization, stage, metastases, cytogenetics, histology<br>Therapy: clinical study participation, treatment protocol, surgery, chemotherapy, radiotherapy, bone marrow transplantation, exact treatment information for non-protocol patients<br>Patient: date of birth, sex, language, nationality, country of birth, address at diagnosis, residence status, contact information, parent's profession, parent's date of birth |
| Since 1976 | All children in the SCCR | **Follow up reports from clinics**: disease: details on relapse, late effects and second malignancies<br>Therapy: follow-up contacts, lost to follow-up, clinical study participation, details on treatment for first diagnosis, relapse or second malignancy<br>Patient: contact information, life status, date and cause of death, patient's paediatrician or general practitioner |
| **Routine data and linkages** | | |
| Since 2005 | All children in the SCCR | **Updates via communities**: vital status, date of death, address history |
| Since 2005 | All deceased children in the SCCR | **Linkage with Swiss mortality statistics**: causes of death |
| Since 2009 | All linkable children in the SCCR | **Linkage with Swiss National Cohort (SNC)**: environmental exposures and socio-economic situation including all information from Swiss Census dataset (1970, 1980, 1990 and 2000), mortality and migration statistics, and (from 2011)[a] birth records:<br>maternal and paternal education and profession<br>no. of rooms per person and persons per household<br>square metre living space per person<br>area-based socio-economic position index<br>maternal and paternal age<br>child's sex, birthweight, birth length, head circumference |
| Since 2010 | All children in the SCCR | **Linkage with cantonal cancer registries**: assessment of secondary malignancies: details of tumour diagnosis, date of diagnosis, causes of death |
| **Surveys and examinations** | | |
| 1994–96 | Children diagnosed 1976–89, $\geqslant$5 years disease free, $\geqslant$2 years off treatment, treated in one of the eight participating SPOG clinics[b] | **Medical history and examination**: patient's history (medical and psychosocial)<br>Standardized clinical investigation: weight, height, blood pressure, screening audiometry (Phonac®)<br>Laboratory: complete blood count, urinalysis, electrolytes, liver, renal, glomerular and tubular function<br>Endocrinological work up: Tanner's pubertal status, age at menarche, bone age, fT4, TSH, FSH/LH, free $\beta$-oestradiol, free testosterone, IGF-1/IGF-BP3<br>Rest echocardiography and ECG (patients treated with anthracylines or mediastinal radiation)<br>Pulmonary function test (patients with respiratory symptoms)<br>Intelligence test: WISC-R < 16 years of age, WAIS-R $\geqslant$16 years of age<br>Socio-economic status of the family: score based on father's profession and mother's schooling |
| 2007–11 (ongoing) | Children diagnosed 1976–2003[c] who survived $\geqslant$5 years | **Postal questionnaire (SCCSS)**: personal information<br>Health-related quality of life<br>Medical care and medication, former disease, somatic and mental health<br>Pregnancy and children (adults)/partner and sexuality (adolescents)<br>Lifestyle and health behaviours<br>Education and social environment |

ECG, electrocardiography; FSH, follicle-stimulating hormone; ft4, free thyroxin; IGF-1, insulin-like growth factor 1; IGF-BP3, insulin-like growth factor-binding protein 3; LH, luteinizing hormone; NA, not applicable; No., number; SES, socio-economic status; SNC, Swiss National Cohort; TSH, thyroid stimulating hormone; WISC-R, Wechsler Intelligence Scale for Children-Revised; WAIS-R, Wechsler Adult Intelligence Scale-Revised; SCCSS, Swiss Childhood Cancer Survival Study; SCCR, Swiss Childhood Cancer Registry; SPOG, Swiss Paediatric Oncology Group.

[a]Children diagnosed in 1991–2006 were included in a first linkage study performed in 2009. The linkage will be repeated in 2011 with the entire cohort.

[b]Participating Swiss Paediatric Oncology Group clinics were: Zurich, Bern, Lucerne, Lausanne, Geneva, St Gall, Aarau and Locarno.

[c]Children diagnosed between 1 May 2003 and 31 December 2005 (new 5-year survivors) will receive the questionnaire in 2011.

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**Table 3** Clinical data, routine data and survey data collected in the SCCSS: available data (*n*) (status December 2010, measurements described in detail in Table 2)

| | Participants (*n*) | | | |
|---|---|---|---|---|
| | | Survivors eligible for questionnaire survey 2007–11 (SCCSS), by age at survey (years) | | |
| **Collection steps** | All children in SCCR | Children (5–15) | Adolescents (16–19) | Adults (⩾20) |
| **Clinical data from medical records** | | | | |
| Report of new cases | 5553 | 621 | 470 | 1647 |
| Follow-up reports from clinics | 3726[a] | 580 | 443 | 1604 |
| **Routine data and linkages** | | | | |
| Updates via communities | 5553 | 621 | 470 | 1647 |
| Linkage with Swiss mortality statistics | 1395[b] | NA | NA | NA |
| Linkage with Swiss National Cohort (SNC) | 1867[c] | 191 | 252 | 596 |
| Linkage with cantonal cancer registries | Is currently being done for all children in the SCCR (5553) | | | |
| **Surveys and examinations** | | | | |
| Medical history and examination (1994–96) | 478[d] | NA[e] | NA[e] | 453 |
| Postal questionnaire (SCCSS) (2007–11) | 1505[f] | NA[g] | 312 | 1193 |

*n*, number; NA, not applicable; SCCSS, Swiss Childhood Cancer Survival Study; SCCR, Swiss Childhood Cancer Registry.
[a]Those 1827 without follow-up report include: 1058 deceased, 132 diagnosed within the last year (2010), 637 lost to follow-up.
[b]Includes deceased children only.
[c]Children diagnosed in 1991–2006 were included in a first linkage study performed in 2009. The linkage will be repeated in 2011.
[d]Eligible were children diagnosed in 1976–1989 who were disease-free for ⩾5 years.
[e]The 5-year survivors in 1994–96 have meanwhile reached an age of ⩾20 years.
[f]Eligible were children diagnosed in 1976–2003 who survived for ⩾5 years ($N=2738$, see Figure 2).
[g]Mailing to families with survivors aged 5–15 years is performed from October 2010 to April 2011.

date of birth, date of death and place of death (the latter two identified via community registration offices). This update, first undertaken in 2005, is being repeated regularly.

Information on peri-natal data, environmental exposures and socio-economic situation for cohort participants and matched controls can be obtained via data linkage with the Swiss National Cohort,[23] a large national cohort study combining data from the Swiss censuses, mortality statistics, migration records and birth records.[18]

Secondly, malignant neoplasms are being assessed (in 2010–11) via linkage with Swiss cantonal cancer registries, organized in the National Institute for Cancer Epidemiology and Registration (NICER; www.nicer.org). For linkage, we use a privacy-protecting technique using Bloom filters.[24] From 2012, this linkage will be repeated annually to detect new cases.

### Surveys and examinations

A first long-term follow-up survey was performed in 1994–96.[15,25–27] A total of 478 5-year survivors attended follow-up at their former hospital for a standardized medical history, a comprehensive clinical examination and additional investigations focusing on somatic, psychosocial and socio-economic outcomes [e.g. intelligence using the Wechsler Intelligence Scale for Children/Wechsler Adult Intelligence Scale (WISC/WAIS)[28]]. Liver, renal, cardiac and lung function were investigated in various subgroups. Participants who had received anthracyclines or mediastinal radiation received a cardiological examination, and patients who had received lung irradiation or chemotherapy with bleomycine or high-dose alkylating agents underwent lung function tests.

A second long-term follow-up survey was performed in 2007–11 (Figure 2), involving a questionnaire to all 5-year survivors who were aged 16–19 years ($N=470$) or ⩾20 years ($N=1647$) at the time of the survey. The mailing to survivors <16 years ($N=621$) is ongoing (2010–11).

## Methodology of the SCCSS: survey 2007–11

### Study logistics

Current addresses, vital status and dates of death for participants of the 2007–11 questionnaire survey were updated via community registration offices (Supplementary Figure S1). All participants with a known address received a study information letter from their former treating hospital. They were asked to indicate if their address had changed, if they required the questionnaire in a language other than

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the information letter (German, French or Italian) or if they did not want to participate. After 2 weeks, they received the questionnaire with a pre-paid return envelope. Non-responders were sent another questionnaire 4–6 weeks later and in case of not answering, were contacted by phone. If they felt that the questionnaire was too long, they were offered a short version with key questions.

Self-reported somatic health problems are validated by comparison with medical records from general practitioners or hospitals. This will be done in 2011 for cardiac disease and SMNs, and will be extended to other outcomes in subsequent years. Informed consent for this validation has been collected in the questionnaire.

### The SCCSS questionnaire

The questionnaire was created based on those used in the US, Canadian and UK childhood cancer survivor studies[3–5] to enable international comparison of health outcomes. It contains the following main domains: QOL, somatic health, current medication, health service utilization, psychological distress, fertility, health behaviour and socio-economic information.

In addition to the questions from the US, UK and Canadian questionnaires, we included the Brief Symptom Inventory (BSI) assessing psychological distress,[29,30] and added more questions on health behaviours and socio-economic information. Unique for the SCCSS is the inclusion of not only the cancer survivors who have reached adulthood, but also younger 5-year survivors.

To account for age-dependent differences, we created three distinct questionnaires: for adult survivors (aged $\geqslant$20 years), adolescents (aged 16–19 years) and children (aged 5–15 years). Details of the content of the questionnaire are described in Table 4. The questionnaires in German, French and Italian are available on our homepage (http://www.childhoodcancerregistry.ch/sccss).

### Control data sets for the questionnaire 2007–11

For comparing answers of study participants with healthy controls, we took two different approaches:

(i) sibling questionnaire—in 2009–11, the same questionnaires (excluding questions on past disease and treatments) are being sent to siblings of the study participants; and
(ii) population health surveys—in addition to questions derived from other childhood cancer survivor studies,[3–5] we included questions on QOL, health behaviours and socio-economic outcomes, which were used during the same years in general population health surveys in Switzerland. This allows a straightforward comparison of specific outcomes between survivors and the Swiss general population (Table 4).[29,31–41]

### Study participation and attrition

In the 1994–96 survey, the SCCR contained information on 914 5-year survivors. All patients ($n = 750$) for whom a valid address was found were invited to attend follow-up at their former hospital, and 478 (64%) participated (Table 3).[26]

In the 2007–11 survey, 2738 eligible survivors were mailed a questionnaire (1647 adults aged 20–49 years at the survey, 470 adolescents aged 16–19 years and 621 children aged 5–15 years; Figure 2). For 134 survivors, we had no valid address, 119 refused and 367 did not answer. Current response rates (31 December 2010) were: 1193 adults (78% of contacted) and 312 adolescents (69% of contacted) (Tables 3 and 5). Mailing of questionnaires to families of children aged 5–15 years and siblings takes place from October 2010 to June 2011. Provisional response rate for the sibling mailing is 451/749 (60%). Respondents to the questionnaire were more likely to be female, German speaking and aged 25–35 years compared with non-respondents (Table 5).

## What has been found? Key findings and publications

### Somatic outcomes

The first survey (1992–94) collected detailed data on somatic and cognitive outcomes.[15,25–27] Moderate to severe late effects were found in 211/621 (34%) survivors.[26] A subgroup of 140 acute lymphoblastic leukaemia (ALL) survivors was studied in detail.[25,27] Of those, 21/140 (15%) had moderate to severe late effects, 8 needed special schooling and 14 had problematic psychosocial adjustments. Most survivors suffered from endocrinological abnormalities (20/140, 14%). Problems of the cardiovascular system, lung, liver and digestion were rare (overall 9/140, 6%).[25] These findings resulted in the development of Swiss recommendations for long-term follow-up of childhood cancer survivors.[15]

In male survivors of acute lymphoblastic leukaemia, we assessed gonadal function and sperm quality. While sex hormone levels were normal, sperm concentration and sperm counts were decreased compared with WHO criteria and healthy controls, suggesting that treatment with moderately dosed chemotherapeutic agents, even without added radiotherapy, might have long-term gonadotoxic effects.[42]

Prevalence of bronchial asthma, assessed in the 2007–11 survey in young adult survivors, was similar to data published from general population samples in Switzerland.[43]

### Psychological and socio-economic outcomes

In the 2007–11 survey, we assessed psychological distress in young adult childhood cancer survivors and found that average distress scores were similar to normal populations. However, the proportion reporting

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**Table 4** Structure of the 2007–11 questionnaires (SCCSS), indicating source of questions and available comparison data (three versions of the questionnaire were made for adult, adolescent and child survivors)

| | Reference questionnaires and comparison data | | |
|---|---|---|---|
| **Sections of questionnaire** | Adults (aged ⩾20 years) | Adolescents (aged 16–19 years) | Children (aged 5–15 years) |
| Personal information | Swiss Census 2000[31]<br>SHS 2007[34] | Swiss Census 2000[31] | Swiss Census 2000[31] |
| Health-related QOL | SF-36[39] | SF-36[39] | KidScreen[40] |
| Former disease and current health status, medical care and medication | CCSS[3]<br>BCCSS[5]<br>BSI[a,29,30] | CCSS[3]<br>BCCSS[5]<br>BSI[a,29,30] | CCSS[3]<br>BCCSS[5]<br>SDC[35] |
| Pregnancy and children/ partner and sexuality | Own questions<br>BCCSS[5] | SMASH 2002 | NA |
| Lifestyle and health behaviours | SHS 2007[34] | SHS 2007[34]<br>SMASH 2002[32]<br>Tobacco-Monitoring[33] | BALLABEINA[36]<br>GABRIEL[37]<br>KIGGS-Study[38] |
| Formation and social environment | Swiss Census 2000[31]<br>European Social Survey[41]<br>SHS 2007[34] | Swiss Census 2000[31]<br>SMASH 2002[32] | Swiss Census 2000[31]<br>SHS 2007[34] |

BCCSS, British Childhood Cancer Survivor Study; CCSS, Childhood Cancer Survivor Study; KidScreen, Health-Related Quality of Life Questionnaire for Children and Young People and their Parents; NA, not applicable; SDC, Strength and Difficulties Questionnaire for Children; SF-36, Short Form-36 (version 2); SHS, Swiss Health Survey 2007; SMASH, Swiss Multicentre Adolescent Survey.
[a]Brief Symptom Inventory (BSI) with reference data from healthy normal populations and psychotherapy patients from the University of Bern Outpatient Clinic.

high distress was disproportionally large, suggesting that a significant number of survivors might benefit from psychological counselling.[30]

A considerable proportion of childhood cancer patients had transient problems with schooling, but final educational attainment in adulthood was comparable with the general population. Only CNS tumour survivors and survivors with a relapse had poorer outcomes.[44]

## Health behaviours

A healthy lifestyle is important to prevent chronic diseases in the general population and even more relevant for childhood cancer survivors. In 835 young adult survivors and 1670 matched controls, latent class analysis identified four distinct behaviour patterns: 'risk-avoiding'—with a generally healthy behaviour; 'moderate drinking'—with higher levels of physical activity[45] but moderate alcohol consumption; 'risk-taking'—engaging in several risk behaviours (alcohol, tobacco and marijuana consumption); and 'smoking'—including smoking but not drinking. A considerable proportion of survivors and controls (14 vs 12%) engaged in multiple risk behaviours. Survivors were more likely to be in the 'moderate drinking' and less likely to be in the 'smoking' group, indicating a greater awareness of health compromising effects of tobacco than alcohol. Compared with the general population,[46] survivors engaged in binge drinking later in life compared with healthy peers.

## Medical care in long-term survivors of childhood cancer

Well-organized medical follow-up is important to detect and treat late effects in survivors. However, we found that only a minority of adult survivors of childhood cancer in Switzerland have regular follow-up, and few received written documentation on their diagnosis, therapy and advice for future medical check-ups.[14] An important barrier for not attending follow-up was the belief that follow-up is not necessary.[47]

## On-going and planned studies

New 5-year survivors are integrated continuously into the SCCSS. This makes numbers of the cohort and response rates fluctuate with time.

We plan to send the participants a follow-up questionnaire every 5 years. The next is planned for 2015.

A study funded by the European Union FP7 (PanCareSurFup; running 2011–15) pools data from the SCCSS with data from other European countries, to construct a European cohort of childhood cancer survivors. It aims to describe late mortality, SMNs and cardiac late effects and determine risk factors.

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**Table 5** Characteristics of the Swiss Childhood Cancer Survivor Study population, for responders and non-responders to the questionnaire survey 2007–11 (5-year survivors currently aged >15 years, diagnosed in 1976–2003, aged 0–15 years at diagnosis, $N = 2117$: 1647 adults and 470 adolescents)

| | **Responders ($n = 1505$: 1193 adults and 312 adolescents)** *n* (%)[a] | **Non-responders ($n = 612$: 454 adults and 158 adolescents)** *n* (%)[a] | ***P*-value** |
|---|---|---|---|
| **Socio-demographic factors** | | | |
| Sex | | | |
| Male | 818 (54.4) | 389 (63.6) | |
| Female | 687 (45.7) | 223 (36.4) | <0.001 |
| Current age (years) | | | |
| 16–19.9 | 166 (11.0) | 73 (11.9) | |
| 20–24.9 | 386 (25.7) | 181 (29.6) | |
| 25–29.9 | 407 (27.0) | 118 (19.3) | |
| 30–34.9 | 266 (17.7) | 114 (18.6) | |
| ⩾35 | 280 (18.6) | 126 (20.6) | 0.006 |
| Language region of Switzerland | | | |
| German speaking | 1123 (74.6) | 385 (64.5) | |
| French speaking | 341 (22.7) | 182 (30.5) | |
| Italian speaking | 41 (2.7) | 30 (5.0) | <0.001 |
| **Clinical factors** | | | |
| Diagnosis (ICCC-3 main groups) | | | |
| (I) Leukaemias | 540 (35.9) | 190 (31.1) | |
| (II) Lymphomas | 287 (19.1) | 131 (21.4) | |
| (III) CNS tumours | 182 (12.1) | 79 (12.9) | |
| (IV) Neuroblastoma | 60 (4.0) | 31 (5.1) | |
| (V) Retinoblastoma | 34 (2.3) | 20 (3.3) | |
| (VI) Renal tumours | 101 (6.7) | 25 (4.1) | |
| (VII) Hepatic tumours | 10 (0.7) | 2 (0.3) | |
| (VIII) Bone tumours | 70 (4.7) | 24 (3.9) | |
| (IX) Soft tissue sarcomas | 81 (5.4) | 41 (6.7) | |
| (X) Germ cell tumours | 47 (3.1) | 24 (3.9) | |
| (XI) Other malignant epithelial neoplasms | 19 (1.3) | 8 (1.3) | |
| (XII) Other and unspecified malignant neoplasms | 4 (0.3) | 1 (0.2) | 0.135 |
| Langerhans cell histiocytosis | 70 (4.7) | 36 (5.9) | |
| Age at diagnosis (years) | | | |
| 0–4.9 | 543 (36.1) | 228 (37.3) | |
| 5–9.9 | 410 (27.2) | 184 (30.1) | |
| ⩾10 | 552 (36.7) | 200 (32.7) | 0.187 |
| Time since diagnosis (years) | | | |
| 5–14.9 | 347 (23.1) | 136 (22.2) | |
| 15–24.9 | 732 (48.6) | 286 (46.7) | |
| ⩾25 | 426 (28.3) | 190 (31.1) | 0.453 |

(continued)

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**Table 5** Continued

| | Responders ($n = 1505$: 1193 adults and 312 adolescents) $n$ (%)[a] | Non-responders ($n = 612$: 454 adults and 158 adolescents) $n$ (%)[a] | *P*-value |
|---|---|---|---|
| Therapy | | | |
| Surgery only | 704 (47.1) | 282 (46.6) | |
| Chemotherapy[b] | 161 (10.8) | 74 (12.2) | |
| Radiotherapy[c] | 517 (34.6) | 228 (37.7) | |
| Bone marrow transplantation[d] | 114 (7.6) | 21 (3.5) | 0.004 |

Percentages are based upon available data for each variable. *n*, number.
[a]Column percentages.
[b]Without radiotherapy, may have surgery.
[c]With or without chemotherapy or surgery.
[d]With or without chemotherapy, radiotherapy or surgery.

Radiation doses and chemotherapeutic agents received will be studied in detail.

An on-going research programme (2009–12) on follow-up care funded by the Swiss National Science Foundation (SNF) studies different models of follow-up for childhood cancer survivors in Switzerland and Europe. In addition, all survivors in Switzerland who replied in 2007–11 will receive a questionnaire about their needs and desires for follow-up care after childhood cancer and how they would like to see it organized. Oncologists and general practitioners receive a similar questionnaire.[48–50]

Two projects nested in the SCCSS (from 2011 to 2014; funded by the SNF and the Swiss Cancer League) focus on transition from paediatric to adult follow-up care in Switzerland.

Results from all these studies will provide the basis to develop a standardized model of follow-up for survivors of childhood and adolescent cancer in Switzerland and Europe.

## What are the main strengths and weaknesses?

Strengths of the SCCSS are:

(i) the close link with the national childhood cancer registry and paediatric oncology clinics allows easy access to routine data and clinical information from medical records. Additionally, research findings can promptly be translated into daily practice;
(ii) the high response rate makes results representative for the majority of childhood cancer survivors in Switzerland;
(iii) the SCCSS can easily be extended to assess later outcomes in current survivors and to include new survivors treated with more recent therapies; and
(iv) results of the SCCSS can be compared with results for representative population-based studies performed simultaneously in Switzerland, with results from siblings and with other childhood cancer survivor studies.

Limitations of the study are:

(i) the number of survivors of certain rare cancers and specific therapies in Switzerland is small, limiting the ability to study rare outcomes. This limitation can be overcome by international pooling of data, as in the incipient EU FP7 survey; and
(ii) although the first late effects study (1994–96) included a standardized medical examination and measurements, outcomes assessed in 2007–11 were based on self-reports from a questionnaire. However, we will validate important outcomes with medical records.

## Can I get hold of the data? Where can I find out more?

The SCCR and the SCCSS are collaborative projects between the Swiss Paediatric Oncology Group (SPOG) and the Institute of Social and Preventive Medicine, University of Bern, Switzerland. Our homepage displays detailed information on methods, results and publications (www.childhoodcancerregistry.ch). Researchers interested in collaborative work can contact the principal investigators (Claudia Kuehni, kuehni@ispm.unibe.ch and Nicolas von der Weid, Nicolas.von-der-Weid@chuv.ch) to discuss planned projects or analyses of existing data. The final decision will be made upon presentation of the project to the Scientific Council of the SPOG.

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## Supplementary Data

Supplementary Data are available at *IJE* online.

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