Published in final edited form as: *Int J Cancer*. 2016 Jun 15;138(12):2856-66. doi: 10.1002/ijc.30029

Socioeconomic Disparities in Childhood Cancer Survival in Switzerland

Martin Adam[1,2,3 #], Corina S. Rueegg[3,4 #], Kurt Schmidlin[3], Adrian Spoerri[3], Felix Niggli[5], Michael Grotzer[5], Nicolas X. von der Weid[6], Matthias Egger[3], Nicole Probst-Hensch[1,2], Marcel Zwahlen[3], Claudia E. Kuehni[3]

[#] both authors contributed equally

[1] Swiss Tropical and Public Health Institute, 4002 Basel, Switzerland

[2] University of Basel, 4001 Basel, Switzerland

[3] Institute of Social and Preventive Medicine, University of Bern, 3012 Bern, Switzerland

[4] Department of Health Sciences and Health Policy, University of Lucerne, 6002 Lucerne, Switzerland

[5] Pediatric Hematology-Oncology Unit, University Children's Hospital Zurich, University of Zurich, 8032 Zurich, Switzerland

[6] Pediatric Hematology-Oncology Unit, University Children's Hospital Basel, University of Basel, 4056 Basel, Switzerland

Short title: Socioeconomic Disparities in Cancer Survival

Article Category: Cancer Epidemiology

Keywords: childhood cancer, mortality, 5-year survival, socioeconomic status, leukemia, central nervous system tumor

Abbreviations: Acute lymphoblastic leukemia (ALL); Central nervous system (CNS); 95% Confidence interval (95%CI); Hazard ratios (HR); International Classification of Childhood Cancer, third revision (ICCC-3); Surveillances, Epidemiology and End Results (SEER); Socioeconomic status (SES); Swiss Childhood Cancer Registry (SCCR); Swiss National Cohort (SNC).

Novelty statement: This study explored the unclear role of socioeconomic status (SES) in childhood cancer survival in Switzerland. By design, we overcame limitations of earlier studies, looking specifically at several tumor groups and applying distinct definitions of SES. We found a never shown, significant socioeconomic gap in survival of pediatric CNS tumor patients. Our findings support the notion to standardize cancer therapy protocols for all tumors, to guarantee universal access to optimal cancer treatment for all patients.

Corresponding Author:
Dr. Martin Adam
Swiss Tropical and Public Health Institute
Socinstrasse 57, 4002 Basel, Switzerland
E-mail: martin.adam@unibas.ch
Phone: +41 61 284 83 96, Fax: +41 61 284 81 05

Published in final edited form as: *Int J Cancer*. 2016 Jun 15;138(12):2856-66. doi: 10.1002/ijc.30029

ABSTRACT

In this study, we investigated whether childhood cancer survival in Switzerland is influenced by socioeconomic status (SES), and if disparities vary by type of cancer and definition of SES (parental education, living condition, area-based SES). Using Cox proportional hazards models, we analyzed 5-year cumulative mortality in all patients registered in the Swiss Childhood Cancer Registry diagnosed 1991-2006 below 16 years. Information on SES was extracted from the Swiss census by probabilistic record linkage. The study included 1602 children (33% with leukemia, 20% with lymphoma, 22% with central nervous system (CNS) tumors); with an overall 5-year survival of 77% (95%CI 75-79%). Higher SES, particularly parents' education, was associated with a lower 5-year cumulative mortality. Results varied by type of cancer with no association for leukemia and particularly strong effects for CNS tumor patients, where mortality hazard ratios for the different SES indicators, comparing the highest with the lowest group, ranged from 0.48 (95%CI: 0.28–0.81) to 0.71 (95%CI: 0.44–1.15). We conclude that even in Switzerland with a high quality health care system and mandatory health insurance, socioeconomic differences in childhood cancer survival persist. Factors causing these survival differences have to be further explored, to facilitate universal access to optimal treatment and finally eliminate social inequalities in childhood cancer survival.

Published in final edited form as: *Int J Cancer*. 2016 Jun 15;138(12):2856-66. doi: 10.1002/ijc.30029

INTRODUCTION

In Europe and the US, cancer is a leading cause of childhood death [1-3]. Although overall 5-year survival increased in the last decades reaching now 81% in Switzerland, large differences between types of cancer and regions remain [4]. In adults and adolescents, socioeconomic status (SES) determines long-term outcome after cancer [5-7]. For childhood cancer in contrast, data on survival and SES are scarce and contradictory. In a recent systematic review the authors concluded that socioeconomic gradients in which low SES is associated with inferior childhood cancer survival are ubiquitous in low income countries and common in high income countries [8]. The review further showed that a majority of the European studies were focused on hematologic malignancies and many studies especially from the UK evaluated area-based SES measures. According to the Organisation for Economic Co-operation and Development (OECD) (http://www.oecdbetterlifeindex.org/countries/switzerland/), Switzerland is a high income country with an above average quality of its educational system, mandatory health insurance and a high quality healthcare system, resulting in one of the highest life expectancies in Europe [3, 9, 10]. Despite all this, it has notable differences in mortality and life expectancy between regions and by socioeconomic status, at least in the German speaking part of Switzerland [11, 12] .

In this study, which linked the Swiss Childhood Cancer Registry to National census records, we investigated whether childhood cancer survival in Switzerland is influenced by the socioeconomic status of the patient. We examined several tumor groups (leukemia, acute lymphoblastic leukemia (ALL), lymphoma, central nervous system (CNS) tumors, bone and soft tissue tumors, and embryonal tumors) to assess potential variation by tumor type; and we applied distinct definitions of SES (parents' education, living condition, area-based SES) to describe their potentially modifying effects on cancer survival.

Published in final edited form as: *Int J Cancer*. 2016 Jun 15;138(12):2856-66. doi: 10.1002/ijc.30029

MATERIAL AND METHODS

Study Population and Data Sources

The Swiss Childhood Cancer Registry

In this nationwide survival study, we included all childhood cancer patients diagnosed between 1991 and 2006 at an age <16 years who were registered in the Swiss Childhood Cancer Registry (SCCR, http://childhoodcancerregistry.ch/) [13, 14]. The SCCR registers since 1976 all patients treated for leukemia, lymphoma, central nervous system (CNS) tumors, malignant solid tumors or Langerhans cell histiocytosis in one of the nine pediatric cancer centers in Switzerland. Since 1995 it registers more than 95% of all children diagnosed below age 16 years in Switzerland [15, 16]. The registry contains detailed individual clinical information on medical history, cancer diagnosis, treatment and follow-up, including date and cause of death, if applicable (see paragraph below on "Outcome Measure: Mortality") [14, 16]. Diagnoses are coded according to the International Classification of Childhood Cancer, third revision (ICCC-3) [17].

The Swiss National Cohort

Information on socioeconomic status was retrieved from the Swiss National Cohort (SNC; www.swissnationalcohort.ch), which we described in detail elsewhere [18]. In short, the SNC is a national longitudinal cohort of Switzerland based on deterministic and probabilistic linkage of Census data with mortality records. Participation in the Swiss census was mandatory and the coverage for the 2000 census was estimated to be 98.6% [19]. To examine the potential bias due to the record linkage we reanalyzed the SNC adding unlinked death records and found no effect on relative mortality estimates [20]. In this study, we used data from the Swiss census 1990 and 2000, which includes detailed information on family characteristics and socioeconomic determinants for all Swiss citizens. We further used a publicly available area-based SES index (SES index) as developed by the Department of Geography at the University of Zurich [21], which had been attached by the SNC to the census data.

Linkage of the two data sources SCCR and SNC

Because routine data in Switzerland are anonymous without personal identifiers, we

Published in final edited form as: *Int J Cancer*. 2016 Jun 15;138(12):2856-66. doi: 10.1002/ijc.30029

linked the cases from the SCCR to the SNC using a probabilistic linkage procedure. Information contained in both datasets (sex, date of birth and place of residence) were used for linking the records. Only cases born before, and diagnosed after a census were included in this study to avoid selection bias related to selective exclusion of children who had died before the census and thus could not have been registered. For children born before 1990 and diagnosed after 2000, we used the census 2000 data to assure that the information on socioeconomic status was contemporary and had always been collected prospectively, before the child had been diagnosed with cancer.

Outcome Measure: Mortality

The assembly of follow-up information and the ascertainment of mortality of the patients recorded in the SCCR, is done actively by data managers from the nine pediatric oncology centers of Switzerland for the duration of follow-up in outpatient clinics (generally 5 to 10 years after diagnosis). During this time the data managers yearly report the date when patients were last known to be alive or date and causes of death if a patient has died. Additionally, information on mortality is updated regularly via comparisons with the National mortality statistics and through requests at the communities of residence.

Explanatory variables: Indicators of Socioeconomic Status

Because previous publications showed conflicting results depending on the definition of SES in use [22-24], we compared the effects of several variables collected in the census representing socioeconomic status. These included individual-based SES information (education of the mother or the father in the household), household-based information (number of rooms per person excluding kitchen and bathrooms, square meter living space per person), and a publicly available area-based SES index representing an average measure of net income, education level and job position of the population living in a respective area (community or quarter). For analysis, we categorized the two continuous variables living space and area-based SES index into tertiles. Parental education was grouped into “compulsory schooling or less” (up to 9 years of education), “secondary education” (10 to 16 years, high school, teachers training colleges, technical colleges and upper vocational education) and “tertiary education” (16 years or more, university degree). Number of habitable rooms per person was grouped into: “<1 room

Published in final edited form as: *Int J Cancer*. 2016 Jun 15;138(12):2856-66. doi: 10.1002/ijc.30029

per person" (more than 1 person per room = overcrowded), "1-1.25 room per person", ">1.25 room per person" [25].

Statistical Analyses

For the 5-year survival analyses, follow-up time was calculated from date of diagnosis until date of death, the last date the patient was known to be alive or exactly 5 years after diagnosis, whichever came first. We calculated survival as cumulative mortality functions (one minus the Kaplan-Meier survival estimates), separately for each SES indicator, first for all cancers together and then stratified by main types of cancer (leukemia, acute lymphoblastic leukemia (ALL), lymphoma, central nervous system (CNS) tumors, bone and soft tissue tumors, and embryonal tumors). Univariable and multivariable Cox proportional hazards regression models were used to assess the association between survival and the different SES measures. We reported hazard ratios (HR) with 95% confidence intervals (95%CI). The multivariable Cox proportional hazards models included, in addition to the SES indicator: gender (male, female); age at diagnosis (0-4, 5-9, 10-13, 14-16); period of diagnosis (1991-1998, 1999-2006); and, for the model including all cancers, type of cancer (leukemia, ALL, lymphoma, CNS tumors, bone and soft tissue tumors, embryonal tumors). To calculate a p-value for trend over the SES levels, we included SES as a continuous variable coded from 1 to 3.

For CNS tumors, we explored in additional analyses whether the strength of the SES survival association was reduced when including in serial manner baseline information known or suspected to be prognostic for survival. We defined baseline information as being prognostic for survival if they were associated with mortality in an univariable Cox Proportional Hazards regression model. We investigated the following prognostic information:: WHO staging (grade I, II, III and IV); histopathological tumor groups (PNET/Medulloblastoma; low-grade glioma; high-grade glioma; ependymoma; and others); first line therapy protocol (surgery only; chemotherapy with/without surgery; radiotherapy with/without surgery or chemotherapy; and, bone marrow transplantation); clinical trial participation status (study patient; not study patient but treated according to protocol; and, not treated according to a study protocol); localization (supratentorial hemispheric; supratentorial midline; infratentorial; and spinal) and, size of the treatment center (>40 patients/year vs. ≤40 patients/year).

Published in final edited form as: *Int J Cancer*. 2016 Jun 15;138(12):2856-66. doi: 10.1002/ijc.30029

All p-values are two sided and a p-value of ≤0.05 was considered as statistically significant. Statistical analyses were performed using STATA, version 12 (StataCorp. 2011. Stata Statistical Software: Release 12. College Station, TX: StataCorp LP).

Published in final edited form as: *Int J Cancer*. 2016 Jun 15;138(12):2856-66. doi: 10.1002/ijc.30029

RESULTS

Characteristics of the Study Population

Overall, 1867 childhood cancer patients met the inclusion criteria for linkage with the census 1990 or 2000. From these we excluded 177 patients with rare or unspecific diagnoses (epithelial neoplasm; malignant melanomas; and, other or unspecified malignant tumors). For 94.8% (1602 of 1690) we had a date the patient was known to be alive, or a date of death. Of these, 56.8% were male, 47.9% were diagnosed after age 10 years, 33.0% (528) had been diagnosed with leukemia (399 with ALL), 22.1% (354) with a CNS tumor, 19.6% (314) with lymphoma, 14.4% (231) with a bone or a soft tissue tumor, and 10.9% (175) with an embryonal tumor (**Tables 1 and S1**).

Socioeconomic Status and Survival

All types of cancer

In the whole population (N=1602) including all diagnostic groups, we calculated a cumulative five year mortality of 23% (95% confidence interval (95%CI) 21-25), highest for patients with CNS tumors (31%; 95%CI 26-35) and lowest for lymphoma patients (8%; 95%CI 5-11). Multivariable cox regression models (including all diagnostic groups) showed higher survial (with higher hazard ratios across all SES indicators) in the highest socioeconomic group (**Table 2**, first column and **Figure 1**, first graph). P-values for trend were below 0.1 for paternal education, maternal education and living space (**Table 2**). Results were similar in the univariable (**Table S2**) and the multivariable (**Table 2**) models.

Survival from Leukemia

For leukemia patients (N=528) both univariable and multivariable models showed no clear evidence for an association between SES and survival, with hazard ratios close to one and all p-values for trend >0.2 (**Tables 2** and **S2**, second column; **Figure 1**, second graph). Results of a sensitivity analysis including only 399 ALL survivors were comparable (**Tables S3** and **S4**, first column).

Survival from CNS tumors

Published in final edited form as: *Int J Cancer*. 2016 Jun 15;138(12):2856-66. doi: 10.1002/ijc.30029

For survivors of CNS tumors (N=354) there was strong evidence for a lower survival in the lowest socioeconomic group (**Tables 2** and **S2,** fourth column). This applied to all SES indicators but was strongest for paternal (**Figure 1**, graph 4) and maternal education, with hazard ratios of 0.48 and 0.52, respectively, and p-values for trend of 0.008 and 0.014, respectively; comparing the highest with the lowest group of education in the multivariable cox models (**Table 2**). The association was somewhat weaker with household-based SES measures with a HR of 0.56 (p=0.023) for rooms per person and 0.61 (p=0.056) for living space; and weakest for the area-based SES index (HR 0.71 for the highest tertile, p=0.170). Results were similar in the univariable regression model (**Table S2).**

As SES disparities in childhood cancer survival were most prominent in CNS patients, we characterized the CNS tumor patients in more detail and explored in additional analyses whether these survival differences could be explained by different clinical baseline information (**Table 3**). Among patients of CNS tumors, most were classified as grade I (41%) or IV (33%) by the WHO, had a tumor histology of low-grade glioma (42%) or PNET/Medulloblastoma (24%) and had an infratentorial localization (53%). About half (49%) were treated with surgery only and 37% with radiotherapy. Almost half of the CNS patients (48%) had not been treated according to a protocol and two thirds had been treated in a large treatment center with more than 40 childhood cancer patients per year.

In the univariable model, WHO grade, histology, therapy and trial participation were all significantly associated with survival (**Table 3**), while tumor localization and size of the treatment center were not associated. Therefore, tumor localization and size of the treatment center were no longer included in the multivariable models to further explore the relationship between survival and SES in CNS tumor patients. When including in serial manner the other variables (WHO grade, histology, therapy, and clinical trial participation) in the multivariable models, the hazard ratio of the SES- survival association in CNS patients remained almost unaffected (**Table 4**).

Survival from lymphoma, embryonal tumors, bone tumors and soft tissue sarcoma

Published in final edited form as: *Int J Cancer*. 2016 Jun 15;138(12):2856-66. doi: 10.1002/ijc.30029

Comparable to the leukemia patients, almost no association between survival and SES levels was found for embryonal tumors, and bone tumor and soft tissue sarcoma in multivariable and univariable cox regression models (**Tables S3** and **S4**, second and third columns; **Figure 1**, last two graphs). Results for lymphoma were more comparable to those found for CNS tumor patients (**Tables 2** and **S2**, third column; **Figure 1**, third graph). However, due to lower patient numbers only the association between paternal education and survival in lymphoma patients was statistically significant (p=0.018) (**Table 2**).

Published in final edited form as: *Int J Cancer*. 2016 Jun 15;138(12):2856-66. doi: 10.1002/ijc.30029

DISCUSSION

In this study we found strong evidence for a deprivation gap in survival of patients with CNS tumors, with survival reduced to half in children from not well-educated families. This is the first population-based study on childhood cancer survival and socioeconomic status of the family that considered several SES indicators collected prospectively in the census before the child's cancer diagnosis. The results were consistent across all SES indicators but most pronounced for paternal and maternal education, and were not readily explained by differences in clinical baseline information or other measures at hand. For other cancer diagnoses, SES disparities in childhood cancer survival were less evident and for leukemia we found none.

Comparison with other studies

For childhood cancer, data on survival and socioeconomic status of the family are scarce and contradictory. In a recent systematic review the authors showed that, while mostly older studies found no evidence for a change in childhood cancer survival by SES, many newer studies found survival rates to be lower in the deprived socioeconomic groups [8]. They further established the fact that survival in patients of childhood cancer varies by type of cancer and SES indicator in use and the socio-cultural context of the patient's country of residence. The overall study's results on childhood cancer survival differentials accentuate the importance to examine different definitions of SES and their distinct associations with cancer types and clinical markers. Especially, when considering the fact that childhood cancer survival, besides tumor type and the child's response to treatment, seems to be mainly explained by differences in patient's tumor stage and the applied therapy [26, 27], and both these factors have shown to be differently influenced by socioeconomic status, depending on the SES definition in use [8, 28]. However, an international comparison of study findings in this context is difficult due to dissimilarities in welfare systems, including access to health care and public family support, coverage and distance to treatment facilities, lifestyle and socio-cultural aspects and methodological differences between studies.

Interestingly, we found no clear trend between survival and SES for leukemia, although this was the largest diagnostic group. Our results were corroborated by a recent

Published in final edited form as: *Int J Cancer*. 2016 Jun 15;138(12):2856-66. doi: 10.1002/ijc.30029

German study which found that socioeconomic factors were not related to ALL survival in children [29]. They claimed their results to be plausible by the fact that irrespective of coverage by private or statutory health insurance (Germany has a similar universal health care system like Switzerland with two main types of health insurance: private insurance and statutory health insurance) and of social background, all children and adolescents have free access to health care. Additionally, they stated that more than 90% of all pediatric oncology patients are included in clinical trials of therapy optimization studies in Germany. This is as well comparable to Switzerland where 73% of the childhood leukemia patients are included in clinical trials and about 92% of the patients are treated according to a study protocol. Nevertheless, recent European studies found children with childhood leukemia from a lower parental socioeconomic level to experience worse survival [26, 30, 31].

To our knowledge, only a few US-based studies, using data from the Surveillances, Epidemiology and End Results (SEER) Program, focused on brain tumor survival in children. Two reported a lower survival in African Americans [32], particularly for astrocytomas [33]. The third found only trends by race for certain histological subtypes, despite a sample size of 2799 [34]. In an English study, CNS tumor survival was influenced only by age, morphology and stage, but not socioeconomic status and region [35].

Generally, our findings fit well into the literature, but the large survival gap found for CNS tumors, with survival reduced to half in children of low educated parents, sticks out. Similar findings were only reported from South Korea [28, 36] The survival gap we found was considerably larger than what has been reported in US studies. A main reason might be the much lower number of Swiss children with CNS tumors being included in clinical trials (25.7%) and treated according to a study protocol (45.4%), when compared with childhood leukemia patients. Another reason might be the inclusion of individual and household-based SES in our study, additionally to the commonly used area-based SES indicators. The survival differentials were in fact smaller for household-based SES indicators and disappeared for the area-based indicator. In analogy, an English study found smaller deprivation gaps in survival of adult cancer for large compared to small geographic units, suggesting a dilution effect caused by aggregated exposure measures [37]. The common use of area-based SES indicators might have diluted survival differentials in many studies.

Published in final edited form as: *Int J Cancer*. 2016 Jun 15;138(12):2856-66. doi: 10.1002/ijc.30029

Potential underlying causes of survival differences in CNS tumor patients

SES disparities in cancer outcome have been explained by three main causes [27, 38]. First, tumor characteristics, particularly differences in stage at diagnosis caused by longer patient or health provider delay [39, 40], misclassification of stage because of less thorough diagnostic work-up, or differences in biological tumor characteristics [41, 42]. Second, patient characteristics, particularly differences in comorbidity, risk behaviors, nutrition and psychosocial factors. Third, differences in treatment, by availability of specialist medical expertise or differences in patient adherence.

Many studies in adults and children have in fact suggested that once treatment is equal, as in clinical trials or highly specialized clinics, SES disparities disappear [41-43]. Comorbidities and health behaviors are unlikely to play a major role in young children. Even in adults, studies looking at relative survival stratified by socioeconomic groups, e.g. compensating for differences in background mortality suggest that comorbidities play a minor role [44].

In our study, we tried to assess the effect of underlying causes as explanatory factors for our findings. Adjustment for WHO grade at diagnosis, histological type and localization did not eliminate the gap in CNS tumor survival, suggesting that delayed diagnosis or differences in tumor morphology or topography between social groups did not play an important role [39, 40]. However, we could include only basic measures and residual confounding is possible. We also tested whether differences in initial treatment or inclusion in a clinical trial explained our findings. Adjustment for these factors did not attenuate but, if anything, accentuate the survival gap. However, the treatment data we had was limited.

In Switzerland almost all children and adolescents with cancer are treated in one of the nine pediatric oncology centers. In contrast to leukemia therapy, the treatment of brain and spinal tumors usually necessitates a very interdisciplinary team including the pediatric oncologist, neurosurgeons and radiotherapists. Usually the latter two professional groups are not pediatric specialists, with exception of specialists in the two largest Swiss centers. Treatment within study protocols and the clinical decision making

Published in final edited form as: *Int J Cancer*. 2016 Jun 15;138(12):2856-66. doi: 10.1002/ijc.30029

process (case discussion in tumor boards, inclusion of national or even international experts) become more and more important, as early diagnosis and therapy (essentially surgery) are of crucial relevance for the therapy success of childhood cancer. In the last twenty-five years over ninety percent of the leukemia patients had been treated by an international standardized protocol, but less than half of the CNS tumor patients. In summary, in comparison with leukemia, CNS tumors are more heterogeneous, have less standardized treatment and typically involve complex, high-skill surgery, necessitating pediatric intensive care admission. Although our data do not allow proving this, we think that ability of wealthier and higher educated parents to obtain second opinion evaluations, better access to a more thorough diagnostic work-up in treatment centers of excellence and higher referral to highly skilled neurosurgeons, radiotherapists and oncologists, could explain our findings. However, such associations are speculative and remain to be assessed in future evaluations.

Strengths and Limitations

Our study design allowed overcoming several limitations of earlier studies on SES and childhood cancer survival. First, the study was nationwide and largely avoided participation bias. We included all cases of the national childhood cancer registry fulfilling the inclusion criteria for linkage with the census. Second, we obtained information on socioeconomic status from the census, avoiding reporting bias. Due to the conditions for linkage (the children had to be born before and diagnosed after the census), the information on SES was always collected prospectively, before the child had been diagnosed. This eliminated the possibility of differential reporting by parents of cured and deceased children, and made sure that the exposure preceded the outcome, i.e. that the SES did not change as a consequence of the diagnosis. Third, the availability of different definitions of socioeconomic status with data on individual-based (parental education), household-based (number of rooms per person, square meter living space per person) and area-based SES information is a unique feature of our study. It allowed assessing the robustness of our findings and analyzing potential differences between the examined SES proxies [22-24]. Last, the availability of detailed clinical information allowed exploring pathways in anadditional analysis of CNS tumor patients. The study has also limitations. First, we excluded children born after 1990 and diagnosed before 2000, potentially introducing selection bias not including children born and diagnosed between the two censuses.

Published in final edited form as: *Int J Cancer*. 2016 Jun 15;138(12):2856-66. doi: 10.1002/ijc.30029

Nevertheless, as survival might be linked to SES, including these children may on the other hand have introduced survivor bias. Second, although we included many SES proxies in the analysis, we lacked a direct measure of income or wealth. Third, our sample size, although nationwide, was reduced by the linkage design, due to missings in the cancer registration and missing patient follow up information (5-10% of all patients), resulting in limited statistical power for analyzing diagnostic subgroups. In addition, the data linkage resulted in a higher proportion of patients with older age at diagnosis, so that relative frequencies of different tumors, and age-sex distribution in our sample differed somewhat from a random, sample of pediatric cancer patients. This should, however, not have affected our findings on the association between SES and survival. Fourth, we assessed the effect of different SES measures individually, and did not develop a score or conjunct measure of SES. Therefore, the total burden of mortality explained by lower socioeconomic status might in fact be even bigger than our results suggest. Last, we had no information on minor comorbidities, health behaviors, social support and patients' adherence to treatment, and the available information on staging, biological prognostic factors and treatment was only basic, leaving room for residual confounding.

Conclusions and implications

In this study, conducted in a high-income country with mandatory health insurance, a high quality health care system and high absolute cancer survival rates, we found a large socioeconomic gap in survival of pediatric CNS tumors. The lack of SES disparities in leukemia, where treatment is highly standardized and most patients are included in clinical trials suggests that the gap found for CNS tumor patients may be explained by differences in the therapeutic process. Complete elimination of the survival differences would lead to an overall 5-year survival of 75% for CNS tumors, the risk observed in the least deprived SES group. Every effort should therefore be made to understand the reasons for the detected survival differences, to improve early diagnosis and facilitate universal access to state-of-the-art treatment in all countries, in order to reduce socioeconomic inequalities and international differences in childhood cancer survival.

Published in final edited form as: *Int J Cancer*. 2016 Jun 15;138(12):2856-66. doi: 10.1002/ijc.30029

ACKNOWLEDGEMENTS

We thank all pediatric cancer centers organized in the SPOG for the data collection within the Swiss Childhood Cancer Registry and Swiss Federal Statistical Office for providing the data necessary to build the Swiss National Cohort. Swiss Pediatric Oncology Group (SPOG) Scientific Committee: Prof. Dr. med. R. Ammann, Bern; Dr. med. R. Angst, Aarau; Prof. Dr. med. A. Ansari, Geneva; PD Dr. med. M. Beck Popovic, Lausanne; Dr. med. E. Bergstraesser, Zurich; Dr. med. P. Brazzola, Bellinzona; Dr. med. J. Greiner, St. Gallen; Prof. Dr. med. M. Grotzer, Zurich; Dr. med. H. Hengartner, St. Gallen; Prof. Dr. med. T. Kuehne, Basel; Prof. Dr. med. C. Kuehni, Bern; Prof. Dr. med. K. Leibundgut, Bern; Prof. Dr. med. F. Niggli, Zurich; PD Dr. med. J. Rischewski, Lucerne; Prof. Dr. med. N. von der Weid, Basel. Swiss National Cohort Study Group (SNC): Matthias Egger (Chairman of the Executive Board), Adrian Spoerri and Marcel Zwahlen (all Bern), Milo Puhan (Chairman of the Scientific Board), Matthias Bopp (both Zurich), Nino Künzli (Basel), Fred Paccaud (Lausanne) and Michel Oris (Geneva).

Conflict of Interest Statement: The authors declare that they do not have any conflicts of interest. No form of payment was given to any of the authors to produce the manuscript. The study received funding through peer-reviewed grants from non-profit organizations (the Swiss Cancer League and the Swiss National Foundation). Those providing the funding had no involvement in 1) study design; 2) collection, analysis, and interpretation of data; 3) writing of the report; or 4) decision to submit the paper for publication.

Funding: This work was supported by Oncosuisse (OCS – 01869 – 02 – 2006, KLS 01869-02-2006) and the Swiss National Science Foundation (Prosper 3233-069348 to CK, and SNC (3347CO-108806, 33CS30_134273 and 33CS30_148415)). The work of the Swiss Childhood Cancer Registry is supported by the Swiss Paediatric Oncology Group (www.spog.ch), Schweizerische Konferenz der kantonalen Gesundheitsdirektorinnen und -direktoren (www.gdk-cds.ch), Swiss Cancer Research (www.krebsforschung.ch), Kinderkrebshilfe Schweiz (www.kinderkrebshilfe.ch), Ernst-Göhner Stiftung, Stiftung Domarena, and National Institute of Cancer Epidemiology and Registration (www.nicer.ch). Those providing funding had no role in study design, data collection and analysis, decision to publish, or preparation of the manuscript.

REFERENCES

1. Bosetti C, Bertuccio P, Chatenoud L, Negri E, Levi F, La Vecchia C. Childhood cancer mortality in Europe, 1970-2007. *Eur J Cancer* 2010;**46**: 384-94.

2. Siegel R, Naishadham D, Jemal A. Cancer statistics, 2013. *CA Cancer J Clin* 2013;**63**: 11-30.

3. Statistik Bf. Statistisches Jahrbuch der Schweiz 2015 Zürich: Neue Zürcher Zeitung, 2015:608.

4. Gatta G, Botta L, Rossi S, Aareleid T, Bielska-Lasota M, Clavel J, Dimitrova N, Jakab Z, Kaatsch P, Lacour B, Mallone S, Marcos-Gragera R, et al. Childhood cancer survival in Europe 1999-2007: results of EUROCARE-5--a population-based study. *The Lancet Oncology* 2014;**15**: 35-47.

5. Ellis L, Coleman MP, Rachet B. How many deaths would be avoidable if socioeconomic inequalities in cancer survival in England were eliminated? A national population-based study, 1996-2006. *Eur J Cancer* 2012;**48**: 270-8.

6. Rachet B, Ellis L, Maringe C, Chu T, Nur U, Quaresma M, Shah A, Walters S, Woods L, Forman D, Coleman MP. Socioeconomic inequalities in cancer survival in England after the NHS cancer plan. *Br J Cancer* 2010;**103**: 446-53.

7. Singh GK, Williams SD, Siahpush M, Mulhollen A. Socioeconomic, Rural-Urban, and Racial Inequalities in US Cancer Mortality: Part I-All Cancers and Lung Cancer and Part II-Colorectal, Prostate, Breast, and Cervical Cancers. *Journal of cancer epidemiology* 2011;**2011**: 107497.

8. Gupta S, Wilejto M, Pole JD, Guttmann A, Sung L. Low socioeconomic status is associated with worse survival in children with cancer: a systematic review. *PloS one* 2014;**9**: e89482.

9. Bopp M, Minder CE, Swiss National C. Mortality by education in German speaking Switzerland, 1990-1997: results from the Swiss National Cohort. *Int J Epidemiol* 2003;**32**: 346-54.

10. Reinhardt UE. The Swiss health system - Regulated competition without managed care. *Jama-J Am Med Assoc* 2004;**292**: 1227-31.

11. Moser A, Panczak R, Zwahlen M, Clough-Gorr KM, Spoerri A, Stuck AE, Egger M, Cohort SN. What does your neighbourhood say about you? A study of life expectancy in 1.3 million Swiss neighbourhoods. *Journal of Epidemiology and Community Health* 2014;**68**: 1125-32.

12. Spoerri A, Zwahlen M, Egger M, Gutzwiller F, Minder C, Bopp M. Educational inequalities in life expectancy in German speaking part of Switzerland 1990-1997: Swiss National Cohort. *Swiss Med Wkly* 2006;**136**: 145-8.

13. Adam M, Kuehni CE, Spoerri A, Schmidlin K, Gumy-Pause F, Brazzola P, Probst-Hensch N, Zwahlen M. Socioeconomic Status and Childhood Leukemia Incidence in Switzerland. *Front Oncol* 2015;**5**: 139.

14. Michel G, von der Weid NX, Zwahlen M, Adam M, Rebholz CE, Kuehni CE, Swiss Childhood Cancer R, Swiss Paediatric Oncology Group Scientific C. The Swiss Childhood Cancer Registry: rationale, organisation and results for the years 2001-2005. *Swiss Med Wkly* 2007;**137**: 502-9.

15. Adam M, von der Weid N, Michel G, Zwahlen M, Lutz JM, Probst-Hensch N, Niggli F, Kuehni C, Swiss Pediatric Oncology G, Swiss Association of Cancer R. Access to specialized pediatric cancer care in Switzerland. *Pediatr Blood Cancer* 2010;**54**: 721-7.

16. Kuehni CE, Rueegg CS, Michel G, Rebholz CE, Strippoli MPF, Niggli FK, Egger M, von der Weid NX. Cohort profile: The Swiss Childhood Cancer Survivor Study. *International Journal of Epidemiology* 2012;**41**: 1553-64.

17. Steliarova-Foucher E, Stiller C, Lacour B, Kaatsch P. International Classification of Childhood Cancer, third edition. *Cancer* 2005;**103**: 1457-67.

18. Bopp M, Spoerri A, Zwahlen M, Gutzwiller F, Paccaud F, Braun-Fahrlander C, Rougemont A, Egger M. Cohort Profile: the Swiss National Cohort--a longitudinal study of 6.8 million people. *Int J Epidemiol* 2009;**38**: 379-84.

19. Renaud A. Methodology Report – Coverage Estimation for the Swiss Population Census 2000. Neuchâtel SSFSO, 2004.

20. Schmidlin K, Clough-Gorr KM, Spoerri A, Egger M, Zwahlen M, Swiss National C.

Impact of unlinked deaths and coding changes on mortality trends in the Swiss National Cohort. *BMC Med Inform Decis Mak* 2013;**13**: 1.

21. Hermann M, Heye C, Leuthold H. Soziokulturelle Unterschiede in der Schweiz. Vier Indizes zu räumlichen Disparitäten, 1990-2000 Neuchâtel: Swiss Federal Statistical Office (SFSO), 2005.

22. Adam M, Rebholz CE, Egger M, Zwahlen M, Kuehni CE. Childhood leukaemia and socioeconomic status: what is the evidence? *Radiat Prot Dosimetry* 2008;**132**: 246-54.

23. Poole C, Greenland S, Luetters C, Kelsey JL, Mezei G. Socioeconomic status and childhood leukaemia: a review. *Int J Epidemiol* 2006;**35**: 370-84.

24. Smith GD, Whitley E, Dorling D, Gunnell D. Area based measures of social and economic circumstances: cause specific mortality patterns depend on the choice of index. *J Epidemiol Community Health* 2001;**55**: 149-50.

25. Myers D, Baer WC, Choi SY. The changing problem of overcrowded housing. *Journal of the American Planning Association* 1996;**62**: 66-84.

26. Syse A, Lyngstad TH, Kravdal O. Is mortality after childhood cancer dependent on social or economic resources of parents? A population-based study. *Int J Cancer* 2012;**130**: 1870-8.

27. Woods LM, Rachet B, Coleman MP. Origins of socio-economic inequalities in cancer survival: a review. *Ann Oncol* 2006;**17**: 5-19.

28. Kong KA, Khang YH, Cha ES, Moon EK, Lee YH, Lee WJ. Childhood cancer mortality and socioeconomic position in South Korea: a national population-based birth cohort study. *Cancer Causes Control* 2010;**21**: 1559-67.

29. Erdmann F, Kaatsch P, Zeeb H, Roman E, Lightfoot T, Schuz J. Survival from childhood acute lymphoblastic leukaemia in West Germany: does socio-demographic background matter? *Eur J Cancer* 2014;**50**: 1345-53.

30. Lightfoot TJ, Johnston WT, Simpson J, Smith AG, Ansell P, Crouch S, Roman E, Kinsey SE. Survival from childhood acute lymphoblastic leukaemia: the impact of social inequality in the United Kingdom. *Eur J Cancer* 2012;**48**: 263-9.

31. Sergentanis T, Dessypris N, Kanavidis P, Skalkidis I, Baka M, Polychronopoulou S, Athanassiadou F, Stiakaki E, Frangandrea I, Moschovi M, Petridou ET. Socioeconomic status, area remoteness, and survival from childhood leukemia: results from the Nationwide Registry for Childhood Hematological Malignancies in Greece. *Eur J Cancer Prev* 2013;**22**: 473-9.

32. Ries LAG, Smith MA, Gurney JG, Linet M, Tamra T, Young JL, Bunin GR. *Cancer Incidence and Survival among Children and Adolescents: United States SEER Program, 1975-1995*ed., vol. NIH Pub. No. 99-4649. Bethesda, MD: National Cancer Institute, SEER Program, 1999.

33. Linabery AM, Ross JA. Childhood and adolescent cancer survival in the US by race and ethnicity for the diagnostic period 1975-1999. *Cancer* 2008;**113**: 2575-96.

34. Barnholtz-Sloan JS, Severson RK, Stanton B, Hamre M, Sloan AE. Pediatric brain tumors in non-Hispanics, Hispanics, African Americans and Asians: differences in survival after diagnosis. *Cancer Causes Control* 2005;**16**: 587-92.

35. Tseng JH, Tseng MY. Survival Analysis of Children with Primary Malignant Brain Tumors in England and Wales: A Population-Based Study. *Pediatric Neurosurgery* 2006;**42**: 67-73.

36. Son M, Kim J, Oh J, Kawachi I. Inequalities in childhood cancer mortality according to parental socioeconomic position: A birth cohort study in South Korea. *Social science & medicine* 2011;**72**: 108-15.

37. Woods LM, Rachet B, Coleman MP. Choice of geographic unit influences socioeconomic inequalities in breast cancer survival. *Br J Cancer* 2005;**92**: 1279-82.

38. Bhatia S. Influence of race and socioeconomic status on outcome of children treated for childhood acute lymphoblastic leukemia. *Curr Opin Pediatr* 2004;**16**: 9-14.

39. Dang-Tan T, Franco EL. Diagnosis delays in childhood cancer: a review. *Cancer* 2007;**110**: 703-13.

40. Kukal K, Dobrovoljac M, Boltshauser E, Ammann RA, Grotzer MA. Does diagnostic delay result in decreased survival in paediatric brain tumours? *Eur J Pediatr* 2009;**168**: 303-10.

41. Byers TE, Wolf HJ, Bauer KR, Bolick-Aldrich S, Chen VW, Finch JL, Fulton JP, Schymura MJ, Shen T, Van Heest S, Yin X, Patterns of Care Study G. The impact of

Published in final edited form as: *Int J Cancer*. 2016 Jun 15;138(12):2856-66. doi: 10.1002/ijc.30029

socioeconomic status on survival after cancer in the United States : findings from the National Program of Cancer Registries Patterns of Care Study. *Cancer* 2008;**113**: 582-91.

42. Rapiti E, Fioretta G, Schaffar R, Neyroud-Caspar I, Verkooijen HM, Schmidlin F, Miralbell R, Zanetti R, Bouchardy C. Impact of socioeconomic status on prostate cancer diagnosis, treatment, and prognosis. *Cancer* 2009;**115**: 5556-65.

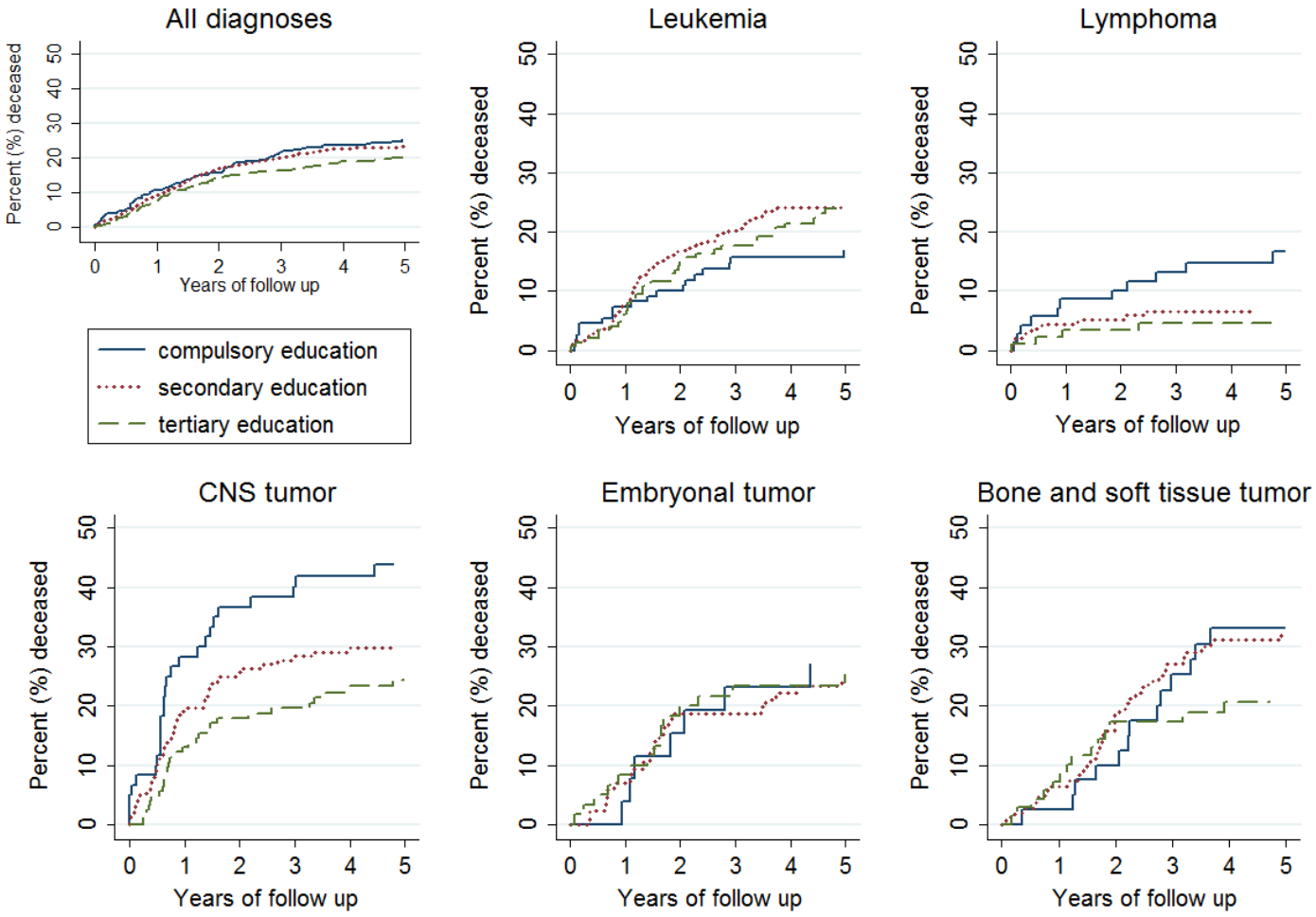
43. Nur U, Rachet B, Parmar MK, Sydes MR, Cooper N, Lepage C, Northover JM, James R, Coleman MP, collaborators A. No socioeconomic inequalities in colorectal cancer survival within a randomised clinical trial. *Br J Cancer* 2008;**99**: 1923-8.

44. Rachet B, Woods LM, Mitry E, Riga M, Cooper N, Quinn MJ, Steward J, Brenner H, Esteve J, Sullivan R, Coleman MP. Cancer survival in England and Wales at the end of the 20th century. *Br J Cancer* 2008;**99 Suppl 1**: S2-10.

Published in final edited form as: *Int J Cancer*. 2016 Jun 15;138(12):2856-66. doi: 10.1002/ijc.30029

Figure 1. Cumulative mortality over the first 5 years after cancer diagnosis by education level of the father, overall and by type of cancer

Figure legend: CNS = Central Nervous System



Published in final edited form as: *Int J Cancer*. 2016 Jun 15;138(12):2856-66. doi: 10.1002/ijc.30029

Table 1. Characteristics of the Study Population: Overall and by Type of Tumor (see online Table S1 for Embryonal Tumors, and Bone and Soft Tissue Tumors)

Characteristics	All diagnoses (N=1602)		Leukemia (N=528)		Lymphoma (N=314)		CNS Tumors (N=354)	
	N	%[a]	N	%[a]	N	%[a]	N	%[a]
Demographic characteristics								
Gender								
Male	910	56.8	317	60.0	197	62.7	186	52.5
Female	692	43.2	211	40.0	117	37.3	168	47.5
Age at diagnosis (years)								
0-4	318	19.9	148	28.0	20	6.4	57	16.1
5-9	516	32.2	174	33.0	83	26.4	151	42.7
10-13	519	32.4	144	27.3	124	39.5	107	30.2
14-16	249	15.5	62	11.7	87	27.7	39	11.0
Period of diagnosis								
1991-1994	462	28.8	174	33.0	79	25.2	82	23.2
1995-1998[b]	276	17.2[b]	88	16.7[b]	66	21.0[b]	62	17.5[b]
1999-2002	421	26.3	131	24.8	82	26.1	100	28.3
2003-2006	443	27.7	135	25.6	87	27.7	110	31.1
Census data used								
1990	841	52.5	282	53.4	173	55.1	163	46.1
2000	761	47.5	246	46.6	141	44.9	191	54.0
Socioeconomic characteristics								
Education status of the father								
Compulsory education	304	20.0	109	21.8	69	23.6	60	17.9
Secondary education	726	47.9	243	48.7	136	46.4	152	45.4
Tertiary education	487	32.1	147	29.5	88	30.0	123	36.7
Missing	85		29		21		19	
Education status of the mother								
Compulsory education	468	29.4	156	29.7	98	31.5	95	27.0
Secondary education	939	58.9	297	56.5	188	60.5	214	60.8
Tertiary education	187	11.7	73	13.9	25	8.0	43	12.2
Missing	8		2		3		2	
Rooms per person								
< 1 room/person	442	27.7	144	27.6	93	29.7	91	25.8
1-1.25 rooms/person	583	36.6	192	36.8	99	31.6	146	41.4
> 1.25 rooms/person	568	35.7	186	35.6	121	38.7	116	32.9
Missing	9		6		1		1	
Living space (in m^2)								
Lower tertile	467	33.8	155	34.7	93	33.9	101	33.3
Medium tertile	457	33.1	139	31.1	92	33.6	100	33.0
Upper tertile	457	33.1	153	34.2	89	32.5	102	33.7
Missing	221		81		40		51	
Area-based SES index								
Lower tertile	545	34.0	164	31.1	116	36.9	116	32.8
Medium tertile	541	33.8	199	37.7	100	31.9	112	31.6
Upper tertile	516	32.2	165	31.3	98	31.2	126	35.6

Abbreviations: CNS, Central Nervous System; N, Number; P, P-value; SES, Socioeconomic Status

Published in final edited form as: *Int J Cancer*. 2016 Jun 15;138(12):2856-66. doi: 10.1002/ijc.30029

[a] Proportions are calculated based on available information within each characteristic.

[b] Small proportion of cancer diagnoses in this period because of fewer linkable cancer survivors with the Census dataset.

Published in final edited form as: *Int J Cancer*. 2016 Jun 15;138(12):2856-66. doi: 10.1002/ijc.30029

Table 2. Association between SES Indicators and Mortality (Multivariable Cox Proportional Hazard Models): Overall and by Type of Tumor (see online Table S2 for Results of the Univariable Cox Models)

	All diagnostic groups[a] (N=1602)				Leukemia (N=528)				Lymphoma (N=314)				CNS Tumors (N=354)			
SES	**HR[b]**	**(95%CI)**	**P**	**P[c]**	**HR[d]**	**(95%CI)**	**P**	**P[c]**	**HR[d]**	**(95%CI)**	**P**	**P[c]**	**HR[d]**	**(95%CI)**	**P**	**P[c]**
Education status of the father				**0.036**				**0.234**				**0.018**				**0.008**
Compulsory education	1				1				1				1			
Secondary education	0.85	(0.64-1.11)	0.226		1.39	(0.81-2.38)	0.228		0.40	(0.16-1.02)	0.055		0.62	(0.38-1.01)	0.055	
Tertiary education	0.72	(0.53-0.98)	0.034		1.45	(0.82-2.58)	0.201		0.26	(0.08-0.85)	0.025		0.48	(0.28-0.81)	0.006	
Education status of the mother				**0.020**				**0.830**				**0.287**				**0.014**
Compulsory education	1				1				1				1			
Secondary education	0.81	(0.65-1.02)	0.078		1.06	(0.69-1.61)	0.797		0.71	(0.30-1.66)	0.428		0.59	(0.39-0.90)	0.013	
Tertiary education	0.67	(0.45-0.98)	0.039		1.05	(0.58-1.91)	0.871		0.40	(0.05-3.19)	0.385		0.52	(0.26-1.05)	0.070	
Rooms per person				**0.111**				**0.406**				**0.060**				**0.023**
< 1 room/person	1				1				1				1			
1-1.25 room/person	0.76	(0.59-0.98)	0.032		0.89	(0.55-1.43)	0.630		0.88	(0.35-2.23)	0.795		0.61	(0.39-0.97)	0.035	
> 1.25 room/person	0.80	(0.62-1.04)	0.095		1.19	(0.76-1.87)	0.454		0.35	(0.12-1.06)	0.062		0.56	(0.34-0.92)	0.021	
Living space (in m^2)				**0.072**				**0.975**				**0.062**				**0.055**
Lower tertile	1				1				1				1			
Medium tertile	0.78	(0.60-1.02)	0.075		0.97	(0.59-1.58)	0.888		0.61	(0.22-1.70)	0.349		0.71	(0.43-1.17)	0.174	
Upper tertile	0.78	(0.60-1.03)	0.076		1.01	(0.62-1.63)	0.981		0.31	(0.08-1.11)	0.072		0.61	(0.37-1.01)	0.053	
Area-based SES index				**0.725**				**0.795**				**0.430**				**0.170**
Lower tertile	1				1				1				1			
Medium tertile	0.93	(0.71-1.20)	0.568		0.90	(0.56-1.42)	0.641		1.09	(0.38-3.09)	0.871		0.70	(0.43-1.15)	0.159	
Upper tertile	0.95	(0.73-1.24)	0.723		1.06	(0.66-1.71)	0.797		1.51	(0.55-4.16)	0.427		0.71	(0.44-1.15)	0.161	

Abbreviations: 95%CI, 95% Confidence Interval; CNS, Central Nervous System; HR, Hazard Ratio; N, Number; P, P-value; SES, Socioeconomic Status

[a] Included ICCC-3 diagnoses: leukemia, lymphoma, CNS tumors, embryonal tumors, malignant bone and soft tissue tumors.

[b] Adjusted for: diagnostic group, gender, age at diagnosis, period of diagnosis.

[c] Two-sided p-value for test of trend.

[d] Adjusted for: gender, age at diagnosis, period of diagnosis.

Published in final edited form as: *Int J Cancer*. 2016 Jun 15;138(12):2856-66. doi: 10.1002/ijc.30029

Table 3. Clinical Characteristics of Patients with Central Nervous System Tumors, and Hazard Ratios for the Association of these Characteristics with Mortality (N=354)

Clinical characteristics	N	%[a]	HR	(95%CI)	P	P[b]
WHO grade						**<0.001**
I	132	41.4	1			
II	45	14.1	5.97	(1.80-19.83)	0.004	
III	37	11.6	42.80	(14.89-123.02)	<0.001	
IV	105	32.9	19.36	(6.98-53.73)	<0.001	
Missing	35					
Histology						**<0.001**
PNET/Medulloblastoma	84	23.9	1			
Low-grade glioma	146	41.5	0.14	(0.07-0.30	<0.001	
High-grade glioma	59	16.8	5.15	(3.25-8.16)	<0.001	
Ependymoma	17	4.8	1.26	(0.58-2.75)	0.556	
Others	46	13.1	0.51	(0.24-1.07)	0.074	
Missing	2					
Localization						**0.178**
Supratentorial hemispheric	67	19.1	1			
Supratentorial midline	84	24.0	0.87	(0.47-1.61)	0.651	
Infratentorial	186	53.1	1.29	(0.77-2.15)	0.327	
Spinal	13	3.7	0.48	(0.11-2.06)	0.322	
Missing	4					
Therapy						**<0.001**
Surgery only	161	48.5	1			
Chemotherapy[c]	40	12.1	6.10	(3.11-11.97)	<0.001	
Radiotherapy[d]	122	36.8	5.24	(3.00-9.14)	<0.001	
BMT	9	2.7	2.22	(0.51-9.66)	0.287	
Missing	22					
Participation to clinical trial						**0.001**
Study patient according to protocol	110	31.4	1			
Non-study patient according to protocol	73	20.9	2.65	(1.57-4.48)	<0.001	
Non-study patient not according to protocol	167	47.7	1.38	(0.83-2.28)	0.210	
Missing	4					
Size of the treatment centre						**0.407**
>40 patients	233	65.8	1			
≤40 patients	121	34.2	0.85	(0.57-1.25)		

Abbreviations: 95%CI, 95% Confidence Interval; BMT, Bone Marrow Transplantation; HR, Hazard Ratio; N, Number; P, P-value

[a] Proportions are calculated based on available information within each characteristic.

[b] Two-sided global p-value from likelihood ratio test.

[c] Without radiotherapy, may have had surgery.

[d] May have had surgery or chemotherapy.

Published in final edited form as: *Int J Cancer*. 2016 Jun 15;138(12):2856-66. doi: 10.1002/ijc.30029

Table 4. Influence of Tumor Stage and Treatment on SES Differential in CNS Tumor Mortality (N=354)

	CNS Tumors (N=354)			+ WHO grade			+ histology			+ therapy			+ study participation		
SES	**HR[a]**	**(95%CI)**	**P[b]**	**HR[c]**	**(95%CI)**	**P[b]**	**HR[c]**	**(95%CI)**	**P[b]**	**HR[c]**	**(95%CI)**	**P[b]**	**HR[c]**	**(95%CI)**	**P[b]**
Education father			**0.008**			**0.013**			**0.184**			**0.012**			**0.016**
Compulsory	1			1			1			1			1		
Secondary	0.62	(0.38-1.01)		0.60	(0.35-1.03)		0.64	(0.39-1.04)		0.68	(0.40-1.16)		0.68	(0.41-1.12)	
Tertiary	0.48	(0.28-0.81)		0.47	(0.26-0.85)		0.68	(0.40-1.16)		0.48	(0.27-0.85)		0.51	(0.30-0.87)	
Education mother			**0.014**			**0.146**			**0.181**			**0.100**			**0.015**
Compulsory	1			1			1			1			1		
Secondary	0.59	(0.39-0.90)		0.60	(0.38-0.97)		0.74	(0.48-1.14)		0.72	(0.46-1.14)		0.60	(0.39-0.91)	
Tertiary	0.52	(0.26-1.05)		0.78	(0.35-1.77)		0.70	(0.34-1.42)		0.56	(0.24-1.31)		0.50	(0.24-1.05)	
Rooms per person			**0.023**			**0.197**			**0.014**			**0.056**			**0.051**
< 1 room/person	1			1			1			1			1		
1-1.25 room/person	0.61	(0.39-0.97)		0.76	(0.44-1.29)		0.65	(0.40-1.06)		0.70	(0.43-1.15)		0.59	(0.37-0.95)	
> 1.25 room/person	0.56	(0.34-0.92)		0.69	(0.39-1.22)		0.52	(0.32-0.87)		0.59	(0.34-1.01)		0.61	(0.37-0.99)	
Living space (in m^2)			**0.055**			**0.176**			**0.035**			**0.097**			**0.088**
Lower tertile	1			1			1			1			1		
Medium tertile	0.71	(0.43-1.17)		0.80	(0.46-1.40)		0.79	(0.47-1.32)		0.82	(0.48-1.40)		0.74	(0.45-1.23)	
Upper tertile	0.61	(0.37-1.01)		0.67	(0.38-1.20)		0.58	(0.35-0.96)		0.63	(0.36-1.09)		0.64	(0.38-1.08)	
Area-based SES index			**0.170**			**0.791**			**0.929**			**0.312**			**0.148**
Lower tertile	1			1			1			1			1		
Medium tertile	0.70	(0.43-1.15)		0.75	(0.43-1.32)		0.90	(0.55-1.48)		0.68	(0.39-1.18)		0.64	(0.38-1.08)	
Upper tertile	0.71	(0.44-1.15)		0.92	(0.53-1.61)		0.98	(0.59-1.61)		0.75	(0.45-1.27)		0.69	(0.42-1.12)	

Abbreviations: 95%CI, 95% Confidence Interval; CNS, Central Nervous System; HR, Hazard Ratio; N, Number; P, P-value; SES, Socioeconomic Status

[a] Adjusted for: gender, age at diagnosis, period of diagnosis.

[b] Two-sided p-value for test of trend.

[c] Adjusted for: gender, age at diagnosis, period of diagnosis plus one at a time: WHO grade, histology, therapy or study participation.