

## ARTICLE

# Socioeconomic Factors and Ninth Grade School Performance in Childhood Leukemia and CNS Tumor Survivors

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## Abstract

**Background:** Childhood cancer survivors can experience deficits in school performance in adolescence. Few studies have investigated how social and socioeconomic factors influence and modify school performance. This study investigates the hypothesis that social and parental socioeconomic factors influence ninth grade school performance in childhood leukemia and central nervous system (CNS) tumor survivors and that the effect is different from that in healthy peers.

**Methods:** We analyzed data from nationwide Danish registers on school grades for children who finished ninth grade during 2002–2015 in Denmark. Using a unique within-school matched design, we compared grades from childhood cancer survivors with grades from healthy peers. Social factors were maternal/paternal civil status, immigrant status, and country of origin. Parental socioeconomic factors were measured by education and income. The study consisted of 36 426 children, of whom 460 and 289 were leukemia and CNS tumor survivors, respectively.

**Results:** School grades varied considerably across social strata. However, the grades among CNS tumor survivors varied notably less in the following effect modifiers: parental educational attainment, income, and immigrant status. On the contrary, no significant effect modifiers were found among leukemia survivors as compared with healthy peers.

**Conclusion:** There is a strong effect of social and parental socioeconomic factors on school performance in healthy adolescence in Denmark. The same pattern is seen in survivors of leukemia, but a different pattern is seen in survivors of CNS tumors. This finding suggests that impairment of school-related functions differ between leukemia and CNS tumor survivors. This study contributes to knowledge on learning in adolescence in childhood cancer survivors by investigating several social and socioeconomic effect modifiers with nationwide register data and a unique statistical method particularly suitable for comparing school grades. Improved insight could make it possible to identify high-risk groups that may need different means of help.

Improvements in diagnostic procedures, risk grouping, and treatment strategies have increased survival rates for childhood leukemias and central nervous system (CNS) tumors (1). Today, the five-year survival rate for childhood acute lymphoblastic leukemia (ALL; the most common childhood cancer) is greater than 90%, whereas for childhood CNS tumors it varies

from 0% for diffuse intrinsic pontine gliomas to more than 90% for fossa posterior pilocytic astrocytoma (1). For the survivors, there is a growing need for mapping the long-term educational attainments, and several studies have identified childhood CNS tumor survivors as being particularly at risk of compromised educational outcomes (2–8). Findings concerning the

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effect of childhood leukemia have been more ambiguous, reporting primarily a negative or no effect on educational outcomes unless CNS irradiation has been part of the therapy (3,4,7–9).

It is known that parental socioeconomic status (SES), family structure, and immigrant status have a positive correlation with school performance in the general population (10–12). Among childhood cancer survivors, parental SES serves as a proxy for possible differences in the home environment and the ability of the parents to guide and meet the educational needs of their children (13). In the literature, most reports have focused on effects of treatment (6–9,14,15), whereas few have focused on the effects of social and socioeconomic factors. Few studies have adjusted for parental SES (6,9,15), but they did not report on effect modification. Earlier literature argues that parental Socioeconomic Position (SEP) is important for the children's school performance. Not only does the parent's SEP account for a significant amount of variation in children's intellect, but also psychological and social aspects of the children's lives are deeply influenced by parental SEP (28). Children with childhood cancer are more dependent on their parents. Thus, one might expect that family resources could be of greater importance for childhood cancer survivors.

Using a population-based setting and taking advantage of the comprehensive nationwide Danish registries, we investigated ninth grade school grades in Danish childhood leukemia and CNS tumor survivors who finished ninth grade in a public school during the period 2002–2015. Our hypothesis was that social and parental socioeconomic factors influence ninth grade school performance in childhood leukemia and central nervous system tumor survivors, and that the effect is different from that in healthy peers. The study could lead to a more thorough understanding of how they may influence survivors of childhood leukemia and CNS tumors and thus a more specialized identification of high-risk groups within the survivor groups.

## Methods

Data from a variety of nationwide Danish registries including the Danish Civil Registration (16), the Attainment Register (17), the Income Statistics Register (18), and the Danish Cancer Registry (19) were merged with registries on school grades (17).

In Denmark, all adolescence attending public schools have their school grades systematically registered from as early ninth grade, and this was chosen as the outcome measure of school performance. We included all Danish pupils included since the start of the registry, that is, pupils who finished ninth grade between 2002 and 2015, making up a population of 858 702 individuals born in the period 1982–2001. Within the population, 460 survivors of leukemia and 289 survivors of CNS tumors were identified in the Danish Cancer Registry (started in 1942) and included in the study population. CNS tumors and leukemia were classified into subgroups according to the childhood cancer classification scheme, third edition (ICCC-3) (20). We compared school performance with the healthy peers. Healthy peers were defined as children with no history of cancer. We included all children who attended the same school at the same year as a CNS tumor/leukemia survivor, thus obtaining a matched study population matched on school and year. In total, the resulting study population included 36 426 individuals born in the period 1983–2000, where 749 children had a previous diagnosis of a

CNS tumor or leukemia before finishing ninth grade and where 35 677 children comprised the population comparison group of healthy peers.

We calculated average mean rank grades for all children in the study population by including all available grades completed by the child including grades in oral examination, written examination, and general proficiency. The overall average was calculated as rank-based grades within each school and graduation year. By applying a matched design, we were able to protect to a certain degree against unmeasured confounding, as all comparisons were done within the same school, teacher, etc. Details about the calculation of rank-based grades are described in Andersen et al. (3).

## Social and Socioeconomic Factors

Parents of study subjects were identified and linked to their children through the Danish Fertility Database (which started in 1980) (21). For all study subjects, we included five different markers of social and SEP to embrace both material and nonmaterial aspects of the survivor's position: disposable income (maternal/paternal), educational attainment (maternal/paternal), civil status (maternal/paternal), the child's immigrant status, and the child's country of origin.

Data on parental educational attainment were obtained from the Attainment Register (which started in 1970) (17). In Denmark, education is mandatory between the ages of six to seven and 16 years, and the government provides free education at all levels (22). Maternal and paternal educational attainments were classified into three groups based on the length of the education and the opportunities the education provided. Basic education: less than 10 years (mandatory); youth education: 10–12 years (secondary education and vocational education); higher education: more than 12 years (short cycle, medium cycle, and long cycle higher education).

Maternal and paternal income was obtained through the Income Statistics Register (which started in 1970) (18). Individuals were grouped into five income groups based on quintiles, the first being the lowest income, and adjusted for sex and birth year.

Information on civil status was collected from the Danish Civil Registration (which started in 1968) and included as a binary variable "married" and "unmarried." "Married" included married couples and registered partnerships. "Unmarried" included individuals who were divorced, widow(er)ed, or never married. Cohabiting status was not taken into account in the analysis.

Data on the child's immigrant status and country of origin were collected from the Danish Civil Registration (which started in 1969). Immigrant status was a binary variable, divided into immigrant/descendant and Danish origin, where immigrant/descendant was defined by having parents who neither were born in Denmark, nor had Danish citizenship. Country of origin was categorized into "Denmark," "Western countries," and "non-Western countries" (23).

## Cancer-Related Factors

The study included the radiation treatment of the survivors, age at diagnosis, and hearing diagnosis as possible confounders or mediators obtained from the Danish Cancer Registry, the National Patient Registry, and the Danish Civil Registration.

## Statistical Methods

Characteristics of the study population were reported as proportions stratified on cancer type. Differences between cancer survivors and healthy peers were tested by means of chi-square tests. Marginal associations were investigated with linear regression models, and differences in mean rank grades were tested between healthy peers, leukemia survivors, and CNS tumor survivors within each strata of the variable.

The effect modification of social and socioeconomic factors and childhood cancer on mean rank grades was estimated and studied considering interaction terms. Parental income was modeled as a continuous variable, while all other variables were modeled as categorical variables.

The possible effect modification of each SES indicator was tested in separate models, adjusted for sex and year of diagnosis. The significance of model terms was evaluated by means of likelihood-ratio test, and a 5% significance level was applied. The statistical analyses were carried out with the statistical software R (24). All statistical tests were two-sided.

## Results

The main results of the study were that leukemia survivors were affected by social and socioeconomic factors similarly as their healthy peers. CNS tumor survivors, however, were affected differently. In general, CNS tumor survivors did more poorly in school than their healthy peers and the social gradient was considerably less among CNS survivors.

The characteristics of the study population are shown in Table 1. In the univariate analysis of the overall mean rank grade shown in Table 2, survivors of leukemia did not differ from their healthy peers in any of the social and socioeconomic factors. Contrarily, CNS tumor survivors had similar grades as their healthy peers on a number of the socioeconomic and social factors, but had significantly lower grades on factors known to be associated with higher grades, namely higher income, higher education, and married parents. As seen from Table 1, we found a deficit in rank grades on average from 1% to 5% points, but for those most affected, up to 13%. Whether this is a large effect or not can be demonstrated using findings from a study from Finland by Huurre et al. (26), which showed that adolescence is an important period for future educational life trajectory. Assuming similar effects as those reported in the Finnish study, we find that a difference of 13% is associated with an increased risk of 78% (95% confidence interval [CI] = 68% to 91%) for not obtaining a higher educational level, whereas a difference of 5% is associated with an increased risk of 20% (95% CI = 18% to 24%).

The main results of the effect modification analysis are illustrated in Figure 1, where the effects of the different modifiers are shown, as well as *P* values of the pairwise likelihood ratio tests.

In the association between being a CNS tumor survivor and mean rank grades, we found four significant effect modifiers: maternal education, maternal income, paternal income, and immigrant status. In low-SES groups, the mean rank grades of CNS tumor survivors and their healthy peers were similar, while in high-SES the mean rank grade of the CNS tumor survivors was on average about 10% lower. Hence, the social gradient was lower for CNS tumor survivors compared with the healthy peers. It is known that CNS tumor survivors are a heterogenic group. An analysis of CNS subgroups, however, could not identify differences in effect modification between the subgroups, which could be due to lack of statistical power.

We did not find any significant effect modification in the association between leukemia survivors and mean rank grades, nor did we find any significant effect modifiers between leukemia survivors and CNS tumor survivors.

## Discussion

Increased survival rates have led to long-term childhood cancer survivors, and the risk of long-term late effects are a mounting concern (1). Earlier studies have found that CNS tumor and leukemia survivors are doing more poorly in school compared with their healthy peers (3,6,9), which can have consequences in adult life, as this affects lifelong academic achievement (25), including educational attainment (26). The objective of this study was to investigate whether school performance deficits were moderated by socioeconomic or social factors. Improved insight might lead to identification of high-risk groups within leukemia and CNS tumor survivors. The existing literature has mainly focused on treatment-related factors, which is why this study adds to the scarce literature of the impact of social and socioeconomic factors on school performance in childhood cancer survivors.

We found a significant modifying relationship between maternal education, maternal/paternal income, and immigrant status and mean rank grades among CNS tumor survivors when compared with healthy peers. The difference in mean rank grade between those from a family with a low SES and those from families with a high SES was smaller among CNS tumor survivors than among healthy peers.

This was surprising, as some childhood cancer survivors and especially CNS tumor and sometimes also leukemia survivors possess increased educational needs. Thus, we would have expected that social and socioeconomic factors like parental education would have had a greater impact on academic achievements in children who had been previously diagnosed with cancer.

The largest difference in grades between CNS tumor survivors and their healthy peers was associated with high parental income or education, while CNS tumor survivors with parents with low parental income or education had similar grades to their healthy peers.

To our knowledge, only the study by Ach et al. (2) has investigated whether SEP's effect differed between survivors and the children in the background population. Ach et al., who measured performance by means of the Wide Range Achievement Test, did not find a modifying relationship between parental education or family SES (measured by occupational prestige) and student achievement overall in the United States, which is in contrast to our findings. Also contrary to the findings in our study, they found that high family SES was significantly associated with a smaller difference in reading skills between CNS tumor survivors and controls. The study by Ach and co-authors is limited by a cross-sectional study design, a small sample size (164 cases and 164 controls), and crude assessment of family variables, which was done by questionnaires completed by caregivers. Moreover, differences between the American and Danish schooling systems and societies make a direct comparison difficult, as the association between cancer, SES, and grades could be affected by different factors and to different degrees.

No significant effect modifiers were found among leukemia survivors, suggesting that survivors from CNS tumors are impaired differently from leukemia survivors. Cranial radiation treatment is a more common treatment among children with

Table 1. Characteristics of leukemia and CNS survivors and the population comparison group of healthy peers\*

| Stratification criteria  | Healthy peers<br>No. (%) | Leukemia<br>survivors No. (%) | CNS tumor<br>survivors No. (%) | Chi <sup>2</sup> P |
|--|--------------------------|-------------------------------|--------------------------------|--------------------|
| Total number   | 35 677                   | 460                           | 289                            |                    |
| Child  |                          |                               |                                |                    |
| Sex  |                          |                               |                                | .080               |
| Male   | 17 758 (49.8)            | 252 (54.8)                    | 138 (47.8)                     |                    |
| Female   | 17 919 (50.2)            | 208 (45.2)                    | 151 (52.2)                     |                    |
| School year  |                          |                               |                                | .479               |
| 2002–2005  | 8105 (22.7)              | 119 (25.9)                    | 64 (22.1)                      |                    |
| 2006–2010  | 12 572 (35.2)            | 162 (35.2)                    | 111 (38.4)                     |                    |
| 2011–2015  | 15 000 (42.0)            | 179 (38.9)                    | 114 (39.4)                     |                    |
| Immigrant status   |                          |                               |                                | .015               |
| Danish origin  | 32 607 (91.4)            | 427 (92.8)                    | 277 (95.8)                     |                    |
| Immigrant/descendant   | 3070 (8.6)               | 33 (7.2)                      | 12 (4.2)                       |                    |
| Country of origin  |                          |                               |                                | .078               |
| Denmark  | 32 607 (91.4)            | 427 (92.8)                    | 277 (95.8)                     |                    |
| Western countries  | 838 (2.3)                | 10 (2.2)                      | 7 (2.4)                        |                    |
| Non-Western countries  | 2229 (6.2)               | 23 (5.0)                      | 5 (1.7)                        |                    |
| Hearing loss   |                          |                               |                                | <.001              |
| No   | 35 219 (98.7)            | 440 (95.7)                    | 267 (92.4)                     |                    |
| Yes  | 458 (1.3)                | 20 (4.3)                      | 22 (7.6)                       |                    |
| Cancer type (ICCC-3) (20)                                      |                          |                               |                                |                    |
| Leukemia   |                          |                               |                                |                    |
| Lymphoid leukemias   | –                        | 387 (84.1)                    | –                              |                    |
| Acute myeloid leukemias  | –                        | 52 (11.3)                     | –                              |                    |
| Chronic myeloproliferative diseases                            | –                        | 6 (1.3)                       | –                              |                    |
| Myelodysplastic syndrome and other myeloproliferative diseases | –                        | 8 (1.7)                       | –                              |                    |
| Unspecified and other specified leukemias                      | –                        | 7 (1.5)                       | –                              |                    |
| CNS tumor  |                          |                               |                                |                    |
| Ependyomas and choroid plexus tumor                            | –                        | –                             | 21 (7.3)                       |                    |
| Astrocytomas   | –                        | –                             | 105 (36.3)                     |                    |
| Intracranial and intraspinal embryonal tumors                  | –                        | –                             | 20 (6.9)                       |                    |
| Other gliomas  | –                        | –                             | 8 (2.8)                        |                    |
| Other specified intracranial and intraspinal neoplasms         | –                        | –                             | 54 (18.7)                      |                    |
| Unspecified intracranial and intraspinal neoplasms             | –                        | –                             | 81 (28.0)                      |                    |
| Year of diagnosis  |                          |                               |                                | <.001              |
| 1987–1994  | –                        | 114 (24.8)                    | 35 (12.1)                      |                    |
| 1995–1999  | –                        | 134 (29.1)                    | 82 (28.4)                      |                    |
| 2000–2004  | –                        | 144 (31.3)                    | 89 (30.8)                      |                    |
| 2005–2014  | –                        | 68 (14.8)                     | 83 (28.7)                      |                    |
| Age at diagnosis, y  |                          |                               |                                | <.001              |
| 0–2  | –                        | 125 (27.2)                    | 37 (12.8)                      |                    |
| 3–5  | –                        | 168 (36.5)                    | 51 (17.6)                      |                    |
| 6–10   | –                        | 92 (20.0)                     | 101 (34.9)                     |                    |
| 11–16  | –                        | 75 (16.3)                     | 100 (34.6)                     |                    |
| Radiation treatment  |                          |                               |                                | <.001              |
| No   | –                        | 436 (94.8)                    | 251 (86.9)                     |                    |
| Yes  | –                        | 24 (5.2)                      | 38 (13.2)                      |                    |
| Parents  |                          |                               |                                |                    |
| Maternal income  |                          |                               |                                | .241               |
| 1st quintile   | 4973 (14.1)              | 65 (14.4)                     | 29 (10.2)                      |                    |
| 2nd quintile   | 6589 (18.7)              | 84 (18.6)                     | 64 (22.5)                      |                    |
| 3rd quintile   | 7451 (21.1)              | 107 (23.7)                    | 68 (23.9)                      |                    |
| 4th quintile   | 8597 (24.4)              | 112 (24.8)                    | 67 (23.5)                      |                    |
| 5th quintile   | 7643 (21.7)              | 83 (18.4)                     | 57 (20.0)                      |                    |
| Paternal income  |                          |                               |                                | .545               |
| 1st quintile   | 5531 (16.1)              | 64 (14.6)                     | 51 (18.3)                      |                    |
| 2nd quintile   | 5973 (17.4)              | 75 (17.1)                     | 50 (18.0)                      |                    |
| 3rd quintile   | 7009 (20.4)              | 96 (21.9)                     | 65 (23.4)                      |                    |
| 4th quintile   | 7710 (22.5)              | 104 (23.7)                    | 48 (17.3)                      |                    |
| 5th quintile   | 8057 (23.5)              | 100 (22.8)                    | 64 (23.0)                      |                    |

(continued)

Table 1. (continued)

| Stratification criteria         | Healthy peers<br>No. (%) | Leukemia<br>survivors No. (%) | CNS tumor<br>survivors No. (%) | Chi <sup>2</sup> P |
|---------------------------------|--------------------------|-------------------------------|--------------------------------|--------------------|
| Maternal educational attainment |                          |                               |                                | .767               |
| Basic education                 | 5604 (16.2)              | 63 (14.2)                     | 45 (16.0)                      |                    |
| Youth education                 | 16 134 (46.6)            | 219 (49.2)                    | 130 (46.3)                     |                    |
| Higher education                | 12 859 (37.2)            | 163 (36.6)                    | 106 (37.7)                     |                    |
| Paternal educational attainment |                          |                               |                                | .084               |
| Basic education                 | 5444 (16.3)              | 67 (15.5)                     | 60 (21.9)                      |                    |
| Youth education                 | 17 443 (52.3)            | 239 (55.5)                    | 138 (50.4)                     |                    |
| Higher education                | 10 459 (31.4)            | 125 (29.0)                    | 76 (27.7)                      |                    |
| Maternal civil status           |                          |                               |                                | .257               |
| Unmarried                       | 9415 (26.8)              | 134 (29.7)                    | 83 (29.1)                      |                    |
| Married                         | 25 741 (73.2)            | 317 (70.3)                    | 202 (70.9)                     |                    |
| Paternal civil status           |                          |                               |                                | .145               |
| Unmarried                       | 8415 (24.8)              | 119 (27.2)                    | 80 (28.9)                      |                    |
| Married                         | 25 568 (75.2)            | 318 (72.8)                    | 197 (71.1)                     |                    |

\*Please note that the percentages do not sum up to 100 due to rounding. CNS = central nervous system.

CNS tumors and is known to be associated with a higher risk of severe cognitive deficits (4,6–8,14). We made a sensitivity analysis in which survivors who received radiation treatment were excluded, and this did not alter our conclusion. Other factors such as insertion of a shunt and cerebral hemisphere tumor location have been found to be predictors for adverse memory outcome (27), but it was not possible to take these factors into account in the analysis. Cognitive deficits in CNS survivors may reduce the effect of SES compared with their healthy peers and, hence, have less impact on school grades. The larger grade difference among high-SES survivors could also be due to decreased expectations for a child who has had a CNS tumor, and thus parents do not encourage the child to do well in school as much as they would with a healthy child. Another explanation could be the fatigue the survivors experience, which is more pronounced among survivors of childhood CNS tumors than survivors of acute lymphoblastic leukemia. While increasing time since cancer treatment leads to decreased fatigue among ALL survivors, it leads to increased fatigue among CNS tumor survivors (28). The fatigue might make it difficult to manage both the social interactions and the academics in school, thus making it a necessity to downgrade time and energy spent on academics to a level where they can balance both. This could lead to similar grades across social strata.

We did not identify effect modification between SES and age at diagnosis on mean rank grade. The study by Patel and co-authors found that parental SES modified the effect of time since diagnosis on processing speed, but not on other cognitive domains (13). Survivors of low parental SES declined in processing speed over time, while it was constant over time for survivors of high parental SES. A limitation of this study, however, was that the sample was small, consisting of only 48 leukemia survivors and parental SES was included as a crude measure, because parental education and occupation were combined. The study by Andersen et al. (3) showed that young age at diagnosis is associated with poorer school performance, albeit they did not consider effect modification by socioeconomic factors. However, as CNS patients often get their diagnosis older than ALL patients ( $P < .001$ ) (Table 1), it is likely that therapy will interfere more with school for CNS patients compared with ALL

patients. This could explain why CNS patients are less sensitive to environmental modifiers.

A strength of the presented study is the availability of the population-based, nationwide Danish registry data on school performance and detailed SES indicators, which to our knowledge makes this the largest and most comprehensive study investigating effect modifiers to date. School performance was measured by overall grades, which is a practice-oriented indicator of how childhood cancer survivors are influenced by late effects in their daily life (3). The continuous measure in terms of mean rank grade, in contrast to the categorical measure of educational attainment, increases the statistical precision and makes it possible to measure even small differences. Furthermore, the mean rank grade is a robust measure that is not affected by shifts in the grade assessing scale, or by potential time trends in grade achievement. The mean rank grade is calculated and compared within the school of the child, which means that the differences we find in our study are the average social gradient within each school.

A limitation of this study is that school grades have only been registered since 2001 and that it only includes data on children who finished ninth grade in a public school, opening possibilities for selection bias. Whether school grades as the outcome measure performance accurately has not been validated. It may be that cancer survivors are treated differently by school teachers and that their grades reflect other aspects than actual performance. In view of this, it is also a limitation that neurocognitive functions were not part of the investigation.

Future studies investigating effect modifiers could benefit from including outcome measures that avoid a selected population, for example, educational attainment, where the availability of data is less likely to depend on SES or the severity of late effects. This could also clarify whether the same effect modification is present in more long-term educational measures. The nationwide, population-based Danish study by Koch and co-authors used this as the outcome measure, but only measured effect modification by a crude highest parental education measurement and found no evidence of risk factors other than those present in the background population (5). Moreover, a larger study, and thus a larger study population, would make it

Table 2. Overall grade means in leukemia and CNS survivors and the population comparison group of healthy peers

| Stratification criteria  | Healthy peers<br>(95% CI) | Leukemia<br>survivors (95% CI) | CNS tumor<br>survivors (95% CI) | t test P | Pairwise<br>t test* |
|--|---------------------------|--------------------------------|---------------------------------|----------|---------------------|
| Total for survivors and population comparisons                 | 50.5 (50.2 to 50.8)       | 48.8 (46.1 to 51.4)            | 45.2 (41.9 to 48.5)             | .003     |                     |
| Child  |                           |                                |                                 |          |                     |
| Sex  |                           |                                |                                 |          |                     |
| Male   | 45.9 (45.5 to 46.4)       | 44.9 (41.4 to 48.4)            | 41.9 (37.2 to 46.7)             | .221     |                     |
| Female   | 55.1 (54.7 to 55.5)       | 53.4 (49.6 to 57.3)            | 48.2 (43.7 to 52.7)             | .009     |                     |
| School year  |                           |                                |                                 |          |                     |
| 2002–2005  | 50.4 (49.8 to 51.0)       | 49.7 (44.8 to 54.6)            | 48.7 (42.1 to 55.4)             | .860     |                     |
| 2006–2010  | 50.6 (50.1 to 51.1)       | 49.1 (44.7 to 53.6)            | 42.9 (37.6 to 48.3)             | .018     |                     |
| 2011–2015  | 50.5 (50.1 to 51.0)       | 47.8 (43.5 to 52.1)            | 45.4 (40.0 to 50.8)             | .087     |                     |
| Immigrant status   |                           |                                |                                 |          |                     |
| Danish origin  | 51.5 (51.2 to 51.8)       | 49.4 (46.7 to 52.1)            | 45.0 (41.6 to 48.3)             | <.001    |                     |
| Immigrant/descendant   | 40.4 (39.4 to 41.5)       | 41.2 (31.2 to 51.2)            | 50.7 (34.1 to 67.3)             | .479     |                     |
| Country of origin  |                           |                                |                                 |          |                     |
| Denmark  | 51.5 (51.2 to 51.8)       | 49.4 (46.7 to 52.1)            | 45.0 (41.6 to 48.3)             | <.001    |                     |
| Western countries  | 44.3 (42.3 to 46.3)       | 41.1 (22.8 to 59.4)            | 49.7 (27.8 to 71.5)             | .839     |                     |
| Non-Western countries  | 39.0 (37.8 to 40.2)       | 41.2 (29.3 to 53.1)            | 52.1 (26.5 to 77.6)             | .567     |                     |
| Hearing loss   |                           |                                |                                 |          |                     |
| No   | 50.6 (50.3 to 50.9)       | 49.1 (46.4 to 51.7)            | 44.6 (41.1 to 48.0)             | .002     |                     |
| Yes  | 45.3 (42.6 to 47.9)       | 42.6 (30.0 to 55.3)            | 53.1 (41.0 to 65.2)             | .413     |                     |
| Cancer type (ICCC-3) (20)                                      |                           |                                |                                 |          |                     |
| Leukemia   |                           |                                |                                 |          |                     |
| Lymphoid leukemias   |                           | 48.2 (45.4 to 51.1)            |                                 |          |                     |
| Acute myeloid leukemias  |                           | 53.3 (45.5 to 61.1)            |                                 |          |                     |
| Chronic myeloproliferative diseases                            |                           | 43.3 (20.3 to 66.3)            |                                 |          |                     |
| Myelodysplastic syndrome and other myeloproliferative diseases |                           | 44.7 (24.7 to 64.6)            |                                 |          |                     |
| Unspecified and other specified leukemias                      |                           | 54.1 (32.8 to 75.4)            |                                 |          |                     |
| CNS tumor  |                           |                                |                                 |          |                     |
| Ependyomas and choroid plexus tumor                            |                           |                                | 44.4 (32.1 to 56.7)             |          |                     |
| Astrocytomas   |                           |                                | 45.2 (39.7 to 50.7)             |          |                     |
| Intracranial and intraspinal embryonal tumors                  |                           |                                | 37.5 (24.9 to 50.1)             |          |                     |
| Other gliomas  |                           |                                | 38.8 (18.9 to 58.7)             |          |                     |
| Other specified intracranial and intraspinal neoplasms         |                           |                                | 52.0 (44.4 to 59.7)             |          |                     |
| Unspecified intracranial and intraspinal neoplasms             |                           |                                | 43.5 (37.2 to 49.7)             |          |                     |
| Year of diagnosis  |                           |                                |                                 |          |                     |
| 1987–1994  |                           | 44.4 (39.3 to 49.6)            | 38.1 (28.8 to 47.5)             | .247     |                     |
| 1995–1999  |                           | 49.6 (44.8 to 54.5)            | 45.3 (39.1 to 51.5)             | .277     |                     |
| 2000–2004  |                           | 48.9 (44.2 to 53.6)            | 45.6 (39.6 to 51.6)             | .397     |                     |
| 2005–2014  |                           | 54.1 (47.0 to 61.2)            | 47.7 (41.3 to 54.1)             | .187     |                     |
| Age at diagnosis, y  |                           |                                |                                 |          |                     |
| 0–2  |                           | 45.7 (40.6 to 50.8)            | 45.2 (41.9 to 48.6)             | .881     |                     |
| 3–5  |                           | 46.1 (42.0 to 50.2)            | 40.1 (33.4 to 46.9)             | .137     |                     |
| 6–10   |                           | 54.8 (47.6 to 62.1)            | 44.9 (38.1 to 51.7)             | .051     |                     |
| 11–16  |                           | 54.7 (48.7 to 60.7)            | 48.8 (43.6 to 54.0)             | .144     |                     |
| Radiation treatment  |                           |                                |                                 |          |                     |
| No   |                           | 48.9 (46.3 to 51.5)            | 45.5 (42.0 to 48.9)             | <.001    |                     |
| Yes  |                           | 47.2 (33.8 to 60.6)            | 43.6 (33.0 to 54.2)             | .674     |                     |
| Parents  |                           |                                |                                 |          |                     |
| Maternal income  |                           |                                |                                 |          |                     |
| 1st quintile   | 42.2 (41.4 to 43.0)       | 40.3 (33.4 to 47.3)            | 51.6 (41.2 to 62.0)             | .184     |                     |
| 2nd quintile   | 45.3 (44.6 to 46.0)       | 41.3 (35.3 to 47.4)            | 40.4 (33.4 to 47.3)             | .176     |                     |
| 3rd quintile   | 49.4 (48.8 to 50.0)       | 47.7 (42.3 to 53.1)            | 42.5 (35.7 to 49.3)             | .116     |                     |
| 4th quintile   | 54.2 (53.6 to 54.8)       | 53.7 (48.5 to 58.9)            | 42.8 (36.1 to 49.5)             | .004     |                     |
| 5th quintile   | 57.8 (57.2 to 58.4)       | 57.1 (51.1 to 63.1)            | 52.8 (45.6 to 60.1)             | .399     |                     |
| Paternal income  |                           |                                |                                 |          |                     |
| 1st quintile   | 43.8 (43.0 to 44.5)       | 45.5 (38.5 to 52.6)            | 45.2 (37.4 to 53.1)             | .831     |                     |
| 2nd quintile   | 45.8 (45.1 to 46.5)       | 42.6 (36.1 to 49.0)            | 45.9 (38.0 to 53.8)             | .619     |                     |
| 3rd quintile   | 49.4 (48.7 to 50.1)       | 44.1 (38.4 to 49.7)            | 43.7 (36.9 to 50.6)             | .051     |                     |
| 4th quintile   | 54.9 (54.2 to 55.5)       | 55.5 (50.1 to 61.0)            | 42.6 (34.6 to 50.5)             | .010     |                     |
| 5th quintile   | 56.8 (56.2 to 57.4)       | 52.7 (47.2 to 58.2)            | 50.4 (43.5 to 57.3)             | .072     |                     |

(continued)

Table 2. (continued)

| Stratification criteria         | Healthy peers<br>(95% CI) | Leukemia<br>survivors (95% CI) | CNS tumor<br>survivors (95% CI) | t test P | Pairwise<br>t test* |
|---------------------------------|---------------------------|--------------------------------|---------------------------------|----------|---------------------|
| Maternal educational attainment |                           |                                |                                 |          |                     |
| Basic education                 | 38.1 (37.4 to 38.8)       | 35.3 (28.6 to 42.1)            | 37.2 (29.3 to 45.2)             | .716     |                     |
| Youth education                 | 47.8 (47.3 to 48.2)       | 45.1 (41.4 to 48.8)            | 43.6 (38.8 to 48.5)             | .095     |                     |
| Higher education                | 60.2 (59.7 to 60.7)       | 59.3 (55.1 to 63.5)            | 49.7 (44.5 to 54.8)             | <.001    | □ □ □               |
| Paternal educational attainment |                           |                                |                                 |          |                     |
| Basic education                 | 40.2 (39.5 to 41.0)       | 39.2 (32.6 to 45.9)            | 40.9 (33.8 to 48.0)             | .942     |                     |
| Youth education                 | 48.4 (47.9 to 48.8)       | 46.0 (42.4 to 49.5)            | 45.0 (40.3 to 49.7)             | .159     |                     |
| Higher education                | 61.3 (60.8 to 61.8)       | 59.5 (54.7 to 64.2)            | 51.4 (45.3 to 57.4)             | .005     | □ □ □               |
| Maternal civil status           |                           |                                |                                 |          |                     |
| Unmarried                       | 45.4 (44.9 to 46.0)       | 44.7 (39.8 to 49.5)            | 41.4 (35.2 to 47.5)             | .411     |                     |
| Married                         | 52.5 (52.2 to 52.9)       | 50.4 (47.2 to 53.5)            | 46.6 (42.6 to 50.5)             | .006     | □ □ □               |
| Paternal civil status           |                           |                                |                                 |          |                     |
| Unmarried                       | 45.7 (45.1 to 46.3)       | 43.3 (38.1 to 48.4)            | 46.0 (39.7 to 52.2)             | .644     |                     |
| Married                         | 52.5 (52.2 to 52.9)       | 50.8 (47.6 to 53.9)            | 45.6 (41.6 to 49.6)             | .002     | □ □ □               |

\*Pairwise t test: pairwise t tests for significant t tests. The first square indicates the healthy peers, the second square the leukemia survivors, and the third square central nervous system survivors. Significant pairwise t tests were illustrated by connecting squares with dotted lines if there was a significant difference between the groups. CNS = central nervous system.

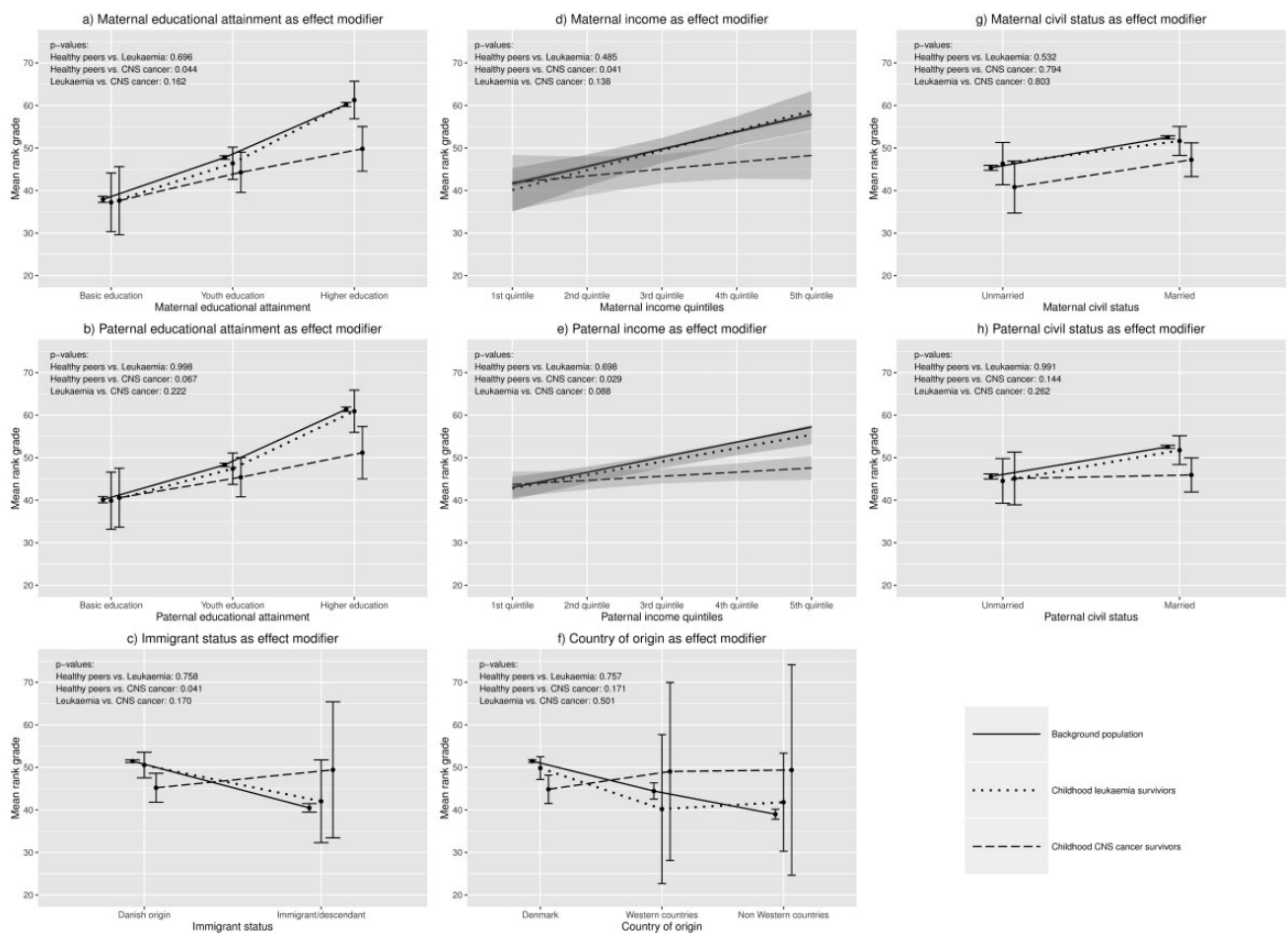


Figure 1. Effect modification of social and socioeconomic factors on school performance. CNS = central nervous system.

possible to examine immigrant status and country of origin as effect modifiers with more precision.

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