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Parental age and childhood cancer risk: A Danish population-based registry study

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Abstract

Background—Though the association between parental age at child's birth and the risk of childhood cancer has been previously investigated, the evidence to date is inconclusive and scarce for rarer cancer types.

Methods—Cancer cases (N=5,856) were selected from all children born from 1968–2014 and diagnosed from 1968–2015 in Denmark at less than 16 years of age listed in the nationwide Danish Cancer Registry. Cases were individually matched to controls (1:100) on sex and year of birth with a total of 585,594 controls randomly sampled from all live births in Denmark from the Danish Central Population Registry. Parental age at child's birth was extracted from the Central Population Registry. Conditional logistic regression models were used to estimate odds ratios for the association between parental age at child's birth and childhood cancer risk. Parental age was modeled as both categorical (referent group, parents aged 25–29) and continuous per 5-year increase in age.

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Author contributions

Zuelma A Contreras: Contributions include analysis and interpretation of study data, drafting and revision of manuscript, and final publication review.

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Results—Offspring of older mothers were at an increased risk of acute lymphoblastic leukemia (ALL) [OR=1.10, 95% CI: (1.02, 1.19) per 5-year increase in age]. Older maternal age (40+) increased the risk of non-Hodgkin lymphoma (NHL) [OR=1.96, 95% CI: (1.12, 3.43)]. The risk of Wilms' tumor also appeared elevated with older paternal age [OR=1.11, 95% CI: (0.97, 1.28) per 5-year increment in age].

Conclusion—Older parental age was a risk factor for various childhood cancers in Danish children. Further investigation of the biological and social factors that may be contributing to these associations is warranted.

Keywords

childhood cancer; parental age; paternal age; maternal age; epidemiology

Introduction

Parental age at child's birth has increased in the US, Europe, and elsewhere. In the United States in 2013, the birth rate for women over 35 years of age (49.3 births per 1,000 women) was at the highest level in 50 years, while the birth rate for all women younger than 30 has dropped, with a 61% drop in the teen birth rate since 1970. The rates of children born to older fathers (ages 35–54) have also increased although less steeply than among mothers [1]. In Denmark, there has been an increasing trend in the average age of first childbirth from 23.1 years in 1960 to 29 years in 2014 [2]. Pregnancy outcomes related to advanced maternal age include low birth weight, preterm birth, and sharp increases in the risk of chromosomal anomalies. Advanced paternal age has been less studied than maternal age, but is related to birth defects associated with single gene mutations (achondroplasia, neurofibromatosis) and chromosomal abnormalities as well as neurodevelopmental disorders [3].

Cancer is the leading cause of death from disease among children younger than 14 and Denmark has among the highest incidence rates of childhood cancer worldwide [4]. Little is known about the etiology of these diseases, with established risk factors limited to ionizing radiation, certain rare genetic syndromes, genetic polymorphisms, congenital anomalies, and parental smoking (only in the case of hepatoblastoma) [5, 6].

Older parental age has been associated with several childhood cancer types, but results across studies have been inconsistent. The most extensively studied cancer type has been leukemia. A recent meta-analysis, including results from 69 case-control studies and 8 cohort studies, found an increased risk of acute lymphoblastic leukemia (ALL) in offspring of older mothers and fathers when examining age as a continuous and categorical variable. Additionally, offspring of younger fathers also had an increased risk of ALL. In terms of acute myeloid leukemia (AML), there was a U-shaped risk with maternal age and the risk of AML was increased only in offspring born to younger fathers. Only 4 of the 77 studies included in this analysis examined the impact of mutual adjustment for maternal and paternal age, and the only notable association that persisted with mutual adjustment was an increased risk of AML with younger maternal age [7].

Population-based studies that have assessed several, rarer cancer types are more limited. A recent study using California Cancer Registry data examined parental age (categorical/per 5-year increment) and found an overall increased risk of ALL, central nervous system (CNS) tumors, hepatic tumors, renal tumors, and lymphomas with older maternal age when adjusting for paternal age. For paternal age, only an increased risk of lymphomas with older paternal age when mutual adjusting was found [8]. A pooled-analysis of registry data from 5 US States (California, Minnesota, New York, Texas, Washington) found an increased risk of several childhood cancer types with advanced maternal age. In particular, leukemia, CNS tumors, neuroblastoma, Wilms' tumors, and soft tissue sarcomas were associated with older maternal age when adjusting for paternal age. Additionally, paternal age was not associated with most childhood cancer types after adjusting for maternal age [9]. A registry-based study in Denmark, including children born 1978–2010, examined paternal age (categorical/per 5-year increment) in relation to various cancer types and found an increased risk of ALL and decreased risk of CNS tumors with older parental age [10]. Specific cancer types have also been individually studied in relation to parental age with varying associations [11–20]. Thus, overall the strongest support exists for a relation between older parental age and ALL. The purpose of this study was to assess the association between parental age and childhood cancer in a large population-based sample of children born in Denmark. Though a previous Danish study has examined paternal age, maternal age was not examined and our study includes more years thus it would expand on this previous study's findings[10].

Methods

Cases for the present study were selected from all primary cancers diagnosed in Denmark born from 1968–2014 and diagnosed from 1968–2015 among children less than 16 years of age and listed in the Danish Cancer Registry [21]. Childhood cancers were grouped according to the International Childhood Cancer Classification (ICCC); ICCC-1 based on the original notification forms corresponding to ICD-O-1 codes until 1977, and ICD-O-1 codes from 1978 until 2003 and ICCC-3 based on ICD-O-3 codes thereafter [22, 23]. We included in analyses the main ICCC groups and specific cancer types with at least 50 cases.

We linked children with cancer to the Central Population Registry (CPR) based on the unique 10-digit Central Person number which is assigned to all persons living in Denmark [24]. From the CPR, we randomly selected controls from all children born in Denmark. We individually matched each case to 100 controls on sex and year of birth. The parent study of this project was designed to assess parental occupational exposures, thus 100 controls were selected to ensure sufficient sample size for rarer exposures. Eligible controls were children who were free of cancer and living in Denmark at the date of their corresponding case's diagnosis.

To obtain covariate information, we also linked children to the Medical Births Registry (MBR) (data available from 1973+) and the Danish National Patient Registry (DNPR) based on their Central Person number. The MBR includes pregnancy information and the DNPR includes all hospital admissions in Denmark since 1977, as well as records for all outpatient visits and emergency room consultations since 1994. Diagnoses are coded according to a modified Danish version of the eighth revision of the International Classification of Diseases

(ICD-8) up to 1993, and thereafter to the tenth revision of the Classification (ICD-10) [25, 26].

As this was a record-based study, we did not seek informed consent from individual subjects. The study received approvals from the human subject's protection boards of the University of California Los Angeles and the Danish Data Protection Agency.

Parental age at child's birth was determined from the date of birth information in the CPR. Given that the previous literature has found mixed results with some studies finding a U-shaped risk with age and others linear increases in risk, we analyzed parental age as both categorical and continuous. We grouped parental age categories as <25, 25–29, 30–34, 35–39, 40–45, 45+, collapsing the top three categories when the number of cases was less than five. The reference group was those in the 25–29 age category. We excluded 6 controls who were born outside of Denmark. Thus, our final sample includes 5,856 cases and 585,594 controls. Supplementary file 1 provides more detailed information on the registries we linked.

We performed conditional logistic regression to assess the effect of parental age on childhood cancer risk. All analyses were conducted using SAS 9.3 software (Cary, NC) and the Proc logistic method with a strata statement to identify our matched sets. We considered covariates for inclusion in the models that have been previously associated with childhood cancer risk, including multiple births, parity, and urban versus rural place of birth [19, 27–30]. Although ethnic group is associated with childhood cancer risk [31], information on ethnic group is not collected in Danish national databases. As a proxy for ethnic group we assessed the inclusion of parental place of birth as a covariate in analyses and categorized it using the definitions of a previous Danish study (Danish/Western/non-Western) [10]. We left parental place of birth and parity in our final models as they changed estimates the most (>5% change). We also performed mutual adjustment for parental age. Due to the large change in estimates with mutual adjustment and the potential collinearity between maternal and paternal age, we present multiple models to show how the estimates changed. Additionally, we conducted a stratified analysis examining the effect of older paternal age (30–34 years and 35+ years vs. <30 yrs) among children with younger (<30 years) mothers to try to tease apart the independent effect of paternal age for ALL. We were unable to look at the effect of older maternal age (35+ years) in younger fathers (<30 years) since there were too few cases that fell into this category (n=5). To assess linear trends in risk with previous studies we modeled maternal and paternal age as continuous variables per 5-year increase in age.

We also conducted analyses stratified by laterality of the tumor for retinoblastoma and Wilms' tumor. Due to its greater frequency of origin in the father's germline [32], bilateral retinoblastoma is typically examined in relation to paternal pre-conception exposures, whereas unilateral disease results from somatic changes in pregnancy or early life, and is studied in relation to maternal exposures [33]. The evidence for a similar presentation of Wilms' tumor is hypothesized but results have been more tenuous for a parent-specific origin.

Social class was defined based on parental job title from criteria developed by the Danish National Center for Social Research (academics or executive managers, middle managers or 3–4 years of further education, other white-collar workers, skilled blue-collar workers, unskilled workers, and unknown or unclassified) [34]. Earlier in the study, job title was reported on income tax forms, whereas in the latter years of the study parents were not required to report their job title in every year, thus the proportion of missing data increased over time. A combined measure of socioeconomic status (SES) for the family was calculated based on the SES of the parent with the highest level. Given the large proportion of missing data we examined the relevance of this covariate in sensitivity analyses only.

Since children with Down syndrome are at an increased risk of leukemia and Down syndrome risk increases with older maternal age [35], we assessed the effect of maternal age on leukemia after excluding Down syndrome cases. Down syndrome information was obtained from the DNPR and the MBR (ICD-8 codes: 759 and ICD-10 codes: Q90). The MBR only collected this variable starting in 1997. Since the DNPR includes only inpatient records for the period prior to 1997, we may have missed some Down syndrome cases. Thus, we also assessed the effect of maternal age on ALL risk excluding subjects born prior to 1997. Furthermore, assisted reproductive technology (ART) started being provided free of charge in 1997 in public hospitals, thus restricting to children born prior to 1997 also allowed us to assess the effect of maternal age on ALL in the period prior to its increased accessibility [36, 37].

Information on parental age is obtained from the CPR, and these parents are legal guardians but not necessarily biological parents. We identified the biological mother from MBR records (data available 1973+) and used those mother's ages in analyses, whereas for the period 1968–1972 we obtained parental ages from CPR records. We conducted sensitivity analyses excluding 1968–1972 to restrict to biological mothers and assess whether estimates changed. For the period starting in 1973, information on the father was obtained from MBR if the father was identified in the birth record by the mother, otherwise we took father's ages from CPR records. For the period 1973–1996 23.1% of fathers are from the MBR and from 1997+ 63.1% are from the MBR, the remaining part are from the CPR. We expect most legal guardians to be biological parents as all children were born in Denmark, and most adoptions in Denmark are of foreign-born children [38]. We analyzed 2014 data – which contained this information – and found that 99.4% of registered legal guardians in our data were the biological parents.

Results

The majority of parents in our sample were 25–29 years of age and first-time parents. Most parents were born in Denmark and children were relatively evenly distributed in the rural, small town, and urban areas of Denmark [Table 1]. We had minimal missing data (<1%) for our main exposures and covariates.

The risk of all cancers was elevated in offspring of mothers aged 35–39 and 40+. We observed an elevated risk of leukemias with older maternal age (35–39) with and without adjustment for paternal age [OR=1.22, 95% CI: (1.11, 1.58), OR=1.36, 95% CI: (1.12,

1.66), respectively] Estimates were very similar in mothers aged 40+, but with wider confidence intervals. For ALL, there was an elevated risk in the 35–39 age group with paternal age adjustment [OR=1.48, 95% CI: 1.19, 1.84], but the estimate dropped in the 40+ age group whereas for AML the risk was highest in the 40+ age group, [OR=2.26, 95% CI: (0.93, 5.45)]. After excluding 544 Down syndrome cases from our analyses, the association between older maternal age and leukemia without mutual adjustment remained similar in the 35–39 age group [OR=1.33, 95% CI: 1.11, 1.59] and in the 40+ age group [OR=1.11, 95% CI: 0.73, 1.69]. The estimates for leukemia after mutual adjustment also did not change in mothers 35–39 [OR=1.36, 95% CI: (1.11, 1.66)] and in mothers 40+. [OR=1.09, 95% CI: 0.70, 1.66]. In subjects born 1997+, the adjusted results for leukemia are the same as those with the exclusion of Down syndrome cases and again similar to our original results in the 35–39 age group [OR=1.33, 95% CI: 1.11, 1.59] and the 40+ age group [OR=1.11, 95% CI: 0.73, 1.69].

We also observed an increased risk of lymphomas with older maternal age, with the strongest associations for Hodgkin lymphomas in the 30–34 age group [OR=1.51, 95% CI: 1.05, 2.18] and NHL in the 35+ group [OR=2.04, 1.26, 3.30] without mutual adjustment. Estimates were slightly attenuated with mutual adjustment. The risk of other specified intracranial and intraspinal neoplasms, germ cell tumors, and other malignant epithelial neoplasms and melanomas were also elevated in mothers 40+ years with and without adjustment for paternal age [Table 2].

For paternal age, we observed a slight increased risk of leukemia and NHL in fathers aged 45+ [OR=1.26, 95% CI: 0.93, 1.70, OR=2.28, 95% CI: 1.06, 4.88, respectively], but it disappeared after adjustment for maternal age. [Table 3].

When modeling parental age as continuous variables per 5-year increase in age, there was an increased risk of cancers overall and leukemias, particularly ALL, for older maternal and paternal age without mutual adjustment. With mutual adjustment associations were attenuated for older paternal age. There was a linear increase in the risk of lymphomas, particularly NHL, with older maternal and paternal age. However, with mutual adjustment associations were slightly attenuated, particularly for paternal age. There was a slightly elevated risk of intracranial and intraspinal embryonal brain tumors, germ cell tumors, and other malignant neoplasms with older maternal age. For paternal age, the risk of Wilms' tumor also appeared elevated with older age [OR=1.11, 95% CI: 0.97, 1.28].

No notable associations by laterality for retinoblastoma and Wilms' tumor were found, although an elevated risk was observed for bilateral Wilms with paternal age over 35 in crude analyses [Table 5].

When we adjusted for family SES, we found similar patterns in cancer risk, but with wider confidence intervals due to the large proportion of missing data for this variable. When we limited our sample to those born 1973 onwards, we found similar estimates for maternal age in relation to childhood cancer risk. Additionally, the effect of paternal age among younger mothers was null for fathers 30–34 years and the 35+ years compared to fathers <30 years

[Adjusted OR=0.95, 95% CI: 0.80, 1.12, Adjusted OR=1.00, 95% CI: [0.77, 1.30], respectively].

Discussion

In this population-based study we estimated an increased risk of leukemia, particularly ALL, NHL, other specified intracranial and intraspinal embryonal brain tumors, germ cell tumors, and other malignant epithelial neoplasms and melanomas with advanced maternal age. These associations were fairly consistent in both categorical and continuous models. For older paternal age, we found an increased risk of leukemia and NHL, but with adjustment for maternal age, results were attenuated. We also found a slight increased risk of Wilms' tumor with older paternal age.

Our findings for ALL largely affirm the results of previous studies which reported an increased risk of ALL with older maternal age [7–9, 16, 19]. However, our results contradict the strong association between older paternal age (45+) and ALL that persisted with adjustment for maternal age in a recent registry-based Danish cohort study [10]. Our study includes more years of data thus we have more cases of ALL (1365 vs. 1110). Their crude and mutually adjusted estimates were very similar, and adjusted for nearly the same variables (parity, parental place of birth, maternal age), with the exception of SES, but in sensitivity analyses SES changed estimates minimally. In our linear analyses, the risk of ALL does appear to be slightly increased with older fathers. It could be that our study had less power to detect these associations since our study was a case-control design and did not have follow-up time.

Interestingly, the findings of a large pooled analysis of 5 US States mirror our results for lymphoma with attenuations with older paternal and maternal age when mutually adjusting [9]. A recent California population-based registry study also found an increased risk of lymphomas for older paternal and maternal age though associations persisted with mutual adjustment [8].

Other specified intracranial and intraspinal embryonal brain tumors, germ cell tumors, and other malignant epithelial neoplasms and melanomas have not been well-studied to date. The only previous case-control study that examined both other specified intracranial and intraspinal embryonal brain tumors and other malignant epithelial neoplasms and melanomas was the California population-based registry, which found an elevated risk for both [8]. Of the two studies that have examined germ cell tumors, the US pooled analysis found no association and the California study found an association with older maternal age [8, 9].

There are various explanations for the increased risk of childhood cancers with older maternal age, but the most commonly cited is the accumulation of chromosomal aberrations and *de novo* mutations in females with older age. An increased rate of *de novo* mutations has been more consistently linked with advanced paternal age than maternal age, likely due to the greater number of cell divisions in spermatogonial cells compared to oogonial cells. Despite more limited evidence on a link between *de novo* point mutations and older

maternal age, older maternal age has been well-established as a risk factor for chromosomal nondisjunction involved in aneuploidies [39]. Down syndrome is one example of a chromosomal abnormality that is mostly of maternal origin and occurs more frequently with older age, with mothers 40+ at childbirth having a 17% higher risk of having a child with Down syndrome [40]. Children with Down syndrome have a 10- to 20- fold increased risk of leukemia, though the exact causes for this are unknown. Currently, older maternal age is the only identified shared risk factor for both Down syndrome and leukemia [35]. However, the association between older maternal age and ALL did not change after exclusion of Down syndrome cases, suggesting that this effect is independent of the higher risk of ALL in children with Down syndrome. Other potential mechanisms that may explain the association between maternal age and childhood cancer risk include age-related changes in hormonal levels or oocyte quality and gene expression, or transgenerational inheritance of epigenetic mutations in oocytes [9, 41, 42].

Another factor that has been well studied with respect to childhood cancers and that is also more prevalent with older age is the use of ART. In Denmark in 1997 about 2.6% of births were born by ART and by 2012 the proportion had risen to 6.1%. [43, 44]. Several European population-based studies, including one using data from Denmark, have shown an increased risk of leukemias, CNS tumors, neuroblastomas, retinoblastomas, and Hodgkin lymphomas in children conceived by ART, with several mechanisms posited to underlie this association [45–48]. It is also hypothesized that the association with childhood cancers may be due to factors related to underlying subfertility rather than the treatment for infertility itself, as assessed in several studies. Most studies that investigated time to pregnancy or the need for medical consultation for infertility found no association with leukemia, but these studies did not differentiate between women who received treatment for infertility or not [49–54]. A study in Denmark obtained information from the Danish Infertility Cohort, which consists of women with fertility problems referred to medical facilities in Denmark and those with a diagnosis of infertility from the National Patient Register or the Danish IVF registry (e.g. this analysis captured all women diagnosed with fertility problems but did not have information on the use of fertility treatment). This study found an increased risk of childhood leukemia and cancer of the endocrine glands with maternal infertility [55]. One study that examined difficulty becoming pregnant (taking more than one year to conceive the index child and/or the need to consult a doctor and/or undergo fertility treatment), and only included women without infertility treatment, found a positive association with ALL [56]. We did not have the data to assess whether ART could have impacted our estimates, but when we looked in the period before 1997 with presumably lower ART use, the effect of older maternal age persisted.

Older paternal age should be particularly relevant for bilateral retinoblastoma since the rate of new mutations in gametes increase with advancing age and there is evidence suggesting that new germline mutations predisposing to these cancers are preferentially inherited from fathers [57–59]. Although Wilms' tumor was originally thought to follow the same model of inheritance as retinoblastoma, the genetics of Wilms' tumor have been shown to be more complex, with the involvement of multiple genes and mechanisms. More recent epidemiological evidence also support that an inherited mutation may not be responsible for bilateral Wilms' tumor as a similar number of familial cases have been found to be

transmitted via fathers and mothers with similar distributions of age at diagnosis [60–62]. Our findings did not corroborate the importance of older paternal age for bilateral retinoblastoma and bilateral Wilms' tumor since we found no notable differences by laterality of the tumor. Several studies have reported an increased risk of retinoblastoma, mostly bilateral, with advanced paternal age [13, 19, 27, 63, 64]. In our study the association between retinoblastoma and paternal age appeared slightly elevated in categorical and linear models, but confidence intervals were too large to report any conclusive findings. For Wilms' tumor, studies with different study designs and using various age groups have reported null results. However, the National Wilms' Tumor study, with the largest case group to date, found an increasing incidence of Wilms' tumor with increasing paternal age and no notable differences by laterality of the tumor [9, 17, 65]. In our study we found a positive association for Wilms' tumor with older paternal age, which was most apparent in linear models.

Potential limitations of our study include the strong correlation between maternal and paternal age ($r=0.71$) which made it difficult to assess the independent influences of each, hence we presented results with and without adjustment to allow for comparison. We also assessed the potential independent impact of older paternal age by restricting to younger mothers and found that there was no increased risk, with largely null estimates, mirroring our results with mutual adjustment for maternal age. This suggests that the increased risk of ALL is likely due to older maternal age, not paternal age, and that mutual adjustment should be done in future studies.

Additionally, there was the possibility of residual confounding for ALL since some diagnoses of Down syndrome might not be captured in the earlier years when the DNPR only collected information on inpatient diagnoses. We were only able to assess whether the inclusion of legal mothers in our sample might affect the results, but not legal fathers. No studies to date have investigated the potential discrepancy between legal and biological parents in the Danish data, though a meta-analysis that included data from various countries found the rate to be about 3.7% [66].

To date most large population-based studies have been limited to more common cancer types, thus a strength of our study is the inclusion of rare cancer types. Additionally, our study design was population-based and validation studies have shown these registers to be of high quality with low rates of misclassification [26, 67–69].

In conclusion, in this population-based study we found a consistently increased risk of ALL among offspring born to older mothers as well as an increased risk of Wilms' tumor with advancing paternal age.

Supplementary Material

Refer to Web version on PubMed Central for supplementary material.

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Highlights

- A linear increase in childhood cancer risk with advancing maternal age was found.
- A linear increase in ALL risk with advancing maternal age was found.
- A linear increase in Wilms' tumor risk with advancing paternal age was found.

Table 1

Parental sociodemographic characteristics of cases and controls, birth years 1968–2014

	Controls	Cases	I. Leukemias	II. Lymphomas	III. CNS tumors	IV. Neuroblastomas and other peripheral nervous cell tumors	V. Retinoblastoma
Cases N	585594	5856	1733	578	1548	346	163
	N (%)	N (%)	N (%)	N (%)	N (%)	N (%)	N (%)
Mother's age at child's birth							
<25 years	158957 (27.1)	1532 (26.2)	434 (25.0)	164 (28.4)	418 (27.0)	94 (27.2)	49 (30.1)
25–29 years	218814 (37.4)	2214 (37.8)	632 (36.5)	196 (33.9)	599 (38.7)	126 (36.4)	58 (35.6)
30–35 years	147890 (25.3)	1441 (24.6)	448 (25.9)	146 (25.3)	381 (24.6)	88 (25.4)	37 (22.7)
35–39 years	51551 (8.8)	578 (9.9)	191 (11.0)	65 (11.3)	125 (8.1)	34 (9.8)	17 (10.4)
40+ years	8381 (1.4)	91 (1.6)	28 (1.6)	7 (1.2)	25 (1.6)	4 (1.2)	2 (1.2)
Missing	1 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
Father's age at child's birth							
<25 years	81167 (13.9)	740 (12.6)	209 (12.1)	80 (13.8)	213 (13.8)	39 (11.3)	20 (12.3)
25–29 years	189912 (32.4)	1927 (32.9)	565 (32.6)	179 (31.0)	516 (33.3)	115 (33.2)	53 (32.5)
30–34 years	178929 (30.6)	1788 (30.5)	531 (30.6)	177 (30.6)	465 (30.0)	110 (31.8)	46 (28.2)
35–39 years	88119 (15.1)	898 (15.3)	261 (15.1)	90 (15.6)	240 (15.5)	54 (15.6)	31 (19.0)
40–44 years	30659 (5.2)	315 (5.4)	105 (6.1)	32 (5.5)	66 (4.3)	17 (4.9)	8 (4.9)
45+ years	13103 (2.2)	142 (2.4)	50 (2.9)	15 (2.6)	30 (1.9)	8 (2.3)	4 (2.5)
Missing	3705 (0.6)	46 (0.8)	12 (0.7)	5 (0.9)	18 (1.2)	3 (0.9)	1 (0.6)
Mother's place of birth							
Danish	548688 (93.7)	5472 (93.4)	1624 (93.7)	535 (92.6)	1452 (93.8)	320 (92.5)	155 (95.1)
Western	6391 (1.1)	74 (1.3)	23 (1.3)	8 (1.4)	20 (1.3)	7 (2.0)	1 (0.6)
Non-Western	29127 (5.0)	296 (5.1)	82 (4.7)	34 (5.9)	73 (4.7)	18 (5.2)	7 (4.3)
Unknown or missing	1388 (0.2)	14 (0.2)	4 (0.2)	1 (0.2)	3 (0.2)	1 (0.3)	0 (0.0)
Father's place of birth							
Danish	541042 (92.4)	5357 (91.5)	1587 (91.6)	526 (91.0)	1426 (92.1)	310 (89.6)	148 (90.8)
Western	9466 (1.6)	99 (1.7)	26 (1.5)	11 (1.9)	24 (1.6)	7 (2.0)	3 (1.8)
Non-Western	29540 (5.0)	321 (5.5)	97 (5.6)	35 (6.1)	72 (4.7)	26 (7.5)	11 (6.8)

	Controls	Cases	I. Leukemias	II. Lymphomas	III. CNS tumors	IV. Neuroblastomas and other peripheral nervous cell tumors	V. Retinoblastoma
Cases N	585594	5856	1733	578	1548	346	163
	N (%)	N (%)	N (%)	N (%)	N (%)	N (%)	N (%)
Unknown or missing	5546 (1.0)	79 (1.4)	23 (1.3)	6 (1.0)	26 (1.7)	3 (0.9)	1 (0.6)
Child's place of birth							
Urban	201070 (34.3)	2039 (34.8)	581 (33.5)	232 (40.1)	549 (35.5)	137 (39.6)	55 (33.7)
Small Towns	185596 (31.7)	1818 (31.1)	539 (31.1)	172 (29.8)	483 (31.2)	105 (30.4)	54 (33.1)
Rural	198928 (34.0)	1999 (34.1)	613 (35.4)	174 (30.1)	516 (33.3)	104 (30.1)	54 (33.1)
Parity							
0	260224 (44.4)	2637 (45.0)	775 (44.7)	275 (47.6)	703 (45.4)	146 (42.2)	70 (42.9)
1	218214 (37.3)	2165 (37.0)	648 (37.4)	207 (35.8)	568 (36.7)	127 (36.7)	58 (35.6)
2	79771 (13.6)	771 (13.2)	228 (13.2)	67 (11.6)	209 (13.5)	55 (15.9)	25 (15.3)
3	19845 (3.4)	213 (3.6)	56 (3.2)	24 (4.2)	50 (3.2)	13 (3.8)	6 (3.7)
4+	7540 (1.3)	70 (1.2)	26 (1.5)	5 (0.9)	18 (1.2)	5 (1.5)	4 (2.5)
Multiple births							
1	569451 (97.2)	5679 (97.0)	1691 (97.6)	558 (96.5)	1496 (96.6)	337 (97.4)	155 (95.1)
2+	16143 (2.8)	177 (3.0)	42 (2.4)	20 (3.5)	52 (3.4)	9 (2.6)	8 (4.9)
Family SES							
1 (highest)	55787 (9.5)	534 (9.1)	150 (8.7)	58 (10.0)	153 (9.9)	33 (9.5)	11 (6.8)
2	71685 (12.2)	728 (12.4)	216 (12.5)	67 (11.6)	195 (12.6)	46 (13.3)	18 (11.0)
3	80333 (13.7)	820 (14.0)	231 (13.3)	77 (13.3)	226 (14.6)	50 (14.5)	18 (11.0)
4	143161 (24.5)	1453 (24.8)	433 (25.0)	153 (26.5)	379 (24.5)	82 (23.7)	51 (31.3)
5 (lowest)	74266 (12.7)	735 (12.6)	224 (12.9)	68 (11.8)	198 (12.8)	42 (12.1)	15 (9.2)
Missing	160362 (27.4)	1586 (27.1)	479 (27.6)	155 (26.8)	397 (25.7)	93 (26.9)	50 (30.7)

	VI. Renal tumors	VII. Hepatic tumors	VIII. Malignant bone tumors	IX. Soft tissue sarcomas	X. Germ cell tumors	XI. Other malignant epithelial neoplasms and malignant melanomas	XII. Other and unspecified malignant neoplasms
Cases N	293	73	266	342	166	268	80
	N (%)	N (%)	N (%)	N (%)	N (%)	N (%)	N (%)
Mother's age at child's birth							

	VI. Renal tumors	VII. Hepatic tumors	VIII. Malignant bone tumors	IX. Soft tissue sarcomas	X. Germ cell tumors	XI. Other malignant epithelial neoplasms and malignant melanomas	XII. Other and unspecified malignant neoplasms
Cases N	293	73	266	342	166	268	80
	N (%)	N (%)	N (%)	N (%)	N (%)	N (%)	N (%)
<25 years	71 (24.2)	14 (19.2)	69 (25.9)	95 (27.8)	39 (23.5)	67 (25.0)	18 (22.5)
25–29 years	121 (41.3)	29 (39.7)	111 (41.7)	145 (42.4)	63 (38.0)	102 (38.1)	32 (40.0)
30–35 years	68 (23.2)	18 (24.7)	55 (20.7)	72 (21.1)	41 (24.7)	67 (25.0)	20 (25.0)
35–39 years	29 (9.9)	10 (13.7)	26 (9.8)	25 (7.3)	17 (10.2)	29 (10.8)	10 (12.5)
40+ years	4 (1.4)	2 (2.7)	5 (1.9)	5 (1.5)	6 (3.6)	3 (1.1)	0 (0.0)
Missing	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
Father's age at child's birth							
<25 years	37 (12.6)	6 (8.2)	27 (10.2)	51 (14.9)	17 (10.2)	34 (12.7)	7 (8.8)
25–29 years	94 (32.1)	24 (32.9)	86 (32.3)	119 (34.8)	54 (32.5)	95 (35.5)	27 (33.8)
30–34 years	91 (31.1)	25 (34.3)	88 (33.1)	90 (26.3)	55 (33.1)	81 (30.2)	29 (36.3)
35–39 years	43 (14.7)	10 (13.7)	39 (14.7)	53 (15.5)	26 (15.7)	39 (14.6)	12 (15.0)
40–44 years	18 (6.1)	7 (9.6)	18 (6.8)	16 (4.7)	12 (7.2)	13 (4.9)	3 (3.8)
45+ years	9 (3.1)	1 (1.4)	5 (1.9)	12 (3.5)	2 (1.2)	5 (1.9)	1 (1.3)
Missing	1 (0.3)	0 (0.0)	3 (1.1)	1 (0.3)	0 (0.0)	1 (0.4)	1 (1.3)
Mother's place of birth							
Danish	282 (96.3)	67 (91.8)	250 (94.0)	315 (92.1)	157 (94.6)	245 (91.4)	70 (87.5)
Western	3 (1.0)	3 (4.1)	3 (1.1)	1 (0.3)	3 (1.8)	1 (0.4)	1 (1.3)
Non-Western	8 (2.7)	2 (2.7)	13 (4.9)	24 (7.0)	6 (3.6)	20 (7.5)	9 (11.3)
Unknown or missing	0 (0.0)	1 (1.4)	0 (0.0)	2 (0.6)	0 (0.0)	2 (0.8)	0 (0.0)
Father's place of birth							
Danish	279 (95.2)	66 (90.4)	244 (91.7)	311 (90.9)	151 (91.0)	244 (91.0)	65 (81.3)
Western	5 (1.7)	1 (1.4)	5 (1.9)	5 (1.5)	6 (3.6)	4 (1.5)	2 (2.5)
Non-Western	5 (1.7)	3 (4.1)	13 (4.9)	24 (7.0)	8 (4.8)	16 (6.0)	11 (13.8)
Unknown or missing	4 (1.4)	3 (4.1)	4 (1.5)	2 (0.6)	1 (0.6)	4 (1.5)	2 (2.5)
Child's place of birth							
Urban	94 (32.1)	16 (21.9)	84 (31.6)	116 (33.9)	58 (34.9)	85 (31.7)	32 (40.0)
Small Towns	103 (35.2)	19 (26.0)	80 (30.1)	120 (35.1)	46 (27.7)	73 (27.2)	24 (30.0)

	VI. Renal tumors	VII. Hepatic tumors	VIII. Malignant bone tumors	IX. Soft tissue sarcomas	X. Germ cell tumors	XI. Other malignant epithelial neoplasms and malignant melanomas	XII. Other and unspecified malignant neoplasms
Cases N	293	73	266	342	166	268	80
	N (%)	N (%)	N (%)	N (%)	N (%)	N (%)	N (%)
Rural	96 (32.8)	38 (52.1)	102 (38.4)	106 (31.0)	62 (37.4)	110 (41.0)	24 (30.0)
Parity							
0	128 (43.7)	33 (45.2)	117 (44.0)	157 (45.9)	69 (41.6)	129 (48.1)	35 (43.8)
1	109 (37.2)	27 (37.0)	96 (36.1)	131 (38.3)	62 (37.4)	103 (38.4)	29 (36.3)
2	41 (14.0)	7 (9.6)	35 (13.2)	42 (12.3)	24 (14.5)	26 (9.7)	12 (15.0)
3	11 (3.8)	5 (6.9)	18 (6.8)	9 (2.6)	9 (5.4)	8 (3.0)	4 (5.0)
4+	4 (1.4)	1 (1.4)	0 (0.0)	3 (0.9)	2 (1.2)	2 (0.8)	0 (0.0)
Multiple births							
1	286 (97.6)	69 (94.5)	259 (97.4)	330 (96.5)	163 (98.2)	260 (97.0)	75 (93.8)
2+	7 (2.4)	4 (5.5)	7 (2.6)	12 (3.5)	3 (1.8)	8 (3.0)	5 (6.3)
Family SES							
1 (highest)	30 (10.2)	8 (11.0)	22 (8.3)	28 (8.2)	15 (9.0)	21 (7.8)	5 (6.3)
2	38 (13.0)	11 (15.1)	35 (13.2)	41 (12.0)	21 (12.7)	36 (13.4)	4 (5.0)
3	43 (14.7)	8 (11.0)	48 (18.1)	48 (14.0)	22 (13.3)	39 (14.6)	10 (12.5)
4	72 (24.6)	16 (21.9)	52 (23.3)	86 (25.2)	40 (24.1)	70 (26.1)	9 (11.3)
5 (lowest)	38 (13.0)	10 (13.7)	26 (9.8)	46 (13.5)	22 (13.3)	36 (13.4)	10 (12.5)
Missing	72 (24.6)	20 (27.4)	73 (27.4)	93 (27.2)	46 (27.7)	66 (24.6)	42 (52.5)

Table 2

Conditional logistic regression models for the association between childhood cancers and mother's age at child's birth

Mother's age (y)	Cases N	Crude OR (95% CI)	Adjusted OR (95% CI) ^a	Adjusted OR (95% CI) ^b
All cancers				
<25	1532	0.95 (0.89, 1.01)	0.93 (0.87, 1.00)	0.97 (0.89, 1.04)
25–29	2214	ref	ref	ref
30–34	1441	0.97 (0.90, 1.03)	0.98 (0.92, 1.05)	0.98 (0.91, 1.06)
35–39	578	1.11 (1.01, 1.22)	1.13 (1.03, 1.25)	1.14 (1.02, 1.27)
40+	91	1.08 (0.87, 1.33)	1.13 (0.91, 1.41)	1.14 (0.91, 1.43)
I. Leukemias				
<25	434	0.93 (0.82, 1.05)	0.90 (0.79, 1.03)	0.94 (0.81, 1.08)
25–29	632	ref	ref	ref
30–34	448	1.05 (0.93, 1.18)	1.09 (0.96, 1.23)	1.11 (0.97, 1.27)
35–39	191	1.25 (1.06, 1.48)	1.22 (1.11, 1.58)	1.36 (1.12, 1.66)
40+	28	1.15 (0.79, 1.69)	1.22 (0.82, 1.81)	1.20 (0.79, 1.82)
Ia. ALL				
<25	336	0.91 (0.79, 1.05)	0.87 (0.76, 1.01)	0.95 (0.81, 1.12)
25–29	498	ref	ref	ref
30–34	362	1.08 (0.94, 1.24)	1.13 (0.98, 1.30)	1.15 (0.99, 1.34)
35–39	159	1.34 (1.12, 1.61)	1.44 (1.19, 1.75)	1.48 (1.19, 1.84)
40+	18	0.95 (0.59, 1.52)	0.99 (0.61, 1.63)	0.98 (0.59, 1.64)
Ib. AML				
<25	69	1.04 (0.75, 1.43)	1.15 (0.82, 1.60)	1.05 (0.72, 1.53)
25–29	92	ref	ref	ref
30–34	59	0.91 (0.65, 1.27)	0.90 (0.64, 1.27)	0.95 (0.66, 1.37)
35–39	28	1.18 (0.77, 1.82)	1.15 (0.72, 1.81)	1.24 (0.74, 2.09)
40+	7	1.90 (0.87, 4.15)	1.98 (0.89, 4.38)	2.26 (0.93, 5.45)
II. Lymphomas				
<25	164	1.12 (0.90, 1.38)	1.06 (0.85, 1.32)	1.11 (0.87, 1.42)
25–29	196	ref	ref	ref
30–34	146	1.11 (0.90, 1.38)	1.17 (0.93, 1.46)	1.13 (0.89, 1.44)
35–39	65	1.43 (1.08, 1.91)	1.59 (1.18, 2.14)	1.54 (1.10, 2.15)
40+	7	0.94 (0.44, 2.00)	1.06 (0.49, 2.29)	1.01 (0.45, 2.25)
IIa. Hodgkin lymphomas				
<25	60	1.30 (0.91, 1.86)	1.25 (0.86, 1.82)	1.33 (0.88, 2.00)
25–29	64	ref	ref	ref
30–34	61	1.50 (1.05, 2.14)	1.51 (1.05, 2.18)	1.45 (0.98, 2.15)
35+	20	1.31 (0.79, 2.17)	1.34 (0.78, 2.28)	1.24 (0.68, 2.24)

Mother's age (y)	Cases N	Crude OR (95% CI)	Adjusted OR (95% CI) ^a	Adjusted OR (95% CI) ^b
IIb. NHL				
<25	55	1.06 (0.74, 1.54)	0.97 (0.66, 1.42)	1.03 (0.67, 1.56)
25–29	64	ref	ref	ref
30–34	40	0.94 (0.63, 1.41)	1.07 (0.71, 1.62)	1.06 (0.68, 1.65)
35+	28	1.69 (1.07, 2.66)	2.04 (1.26, 3.30)	1.96 (1.12, 3.43)
IIc. Burkitt lymphoma				
<25	29	1.13 (0.69, 1.85)	1.11 (0.66, 1.85)	1.18 (0.66, 2.09)
25–29	38	ref	ref	ref
30–34	24	0.86 (0.51, 1.44)	0.87 (0.51, 1.48)	0.84 (0.48, 1.49)
35+	13	1.03 (0.54, 1.97)	1.18 (0.60, 2.32)	1.34 (0.61, 2.91)
III. CNS tumors				
<25	418	0.98 (0.86, 1.11)	0.97 (0.85, 1.11)	0.96 (0.83, 1.12)
25–29	599	ref	ref	ref
30–34	381	0.95 (0.84, 1.09)	0.96 (0.84, 1.01)	0.97 (0.84, 1.12)
35–39	125	0.92 (0.75, 1.11)	0.89 (0.73, 1.10)	0.93 (0.74, 1.16)
40+	25	1.15 (0.77, 1.72)	1.20 (0.79, 1.81)	1.33 (0.86, 2.06)
IIIa. Ependymomas				
<25	46	1.34 (0.88, 2.03)	1.44 (0.92, 2.23)	1.43 (0.88, 2.32)
25–29	46	ref	ref	ref
30–34	27	0.93 (0.57, 1.50)	0.92 (0.56, 1.51)	1.01 (0.59, 1.71)
35+	15	1.30 (0.72, 2.35)	1.19 (0.63, 2.26)	1.43 (0.68, 3.02)
IIIb. Astrocytomas				
<25	147	0.99 (0.80, 1.23)	0.98 (0.79, 1.23)	1.01 (0.79, 1.30)
25–29	205	ref	ref	ref
30–34	118	0.90 (0.71, 1.13)	0.92 (0.73, 1.17)	0.92 (0.71, 1.18)
35–39	37	0.88 (0.62, 1.26)	0.86 (0.59, 1.25)	0.88 (0.58, 1.32)
40+	6	0.82 (0.36, 1.87)	0.86 (0.38, 1.99)	1.02 (0.43, 2.42)
IIIc. Intracranial and intraspinal embryonal tumors				
<25	74	1.08 (0.79, 1.46)	1.04 (0.75, 1.44)	1.03 (0.72, 1.47)
25–29	97	ref	ref	ref
30–34	57	0.87 (0.62, 1.21)	0.91 (0.65, 1.28)	1.01 (0.70, 1.45)
35+	27	1.04 (0.67, 1.61)	1.18 (0.75, 1.87)	1.50 (0.89, 2.54)
IIIc1. Medulloblastomas				
<25	71	1.09 (0.79, 1.50)	1.05 (0.75, 1.46)	1.04 (0.72, 1.51)
25–29	88	ref	ref	ref
30–34	50	0.87 (0.61, 1.24)	0.92 (0.64, 1.32)	1.04 (0.71, 1.54)
35+	24	1.09 (0.69, 1.74)	1.23 (0.76, 2.00)	1.59 (0.91, 2.77)
IIIe. Other specified intracranial and intraspinal neoplasms				
<25	118	0.83 (0.66, 1.04)	0.81 (0.64, 1.03)	0.80 (0.61, 1.04)

Mother's age (y)	Cases N	Crude OR (95% CI)	Adjusted OR (95% CI) ^a	Adjusted OR (95% CI) ^b
25–29	211	ref	ref	ref
30–34	153	1.04 (0.84, 1.28)	1.03 (0.83, 1.28)	1.00 (0.79, 1.26)
35–39	40	0.75 (0.53, 1.06)	0.71 (0.49, 1.02)	0.70 (0.47, 1.04)
40+	15	1.81 (1.06, 3.07)	1.85 (1.07, 3.20)	2.00 (1.09, 3.67)
IIIc. Unspecified intracranial and intraspinal neoplasms				
<25	31	0.89 (0.58, 1.37)	0.88 (0.56, 1.38)	0.82 (0.49, 1.36)
25–29	72	ref	ref	ref
30–34	68	1.05 (0.75, 1.47)	0.95 (0.67, 1.34)	0.90 (0.62, 1.30)
35–39	20	0.76 (0.46, 1.26)	0.67 (0.40, 1.14)	0.62 (0.35, 1.11)
40+	6	1.40 (0.60, 3.26)	1.36 (0.57, 3.23)	1.23 (0.47, 3.17)
IV. Neuroblastoma and other peripheral nervous cell tumors				
<25	94	1.00 (0.76, 1.32)	1.00 (0.75, 1.33)	1.11 (0.81, 1.51)
25–29	126	ref	ref	ref
30–34	88	1.03 (0.78, 1.36)	0.99 (0.75, 1.32)	0.99 (0.73, 1.34)
35+	38	1.12 (0.77, 1.62)	1.05 (0.71, 1.56)	1.10 (0.71, 1.72)
IVa. Neuroblastoma and ganglioneuroblastoma				
<25	91	1.02 (0.77, 1.34)	1.04 (0.77, 1.39)	1.14 (0.83, 1.57)
25–29	119	ref	ref	ref
30–34	85	1.06 (0.80, 1.40)	1.01 (0.75, 1.35)	1.01 (0.74, 1.38)
35+	35	1.10 (0.75, 1.61)	1.03 (0.68, 1.54)	1.09 (0.69, 1.72)
V. Retinoblastoma				
<25	49	1.20 (0.81, 1.78)	1.24 (0.82, 1.86)	1.36 (0.87, 2.12)
25–29	58	ref	ref	ref
30–34	37	0.93 (0.61, 1.41)	0.86 (0.56, 1.32)	0.82 (0.52, 1.29)
35+	19	1.13 (0.67, 1.92)	0.98 (0.56, 1.73)	0.90 (0.48, 1.68)
VI. Renal tumors				
<25	71	0.73 (0.54, 0.98)	0.77 (0.56, 1.05)	0.80 (0.56, 1.14)
25–29	121	ref	ref	ref
30–34	68	0.86 (0.64, 1.17)	0.82 (0.60, 1.13)	0.77 (0.55, 1.08)
35+	33	1.00 (0.68, 1.49)	0.94 (0.62, 1.44)	0.80 (0.49, 1.30)
VIa. Nephroblastoma and other nonepithelial renal tumors^c				
<25	69	0.80 (0.59, 1.09)	0.85 (0.62, 1.17)	0.89 (0.62, 1.28)
25–29	106	ref	ref	ref
30–34	61	0.89 (0.65, 1.23)	0.86 (0.61, 1.19)	0.78 (0.55, 1.11)
35+	30	1.05 (0.69, 1.58)	0.98 (0.63, 1.53)	0.80 (0.48, 1.34)
VII. Hepatic tumors				
<25	14	0.77 (0.40, 1.47)	0.80 (0.40, 1.57)	0.91 (0.43, 1.91)
25–29	29	ref	ref	ref
30–34	18	0.87 (0.48, 1.59)	0.91 (0.49, 1.72)	0.92 (0.47, 1.79)

Mother's age (y)	Cases N	Crude OR (95% CI)	Adjusted OR (95% CI) ^a	Adjusted OR (95% CI) ^b
35+	12	1.49 (0.75, 2.98)	1.63 (0.77, 3.45)	1.68 (0.70, 4.01)
VIIa. Hepatoblastoma				
<25	11	0.70 (0.34, 1.44)	0.71 (0.33, 1.51)	0.74 (0.31, 1.74)
25–29	25	ref	ref	ref
30–34	14	0.77 (0.40, 1.50)	0.82 (0.41, 1.67)	0.79 (0.38, 1.68)
35+	9	1.25 (0.57, 2.73)	1.41 (0.60, 3.30)	1.28 (0.47, 3.46)
VIII. Malignant bone tumors				
<25	69	0.85 (0.63, 1.16)	0.82 (0.60, 1.14)	0.99 (0.69, 1.41)
25–29	111	ref	ref	ref
30–34	55	0.76 (0.55, 1.06)	0.76 (0.54, 1.06)	0.72 (0.50, 1.02)
35–39	26	1.06 (0.68, 1.63)	1.02 (0.65, 1.62)	0.97 (0.58, 1.62)
40+	5	1.26 (0.51, 3.11)	1.27 (0.51, 3.20)	1.17 (0.44, 3.15)
IX. Soft tissue sarcomas				
<25	95	0.93 (0.71, 1.21)	0.90 (0.69, 1.19)	0.86 (0.63, 1.16)
25–29	145	ref	ref	ref
30–34	72	0.72 (0.54, 0.97)	0.73 (0.54, 0.98)	0.72 (0.52, 0.98)
35–39	25	0.70 (0.46, 1.08)	0.70 (0.45, 1.11)	0.63 (0.38, 1.04)
40+	5	0.86 (0.35, 2.13)	0.93 (0.37, 2.31)	0.77 (0.29, 2.02)
IXa. Rhabdomyosarcoma				
<25	44	1.09 (0.74, 1.63)	1.16 (0.77, 1.77)	1.06 (0.68, 1.68)
25–29	60	ref	ref	ref
30–34	32	0.74 (0.48, 1.15)	0.71 (0.45, 1.10)	0.83 (0.51, 1.36)
35+	17	0.93 (0.54, 1.62)	0.82 (0.45, 1.48)	0.95 (0.48, 1.88)
X. Germ cell tumors				
<25	39	0.83 (0.55, 1.25)	0.82 (0.53, 1.24)	0.90 (0.57, 1.44)
25–29	63	ref	ref	ref
30–34	41	0.98 (0.66, 1.46)	0.97 (0.65, 1.46)	0.95 (0.62, 1.47)
35–39	17	1.24 (0.72, 2.14)	1.22 (0.69, 2.17)	1.27 (0.67, 2.41)
40+	6	2.35 (1.00, 5.53)	2.32 (0.96, 5.61)	2.49 (0.93, 6.72)
XI. Other malignant epithelial neoplasms and malignant melanomas				
<25	67	0.96 (0.70, 1.31)	0.88 (0.64, 1.22)	0.88 (0.61, 1.26)
25–29	102	ref	ref	ref
30–34	67	0.98 (0.72, 1.33)	1.06 (0.77, 1.47)	1.14 (0.81, 1.61)
35+	32	1.22 (0.81, 1.82)	1.37 (0.89, 2.10)	1.57 (0.96, 2.57)
XId. Melanoma				
<25	19	0.91 (0.51, 1.62)	0.86 (0.47, 1.55)	0.88 (0.46, 1.69)
25–29	34	ref	ref	ref
30–34	14	0.63 (0.33, 1.18)	0.66 (0.35, 1.25)	0.73 (0.37, 1.44)
35+	7	0.82 (0.36, 1.87)	0.96 (0.41, 2.25)	1.16 (0.44, 3.04)

Mother's age (y)	Cases N	Crude OR (95%CI)	Adjusted OR (95% CI) ^a	Adjusted OR (95% CI) ^b
XII. Other and unspecified malignant neoplasms				
<25	18	0.90 (0.50, 1.62)	0.85 (0.46, 1.56)	0.96 (0.49, 1.87)
25–29	32	ref	ref	ref
30–34	20	0.77 (0.44, 1.35)	0.71 (0.40, 1.28)	0.79 (0.42, 1.46)
35+	10	0.92 (0.45, 1.90)	0.84 (0.38, 1.84)	1.16 (0.47, 2.83)

^a Adjusted for parental place of birth, parity

^b Adjusted for parental place of birth, parity, maternal age

^c Wilms' tumor cases corresponding to ICCC VIa1 are not shown as a separate category because they overlap completely with this category in our sample

Table 3

Conditional logistic regression models for the association between childhood cancers and father's age at child's birth

Father's age (y)	Cases N	Crude OR (95%CI)	Adjusted OR (95% CI) ^a	Adjusted OR (95% CI) ^b
All cancers				
<25	740	0.90 (0.82, 0.98)	0.89 (0.82, 0.97)	0.90 (0.82, 0.99)
25–29	1927	ref	ref	ref
30–34	1788	0.99 (0.93, 1.05)	1.00 (0.94, 1.07)	1.00 (0.93, 1.07)
35–39	898	1.01 (0.93, 1.09)	1.02 (0.94, 1.11)	0.99 (0.90, 1.09)
40–44	315	1.02 (0.90, 1.15)	1.03 (0.91, 1.17)	0.97 (0.85, 1.11)
45+	142	1.07 (0.90, 1.27)	1.07 (0.90, 1.28)	1.00 (0.83, 1.21)
I. Leukemias				
<25	209	0.84 (0.72, 0.99)	0.84 (0.71, 0.98)	0.86 (0.72, 1.03)
25–29	565	ref	ref	ref
30–34	531	0.99 (0.88, 1.12)	1.00 (0.89, 1.13)	0.95 (0.84, 1.09)
35–39	261	0.97 (0.84, 1.13)	1.00 (0.85, 1.16)	0.89 (0.74, 1.05)
40–44	105	1.13 (0.91, 1.39)	1.14 (0.91, 1.42)	0.98 (0.77, 1.24)
45+	50	1.26 (0.94, 1.68)	1.26 (0.93, 1.70)	1.07 (0.78, 1.48)
Ia. ALL				
<25	150	0.76 (0.63, 0.92)	0.75 (0.62, 0.90)	0.76 (0.62, 0.93)
25–29	450	ref	ref	ref
30–34	434	1.02 (0.89, 1.16)	1.04 (0.91, 1.19)	0.98 (0.85, 1.13)
35–39	208	0.99 (0.83, 1.17)	1.02 (0.86, 1.22)	0.89 (0.73, 1.08)
40–44	85	1.15 (0.91, 1.46)	1.19 (0.93, 1.52)	1.00 (0.76, 1.31)
45+	38	1.22 (0.87, 1.71)	1.22 (0.86, 1.73)	1.05 (0.72, 1.51)
Ib. AML				
<25	38	1.07 (0.73, 1.58)	1.16 (0.78, 1.72)	1.12 (0.73, 1.73)
25–29	83	ref	Ref	ref
30–34	71	0.88 (0.64, 1.21)	0.85 (0.61, 1.19)	0.87 (0.61, 1.24)
35–39	42	0.99 (0.68, 1.45)	0.96 (0.65, 1.42)	0.92 (0.59, 1.44)
40–44	13	0.92 (0.51, 1.67)	0.82 (0.44, 1.53)	0.71 (0.36, 1.41)
45+	7	1.09 (0.50, 2.37)	1.06 (0.48, 2.34)	0.82 (0.34, 1.97)
II. Lymphomas				
<25	80	1.03 (0.79, 1.35)	0.98 (0.75, 1.29)	0.94 (0.70, 1.26)
25–29	179	ref	ref	ref
30–34	177	1.07 (0.87, 1.32)	1.12 (0.90, 1.39)	1.09 (0.87, 1.38)
35–39	90	1.13 (0.87, 1.46)	1.20 (0.92, 1.57)	1.08 (0.80, 1.45)
40–44	32	1.16 (0.79, 1.70)	1.23 (0.84, 1.82)	1.06 (0.69, 1.62)
45+	15	1.26 (0.74, 2.14)	1.34 (0.78, 2.30)	1.19 (0.67, 2.10)

Father's age (y)	Cases N	Crude OR (95%CI)	Adjusted OR (95% CI) ^a	Adjusted OR (95% CI) ^b
IIa. Hodgkin lymphomas				
<25	29	1.08 (0.69, 1.69)	1.01 (0.64, 1.59)	0.92 (0.56, 1.49)
25–29	62	ref	ref	ref
30–34	63	1.10 (0.77, 1.57)	1.13 (0.79, 1.63)	1.08 (0.73, 1.59)
35–39	32	1.22 (0.79, 1.88)	1.23 (0.79, 1.93)	1.11 (0.67, 1.83)
40+	17	1.31 (0.76, 2.26)	1.32 (0.75, 2.32)	1.21 (0.64, 2.27)
IIb. NHL				
<25	26	0.91 (0.57, 1.44)	0.84 (0.53, 1.35)	0.83 (0.50, 1.37)
25–29	63	ref	ref	ref
30–34	49	0.88 (0.60, 1.28)	0.94 (0.64, 1.38)	0.91 (0.61, 1.38)
35–39	32	1.16 (0.75, 1.80)	1.32 (0.84, 2.07)	1.11 (0.67, 1.86)
40–44	8	0.84 (0.40, 1.77)	0.92 (0.43, 1.95)	0.68 (0.30, 1.54)
45+	8	2.17 (1.03, 4.58)	2.28 (1.06, 4.88)	1.68 (0.73, 3.83)
IIc. Burkitt lymphoma				
<25	14	1.14 (0.60, 2.16)	1.14 (0.60, 2.18)	1.05 (0.53, 2.10)
25–29	31	ref	ref	ref
30–34	37	1.19 (0.73, 1.93)	1.25 (0.76, 2.06)	1.35 (0.79, 2.31)
35–39	15	0.94 (0.50, 1.77)	1.02 (0.53, 1.96)	1.03 (0.49, 2.16)
40+	6	0.76 (0.31, 1.84)	0.82 (0.33, 2.04)	0.77 (0.28, 2.13)
III. CNS tumors				
<25	213	0.99 (0.84, 1.17)	0.99 (0.84, 1.17)	1.01 (0.85, 1.20)
25–29	516	ref	ref	ref
30–34	465	0.96 (0.85, 1.09)	0.97 (0.85, 1.11)	0.97 (0.85, 1.20)
35–39	240	1.02 (0.87, 1.20)	1.03 (0.87, 1.21)	1.04 (0.87, 1.24)
40–44	66	0.82 (0.63, 1.06)	0.82 (0.63, 1.07)	0.81 (0.61, 1.08)
45+	30	0.87 (0.60, 1.26)	0.86 (0.58, 1.25)	0.82 (0.55, 1.23)
IIIa. Ependymomas				
<25	22	1.03 (0.62, 1.72)	1.05 (0.63, 1.77)	0.90 (0.52, 1.57)
25–29	48	ref	ref	ref
30–34	37	0.85 (0.55, 1.32)	0.84 (0.54, 1.31)	0.89 (0.55, 1.43)
35–39	16	0.76 (0.43, 1.35)	0.73 (0.40, 1.33)	0.72 (0.37, 1.41)
40+	8	0.79 (0.37, 1.68)	0.80 (0.37, 1.74)	0.73 (0.30, 1.77)
IIIb. Astrocytomas				
<25	70	0.89 (0.68, 1.18)	0.87 (0.66, 1.15)	0.86 (0.64, 1.17)
25–29	186	ref	ref	ref
30–34	140	0.84 (0.67, 1.05)	0.86 (0.69, 1.08)	0.89 (0.70, 1.13)
35–39	90	1.13 (0.87, 1.46)	1.14 (0.87, 1.49)	1.20 (0.89, 1.62)
40–44	17	0.63 (0.38, 1.03)	0.64 (0.39, 1.07)	0.68 (0.40, 1.17)
45+	6	0.52 (0.23, 1.17)	0.53 (0.23, 1.21)	0.56 (0.24, 1.31)

Father's age (y)	Cases N	Crude OR (95%CI)	Adjusted OR (95% CI) ^a	Adjusted OR (95% CI) ^b
IIIc. Intracranial and intraspinal embryonal tumors				
<25	35	0.93 (0.63, 1.37)	0.93 (0.63, 1.39)	0.92 (0.60, 1.41)
25–29	92	ref	ref	ref
30–34	77	0.88 (0.65, 1.20)	0.92 (0.67, 1.25)	0.91 (0.65, 1.27)
35–39	31	0.73 (0.48, 1.10)	0.78 (0.51, 1.20)	0.71 (0.44, 1.14)
40–44	12	0.79 (0.43, 1.44)	0.77 (0.40, 1.46)	0.64 (0.32, 1.30)
45+	5	0.75 (0.30, 1.86)	0.63 (0.23, 1.73)	0.53 (0.19, 1.51)
IIIc1. Medulloblastomas				
<25	32	0.85 (0.57, 1.28)	0.85 (0.56, 1.29)	0.83 (0.53, 1.30)
25–29	89	ref	ref	ref
30–34	66	0.81 (0.58, 1.12)	0.84 (0.60, 1.17)	0.82 (0.58, 1.17)
35–39	27	0.69 (0.45, 1.07)	0.74 (0.47, 1.16)	0.65 (0.39, 1.08)
40–44	11	0.80 (0.42, 1.50)	0.76 (0.39, 1.50)	0.62 (0.30, 1.30)
45+	5	0.82 (0.33, 2.03)	0.66 (0.24, 1.84)	0.55 (0.19, 1.57)
IIIe. Other specified intracranial and intraspinal neoplasms				
<25	64	0.99 (0.74, 1.33)	0.99 (0.74, 1.34)	1.11 (0.80, 1.53)
25–29	162	ref	ref	ref
30–34	175	1.09 (0.88, 1.35)	1.10 (0.88, 1.37)	1.06 (0.84, 1.34)
35–39	93	1.18 (0.91, 1.53)	1.18 (0.90, 1.55)	1.19 (0.88, 1.61)
40–44	24	0.87 (0.57, 1.35)	0.88 (0.57, 1.38)	0.85 (0.53, 1.38)
45+	12	1.03 (0.57, 1.86)	1.04 (0.57, 1.90)	0.89 (0.47, 1.71)
IIIf. Unspecified intracranial and intraspinal neoplasms				
<25	17	1.22 (0.69, 2.15)	1.31 (0.74, 2.32)	1.44 (0.78, 2.67)
25–29	45	ref	ref	ref
30–34	74	1.28 (0.88, 1.86)	1.17 (0.80, 1.72)	1.19 (0.80, 1.78)
35–39	38	1.21 (0.78, 1.87)	1.12 (0.71, 1.75)	1.23 (0.75, 2.02)
40–44	13	1.16 (0.62, 2.16)	1.10 (0.58, 2.08)	1.20 (0.60, 2.41)
45+	6	1.32 (0.56, 3.11)	1.28 (0.54, 3.08)	1.35 (0.52, 3.48)
IV. Neuroblastoma and other peripheral nervous cell tumors				
<25	39	0.78 (0.54, 1.12)	0.78 (0.54, 1.13)	0.75 (0.50, 1.11)
25–29	115	ref	ref	ref
30–34	110	1.04 (0.80, 1.35)	1.03 (0.78, 1.35)	1.05 (0.79, 1.40)
35–39	54	1.03 (0.74, 1.43)	0.99 (0.71, 1.40)	1.00 (0.68, 1.47)
40–44	17	0.92 (0.55, 1.54)	0.87 (0.51, 1.48)	0.86 (0.49, 1.52)
45+	8	1.00 (0.48, 2.05)	0.94 (0.45, 1.95)	0.92 (0.43, 1.99)
IVa. Neuroblastoma and ganglioneuroblastoma				
<25	38	0.79 (0.55, 1.15)	0.81 (0.56, 1.19)	0.77 (0.52, 1.15)
25–29	109	ref	ref	ref
30–34	107	1.07 (0.82, 1.40)	1.05 (0.79, 1.38)	1.07 (0.80, 1.44)

Father's age (y)	Cases N	Crude OR (95%CI)	Adjusted OR (95% CI) ^a	Adjusted OR (95% CI) ^b
35–39	49	1.00 (0.71, 1.40)	0.95 (0.67, 1.36)	0.96 (0.65, 1.43)
40–44	16	0.91 (0.54, 1.55)	0.86 (0.50, 1.48)	0.86 (0.48, 1.54)
45+	8	1.06 (0.51, 2.18)	0.99 (0.48, 2.07)	0.99 (0.46, 2.15)
V. Retinoblastoma				
<25	20	0.86 (0.51, 1.45)	0.86 (0.51, 1.47)	0.76 (0.44, 1.33)
25–29	53	ref	ref	ref
30–34	46	0.90 (0.61, 1.35)	0.89 (0.59, 1.33)	1.01 (0.65, 1.55)
35–39	31	1.20 (0.76, 1.89)	1.14 (0.71, 1.83)	1.33 (0.78, 2.27)
40+	12	0.96 (0.51, 1.80)	0.88 (0.46, 1.72)	1.03 (0.50, 2.15)
VI. Renal tumors				
<25	37	0.87 (0.59, 1.27)	0.88 (0.60, 1.31)	0.98 (0.64, 1.49)
25–29	94	ref	ref	ref
30–34	91	1.09 (0.82, 1.47)	1.05 (0.77, 1.41)	1.08 (0.79, 1.48)
35–39	43	1.10 (0.76, 1.59)	1.09 (0.74, 1.59)	1.18 (0.78, 1.79)
40–44	18	1.26 (0.75, 2.10)	1.25 (0.74, 2.13)	1.38 (0.77, 2.46)
45+	9	1.41 (0.70, 2.81)	1.42 (0.70, 2.88)	1.56 (0.74, 3.31)
VIa. Nephroblastoma and other nonepithelial renal tumors^c				
<25	36	0.94 (0.64, 1.40)	0.96 (0.64, 1.43)	1.01 (0.65, 1.56)
25–29	83	ref	ref	ref
30–34	81	1.12 (0.82, 1.53)	1.08 (0.78, 1.48)	1.13 (0.81, 1.58)
35–39	41	1.21 (0.82, 1.77)	1.18 (0.79, 1.76)	1.30 (0.84, 2.02)
40–44	17	1.35 (0.79, 2.30)	1.33 (0.77, 2.31)	1.49 (0.81, 2.72)
45+	8	1.42 (0.68, 2.95)	1.44 (0.68, 3.04)	1.61 (0.73, 3.56)
VII. Hepatic tumors				
<25	6	0.65 (0.26, 1.61)	0.70 (0.28, 1.76)	0.73 (0.27, 1.95)
25–29	24	ref	ref	ref
30–34	25	1.04 (0.59, 1.84)	1.15 (0.63, 2.08)	1.14 (0.61, 2.14)
35–39	10	0.82 (0.39, 1.75)	0.96 (0.44, 2.11)	0.85 (0.35, 2.03)
40+	8	1.35 (0.60, 3.05)	1.54 (0.65, 3.63)	1.21 (0.45, 3.24)
VIIa. Hepatoblastoma				
<25	6	0.88 (0.35, 2.25)	0.95 (0.37, 2.49)	1.09 (0.38, 3.10)
25–29	18	ref	ref	ref
30–34	21	1.15 (0.61, 2.18)	1.32 (0.67, 2.60)	1.32 (0.65, 2.68)
35–39	6	0.66 (0.26, 1.68)	0.83 (0.31, 2.21)	0.79 (0.27, 2.29)
40+	8	1.78 (0.76, 4.16)	2.11 (0.85, 5.26)	1.84 (0.64, 5.31)
VIII. Malignant bone tumors				
<25	27	0.70 (0.46, 1.09)	0.69 (0.45, 1.08)	0.69 (0.43, 1.10)
25–29	86	ref	ref	ref
30–34	88	1.13 (0.84, 1.53)	1.15 (0.85, 1.56)	1.24 (0.90, 1.72)

Father's age (y)	Cases N	Crude OR (95%CI)	Adjusted OR (95% CI) ^a	Adjusted OR (95% CI) ^b
35–39	39	1.01 (0.69, 1.48)	0.98 (0.65, 1.46)	1.08 (0.69, 1.68)
40–44	18	1.33 (0.80, 2.23)	1.34 (0.79, 2.28)	1.41 (0.78, 2.54)
45+	5	0.95 (0.38, 2.34)	0.99 (0.40, 2.47)	1.01 (0.39, 2.64)
IX. Soft tissue sarcomas				
<25	51	1.05 (0.75, 1.46)	1.03 (0.73, 1.44)	1.09 (0.76, 1.57)
25–29	119	ref	ref	ref
30–34	90	0.80 (0.60, 1.05)	0.81 (0.61, 1.08)	0.87 (0.65, 1.17)
35–39	53	0.94 (0.67, 1.30)	0.97 (0.68, 1.36)	1.14 (0.78, 1.66)
40–44	16	0.80 (0.47, 1.36)	0.84 (0.49, 1.45)	1.02 (0.57, 1.82)
45+	12	1.39 (0.76, 2.54)	1.34 (0.71, 2.53)	1.61 (0.81, 3.19)
IXa. Rhabdomyosarcoma				
<25	21	0.85 (0.52, 1.40)	0.90 (0.54, 1.49)	0.87 (0.50, 1.49)
25–29	62	ref	ref	ref
30–34	34	0.54 (0.35, 0.83)	0.52 (0.34, 0.79)	0.55 (0.35, 0.87)
35–39	25	0.77 (0.48, 1.24)	0.70 (0.42, 1.14)	0.75 (0.43, 1.32)
40+	10	0.62 (0.31, 1.21)	0.59 (0.29, 1.18)	0.62 (0.29, 1.36)
X. Germ cell tumors				
<25	17	0.74 (0.43, 1.28)	0.76 (0.44, 1.33)	0.79 (0.44, 1.44)
25–29	54	ref	ref	ref
30–34	55	1.11 (0.76, 1.62)	1.12 (0.76, 1.65)	1.10 (0.73, 1.67)
35–39	26	1.11 (0.69, 1.79)	1.09 (0.66, 1.79)	1.01 (0.58, 1.76)
40+	14	1.22 (0.67, 2.22)	1.20 (0.64, 2.23)	0.92 (0.44, 1.91)
XI. Other malignant epithelial neoplasms and malignant melanomas				
<25	34	0.88 (0.59, 1.31)	0.85 (0.57, 1.27)	0.91 (0.59, 1.40)
25–29	95	ref	ref	ref
30–34	81	0.88 (0.65, 1.19)	0.94 (0.69, 1.29)	0.88 (0.63, 1.22)
35–39	39	0.87 (0.60, 1.28)	1.00 (0.67, 1.47)	0.84 (0.54, 1.30)
40–44	13	0.84 (0.47, 1.50)	0.94 (0.52, 1.70)	0.73 (0.38, 1.40)
45+	5	0.78 (0.32, 1.92)	0.85 (0.34, 2.12)	0.65 (0.25, 1.69)
XId. Melanoma				
<25	9	0.78 (0.37, 1.65)	0.75 (0.35, 1.61)	0.78 (0.35, 1.77)
25–29	30	ref	ref	ref
30–34	22	0.77 (0.44, 1.34)	0.80 (0.45, 1.42)	0.84 (0.46, 1.52)
35+	13	0.63 (0.32, 1.22)	0.68 (0.34, 1.35)	0.69 (0.31, 1.52)
XII. Other and unspecified malignant neoplasms				
<25	7	0.65 (0.28, 1.51)	0.63 (0.27, 1.47)	0.63 (0.26, 1.55)
25–29	27	ref	ref	ref
30–34	29	0.98 (0.57, 1.67)	1.01 (0.58, 1.75)	1.06 (0.59, 1.90)
35+	16	0.68 (0.36, 1.27)	0.62 (0.31, 1.22)	0.62 (0.28, 1.35)

^a Adjusted for parental place of birth, parity

^b Adjusted for parental place of birth, parity, maternal age

^c Wilms' tumor cases corresponding to ICCC VIa1 are not shown as a separate category because they overlap completely with this category in our sample

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Table 4

Conditional logistic regression models for the association between childhood cancers and a 5-year increase in parental age at child's birth

	Maternal age at child's birth					Paternal age at child's birth				
	Cases N	Crude OR	Adjusted OR ^a (95%CI)	Adjusted OR ^b (95%CI)		Cases N	Crude OR	Adjusted OR ^a (95%CI)	Adjusted OR ^c (95%CI)	
All cancers	5856	1.03 (1.01, 1.06)	1.05 (1.02, 1.09)	1.05 (1.01, 1.09)		5810	1.03 (1.00, 1.05)	1.03 (1.01, 1.06)	1.01 (0.98, 1.04)	
I. Leukemias	1733	1.08 (1.03, 1.13)	1.11 (1.05, 1.18)	1.10 (1.02, 1.18)		1721	1.05 (1.01, 1.10)	1.06 (1.02, 1.11)	1.02 (0.96, 1.08)	
Ia. ALL	1373	1.09 (1.03, 1.15)	1.13 (1.06, 1.21)	1.10 (1.02, 1.19)		1365	1.07 (1.02, 1.12)	1.09 (1.03, 1.14)	1.04 (0.98, 1.11)	
Ib. AML	255	1.08 (0.95, 1.23)	1.05 (0.90, 1.21)	1.13 (0.93, 1.37)		254	0.99 (0.89, 1.11)	0.97 (0.86, 1.09)	0.91 (0.78, 1.06)	
II. Lymphomas	578	1.05 (0.96, 1.14)	1.10 (1.00, 1.22)	1.07 (0.95, 1.21)		573	1.04 (0.97, 1.12)	1.07 (1.00, 1.16)	1.04 (0.94, 1.14)	
IIa. Hodgkin lymphomas	205	1.04 (0.90, 1.20)	1.05 (0.90, 1.24)	1.04 (0.84, 1.28)		203	1.03 (0.91, 1.16)	1.04 (0.92, 1.18)	1.02 (0.87, 1.20)	
IIb. NHL	187	1.09 (0.94, 1.26)	1.20 (1.02, 1.42)	1.16 (0.94, 1.44)		186	1.07 (0.95, 1.21)	1.12 (0.98, 1.27)	1.04 (0.88, 1.23)	
IIc. Burkitt lymphoma	104	0.93 (0.76, 1.14)	0.96 (0.76, 1.21)	0.93 (0.69, 1.25)		103	0.98 (0.82, 1.16)	1.00 (0.83, 1.20)	1.04 (0.82, 1.31)	
III. CNS tumors	1548	0.99 (0.94, 1.04)	1.00 (0.94, 1.06)	1.02 (0.94, 1.10)		1530	0.98 (0.94, 1.03)	0.98 (0.94, 1.03)	0.98 (0.92, 1.04)	
IIIa. Ependymomas	134	0.95 (0.79, 1.14)	0.93 (0.75, 1.14)	0.98 (0.75, 1.28)		131	0.93 (0.79, 1.08)	0.92 (0.77, 1.10)	0.93 (0.75, 1.16)	
IIIb. Astrocytomas	513	0.96 (0.87, 1.05)	0.97 (0.87, 1.08)	0.98 (0.86, 1.12)		509	0.96 (0.89, 1.04)	0.97 (0.89, 1.06)	0.98 (0.88, 1.09)	
IIIc. Intracranial and intraspinal embryonal tumors	255	0.98 (0.86, 1.12)	1.04 (0.90, 1.21)	1.15 (0.95, 1.40)		252	0.94 (0.84, 1.05)	0.94 (0.83, 1.06)	0.88 (0.75, 1.02)	
IIId. Medulloblastomas	233	0.98 (0.86, 1.13)	1.05 (0.90, 1.23)	1.16 (0.95, 1.42)		230	0.95 (0.84, 1.06)	0.94 (0.83, 1.07)	0.88 (0.74, 1.03)	
IIIe. Other specified intracranial and intraspinal neoplasms	537	1.04 (0.96, 1.14)	1.05 (0.95, 1.16)	1.05 (0.92, 1.19)		530	1.03 (0.95, 1.11)	1.03 (0.95, 1.11)	1.01 (0.91, 1.11)	
IIIf. Unspecified intracranial and intraspinal neoplasms	197	0.98 (0.85, 1.14)	0.94 (0.80, 1.12)	0.91 (0.73, 1.12)		193	1.03 (0.91, 1.17)	1.01 (0.88, 1.15)	1.06 (0.89, 1.24)	
IV. Neuroblastomas and other peripheral nervous cell tumors	346	1.05 (0.94, 1.18)	1.04 (0.92, 1.18)	1.06 (0.90, 1.24)		343	1.03 (0.94, 1.12)	1.01 (0.91, 1.11)	0.98 (0.86, 1.11)	

	Maternal age at child's birth				Paternal age at child's birth			
	Cases N	Crude OR (95%CI)	Adjusted OR ^a (95%CI)	Adjusted OR ^b (95%CI)	Cases N	Crude OR (95%CI)	Adjusted OR ^a (95%CI)	Adjusted OR ^c (95%CI)
IVa. Neuroblastoma and ganglioneuroblastoma	330	1.05 (0.94, 1.18)	1.03 (0.91, 1.18)	1.06 (0.90, 1.25)	327	1.02 (0.93, 1.12)	1.00 (0.90, 1.11)	0.97 (0.85, 1.11)
V. Retinoblastoma	163	0.95 (0.81, 1.12)	0.91 (0.75, 1.10)	0.84 (0.66, 1.06)	162	1.05 (0.92, 1.20)	1.03 (0.89, 1.19)	1.12 (0.94, 1.33)
VI. Renal tumors	293	1.07 (0.95, 1.21)	1.03 (0.90, 1.18)	0.96 (0.81, 1.15)	292	1.07 (0.97, 1.18)	1.07 (0.96, 1.19)	1.09 (0.95, 1.24)
Via. Nephroblastoma and other nonepithelial renal tumors ^d	266	1.06 (0.93, 1.20)	1.01 (0.88, 1.17)	0.93 (0.77, 1.12)	266	1.08 (0.98, 1.19)	1.07 (0.96, 1.20)	1.11 (0.97, 1.28)
VII. Hepatic tumors	73	1.21 (0.95, 1.54)	1.24 (0.94, 1.64)	1.28 (0.90, 1.82)	73	1.04 (0.85, 1.27)	1.08 (0.87, 1.34)	0.96 (0.73, 1.27)
VIIa. Hepatoblastoma	59	1.17 (0.89, 1.52)	1.21 (0.89, 1.65)	1.21 (0.82, 1.80)	59	1.04 (0.83, 1.30)	1.10 (0.87, 1.40)	1.00 (0.73, 1.37)
VIII. Malignant bone tumors	266	1.05 (0.92, 1.19)	1.06 (0.92, 1.23)	1.01 (0.84, 1.22)	263	1.06 (0.96, 1.18)	1.06 (0.95, 1.19)	1.06 (0.92, 1.22)
IX. Soft tissue sarcomas	342	0.92 (0.82, 1.03)	0.94 (0.83, 1.07)	0.90 (0.77, 1.06)	341	0.99 (0.90, 1.09)	1.00 (0.91, 1.11)	1.05 (0.93, 1.19)
IXa. Rhabdomyosarcoma	153	0.91 (0.76, 1.07)	0.86 (0.70, 1.04)	0.95 (0.74, 1.22)	152	0.88 (0.76, 1.02)	0.85 (0.73, 1.00)	0.87 (0.71, 1.07)
X. Germ cell tumors	166	1.16 (0.99, 1.36)	1.17 (0.98, 1.40)	1.17 (0.93, 1.47)	166	1.09 (0.96, 1.24)	1.08 (0.94, 1.24)	1.00 (0.83, 1.20)
XI. Other malignant epithelial neoplasms and malignant melanomas	268	1.04 (0.92, 1.18)	1.12 (0.97, 1.29)	1.17 (0.97, 1.40)	267	0.98 (0.88, 1.09)	1.02 (0.91, 1.14)	0.95 (0.82, 1.10)
XId. Melanoma	74	0.97 (0.76, 1.24)	1.06 (0.81, 1.39)	1.19 (0.84, 1.70)	74	0.91 (0.74, 1.12)	0.94 (0.75, 1.17)	0.86 (0.64, 1.14)
XII. Other and unspecified malignant neoplasms	80	0.91 (0.72, 1.15)	0.90 (0.69, 1.18)	1.05 (0.74, 1.48)	79	0.87 (0.71, 1.06)	0.84 (0.68, 1.05)	0.82 (0.62, 1.09)

^a Adjusted for parental place of birth, parity^b Adjusted for parental place of birth, parity, paternal age^c Adjusted for parental place of birth, parity, maternal age^d Wilms' tumor cases corresponding to ICCC VIa1 are not shown as a separate category because they overlap completely with this category in our sample

Table 5

Conditional logistic regression models for the association between retinoblastoma and Wilms' tumor and parental age at child's birth by laterality of tumor

Maternal age, y				
	Cases N	Crude OR	Adjusted OR^a (95%CI)	Adjusted OR^b (95%CI)
Unilateral retinoblastoma				
<25	37	1.22 (0.77, 1.93)	1.24 (0.77, 2.00)	1.32 (0.78, 2.24)
25–29	41	ref	ref	ref
30–34	27	0.99 (0.61, 1.62)	0.94 (0.56, 1.55)	0.87 (0.51, 1.49)
35+	15	1.34 (0.73, 2.46)	1.19 (0.62, 2.28)	1.12 (0.54, 2.31)
Bilateral retinoblastoma				
<25	11	1.05 (0.48, 2.29)	1.08 (0.48, 2.42)	1.43 (0.61, 3.32)
25–29	17	ref	ref	ref
30–34	10	0.79 (0.36, 1.75)	0.72 (0.32, 1.64)	0.70 (0.29, 1.68)
35+	4	0.71 (0.23, 2.15)	0.61 (0.19, 1.98)	NE
Unilateral Wilms				
<25	66	0.79 (0.57, 1.09)	0.84 (0.60, 1.17)	0.87 (0.60, 1.27)
25–29	99	ref	ref	ref
30–34	53	0.84 (0.60, 1.18)	0.81 (0.57, 1.15)	0.75 (0.52, 1.09)
35+	26	0.98 (0.63, 1.53)	0.95 (0.59, 1.52)	0.83 (0.48, 1.42)
Bilateral Wilms' tumor				
<25	2	1.21 (0.22, 6.70)	NE	NE
25–29	4	ref	ref	ref
30–34	6	1.82 (0.51, 6.52)	NE	NE
35+	4	2.72 (0.66, 11.17)	NE	NE
Paternal age, y				
	Cases N	Crude OR	Adjusted OR^a (95%CI)	Adjusted OR^c (95%CI)
Unilateral retinoblastoma				
<25	17	1.06 (0.59, 1.89)	1.08 (0.60, 1.95)	0.96 (0.51, 1.79)
25–29	36	ref	ref	ref
30–34	35	1.06 (0.66, 1.69)	1.03 (0.63, 1.66)	1.13 (0.68, 1.89)
35–39	23	1.37 (0.80, 2.33)	1.29 (0.74, 2.25)	1.41 (0.75, 2.64)
40+	8	0.97 (0.45, 2.11)	0.87 (0.39, 1.97)	0.92 (0.38, 2.24)
Bilateral retinoblastoma				
<25	2	0.28 (0.06, 1.23)	NE	NE
25–29	17	ref	ref	ref
30–34	11	0.61 (0.28, 1.31)	0.61 (0.28, 1.34)	0.73 (0.32, 1.66)
35+	12	0.89 (0.42, 1.93)	0.87 (0.39, 1.98)	1.22 (0.48, 3.08)
Unilateral Wilms' tumor				

Maternal age, y				
	Cases N	Crude OR	Adjusted OR ^a (95%CI)	Adjusted OR ^b (95%CI)
<25	35	0.97 (0.65, 1.45)	0.99 (0.66, 1.49)	1.05 (0.67, 1.64)
25–29	77	ref	ref	1.20 (0.85, 1.70)
30–34	77	1.18 (0.86, 1.63)	1.14 (0.82, 1.58)	1.21 (0.85, 1.93)
35–39	34	1.11 (0.74, 1.68)	1.09 (0.71, 1.68)	ref
40–44	14	1.24 (0.69, 2.21)	1.24 (0.68, 2.25)	1.37 (0.71, 2.64)
45+	7	1.35 (0.62, 2.94)	1.40 (0.63, 3.09)	1.54 (0.66, 3.60)
Bilateral Wilms' tumor				
<25	1	3.55 (0.22, 57.49)	NE	NE
25–29	1	ref	ref	ref
30–34	4	2.84 (0.32, 25.58)	NE	NE
35+	10	10.36 (1.20, 82.42)	NE	NE

^a Adjusted for parental place of birth, parity

^b Adjusted for parental place of birth, parity, paternal age

^c Adjusted for parental place of birth, parity, maternal age

NE=not estimable, reference group has <5 cases