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Cancer risk among children with very low birth weight

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Abstract

Objective: Risk of hepatoblastoma is strongly increased among children with very low birth weight (VLBW: <1,500 grams). Because data on VLBW and other childhood cancers is sparse, we examined the risk of malignancy following VLBW in a large dataset.

Methods: We combined case-control datasets created by linking the cancer and birth registries of California, Minnesota, New York, Texas, and Washington states, which comprised 17,672 children diagnosed with cancer at 0-14 years of age and 57,966 randomly selected controls. Unconditional logistic regression was used to examine the association of cancer with VLBW and moderately low birth weights (1,500-1,999g and 2,000-2,499g) compared to moderate/high birth weight ($\geq 2,500$) adjusting for sex, gestational age, birth order, plurality, maternal age, maternal race, state, and year of birth.

Results: Most childhood cancers were not associated with low birth weights. However, retinoblastoma and gliomas other than astrocytomas and ependymomas were possibly associated with VLBW, with respective odds ratios (OR) of 2.43 (95% Confidence Interval (CI): 1.00-5.89) and 2.13 (95% CI: 0.71-6.39). Risk of other gliomas was also increased among children weighing 1,500-1,999g at birth (OR = 3.58; 95% CI: 1.98-6.47). For hepatoblastoma the ORs associated with birth weights of 2,000-2,499g, 1,500-1,999g, and 350-1,499g were 1.56 (95% CI: 0.81-2.98), 3.37 (95% CI: 1.44-7.88), and 17.18 (95% CI: 7.46-39.54), respectively

Conclusions: These data suggest no association between most cancers and VLBW with the exception of the known association with hepatoblastoma and possible moderately increased risks of other gliomas and retinoblastoma, which may warrant confirmation.

Keywords

Infant; very low birth weight; cancer; case-control studies; registries

INTRODUCTION

As survival of very low birth weight (VLBW, usually defined as <1,500 grams) infants has improved markedly in recent decades (1), the long-term health of these children requires increasing attention, with much research focusing on neurocognitive outcomes(2,3), growth and development (4,5), and the metabolic syndrome (6,7). Childhood cancer has not often been studied, but it has been demonstrated that incidence of a rare embryonal liver tumor, hepatoblastoma, is at least a magnitude greater among VLBW children than among children with moderate birth weights (8-12). As VLBW infants are exposed to multiple medical interventions in neonatal intensive care units (NICUs) (13,14) at a time in development when antioxidant capacity is diminished (15,16) and xenobiotic-metabolizing enzyme expression is variable(17,18), an iatrogenic etiology is plausible.

Other childhood cancers might also be associated with VLBW for similar reasons, although no similar-sized associations have been noted to date. While birth weight has been examined frequently in relation to various childhood cancers (19-21), small or moderately increased risks associated with VLBW may not have been detected. Nearly all studies have grouped all infants <2,500 grams, possibly obscuring differences in biology and medical exposures between moderately and very low birth weight infants. Moreover, as the prevalence of VLBW is low, presently about 1% of births in the United States (1), the large sample sizes required to detect small-to-moderate relative risks are not generally available in studies of childhood cancers.

Our objective was to fill a gap in the literature by examining whether specific childhood cancers, in addition to hepatoblastoma, demonstrate associations with VLBW. Although high birth weight is a risk factor for several pediatric malignancies (20-23), we report here on VLBW alone, because the putative mechanism to explain increased cancer risk in large infants, growth factor excess (22,24), differs from mechanisms we hypothesize for small infants. Our analysis constitutes the first comprehensive examination of cancer risk among children born at the lowest end of the birth weight distribution.

METHODS

Study design

We pooled data from population-based case-control studies conducted in California, Minnesota, New York (excluding New York City), Texas and Washington states (8,10,12, 25,26). Institutional Review Board approvals were obtained from each participating institution for the conduct of this analysis. Table 1 provides information about each component study. Cases of childhood cancer meeting eligibility criteria were identified in each population-based cancer registry and matched to birth records using sequential deterministic or probabilistic record linkage (27). Cases were classified according to the International Classification of Childhood Cancer 3rd edition (ICCC-3) (28).

Controls were selected at random from birth records in ratios to cases ranging from 1 to 10, with frequency matching used in four states and individual matching in one (California). All states matched on year of birth and two also matched on sex (6,16-19). Cases selected as controls in Minnesota and New York were excluded from analysis, as were subjects with reported Down syndrome. However, this condition was not recorded in Texas before 1984 and Washington before 1989. Cases diagnosed before 28 days of life and controls that died prior

to then were also excluded from analysis. The final pooled dataset consisted of 17,672 cases and 57,966 controls.

Variable specification

Birth weight, gestational age, plurality, sex, birth order, year of birth, and maternal age and race were obtained from birth records. Maternal education was not recorded by all states until 1992 and so was used only in secondary analyses. Gestational ages calculated from last menstrual period (LMP) and a clinical estimate were provided by four states, whereas California recorded only the former. A combined gestational age variable was developed that gave preference to the calculated estimate when available and used the clinical estimate otherwise.

Birth weights of <350g and gestational lengths <20 or >45 weeks were considered implausible and treated as missing. For the purposes of sensitivity analysis, we also identified subjects with implausible birth weights for gestational age using guidelines derived from expert clinical opinion(29).

Continuous and discrete variables were grouped using cut points determined *a priori*. Categories of birth weight were 350-1,499 grams (g), 1,500-1,999g, and 2,000-2,499g with a referent of $\geq 2,500$ g, thereby delineating groups with decreasing NICU utilization (30,31). Separating high (>4,000g) from normal (2,500-3,999g) birth weight and using the latter as referent only minimally affected results for low birth weights (data not shown). High birth weight was therefore included in the referent category of $\geq 2,500$ g to simplify presentation. Categories of gestational age were <32 weeks, 32-36 weeks, and ≥ 37 weeks. Because methods for gestational age estimation shifted over the wide study period, adding to common concerns about the accuracy of early gestational ages(32), we did not pursue any finer discrimination of preterm weeks of gestation. Categorizations of other variables are shown in Table 3 and the footnotes to tables 4 and 5.

Statistical analysis

Analyses were performed using SAS 9.1 (SAS Institute, Cary, NC). Odds ratios (OR) and two-sided 95% confidence intervals (CI) were obtained using unconditional logistic regression, with individual matching in the California dataset broken to allow use of this method. Risk estimates were adjusted for the matching variables state, year of delivery (1970-1985, 1986-1989, 1990-1993, 1994-2004), and infant sex (matched in 2 states only). We decided *a priori* to adjust all risk estimates for maternal age (<20, 20-24, 25-29, 30-34, 35-39, 40+ years), plurality (singleton/multiple delivery), birth order (1,2,3,4,5+), and maternal race/ethnicity as well, since these variables are associated with birth weight(33) and are established or suspected risk factors for several childhood cancers (34). Analyses of birth weight (<1500, 1500-1999, 2000-2499, 2500+ g) were additionally adjusted for gestational age (<32, 32-36, 37+ weeks), and vice versa.

ORs for birth weight and gestational age are presented for all cancers combined and for the 17 ICCC-3 cancer types with >200 cases in the dataset (excluding heterogeneous “other” and unspecified tumor categories). Several secondary analyses were also conducted, including: exclusion of subjects with implausible birth weight for gestational age, adjustment for maternal education during the years data were available, restriction to subjects with birth years coextensive with registry operation, and use of the alternate gestational age variable that gave preference to the clinical estimate.

RESULTS

Diagnoses were distributed approximately as would be expected based on national surveillance data (Table 2) (35). Male sex and white race were somewhat more frequent among cases compared to controls, while there were no appreciable differences regarding other variables (Table 3). Values for all variables (except maternal education) were available for 93.7% of cases and 92.7% of controls.

Childhood cancer overall and most cancer types, including those not shown in the table, did not have increased ORs for the associations of moderately or VLBW (Table 4). Having a birth weight of 350-1499g was associated with a greatly increased risk of hepatoblastoma (OR = 17.18; 95% CI: 7.46-39.54) relative to weighing > 2,500g at birth. Less marked, but still increased ORs were observed for birth weights of 1,500-1,999g (OR = 3.37; 95% CI: 1.44-7.88) and 2,000-2,499g (OR = 1.56; 95% CI: 0.81-2.98). The large number of hepatoblastoma cases with birth weights <1,500g allowed further division of VLBW into categories of 350-749g and 750-1,499g, with respective ORs of 46.78 (95% CI: 16.36-133.74) and 13.73 (95% CI: 5.63-33.48).

VLBW was associated with greater than two-fold increased ORs for two other tumor types, including gliomas other than astrocytomas and ependymomas (i.e. "other gliomas") (OR = 2.13, 95% CI: 0.71-6.39 for birth weight <1500g; OR = 3.58, 95% CI: 1.98-6.47 for birth weight 1,500-1,999g) and retinoblastoma (OR = 2.43, 95% CI: 1.00-5.89 for birth weight <1500g). There was a significant OR of 1.42 (95% CI: 1.01-1.99) for intracranial embryonal tumors associated with birth weights of 2,000-2,499g group alone.

Excluding the 308 subjects with implausible birth weight for gestational age did not substantially alter most ORs or suggest associations of VLBW with cancers not apparent in the main analyses. However, the association of retinoblastoma with VLBW became markedly stronger (OR = 3.95; 95% CI: 1.55-10.07) and the OR for other gliomas increased slightly (OR = 2.60; 95% CI: 0.82-8.22). Hepatoblastoma remained strongly associated with VLBW but the OR was somewhat attenuated (1.55; 95% CI: 4.52-29.55). Results of the other sensitivity analyses, including adjustment of birth weight for maternal education and use of the alternate gestational age variable giving preference to the clinical estimate, were not materially different from those in the main analysis (data not shown).

Although there were modestly increased ORs for several tumors associated with very preterm delivery (<32 weeks), all confidence intervals included one (Table 5). Wilms tumor (OR = 1.51; 95% CI: 1.21-1.88) and Ewing sarcoma (OR = 1.68; 95% CI: 1.03-2.76) were associated with moderately preterm delivery (32-36 weeks). Using the alternate gestational age variable that gave preference to the calculated estimate produced similar results (data not shown), with the exception that Ewing sarcoma displayed somewhat stronger ORs for both moderately (OR = 2.14; 95% CI: 1.32-3.47) and very preterm delivery (OR = 3.11; 95% CI: 0.89-10.88).

DISCUSSION

As the risk of most cancers among children with the lowest birth weights has not been adequately assessed we undertook to examine this issue in a large population-based dataset. The strong inverse association between hepatoblastoma and birth weight was confirmed, with relative risks estimated more precisely here than in most previous studies (8-12). Most other cancers were not associated with moderately or very low birth weight, although retinoblastoma and other gliomas displayed possibly increased risks.

The size of association with VLBW that we were able to detect is an important consideration. Analysis of confidence limits is the preferred method for determining the size of association

compatible with the data (36). Table 4 shows upper confidence limits of 1.50 and 1.13 for all childhood cancers and acute lymphoid leukemia, respectively, while upper confidence limits ranging from about 2 to 4 were found for most other cancers; ORs larger than the upper confidence limits are unlikely to have been missed. Thus our results indicate that no moderate to strong associations of VLBW with most types of childhood cancer were present in this dataset, notwithstanding possible biases and other limitations to interpretation.

The association of VLBW with hepatoblastoma is unlikely to be due to chance or bias, having been observed in the United Kingdom (11) and Japan (9) as well as in the current United States study (which included data reported in three prior publications (8,10,12)). Our findings regarding other gliomas and retinoblastomas may however be due to random error, given the number of comparisons made, and less weight may also be attributed to the observations since there was a lack of clear evidence of dose-response between lower birth weights and these cancers. However, if real these associations warrant some explanation, though necessarily speculative.

We posited that the increased risk of hepatoblastoma among VLBW infants may be attributable to exposures in the NICU, and sought to determine if similar, but weaker, associations existed with other childhood cancers. The list of possible iatrogenic hazards in NICUs, recently reviewed by Lai and Bearer,(14) includes light, oxygen, irradiation, electromagnetic fields, plasticizers, medications, and total parenteral nutrition. Among these exposures, irradiation and oxidative stress, through high fraction oxygenation or lipid peroxidation, stand out for their known carcinogenicity (37,38). The plasticizer di-(2-ethylhexyl)phthalate (DEHP) is also considered a “probable human carcinogen” (39). The possible role of NICU exposures in causing hepatoblastoma has been examined in three small Japanese studies with 5 to 15 cases; greater lengths of oxygen therapy, furosemide use, and hospitalization were observed among VLBW cases compared to weight-matched controls (40-42). Larger studies may provide more definitive answers.

One limitation of our record-linkage study is that we did not have access to NICU exposure information. The use of birth weight as a proxy for medical exposures also requires caution for several reasons. First, even among VLBW infants, almost all of whom spend some time in a NICU, there is variation in treatment. For instance, among infants with birth weights of 501-1,500g tracked by the NICHD Neonatal Research Network during 1999-2000, 57% received surfactant, 27% received oxygen therapy at 28 days of life, and 20% received postnatal steroids (43). Moreover, as medical practice has changed over time (e.g. no infants in the aforementioned series received surfactant in 1987-1988), VLBW may have acted as proxy for differing exposures during the long period of this study.

VLBW may also signal the underlying pathologic processes that produced small size rather than (or in addition to) postnatal treatments, although the effect of such confounding is difficult to predict and may differ by cancer type. Congenital anomalies are both overrepresented among VLBW infants compared to those with normal birth weights (44) and among children with cancer (45); the net effect of these tendencies would be to exaggerate associations of VLBW with malignancies. Conversely, high birth weight was associated with risk of acute lymphoid leukemia, Wilms tumor, and astrocytoma in our data (not shown) as in others (20-23), which would tend to countervail any increase in risk due to medical exposures among VLBW infants. In this context we note that the OR of 1.48 relating VLBW to astrocytomas was possibly inconsistent with the overall significant linear trend in risk of this tumor with increasing birth weight. The ORs relating VLBW to acute lymphoid leukemia and Wilms tumor, by contrast, supported the overall linear trends. Absent additional information about the causes of VLBW our data could not address these concerns.

We controlled for gestational age in analysis of birth weight and observed few associations of childhood cancers with preterm birth itself. However, we cannot dismiss the possibility that our results for VLBW were actually due to residual confounding by length of gestation, since the limitations of measurement of gestational age in vital records necessitated using broad categories of preterm birth (32).

The use of population-based cancer surveillance data and prospectively collected birth records were major strengths of this study. Birth weight is considered generally accurate in vital records, as are the other variables we used, apart from gestational age (46). Several limitations must also be noted. We may have missed cancer diagnoses among controls who were sampled from birth years prior to the inception of their respective cancer registries or who moved out of state, but estimate based on U.S. surveillance data (35) that only about 125 cancers would be expected among controls if all were lost to follow-up. Thus even under the most extreme assumption disease misclassification would be unlikely to bias our results. Mortality among VLBW infants is also many times greater than at higher birth weights (1). Limiting subjects to those who survived to 28 days of life minimized this issue since most deaths among VLBW infants occur before then (47). However, person-time at risk among VLBW controls was probably still overestimated relative to children with normal birth weight since later mortality was not accounted for in these data. This would result in underestimation of the ORs for VLBW, although it is not possible for us to gauge the extent of any such bias. Lastly, we could not control completely for socioeconomic status, which is associated with both VLBW(48) and some childhood cancers(49) However, subanalyses adjusting for maternal education as a marker for socioeconomic status were concordant with the main analysis

CONCLUSIONS

Medical exposures in the NICU, combined with the immature defenses of premature infants, may plausibly affect future cancer risk. Apart from hepatoblastoma, associations with most childhood cancers were not increased, although possible moderate increases in risks of other gliomas and retinoblastoma were noted and may warrant confirmation. These results may be reassuring to practitioners and families concerned with the long-term health of VLBW infants.

Abbreviations

CI, Confidence interval; NICU, Neonatal Intensive Care Unit; OR, Odds ratio; VLBW, very low birth weight.

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Table 1

Details of studies included in the pooled dataset

State	Ages at diagnoses	Years of diagnoses	Years of birth	N cases included	N controls included	Matching factors
California	28 days – 4 years	1988-1997	1983-1997	4177	8730	Birth Year, Sex
Minnesota	28 days – 14 years	1988-2004	1976-2004	2170	8735	Birth Year
New York	28 days – 14 years	1985-2001	1970-2001	4357	12041	Birth Year
Texas	28 days – 14 years	1990-1998	1975-1998	4647	4732	Birth Year, Sex
Washington	28 days – 14 years	1980-2004	1980-2004	2321	23728	Birth Year

Table 2

Number of subjects by diagnosis*

Cancer type	Number of cases ^{**}
Leukemia	5908
Lymphoid leukemia	4756
Acute myeloid leukemia	849
Chronic myeloproliferative diseases	110
Lymphoma	1545
Hodgkin lymphoma	501
Non-Hodgkin lymphoma	605
Burkitt lymphoma	234
Central nervous system tumors	3807
Ependymoma	390
Astrocytoma	1685
Intracranial embryonal	903
Other gliomas	499
Neuroblastoma	1482
Retinoblastoma	684
Wilms tumor	1176
Hepatoblastoma	273
Bone tumors	573
Osteosarcoma	293
Ewing sarcoma	219
Soft tissue sarcoma	1067
Rhabdomyosarcoma	583
Fibrosarcoma	131
Germ cell tumors	572
Intracranial GCT	131
Extracranial GCT	134
Gonadal GCT	281
Carcinomas	409
Thyroid carcinoma	159
Melanoma	126
Total cancers	17672 [†]
Controls	57966

* Cases grouped according to the International Classification of Childhood Cancer 3

^{**} Cases with non-missing data for maternal race, maternal age, sex, gestational age, plurality, birth order, and birth weight[†] Sum of specific diagnoses does not equal total because unspecified tumors were omitted from table.

Table 3
Characteristics of childhood cancer cases and controls

Variable	Category	Cases (%)	Controls (%)
Age at diagnosis (cases)	28 days - 4 years	10977 (62.1)	
	5 – 9 years	3403 (19.3)	
	10 – 14 years	3292 (18.6)	
	Mean (SD) (months)	62.42 (50.80)	
<i>Maternal characteristics</i>			
Age at delivery (years)	< 20	1821 (10.3)	6220 (10.7)
	20-24	4448 (25.2)	15268 (26.3)
	25-29	5682 (32.2)	18427 (31.8)
	30-34	3908 (22.1)	12521 (21.6)
	35-39	1537 (8.7)	4670 (8.1)
	≥ 40	270 (1.5)	839 (1.4)
	Mean (SD)	26.91 (5.70)	26.71(5.67)
	Missing	6	21
Education (years)	< 12	2482 (20.2)	7246 (19.2)
	12	4346 (35.4)	13586 (36.1)
	13-16	4381 (35.7)	13815 (36.7)
	≥17	1053 (8.6)	3017 (8.0)
	Mean (SD) *	12.66 (2.88)	12.71 (2.79)
	Missing	5410	20302
Race	White	15243 (87.8)	48568 (85.1)
	Black	1147 (6.6)	3478 (6.1)
	Asian	694 (4.0)	2590 (4.5)
	Other	284 (1.6)	2448 (4.3)
	Missing	304	882
<i>Child's characteristics</i>			
Sex	Male	9728 (55.1)	30573 (52.8)
	Female	7942 (44.9)	27383 (47.2)
	Missing	2	10
Birth weight (grams)	< 1,500	155 (0.9)	411 (0.7)
	1,500-1,999	204 (1.2)	634 (1.1)
	2,000-2,499	639 (3.7)	2108 (3.7)
	≥ 2,500	16436 (94.3)	54438 (94.5)
	Mean (SD)	3420.66 (592.64)	3408.76 (572.67)
	Missing	238	375
Gestational age (weeks)	< 32	236 (1.4)	628 (1.1)
	32-36	1252 (7.4)	3776 (6.8)
	≥ 37	15480 (91.2)	50858 (92.0)
	Mean (SD)	39.39 (2.45)	39.52 (2.40)
	Missing	704	2704
Plurality	Singleton	17311 (98.0)	56626 (97.7)
	Multiple	357 (2.0)	1307 (2.3)
	Missing	4	33

Variable	Category	Cases (%)	Controls (%)
Birth order	First	7186 (41.3)	23131 (41.0)
	Second	5718 (32.9)	18383 (32.6)
	Third	2745 (15.8)	9092 (16.1)
	Fourth	1076 (6.2)	3454 (6.1)
	Fifth or higher	675 (3.9)	2373 (4.2)
	Mean (SD)	2.02 (1.23)	2.04 (1.25)
	Missing	272	1533

* Years of education was not included as a continuous variable in NY from 1988-1990, since a larger number of missing data is present for the continuous variable, the categorical variable was used for comparison.

Table 4

Adjusted odds ratios (OR) and 95% confidence intervals (CI) relating moderately and very low birth weight with childhood cancers

		Birth weight (grams)			
		>=2500	2000-2499	1500-1999	350-1499
All cancers	N ^a	16436	639	204	155
	OR ^b (95%CI)		0.97 (0.87-1.08)	0.98 (0.81-1.18)	1.15 (0.89-1.50)
Acute lymphoid leukemia	N ^a	4492	157	44	22
	OR ^b (95%CI)		0.90 (0.75-1.08)	0.81 (0.57-1.15)	0.65 (0.38-1.13)
Acute myeloid leukemia	N ^a	791	29	9	8
	OR ^b (95%CI)		0.98 (0.65-1.47)	1.06 (0.51-2.17)	1.39 (0.53-3.64)
Hodgkin lymphoma	N ^a	450	16	6	2
	OR ^b (95%CI)		0.76 (0.42-1.37)	1.23 (0.50-3.03)	--
Non-Hodgkin lymphoma	N ^a	552	30	6	4
	OR ^b (95%CI)		1.38 (0.90-2.12)	1.00 (0.41-2.42)	0.85 (0.26-2.83)
Burkitt lymphoma	N ^a	224	5	2	1
	OR ^b (95%CI)		0.52 (0.20-1.32)	--	--
Ependymoma	N ^a	373	6	5	3
	OR ^b (95%CI)		0.46 (0.20-1.05)	1.19 (0.44-3.23)	--
Astrocytoma	N ^a	1577	62	10	11
	OR ^b (95%CI)		1.15 (0.87-1.52)	0.57 (0.27-1.18)	1.48 (0.66-3.31)
Intracranial embryonal	N ^a	839	43	7	5
	OR ^b (95%CI)		1.42 (1.01-1.99)	0.68 (0.29-1.60)	1.06 (0.36-3.14)
Other gliomas	N ^a	454	17	17	5
	OR ^b (95%CI)		0.88 (0.51-1.51)	3.58 (1.98-6.47)	2.13 (0.71-6.39)
Neuroblastoma	N ^a	1386	59	23	13
	OR ^b (95%CI)		1.14 (0.85-1.52)	1.35 (0.84-2.18)	1.03 (0.50-2.11)
Retinoblastoma	N ^a	637	25	8	12
	OR ^b (95%CI)		0.91 (0.59-1.41)	0.97 (0.45-2.07)	2.43 (1.00-5.89)
Wilms tumor	N ^a	1113	42	14	7
	OR ^b (95%CI)		0.80 (0.57-1.13)	0.77 (0.41-1.42)	0.83 (0.33-2.07)

		Birth weight (grams)			
		>=2500	2000-2499	1500-1999	350-1499
Hepatoblastoma	N ^a	212	12	8	41
	OR ^b (95%CI)	1	1.56 (0.81-2.98)	3.37 (1.44-7.88)	17.18 (7.46-39.54)
Osteosarcoma	N ^a	258	13	1	1
	OR ^b (95%CI)	1	1.04 (0.55-1.97)	--	--
Ewing sarcoma	N ^a	200	12	3	0
	OR ^b (95%CI)	1	1.38 (0.72-2.64)	--	--
Rhabdomyosarcoma	N ^a	555	15	5	2
	OR ^b (95%CI)	1	0.66 (0.38-1.13)	0.77 (0.30-1.98)	--
Gonadal germ cell tumor	N ^a	257	14	2	1
	OR ^b (95%CI)	1	1.23 (0.66-2.31)	--	--
Controls	N ^a	54438	2108	634	411

^aNumber of cases with non-missing birth weight.

^bAdjusted for sex, gestational age, plurality, birth order, maternal age, maternal race, state, and year of birth

Table 5

Adjusted odds ratios (OR) and 95% confidence intervals (CI) relating gestational age with childhood cancers

		Gestational Age		
		>=37 weeks	32-36 weeks	<32 weeks
All cancers	N ^a	15480	1252	236
	OR ^b (95%CI)	1	1.07 (0.99-1.15)	1.13 (0.92-1.40)
Acute lymphoid leukemia	N ^a	4199	324	47
	OR ^b (95%CI)	1	1.06 (0.93-1.21)	1.05 (0.72-1.54)
Acute myeloid leukemia	N ^a	758	50	11
	OR ^b (95%CI)	1	0.86 (0.63-1.17)	0.97 (0.45-2.12)
Hodgkin lymphoma	N ^a	431	30	4
	OR ^b (95%CI)	1	0.92 (0.61-1.40)	0.75 (0.24-2.38)
Non-Hodgkin lymphoma	N ^a	522	37	10
	OR ^b (95%CI)	1	0.89 (0.61-1.28)	1.63 (0.73-3.63)
Burkitt lymphoma	N ^a	200	22	1
	OR ^b (95%CI)	1	1.53 (0.94-2.47)	--
Ependymoma	N ^a	355	19	5
	OR ^b (95%CI)	1	0.80 (0.49-1.31)	1.29 (0.42-3.95)
Astrocytoma	N ^a	1495	96	12
	OR ^b (95%CI)	1	0.83 (0.66-1.05)	0.58 (0.28-1.20)
Intracranial embryonal	N ^a	803	63	8
	OR ^b (95%CI)	1	0.97 (0.73-1.29)	0.80 (0.34-1.90)
Other gliomas	N ^a	424	42	8
	OR ^b (95%CI)	1	1.07 (0.74-1.56)	0.76 (0.31-1.88)
Neuroblastoma	N ^a	1308	109	25
	OR ^b (95%CI)	1	1.03 (0.83-1.29)	1.33 (0.78-2.29)
Retinoblastoma	N ^a	603	52	12
	OR ^b (95%CI)	1	1.05 (0.77-1.45)	0.87 (0.38-2.03)
Wilms tumor	N ^a	1023	109	11
	OR ^b (95%CI)	1	1.51 (1.21-1.88)	0.96 (0.46-2.03)
Hepatoblastoma	N ^a	207	18	38
	OR ^b (95%CI)	1	0.69 (0.39-1.23)	1.59 (0.70-3.64)
Osteosarcoma	N ^a	251	22	2
	OR ^b (95%CI)	1	1.31 (0.81-2.11)	--
Ewing sarcoma	N ^a	181	22	3
	OR ^b (95%CI)	1	1.68 (1.03-2.76)	2.32 (0.67-8.02)
Rhabdomyosarcoma	N ^a	522	40	2
	OR ^b (95%CI)	1	1.08 (0.76-1.53)	--
Gonadal germ cell tumor	N ^a	249	20	5
	OR ^b (95%CI)	1	1.11 (0.68-1.81)	2.44 (0.89-6.74)

		Gestational Age		
		>=37 weeks	32-36 weeks	<32 weeks
Controls	N ^a	50858	3776	628

^a Number of cases with non-missing birth weight

^b Adjusted for sex, birth weight, plurality, birth order, maternal age, maternal race, state, and year of birth