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Associations between Vaccination and Childhood Cancers in Texas Regions

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Abstract

Objectives—To determine whether children born in Texas regions with higher vaccination coverage had reduced risk of childhood cancer.

Study design—The Texas Cancer Registry identified 2800 cases diagnosed from 1995 to 2006 who were (1) born in Texas and (2) diagnosed at ages 2 to 17 years. The state birth certificate data were used to identify 11 200 age- and sex-matched control subjects. A multilevel mixed-effects regression model compared vaccination rates among cases and control subjects at the public health region and county level.

Results—Children born in counties with higher hepatitis B vaccine coverage had lower odds of all cancers combined (OR = 0.81, 95% CI: 0.67 to 0.98) and acute lymphoblastic leukemia (ALL) specifically (OR = 0.63, 95% CI: 0.46 to 0.88). A decreased odds for ALL also was associated at the county level with higher rates of the inactivated poliovirus vaccine (OR = 0.67, 95% CI: 0.49 to 0.92) and 4–3-1–3-3 vaccination series (OR = 0.62, 95% CI: 0.44 to 0.87). Children born in public health regions with higher coverage levels of the *Haemophilus influenzae* type b-conjugate vaccine had lower odds of ALL (OR: 0.58; 95% CI: 0.42 to 0.82).

Conclusions—Some common childhood vaccines appear to be protective against ALL at the population level.

Despite dedicated research, more than 95% of the causes of childhood cancer remain undetermined.[1] In his "delayed-infection hypothesis," Greaves asserts that postponed exposure to common infections increases the risk of childhood leukemia.[2–5] Early exposure of young children to a limited dose of pathogens primes immunologic mechanisms for future

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exposures.[3] Hygienic advancements in more developed countries have reduced young children's exposure to pathogens, which may compromise the natural development of the immune system.[2–5] In genetically predisposed children, delayed exposure to common infections may increase the risk of leukemia.[2,3]

Vaccinations prompt an immune response often similar to the natural infection.[6] Although particular biologic mechanisms have not been identified, vaccinations may play a role in regulating the risk of childhood cancer by nonspecific stimulation of certain macrophages and natural killer cells that target tumors.[6–9] In addition, a properly modulated adaptive immune system promotes possible antitumor activity of T-helper 1 responses.[7,10,11] Thus vaccinations may be a factor in regulating the risk of childhood cancer because of their role in modulating the immune system. Several studies reported a protective effect against childhood leukemia associated with the conjugate *Haemophilus influenzae* type b-conjugate (Hib) vaccine,[12–15] showing a dose-response relationship with the number of vaccinations received,[12,13] most significant in children vaccinated at the youngest ages.[1,16] The aim of this study was to determine whether children born in Texas regions with higher levels of vaccination coverage had a reduced risk of childhood cancer.

Methods

We conducted a case-control study using multi-level data to examine the association between childhood cancers, specifically acute lymphoblastic leukemia (ALL), medulloblastoma, and non-Hodgkin lymphoma (NHL), and vaccination rates in Texas. This research project was approved by the Texas Department of State Health Services Institutional Review Board (IRB# 08–089). The Texas Cancer Registry (TCR) provided data on 3871 childhood cancer cases diagnosed between 1995 and 2006. Cases who were not born in Texas (n = 8) were removed from the sample because relevant comparator vaccination rates were not available for such individuals. Cases who were diagnosed before age 2 years (n = 1063) also were eliminated because vaccination rate data were based on completion of vaccination series at 2 years of age. For our final analyses, 2800 cases remained.

A pool of 38 601 randomly selected control subjects without cancer were obtained by the TCR from birth records provided by Child Health Statistics. Personnel from the TCR conducted the data linkage between the incidence cases and potential birth-certificate control subjects to ensure that the control subjects were not included in the cancer incidence files. The randomly selected control subjects were matched by frequency to cases (4 control subjects/1 case) on sex and birth year (as a continuous variable), yielding 11 200 control subjects for the analysis. We also acquired de-identified demographic information on the parents and infant such as county of birth and race; as well as maternal and infant health information such as pregnancy history, medical risk for the pregnancy, and methods of delivery for both cases and control subjects through their birth certificates supplied by Child Health Statistics.

Vaccination rates from the Texas Department of State Health Services (DSHS) for the 11 public health regions for 1999 were available for all cases and control subjects. These data

were collected as part of the Texas Retrospective Immunization Survey, which is a retrospective survey of the vaccination coverage levels of public school kindergarteners when they were 24 months of age. These data were validated by comparison with vaccination records and were found to be more accurate than maternal self-report. Vaccination rates for Texas counties for the year 2007 to 2008 were obtained from the DSHS, as part of the state's active immunization surveillance system, and the Centers for Disease Control and Prevention (CDC). If the 2007 to 2008 yearly data were not available, we used 2005 to 2006 or 2006 to 2007 rates. The shaded counties in the Figure highlight the 91 counties for which we also had access to county vaccination coverage levels. For Harris County, we used the Houston city vaccination rates because most of Harris County is included within the City of Houston. We obtained county-level vaccination rates for 1707 cases and 6828 control subjects (61.0%). The Advisory Committee on Immunization Practices, DSHS, and CDC report completeness of vaccine series by 2 years of age for the following sets of vaccines: (1) four doses of the diphtheria toxoid, tetanus toxoid, and acellular pertussis antigen (DTaP) vaccine; (2) three doses of the inactivated polio virus vaccine (IPV); (3) one dose of the measles, mumps, and rubella (MMR) vaccine; (4) three doses of the Hib-conjugate vaccine; (5) three doses of the hepatitis B vaccine; (6) one dose of the varicella zoster virus vaccine; (7) the 4–3-1 vaccination series, which consists of four doses of the DTaP vaccine, three doses of the IPV, and one dose of the MMR vaccine; (8) the 4–3-1–3 vaccination series, which includes four doses of the DTaP vaccine, three doses of the IPV, one dose of the MMR vaccine, and three doses of the Hib vaccine; (9) the 4–3-1–3-3 vaccination series, which includes four doses of the DTaP vaccine, three doses of the IPV, one dose of the MMR vaccine, three doses of the Hib vaccine, and three doses of the hepatitis B vaccine; (10) and the 4–3-1–3-3–1 series, which consists of four doses of the DTaP vaccine, three doses of the IPV, one dose of the MMR vaccine, three doses of the Hib vaccine, three doses of the hepatitis B vaccine, and one dose of the varicella zoster virus vaccine.[17]

For the specific vaccines (ie, DTaP), children born in counties or public health regions with vaccination coverage levels at or above the 90th percentile were considered exposed. For the combination series (ie, 4–3-1), individuals born in counties or public health regions with vaccination coverage levels at or above the 80th percentile were considered exposed. These cut-offs were based on the United States Department of Health and Human Service's Healthy People 2010 goals for vaccination coverage levels.[18] Pearson's χ^2 test was used to test for differences in characteristics between the cases and the control subjects. We also assessed potential confounding and effect measure modification of the study variables using unconditional logistic regression. The variables examined included infant sex, race/ethnicity, maternal age at birth, birth weight, and parity. We performed stratified analyses to determine whether conditioning on any of the observed covariates greatly affected the OR relating vaccination rates to the odds of childhood cancer.

We used a multilevel mixed-effects logistic regression model to evaluate the association between group vaccination rates and individual disease outcome for each vaccine group. In this context, the cases with cancer and their matched control subjects provided the individual data, and the county and public health region vaccination rates were used as the aggregate data. One model, limited to the cases and control subjects born in the 91 counties with

available vaccination rates, assessed the relationship between childhood cancer and vaccination rates at the county level. A separate model included all cases and control subjects to evaluate the association between childhood cancer and public health region vaccine coverage levels. The association between vaccination rates and childhood cancers was measured by the OR and 95% CI were constructed as estimates of precision. All data were edited, cleaned, and analyzed by use of Intercooled Stata version 10.0 (Stata Corp, College Station, Texas).

Results

For the final analyses, a total of 2800 cases and 11 200 control subjects were available to measure the association between vaccination coverage rates and childhood cancer. Of the cases, 895 were diagnosed with ALL (32.0%), 114 with medulloblastoma (4.1%), and 116 with NHL (4.1%). No statistically significant differences ($P < .05$) existed between cases and control subjects for the following birth and maternal characteristics: birth year, birth type, birth order, premature birth, maternal education, maternal marital status, prior births, diabetes, preterm labor, tobacco use, and alcohol use (data not shown). We found a larger percentage of males in the medulloblastoma subtype compared with females. Although both cases and control subjects were predominantly Hispanic, compared with control subjects, a lower percentage of black and other ethnicities was seen in all cancers combined ($P < .001$) and in all subgroups (ALL: $P < 0.001$; NHL: $P = .03$) except for medulloblastoma (Table I). Compared with control subjects, children born at a high birth weight represented a larger percentage of ALL ($P = .005$) and all cancers combined ($P < .001$). Compared with control subjects, a higher number of children were born to mothers 35 years or older for all cancers combined ($P = .01$) and the ALL subgroup ($P = .02$).

We examined potential confounders using unconditional logistic regression analysis for selected birth and maternal characteristics (data not shown). Compared with males, females showed a decreased risk for development of medulloblastoma (OR = 0.56, 95% CI: 0.38 to 0.84). Black subjects had a lower risk for all cancer types combined (OR = 0.71, 95% CI: 0.61 to 0.82), the ALL subgroup (OR = 0.42, 95% CI: 0.31 to 0.58), and the NHL subgroup (OR = 0.29, 95% CI: 0.12 to 0.73) relative to white subjects. A higher risk for development of ALL was found for Hispanics compared with white subjects (OR = 1.17, 95% CI: 1.01 to 1.36). Taking into account the results from the logistic regression analysis and information provided in the current literature, child's ethnicity, child's birth weight, and mother's age at child's birth were adjusted for in the multilevel mixed-effects logistic regression. Sex and birth year also were adjusted for in the model to avoid confounding bias because of differences not completely adjusted by the frequency matching design. Parity was examined but was not determined to be a confounder between vaccination rate and cancer risk.

Children born in public health regions (Table II) with Hib vaccine rates at or above the 90th percentile had lower odds of ALL (OR: 0.58; 95% CI: 0.42 to 0.82). We also observed a decreased odds of ALL associated with higher 4–3-1 combination series rates (OR: 0.77, 95% CI: 0.60 to 1.00), as well as with higher Hib vaccine rates in all cancer types (OR: 0.84; 95% CI: 0.70 to 1.00) at the public health region level.

Children born in counties (Table III) with hepatitis B vaccine rates at or above the 90th percentile revealed negative associations with all cancers combined (OR = 0.81, 95% CI: 0.67 to 0.98) and the ALL subgroup (OR = 0.63, 95% CI: 0.46 to 0.88). The lower risk for ALL was evident for children born in counties with higher levels of the IPV (OR = 0.67, 95% CI: 0.49 to 0.92) and 4–3-1–3-3 vaccination series (OR = 0.62, 95% CI: 0.44 to 0.87) as well. In contrast, the children born in counties with MMR vaccine rates at or above the 90th percentile had higher odds of NHL (OR = 2.81, 95% CI: 1.27 to 6.22). A similar positive association between higher Hib vaccine rates at the county level and odds for medulloblastoma also was found (OR: 1.62; 95% CI: 1.00 to 2.62).

Discussion

We found novel and confirmatory results for the associations between specific vaccines and for the common vaccine series in relation to risk of ALL, NHL, and medulloblastoma. In addition, because we used a large pool of population-based control subjects, the distribution of potential risk factors between the cases and control subjects was similar and reduced the possibility that our significant results were due to confounding.

In support of recently reported inverse associations,[12,14,16] we found a decreased odds for all cancers, specifically ALL, for the Hib vaccine in the adjusted logistic regression model utilizing public health region vaccination rates. We also found that children born in counties with higher hepatitis B vaccine or IPV rates had lower odds of all cancers combined, specifically ALL. The negative associations for these specific vaccines are supported by nonsignificant inverse associations reported in the recent literature.[19] However, wide-spread vaccination programs in the United States have resulted in a narrowing of the variation in direct vaccine exposure between cases and control subjects.[12] Thus the lack of significant results in past studies that have used personal vaccine information may reflect the low statistical power of the studies rather than a nonexistent association between childhood cancer and vaccinations.

The decreased odds for ALL in children born in counties with 4–3-1–3-3 series rates at or above the 80th percentile deserves special attention. Although higher county coverage rates for the DTaP, MMR, and Hib vaccines did not produce significant associations individually, the associations between ALL and higher rates of the MMR and Hib vaccines demonstrated a negative trend. Two other studies have found a nonsignificant inverse association between MMR and leukemia.[19,20] Although the question cannot be completely answered within this study, in the future, we may be able to ascertain whether the IPV and hepatitis B vaccine are wholly responsible for the inverse association or if the MMR and Hib vaccines' beneficial effects emerge only in combination. Similarly, the borderline significant results found in children born in public health regions with higher rates of the 4–3-1 series point to a possible additive or synergistic effect because higher rates of the DTaP vaccine, IPV, and MMR vaccine demonstrated negative trends. These results may support our hypothesis that children born in Texas counties with higher vaccination rates for the hepatitis B vaccine, IPV, and Hib vaccine have decreased odds of development of all cancers combined, specifically ALL.

Conversely, a positive association existed between children born in counties with MMR vaccine rates at or above the 90th percentile and NHL. Elevated, although nonsignificant, ORs were also found with higher county coverage rates for the DTaP vaccine, 4–3-1 series, and 4–3-1–3-3 series. The wide confidence intervals are most likely due to the small number of cases for the subtype. Consequently, the results should be interpreted with caution until future case-control studies with larger sample sizes and individual vaccination information are conducted to confirm or refute the findings.

The medulloblastoma results are interesting as a whole because higher vaccination rates for all but the varicella zoster vaccination rates were related to an increased risk in the subtype both at the county and public health region level. The nonsignificant decrease in risk for medulloblastoma for children born in counties with higher rates of the varicella zoster virus vaccine warrants consideration in light of previous research which suggested a possible inverse association between chicken pox and adult gliomas.[21,22] Ultimately, we must perform further investigations to verify whether our results were caused by inadequate numbers or if medulloblastomas truly react differently to vaccinations.

The larger percentage of males with medulloblastoma in our data is supported by reports in the literature regarding lower rates of medulloblastoma incidence in females.[23] The increased risk in the children with higher birth weights also is in concordance with findings in previous research that found an association between higher birth weight and cancer risk, particularly ALL.[24,25] The higher risk for development of all cancer types and ALL specifically in children born to mothers 35 years or older is not surprising because the probability for chromosomal abnormalities such as Down syndrome increase with mother’s age, with the relationship between Down syndrome and the increased risk for development of leukemia being well documented.[26] The inverse association between children of unwed mothers and medulloblastoma may indirectly reflect the finding that unwed mothers are usually younger in age than mothers who are married. In this regard, cancer is a disease diagnosed mostly in the upper and middle class, and, in general, unmarried mothers report lower socioeconomic status.[27,28]

The use of birth certificate control subjects has been criticized because the reliability and validity of certain birth certificate variables remains questionable. For example, studies have shown that birth weight has been more accurately reported than information on complications during the pregnancy, and self-reported tobacco use is an inaccurate measure of maternal exposure.[29] Although we included some of these variables in our analyses of potential confounders and effect modifiers, we were aware of the limitations of the potential risk factors, and the variables that we used from the birth record are ones that are known to be more accurately reported.

Unlike a traditional case-control study, we did not have access to the vaccination records for each study participant. One of the major limitations of our study stemmed from the use of aggregate data for our primary vaccination exposure when trying to infer the risk of childhood cancer at an individual level. However, we may still draw accurate conclusions about the exposure-disease relationship from our results.[30] Because vaccine data for children in Texas may be similar because of immunization programs, a relationship between

vaccination rates and childhood cancer may not be evident in a study observing individuals. However, significant associations with childhood cancer were seen in our study that compared counties with diverse vaccine coverage levels.[30] As such, the multi-level logistic regression model allowed us to still take advantage of the available data and derive meaningful results to guide future studies.

Another potential limitation related to the use of vaccination rates on the basis of the study participants' birth counties and public health regions is the issue of residential mobility. Overall, 1944 of 2800 (69.4%) of the cases in our study were diagnosed in the same county where they were born, and we had no residential mobility history for the control subjects. However, we found no relationships between the residential mobility of the cases and any of the covariates included in the statistical model. We also found no relationship between residential mobility and our exposure, being born in Texas regions above the designated cut-off levels. In addition, on the basis of the U.S. Census Bureau general mobility data for 2000, the proportion of children 1 to 4 years old who remained at the same address or who moved within the same county was approximately 89.3%. Thus most of our study participants most likely received the required vaccinations before age 2 in the same county in which they were born.

Another limitation of the study stemmed from the limited availability of 2007 to 2008 county-level vaccine data. As such, we were forced to use 2005 to 2006 and 2006 to 2007 vaccination rates. However, 2007 to 2008 information was used for most of the cases and control subjects (97.1%). As a result, the percentage of vaccine data from prior years used was small, and inconsistencies in the primary vaccination exposure were minimal. Because vaccination rates used in our study were taken from years after the cases were diagnosed, we wanted to determine whether vaccination rates remained stable over time. To address this issue, we examined annual vaccine coverage rates from 1995 to 2007 available for Bexar County, Dallas County, and El Paso County from the CDC. We used these data to perform a time trend analysis by use of linear regression to examine differences in the vaccination rates for each vaccine over these years (results not shown). The results of this analysis describe the consistency of vaccine coverage levels for the 3 counties that contribute 25% of the total number of cases. The time trend results indicated that vaccination rates have increased over the years, which reveals the potential for nondifferential misclassification bias.[30] Children who would have been considered unexposed in the past may have been misclassified as exposed because of currently higher vaccine coverage levels. However, because the misclassification of exposure would not have been different between cases and control subjects, ORs would be biased toward null associations. As such, our significant results may be underestimations of the true associations.

In future studies using personal information, we may be able to discover whether simply obtaining common vaccines lowers the risk for development of pediatric cancer or whether children must acquire the vaccinations at the recommended ages to experience such benefits. In addition, we could examine differences in association for variations of a vaccine against the same agent (ie, DTaP vs diphtheria, tetanus, and whole-cell pertussis),[14] because the differing biologic make-up of the vaccines may induce distinct immunologic responses that may be expressed in cancer development. By obtaining participants' medical histories, as

well as vaccination records, we could better separate and distinguish the effects of vaccinations and actual infections in the development of childhood cancer. We could also investigate newly created vaccines for the pneumococcal virus, rotavirus, and hepatitis A virus not included in this study.

Although the biologic mechanism behind the effect of vaccinations on childhood cancer remains to be determined, our results corroborate findings from previous studies that point to a reduced risk from common vaccines against the development of ALL. Immunization programs may not only reduce the number of infectious diseases in childhood but also contribute to some immunologic defense against the development of certain cancers. Our findings must be verified in larger studies with individual vaccination histories. ■

Glossary

ALL	Acute lymphoblastic leukemia
CDC	Centers for Disease Control and Prevention
DSHS	Texas Department of State Health Services
DTaP	Diphtheria, tetanus, and acellular pertussis
HiB	*Haemophilus influenzae* type B
IPV	Inactivated polio virus
MMR	Measles, mumps, and rubella
NHL	Non-Hodgkin lymphoma
TCR	Texas Cancer Registry

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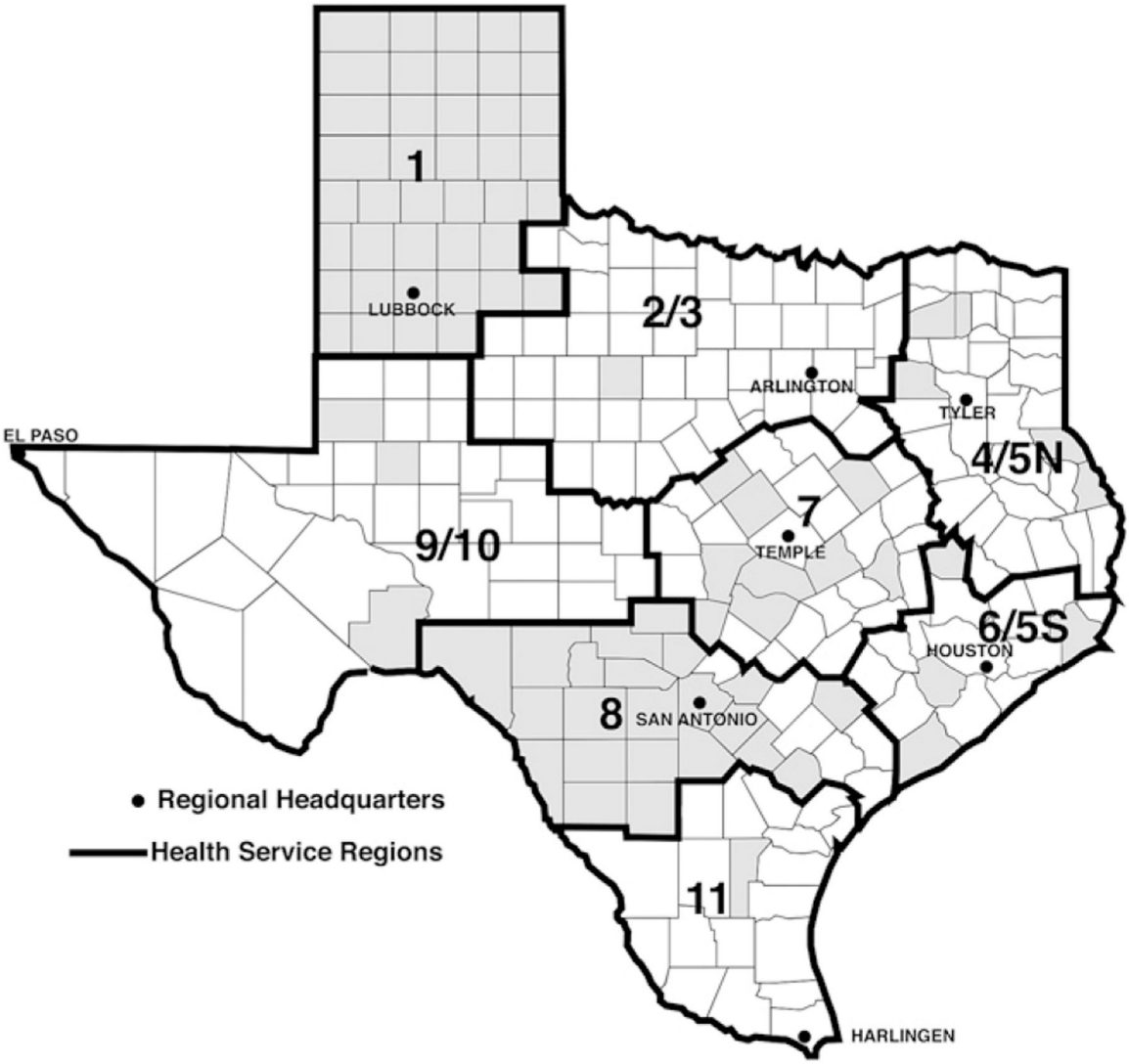

Figure.

Map of Texas Counties by Public Health Service Regions (http://www.dshs.state.tx.us/immunize/coverage/tcriss.shtm). *Shaded Counties* indicate that county-level vaccine coverage data were available and used in the county-level analysis. Vaccine Coverage data were available at the public health service region level for all regions.

Table I.

Distribution of selected birth & maternal characteristics obtained from birth certificate records for controls, all cancer cases, and specified cancer subtypes, Texas Cancer Registry, 1995 to 2006

	Control subjects (n = 11 200)		Total cases (n = 2800)		ALL (n = 895)		Medulloblastoma (n = 114)		Non-Hodgkin lymphoma(n = 115)	
	No.	%	No.	%	No.	%	No.	%	No.	%
Sex										
Male	6160	55.00	1540	55.00	493	55.08	78	68.42	73	63.48
Female	5040	45.00	1260	45.00	402	44.92	36	31.58	42	36.52
P value *				1.00		.92		.004		.07
Ethnicity										
White	4034	36.02	1070	38.21	322	35.98	44	38.60	50	43.48
Black	1395	12.46	261	9.32	46	5.14	17	14.91	5	4.35
Hispanic	5482	48.95	1414	50.50	510	56.98	51	44.74	55	47.83
Other	289	2.58	55	1.96	17	1.90	2	1.75	5	4.35
P value *				<.001		<.001		.69		.03
Birth weight										
Low	794	7.09	180	6.43	39	4.36	9	7.89	6	5.22
Normal	9439	84.28	2326	83.07	746	83.35	88	77.19	95	82.61
High	967	8.63	294	10.50	110	12.29	17	14.91	14	12.17
P value *				.005		<.001		.05		.33
Maternal education										
< High school	3647	32.56	875	31.25	293	33.30	33	28.95	42	36.52
High school	3418	30.52	861	30.75	267	29.83	33	28.95	36	31.30
Some college	1913	17.08	515	18.39	159	17.76	22	19.30	15	13.04
Bachelors degree	1171	10.46	304	10.86	96	10.72	16	14.04	11	9.57
Graduate degree	881	7.87	209	7.46	70	7.82	9	7.89	9	7.83
Unknown	170	1.52	36	1.29	10	1.12	1	0.88	2	1.74
P value *				.41		.99		.77		.88
Prior births										
0	4365	38.97	1117	38.89	345	38.55	37	32.46	50	43.48

	Control subjects (n = 11 200)		Total cases (n = 2800)		ALL (n = 895)		Medulloblastoma (n = 114)		Non-Hodgkin lymphoma(n = 115)	
	No.	%	No.	%	No.	%	No.	%	No.	%
1	3547	31.67	885	31.61	266	29.72	41	35.96	37	32.17
≥2	3152	28.15	762	28.21	271	30.28	35	30.70	28	24.35
Missing	136	1.21	36	1.29	13	1.45	1	0.88	0	
P value *				.90		.62		.73		.22
Maternal age at child's birth (years)										
<35	10 092	90.11	2478	88.46	783	87.49	108	94.74	104	90.43
≥35	1108	9.89	322	11.54	112	12.51	6	5.26	11	9.57
P value *				.01		.02		.09		.91

* *P* values derived from Pearson χ^2 function or Student *t* test where appropriate in comparison to control group.

Table II.

Multivariable multi-level logistic regression of specific vaccines and combination series for all cancer cases and specific cancer subtypes with public health region vaccination rates, Texas Cancer Registry, 1995–2006

	Total cases (n = 2800)			ALL (n = 895)			Non-Hodgkin lymphoma (n = 115)			Medulloblastoma (n = 114)		
	OR*	*P*	95% CI	OR*	*P*	95% CI	OR*	*P*	95% CI	OR*	*P*	95% CI
DTaP†	0.92	.28	0.80 – 1.07	0.82	.12	0.63 – 1.06	0.88	.53	0.58 – 1.32	1.11	.65	0.71 – 1.73
IPV‡	0.93	.30	0.81 – 1.07	0.83	.17	0.63 – 1.09	1.01	.98	0.59 – 1.74	1.49	.13	0.89 – 2.52
MMR§	0.92	.11	0.82 – 1.02	0.87	.21	0.71 – 1.08	0.99	.96	0.63 – 1.55	1.10	.68	0.70 – 1.72
Hib¶	**0.84**	**.05**	**0.70 – 1.00**	**0.58**	**.002**	**0.42 – 0.82**	0.65	.34	0.26 – 1.59	1.45	.28	0.75 – 2.80
4–3-1**	0.90	.13	0.80 – 1.03	**0.77**	**.05**	**0.60 – 1.00**	0.98	.95	0.59 – 1.64	1.39	.19	0.85 – 2.27
4–3-1–3††	0.98	.78	0.87 – 1.11	1.04	.80	0.74 – 1.47	1.18	.54	0.70 – 1.98	1.46	.12	0.90 – 2.36

Bolded results denote significant results ($P < .05$) or borderline significant results ($P = .05$).

*OR adjusted for sex, child's birth year, child's ethnicity, child's birth weight, and mother's age at child's birth.

†Four doses of the DTaP vaccine.

‡Three doses of the IPV.

§One dose of the MMR vaccine.

¶Three doses of the Hib vaccine.

**Four doses of the DTaP vaccine, 3 doses of the IPV, and 1 dose of the MMR vaccine.

††Four doses of the DTaP vaccine, 3 doses of the IPV, 1 dose of the MMR vaccine, and three doses of the Hib vaccine.

Table III.

Multivariable multi-level logistic regression of specific vaccines and combination series for all cancer cases and specific cancer subtypes by use of county-level vaccination rates, Texas Cancer Registry, 1995–2006

	Total cases (n = 1707)			ALL (n = 547)			Non-Hodgkin lymphoma (n = 71)			Medulloblastoma (n = 70)		
	OR*	*P*	95% CI	OR*	*P*	95% CI	OR*	*P*	95% CI	OR*	*P*	95% CI
DTaP†	1.20	.21	0.90–1.60	1.02	.92	0.61–1.72	2.34	.07	0.93–5.90	1.43	.55	0.44– 4.63
IPV‡	0.88	.17	0.74–1.05	**0.67**	**.01**	**0.49–0.92**	0.73	.47	0.31–1.72	1.47	.28	0.73– 2.96
MMR§	1.10	.48	0.84–1.45	0.84	.49	0.51–1.39	**2.81**	**.01**	**1.27–6.22**	1.20	.76	0.37– 3.88
Hib¶	0.92	.18	0.82–1.04	0.76	.13	0.54–1.08	0.98	.94	0.59–1.64	**1.62**	**.05**	**1.00– 2.62**
Hepatitis B**	**0.81**	**.03**	**0.67–0.98**	**0.63**	**.006**	**0.46–0.88**	0.77	.54	0.32–1.81	1.39	.38	0.67– 2.91
Varicella Zoster††	1.03	.60	0.92–1.16	1.07	.67	0.78–1.47	0.97	.91	0.58–1.62	0.90	.70	0.54– 1.51
4–3-1‡‡	1.00	.93	0.89–1.11	0.73	.10	0.51–1.06	1.13	.60	0.71–1.82	1.14	.69	0.60– 2.18
4–3-1–3-3§§	0.90	.28	0.74–1.09	0.62	**.007**	**0.44–0.87**	1.22	.72	0.40–3.69	1.58	.22	0.76– 3.30
4–3-1–3-3–1¶¶	0.98	.77	0.88–1.10	0.77	.22	0.50–1.17	0.84	.49	0.51–1.38	1.12	.74	0.58– 2.17

Bolded results denote significant results ($P < .05$) or borderline significant results ($P = .05$).

*OR adjusted for sex, child's birth year, child's ethnicity, child's birth weight, and mother's age at child's birth.

†Four doses of the DTaP vaccine.

‡Three doses of the IPV.

§One dose of the MMR vaccine.

¶Three doses of the Hib vaccine.

**Three doses of the hepatitis B vaccine.

††One dose of the varicella zoster vaccine.

‡‡Four doses of the DTaP vaccine, three doses of the IPV, and one dose of the MMR vaccine.

§§Four doses of the DTaP vaccine, three doses of the IPV, one dose of the MMR vaccine, and three doses of the Hib vaccine.

¶¶Four doses of the DTaP vaccine, three doses of the IPV, one dose of the MMR vaccine, three doses of the Hib vaccine, three doses of the hepatitis B vaccine, and one dose of the varicella zoster vaccine.