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Maternal and paternal occupational exposures and hepatoblastoma: results from the HOPE study through the Children's Oncology Group (COG)

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Abstract

Introduction—Little is known about the etiology of hepatoblastoma. We aimed to confirm the results of a previous study evaluating the association between parental occupational exposures and hepatoblastoma.

Methods—In our case-control study, we identified cases (n=383) from the Children's Oncology Group and controls from birth certificates (n=387), which were frequency matched to cases on year and region of birth, sex, and birth weight. Occupational exposure in the year prior to and during the index pregnancy was collected through maternal interview and analyzed using unconditional logistic regression.

Results—The odds of both paternal and maternal "Likely" exposure to paints was elevated among cases compared to controls (Paternal Odds Ratio [OR]: 1.71, 95% Confidence Interval [CI]: 1.04, 2.81; Maternal OR: 3.29, 95% CI: 0.32, 33.78) after adjustment for matching factors and the confounding factors of maternal race (maternal only) and household income. In addition, paternal exposure to other chemicals was also elevated when adjusting for matching factors only (OR: 1.53, 95% CI: 1.02, 2.30).

Discussion—The results of our study provide further evidence of an association between parental occupation and hepatoblastoma. These results warrant further investigation of the

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Conflict of interest

The authors declare no conflict of interest.

etiologically relevant timing of occupational exposure to fumes and chemicals related to hepatoblastoma.

Keywords

cancer; child exposure/health; epidemiology

Background

Little is known about the etiology of the rare pediatric liver tumor hepatoblastoma. The age-adjusted incidence rate from 2009–2013 was 2.6 per million among children aged 0–14 years.(1) The incidence was highest among infants under 1 year of age at 12.1 per million, followed by children 1–4 years of age at 6.4 per million.(1) Among children and adolescents aged 0–19 years, the five-year relative survival rate was 84.2%, which has increased from 69.5% during 1999–2005.(2)

Known risk factors for hepatoblastoma include syndromes, such as Beckwith-Wiedemann syndrome, hemihypertrophy, Familial Adenomatous Polyposis, and Gardner's Syndrome.(3, 4) Other potential risk factors include congenital anomalies, very low and moderately low birth weight, parental tobacco use and parental occupational exposures.(4) Only one study previously evaluated parental occupational exposures in a matched case-control study of hepatoblastoma in North American children aged 0–15 years from 1980–1983.(5) Among maternal exposures, the authors observed elevated odds ratios (ORs) for exposure to paints or pigments (OR 3.7), oil or coal products (OR: 3.7), and metals (OR: 7.0). ORs for paternal occupational exposures were attenuated compared to maternal exposures, with the only significant association for oil or coal products (OR: 1.9), although the OR for metals was of marginal significance (OR: 3.0).(5)

In order to confirm the results observed in Buckley et al.,(5) we aimed to further evaluate the association between maternal and paternal occupational exposures and hepatoblastoma.

Methods

We conducted a case-control study, the HOPE study, comparing children diagnosed with hepatoblastoma at a Children's Oncology Group (COG) institution (n=383) to children without hepatoblastoma with ascertainment through birth certificates as the source for controls (n=387). Details of the study design have been published previously.(6–8) Briefly, cases were recruited from United States COG institutions and included children diagnosed with hepatoblastoma (International Classification of Childhood Cancers histology code 8970) prior to 15 years of age between January 1, 2000 and December 31, 2008. Other inclusion criteria include birth in the United States, birth mother available for interview who speaks English or Spanish, and physician permission to contact cases. Diagnosis of hepatoblastoma was confirmed through pathologic review. Controls were obtained from birth certificates from 32 state birth registries from 1994–2008 and frequency matched to cases on year of birth (quartiles), region of birth, sex, and birth weight (<1500 grams, 1500–2499 grams, and ≥2500 grams). Details on control selection were published previously.(7, 8)

The study had approximately 80% power to detect an OR of at least 1.5 assuming 30% of controls were exposed.

Occupational exposures for participant mothers and fathers were obtained through maternal phone interview following a computer-assisted structured questionnaire after obtaining verbal informed consent. Mothers were asked about jobs held from one year prior to becoming pregnant through the index child's birth. Self-report of occupational exposures for mothers was also collected. These included exposures to chemical, welding, solder/flux, plastic, paint (such as varnish and shellac), gasoline/diesel, or other types of fumes or other chemicals including solvents, glues/resins/pigments, or any other types of chemicals at the job at least once a week for six months in a row. In addition, job titles, duties, and time period of the job (prior to pregnancy, during pregnancy, or both) were collected. Mothers also reported jobs and exposures for the biologic father for the year prior to and during her pregnancy with the index child. An exposure matrix was subsequently developed by an industrial hygienist (G.R.) to estimate the level of exposure based on job classification,(9, 10) which assigned exposure to the fumes and chemicals described above. The exposure matrix classified exposure as unlikely, possible, or likely to each type of occupational exposure depending on the job category. Since mothers and fathers could hold multiple jobs during the time period of interest, we combined occupational exposure into a single exposure variable in order to evaluate exposure to each chemical/fume included. Therefore, any "Likely" occupational exposure to specific fumes/chemicals during the time period of interest was classified as "Likely", any job with "Possible" exposure was classified as "Possible" as long as the parent had no "Likely" exposures, and all others were classified as "Unlikely" to be exposed to the fume or chemical. Mothers and fathers who reported having no jobs in the year prior to or during the index pregnancy were classified into the "Unlikely" category. We analyzed maternal and paternal exposures separately. We evaluated exposures in three categories (Unlikely, Possible, and Likely) and as a dichotomous variable (Unlikely and Possible/Likely) due to small sample size in the "Likely" category for mothers.

Covariates of interest were also collected through maternal interview and included maternal and paternal race, pregnancy complications, maternal pre-pregnancy weight, maternal age, birth weight, gestational age at delivery, plurality, sex of the child, congenital anomalies, maternal tobacco use, child's age at interview, and socioeconomic status (maternal education and household income).

We used unconditional logistic regression to evaluate the association between maternal and paternal occupational exposures adjusted for the matching factors. We used a directed acyclic graph to identify potential confounders.(11) For maternal occupational exposures and hepatoblastoma, the minimally sufficient set to control confounding included maternal race and household income as a surrogate for socioeconomic status. For paternal exposures, we identified household income as the minimally sufficient set to control confounding. However, most covariates were based on maternal factors, resulting in limited covariates available for fathers. We used backwards selection to determine whether removing a covariate from the logistic regression model changed the odds ratio (OR) more than 15%. (12) We also evaluated effect modification using a test for interaction between the exposure and covariates of interest in a logistic regression model. To evaluate potential recall bias, we

stratified by age at interview. All analyses were conducted in SAS v. 9.4 and used an alpha of 0.05 to define statistical significance for two-sided tests. SAS code is available upon request.

This study was approved by the Institutional Review Board at the University of Minnesota, the coordinating center, and all participating COG institutions.

Results

In our study population, we observed differences in both maternal and paternal race/ethnicity by case/control status, with a higher percentage of case mothers and fathers reporting Hispanic ethnicity but a lower percentage of African Americans compared to controls (Table 1). We also observed a higher percentage of case households with income below \$30,000 per year compared to controls. Regarding birth characteristics, a lower percentage of cases weighed 1,500–2,499 grams at birth compared to controls. We observed no differences in maternal smoking during pregnancy or regarding employment status for mothers or fathers.

Regarding maternal occupational exposures, few were classified in the “Likely” exposure category for exposure to many fumes/chemicals. Although we observed no statistically significant associations, the odds of “Likely” maternal exposure to paint was more than three times higher among cases compared to controls after adjustment for matching factors in addition to household income and maternal race (OR: 3.29, 95% CI: 0.32, 33.78), with three cases in the “Likely” exposure category (Table 2). Furthermore, “Possible” exposure to paints was also elevated, though attenuated, indicating a possible dose-response relationship. Additionally, the adjusted odds of “Likely” exposure to plastics was more than two times higher among cases compared to controls (OR: 2.19, 95% CI: 0.39, 12.29).

Similar to mothers, the odds of “Likely” paternal exposure to paint was significantly elevated among cases compared to controls after adjustment for household income (OR: 1.71, 95% CI: 1.04, 2.81) (Table 2). Paternal exposure to paints also demonstrates a potential dose-response relationship. Exposure to other chemicals was also significantly elevated when adjusting for matching factors only (OR: 1.53, 95% CI: 1.02, 2.30). With the exception of gasoline exposure, the remaining paternal occupational exposures were elevated, though none were statistically significant.

After dichotomizing occupational exposures, we observed similar results to our analysis of maternal exposure to three categories, with elevated and more precise ORs for welding, plastic, paint, other fumes, solvents, glues, and other chemicals (Table 3). Results for paternal occupations were similar to those when evaluating three categories of exposure, with paint remaining significantly associated with hepatoblastoma.

Additionally, we analyzed maternal self-reported occupational exposures to specific types of fumes and other chemicals (Supplemental Table 1). While none of the estimates were statistically significant, we observed elevated ORs for welding, solder, paint, and glues exposures.

When we analyzed the data by age group, we observed stronger ORs among children aged 0–4 years compared to those aged 5–14 years for several maternal and all paternal occupational exposures using the exposure matrix (Supplemental Table 2). However, for the maternal self-reported exposures, the ORs were generally stronger in the 5–14 year age group compared to the 0–4 year age group, though estimates were imprecise (Supplemental Table 3).

Discussion

We observed elevated odds of both maternal and paternal paint exposures for hepatoblastoma cases compared controls, although only the association for paternal exposures was significantly elevated. We also observed that paternal exposure to other chemicals was associated with hepatoblastoma, with no association among the remaining occupational exposures measured in this study.

As stated previously, there has been one other study evaluating parental occupational exposures and hepatoblastoma.(5) Mothers and fathers, when available, were interviewed regarding job history including title, industry, time period and length of job, and exposure to specific chemicals and substances. The authors observed a significantly elevated association with maternal paint exposures (OR: 3.7, $p<0.05$) and a non-significantly elevated association with paternal paint exposures (OR: 1.5). These results were of similar magnitude as the estimates for maternal and paternal paint exposures in our study, though we only observed statistically significant results for paternal paint exposure. In the Buckley et al. (5) study, there were fewer than five controls for all maternal occupational exposures except solvents/ cleaning agents, resulting in imprecise estimates. The authors also explored timing of exposure related to pregnancy and reported that maternal paint exposures primarily occurred prior to the index pregnancy in brief periods, but the timing of exposure during pregnancy varied. The estimated OR observed in our study for both maternal self-reported exposure to paint and “Likely” exposure based on job title was similar to that reported in Buckley et al. (5), though not statistically significant.

While studies of occupational exposure and risk of hepatoblastoma are rare, several studies have identified positive associations between parental occupational exposures and other childhood cancers, primarily leukemia.(13–20) In a systematic review, Colt and Blair(21) reported consistently elevated relative risks of leukemia and central nervous system tumors among children whose fathers were exposed to paints/pigments and solvents (leukemia only) across multiple studies. Maternal occupational exposures were studied less frequently, but elevated relative risks were reported for mothers in personal service, textiles, and metals and childhood leukemia. Furthermore, moderately elevated relative risks were observed for paternal exposure to hydrocarbons and urinary tract cancers.

To date, there is no clear biologic mechanism for parental occupational exposures to cause hepatoblastoma in the offspring. However, chemicals are often metabolized by the liver and may be attracted to the liver based on rich blood supply.(22) In addition, laboratory studies, primarily in animals, have demonstrated that chemicals can affect the fetal liver through transplacental exposure.(23)

Misclassification of occupational exposures was of concern in our study. Schuz, Spector, and Ross (24) evaluated parental occupational exposures and childhood cancer in a pooled analysis of several case-control studies conducted in Germany. The authors observed evidence of recall bias for paternal exposures in their analysis by comparing those with shorter times between birth and interview to those with longer times and observed increased prevalence of exposure among cases during the shorter time period, but not controls. Furthermore, the authors compared self-reported exposures to specific chemicals by job title and observed misclassification for some job categories, including both under and over-reporting of exposures.

To evaluate the potential for recall bias in our study, we stratified by age. We generally observed stronger estimates for maternal and paternal exposures using the exposure matrix in the younger age group, but the trend was unclear for maternal self-report of exposure. Although it is unclear whether recall bias was present in the self-reported data, using a job-exposure matrix provided an improvement over self-report of exposure or occupation obtained existing records, such as birth certificates.(21) However, fathers were not interviewed regarding their occupational history and mothers provided surrogate information on paternal exposures, which may be an additional source of misclassification. It is notable that the cases of hepatoblastoma in older children are often a mixture of hepatoblastoma and hepatocellular carcinoma (HCC) (25). While the precise classification of these liver tumors in older children is undergoing evolution, it is plausible that the etiology in these older children may also differ from that in younger children.

Another limitation of our study was the inclusion of household income as a potential confounder for the association between paternal exposures and hepatoblastoma. Paternal income may be misclassified in this study since income was reported by the mother and may differ from that of the father if they are not cohabiting. Furthermore, exposure to occupational chemicals and fumes was not directly measured. This study was retrospective and relied on maternal self-report of both maternal and paternal occupation and exposures. Questions were asked about job type, duties, and length and exposure to specific chemicals during the year prior to pregnancy through the child's birth. This provides a methodologic improvement in that exposure was estimated near the etiologically-relevant window of exposure. However, we did not restrict to exposures that only occurred during the pregnancy due to the inability to determine which jobs occurred during which time period. Furthermore, because likely maternal exposure was rare, the estimates were imprecise and limited our ability to evaluate a dose-response relationship. While we conducted multiple statistical tests in our study, there is disagreement among epidemiologists on the importance of controlling for multiple tests. Our study tested a relatively low number of tests compared with genetic studies which perform thousands of statistical tests, thus we did not adjust the level of significance.(26, 27)

A strength of this study was the ability to assess a rare cancer on a national level through a high quality childhood cancer clinical trials consortium resulting in the largest study on hepatoblastoma to date. In addition, controls were population-based with selection from birth certificates, which has advantages compared to random digit dialing including the ability to more quickly identify eligible controls and collect limited parental demographic

data.(28) However, despite identifying controls through birth certificates, participation rates were low, resulting in the potential for selection bias. Furthermore, the underlying distribution of controls differed from the general US population for maternal race, age, and education, although the impact on the results was minimal.(8)

Future studies should consider interviewing both mothers and fathers on occupational history, although this can be challenging if the biological parents are not residing together at the time of interview. It would also be informative to have information on whether the biological father resided in the home with the mother/child during the relevant timing of exposure. This could allow investigators to estimate whether exposure occurred through germ cells prior to conception or domestically during pregnancy/early childhood. Additionally, obtaining biomarkers of occupational exposures would provide a more objective measure of exposure to specific chemicals. However, the metabolism of each type of fume or chemical may differ and may require measurement close to the time of exposure. Due to the resources required to follow a large, occupationally exposed cohort over time for a rare outcome, this is infeasible in studying such a rare disease. In summary, this study provided additional evidence regarding the association between occupational exposures and hepatoblastoma, a rare childhood cancer. The results of this study warrant further investigation related to timing of exposure and understanding the biologic mechanism for occupational exposures to chemicals and fumes to be a cause of hepatoblastoma.

Supplementary Material

Refer to Web version on PubMed Central for supplementary material.

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References

1. Howlader, N., Noone, AM., Krapcho, M., Miller, D., Bishop, K., Altekruse, SF., et al. SEER Cancer Statistics Review, 1975–2013. Bethesda, MD: National Cancer Institute; 2016.
2. Horner, MJ., Ries, LAG., Krapcho, M., Neyman, N., Aminou, R., Howlader, N., et al. SEER Cancer Statistics Review, 1975–2006. Bethesda, MD: National Cancer Institute; 2009.
3. Bulterys, M., Goodman, MT., Smith, MA., Buckley, J. Hepatic Tumors. In: Ries, LAG.Smith, MA.Gurney, JG.Linet, M.Tamra, T.Young, JL., et al., editors. Cancer Incidence and Survival among Children and Adolescents: United States SEER Program 1975–1995. Bethesda, MD: National Cancer Institute, SEER Program; 1999.
4. Spector LG, Birch J. The epidemiology of hepatoblastoma. *Pediatr Blood Cancer*. 2012; 59(5):776–9. [PubMed: 22692949]
5. Buckley JD, Sather H, Ruccione K, Rogers PC, Haas JE, Henderson BE, et al. A case-control study of risk factors for hepatoblastoma. A report from the Childrens Cancer Study Group. *Cancer*. 1989; 64(5):1169–76. [PubMed: 2547509]
6. Turcotte LM, Georgieff MK, Ross JA, Feusner JH, Tomlinson GE, Malogolowkin MH, et al. Neonatal medical exposures and characteristics of low birth weight hepatoblastoma cases: a report from the Children's Oncology Group. *Pediatr Blood Cancer*. 2014; 61(11):2018–23. [PubMed: 25044669]

7. Musselman JR, Georgieff MK, Ross JA, Tomlinson GE, Feusner J, Krailo M, et al. Maternal pregnancy events and exposures and risk of hepatoblastoma: a Children's Oncology Group (COG) study. *Cancer epidemiol.* 2013; 37(3):318–20. [PubMed: 23312454]
8. Puumala SE, Ross JA, Feusner JH, Tomlinson GE, Malogolowkin MH, Krailo MD, et al. Parental infertility, infertility treatment and hepatoblastoma: a report from the Children's Oncology Group. *Hum Reprod.* 2012; 27(6):1649–56. [PubMed: 22473396]
9. Ramachandran, G. Occupational Exposure Assessment for Air Contaminants. Boca Raton, FL: CRC Press; 2005.
10. Jahn, S., Bullock, WH., Ignacio, J. A Strategy for Assessing and Managing Occupational Exposures. 4. Fairfax, VA: American Industrial Hygiene Association; 2015.
11. Greenland S, Pearl J, Robins JM. Causal diagrams for epidemiologic research. *Epidemiology.* 1999; 10(1):37–48. [PubMed: 9888278]
12. Kleinbaum, DG., Kupper, LL., Nizam, A., Muller, KE. Applied Regression Analysis and Other Multivariable Methods. 4. 2008.
13. Sung TI, Wang JD, Chen PC. Increased risk of cancer in the offspring of female electronics workers. *Reprod Toxicol.* 2008; 25(1):115–9. [PubMed: 17923386]
14. Pearce MS, Hammal DM, Dorak MT, McNally RJ, Parker L. Paternal occupational exposure to electro-magnetic fields as a risk factor for cancer in children and young adults: a case-control study from the North of England. *Pediatr Blood Cancer.* 2007; 49(3):280–6. [PubMed: 16941646]
15. McKinney PA, Fear NT, Stockton D. Investigators UKCCS. Parental occupation at periconception: findings from the United Kingdom Childhood Cancer Study. *Occup Environ Med.* 2003; 60(12): 901–9. [PubMed: 14634180]
16. Mutanen P, Hemminki K. Childhood cancer and parental occupation in the Swedish Family-Cancer Database. *Journal of Occupational & Environmental Medicine.* 2001; 43(11):952–8. [PubMed: 11725335]
17. Schuz J, Kaletsch U, Meinert R, Kaatsch P, Michaelis J. Risk of childhood leukemia and parental self-reported occupational exposure to chemicals, dusts, and fumes: results from pooled analyses of German population-based case-control studies. *Cancer Epidemiol Biomarkers Prev.* 2000; 9(8): 835–8. [PubMed: 10952101]
18. Heacock H, Hertzman C, Demers PA, Gallagher R, Hogg RS, Teschke K, et al. Childhood cancer in the offspring of male sawmill workers occupationally exposed to chlorophenolate fungicides. *Environ Health Perspect.* 2000; 108(6):499–503. [PubMed: 10856022]
19. Smulevich VB, Solionova LG, Belyakova SV. Parental occupation and other factors and cancer risk in children: II. Occupational factors. *Int J Cancer.* 1999; 83(6):718–22. [PubMed: 10597184]
20. Shu XO, Stewart P, Wen WQ, Han D, Potter JD, Buckley JD, et al. Parental occupational exposure to hydrocarbons and risk of acute lymphocytic leukemia in offspring. *Cancer Epidemiol Biomarkers Prev.* 1999; 8(9):783–91. [PubMed: 10498397]
21. Colt JS, Blair A. Parental occupational exposures and risk of childhood cancer. *Environ Health Perspect.* 1998; 106(Suppl 3):909–25. [PubMed: 9646055]
22. Rapisarda V, Loreto C, Malaguarnera M, Ardiri A, Proiti M, Rigano G, et al. Hepatocellular carcinoma and the risk of occupational exposure. *World journal of hepatology.* 2016; 8(13):573–90. [PubMed: 27168870]
23. International Agency for Research on Cancer. Chemical Agents and Related Occupations. Lyon, France: 2012.
24. Schuz J, Spector LG, Ross JA. Bias in studies of parental self-reported occupational exposure and childhood cancer. *Am J Epidemiol.* 2003; 158(7):710–6. [PubMed: 14507608]
25. Lopez-Terrada D, Alaggio R, de Davila MT, Czauderna P, Hiyama E, Katzenstein H, et al. Towards an international pediatric liver tumor consensus classification: proceedings of the Los Angeles COG liver tumors symposium. *Mod Pathol.* 2014; 27(3):472–91. [PubMed: 24008558]
26. Greenland S. Multiple comparisons and association selection in general epidemiology. *Int J Epidemiol.* 2008; 37(3):430–4. [PubMed: 18453632]
27. Rothman KJ. No adjustments are needed for multiple comparisons. *Epidemiology.* 1990; 1(1):43–6. [PubMed: 2081237]

28. Spector LG, Ross JA, Puumala SE, Roesler M, Olshan AF, Bunin GR. Feasibility of nationwide birth registry control selection in the United States. *Am J Epidemiol.* 2007; 166(7):852–6. [PubMed: 17623744]

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Table 1

Distribution of demographic factors for hepatoblastoma cases and controls

	Cases (n=383)		Controls (n=387)		
	N	%	N	%	
Maternal Race/Ethnicity					0.0003
African American	18	4.8	33	8.7	
Hispanic	72	19.0	34	8.9	
Other	28	7.4	30	7.9	
Non-Hispanic White	261	68.9	284	74.5	
Paternal Race/Ethnicity					<0.0001
African American	23	6.1	41	10.8	
Hispanic	79	20.8	34	8.9	
Other	32	8.4	27	7.1	
Non-Hispanic White	245	64.6	279	73.2	
Maternal Age (years)					0.16
<20	27	7.1	15	3.9	
20–24	59	15.4	66	17.2	
25–29	101	26.4	122	31.8	
30–34	127	33.2	113	29.4	
35+	69	18.0	68	17.7	
Household Income (per year)					0.04
<\$30,000	117	31.1	88	23.0	
\$30,000 - \$75,000	143	38.0	166	43.5	
\$75,000	116	30.9	128	33.5	
Gestational Age at Delivery (weeks)					0.006
<34	62	16.3	69	18.0	
34–36	25	6.6	50	13.0	
37+	293	77.1	265	69.0	
Birthweight (grams)					<0.0001
<1500	57	14.9	65	16.8	
1500–2499	23	6.0	79	20.4	

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	Cases (n=383)		Controls (n=387)		
	N	%	N	%	
2500	303	79.1	243	62.8	0.7
Sex					
Female	155	40.5	162	41.9	
Male	228	59.5	225	58.1	0.93
Maternal Smoking during Pregnancy					
Yes	34	8.9	35	9.1	
No	347	91.1	349	90.9	0.69
Mother Employment [/]					
Yes	300	78.7	306	79.9	
No	81	21.3	77	20.1	0.26
Father Employment [/]					
Yes	367	96.6	374	97.9	
No	13	3.4	8	2.1	

[/]Employment from one year prior to and during pregnancy

Table 2

Odds ratios and 95% confidence intervals for parental occupational exposures and childhood hepatoblastoma

	Maternal Exposures				Paternal Exposures			
	N	Model 1 [†] OR (95% CI)	Model 2 [‡] OR (95% CI)	N	Model 1 [†] OR (95% CI)	Model 2 [‡] OR (95% CI)		
Welding								
Unlikely	731	Referent	Referent	514	Referent	Referent	Referent	
Possible	13	1.20 (0.38, 3.77)	1.27 (0.40, 3.99)	62	1.12 (0.63, 1.98)		1.17 (0.66, 2.08)	
Likely	9	1.16 (0.29, 4.67)	1.09 (0.28, 4.32)	165	1.23 (0.84, 1.80)		1.17 (0.79, 1.73)	
Solder								
Unlikely	722	Referent	Referent	515	Referent	Referent	Referent	
Possible	14	1.03 (0.34, 3.12)	1.05 (0.34, 3.20)	73	0.86 (0.50, 1.46)		0.87 (0.51, 1.50)	
Likely	17	0.96 (0.35, 2.63)	0.88 (0.32, 2.43)	153	1.31 (0.88, 1.93)		1.25 (0.84, 1.86)	
Plastic								
Unlikely	740	Referent	Referent	571	Referent	Referent	Referent	
Possible	7	0.94 (0.19, 4.56)	1.00 (0.20, 4.98)	46	1.29 (0.67, 2.48)		1.33 (0.69, 2.56)	
Likely	6	2.19 (0.39, 12.29)	2.07 (0.36, 11.84)	124	1.21 (0.79, 1.85)		1.14 (0.74, 1.76)	
Paint								
Unlikely	726	Referent	Referent	522	Referent	Referent	Referent	
Possible	23	1.65 (0.68, 4.02)	1.49 (0.61, 3.60)	125	1.47 (0.96, 2.24)		1.40 (0.91, 2.15)	
Likely	4	3.73 (0.38, 36.97)	3.29 (0.32, 33.78)	94	1.77 (1.09, 2.88)		1.71 (1.04, 2.81)	
Gasoline								
Unlikely	718	Referent	Referent	489	Referent	Referent	Referent	
Possible	18	0.59 (0.21, 1.64)	0.51 (0.18, 1.44)	128	1.11 (0.73, 1.70)		1.05 (0.68, 1.61)	
Likely	17	1.29 (0.46, 3.64)	1.03 (0.36, 2.97)	124	0.97 (0.63, 1.49)		0.87 (0.55, 1.36)	
Other Fumes								
Unlikely	709	Referent	Referent	509	Referent	Referent	Referent	
Possible	42	1.69 (0.85, 3.34)	1.69 (0.84, 3.40)	114	1.17 (0.75, 1.81)		1.10 (0.71, 1.72)	
Likely	2	1.20 (0.07, 19.76)	1.10 (0.07, 18.52)	118	1.32 (0.85, 2.05)		1.25 (0.80, 1.96)	
Solvents								
Unlikely	685	Referent	Referent	481	Referent	Referent	Referent	
Possible	46	1.27 (0.66, 2.42)	1.27 (0.65, 2.47)	122	1.03 (0.67, 1.58)		0.99 (0.64, 1.52)	

		Maternal Exposures				Paternal Exposures					
		N	Model 1 ¹	OR (95% CI)	Model 2 ²	OR (95% CI)	N	Model 1 ¹	OR (95% CI)	Model 2 ³	OR (95% CI)
Likely		22	1.15 (0.47, 2.84)		0.97 (0.39, 2.43)		138	1.37 (0.90, 2.08)		1.27 (0.83, 1.95)	
Glues											
Unlikely		657	Referent		Referent		459	Referent		Referent	
Possible		69	1.48 (0.86, 2.56)		1.30 (0.75, 2.27)		150	1.21 (0.81, 1.80)		1.13 (0.75, 1.69)	
Likely		27	0.77 (0.33, 1.79)		0.72 (0.30, 1.69)		132	1.52 (0.99, 2.32)		1.43 (0.93, 2.21)	
Other Chemicals											
Unlikely		632	Referent		Referent		420	Referent		Referent	
Possible		94	1.41 (0.88, 2.26)		1.28 (0.79, 2.09)		169	1.27 (0.86, 1.86)		1.18 (0.80, 1.76)	
Likely		27	0.77 (0.33, 1.80)		0.72 (0.31, 1.70)		152	1.53 (1.02, 2.30)		1.45 (0.95, 2.20)	

¹ Adjusted for matching factors of year of birth, region of birth, sex, and birth weight

² Adjusted for household income, maternal race and matching factors

³ Adjusted for household income and matching factors

Bold indicates statistically significant results.

Table 3

Odds ratios and 95% confidence intervals for dichotomous parental occupational exposures and childhood hepatoblastoma.

	Maternal Exposures				Paternal Exposures			
	N	Model 1 [†] OR (95% CI)	Model 2 [‡] OR (95% CI)	N	Model 1 [†] OR (95% CI)	Model 2 [‡] OR (95% CI)	Model 3 [§] OR (95% CI)	
Welding								
Unlikely	731	Referent	Referent	514	Referent	Referent	Referent	
Possible/Likely	22	1.18 (0.48, 2.89)	1.19 (0.49, 2.91)	227	1.20 (0.85, 1.68)	1.17 (0.83, 1.65)		
Solder								
Unlikely	722	Referent	Referent	515	Referent	Referent	Referent	
Possible/Likely	31	0.99 (0.46, 2.10)	0.95 (0.44, 2.04)	226	1.14 (0.81, 1.60)	1.11 (0.79, 1.57)		
Plastic								
Unlikely	740	Referent	Referent	571	Referent	Referent	Referent	
Possible/Likely	13	1.39 (0.45, 4.36)	1.41 (0.44, 4.47)	170	1.23 (0.85, 1.79)	1.19 (0.81, 1.74)		
Paint								
Unlikely	726	Referent	Referent	522	Referent	Referent	Referent	
Possible/Likely	27	1.86 (0.82, 4.24)	1.66 (0.73, 3.79)	219	1.59 (1.12, 2.24)	1.52 (1.07, 2.16)		
Gasoline								
Unlikely	718	Referent	Referent	489	Referent	Referent	Referent	
Possible/Likely	35	0.86 (0.42, 1.76)	0.72 (0.34, 1.50)	252	1.04 (0.75, 1.45)	0.96 (0.68, 1.35)		
Other Fumes								
Unlikely	709	Referent	Referent	509	Referent	Referent	Referent	
Possible/Likely	44	1.66 (0.85, 3.22)	1.65 (0.84, 3.26)	232	1.24 (0.89, 1.74)	1.17 (0.83, 1.66)		
Solvents								
Unlikely	685	Referent	Referent	481	Referent	Referent	Referent	
Possible/Likely	68	1.23 (0.72, 2.10)	1.16 (0.67, 2.01)	260	1.20 (0.86, 1.66)	1.12 (0.80, 1.57)		
Glues								
Unlikely	657	Referent	Referent	459	Referent	Referent	Referent	
Possible/Likely	96	1.23 (0.77, 1.96)	1.10 (0.68, 1.77)	282	1.34 (0.97, 1.85)	1.26 (0.90, 1.75)		
Other Chemicals								
Unlikely	632	Referent	Referent	420	Referent	Referent	Referent	
Possible/Likely	121	1.23 (0.81, 1.87)	1.13 (0.73, 1.73)	321	1.38 (1.01, 1.90)	1.30 (0.94, 1.80)		

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² Adjusted for household income, maternal race and matching factors

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Bold indicates statistically significant results.