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Maternal occupation and the risk of major birth defects: A follow-up analysis from the National Birth Defects Prevention Study

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Abstract

This study further examined the association between selected maternal occupations and a variety of birth defects identified from prior analysis and explored the effect of work hours and number of jobs held and potential interaction between folic acid and occupation. Data from a population-based, multi-center case-control study was used. Analyses included 45 major defects and specific sub-occupations under five occupational groups: healthcare workers, cleaners, scientists, teachers and personal service workers. Both logistic regression and Bayesian models (to minimize type-1 errors) were used, adjusted for potential confounders. Effect modification by folic acid was also assessed. More than any other occupation, nine different defects were positively associated with maids or janitors [odds ratio (OR) range: 1.72-3.99]. Positive associations were also seen between the following maternal occupations and defects in their children (OR range: 1.35-3.48): chemists/conotruncal heart and neural tube defects (NTDs), engineers/conotruncal defects, preschool teachers/cataracts and cleft lip with/without cleft palate (CL/P), entertainers/athletes/gastroschisis, and nurses/hydrocephalus and left ventricular outflow tract heart defects. Non-preschool teachers had significantly lower odds of oral clefts and gastroschisis in their offspring (OR range: 0.53-0.76). There was a suggestion that maternal folic acid use modified the effects with occupations including lowering the risk of NTDs and CL/P. No consistent patterns were found between maternal work hours or multiple jobs by occupation and the risk of birth defects. Overall, mothers working as maids, janitors, biologists, chemists, engineers, nurses, entertainers, child care workers and preschool teachers had increased risks of several malformations and non-preschool teachers had a lower risk of some defects. Maternal folic acid use reduced the odds of NTDs and CL/P among those with certain occupations. This hypothesis-generating study will provide clues for future studies with better exposure data.

Keywords

occupation; birth defects; folic acid

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Introduction

Associations between maternal occupations and certain birth defect outcomes have been studied, though not thoroughly. Studies have shown oral clefts (Cordier et al., 1992; Lorente et al., 2000), neural tube defects (NTDs) (Brender et al., 2002), spina bifida (Blatter et al., 1996), and chromosomal single birth defects (Chi et al., 2003) to be associated with the maternal occupations of janitors or cleaners. A French study found that nurses, laboratory workers, hairdressers, and cleaners may be exposed to solvents and that maternal exposure to solvents was associated with major malformations, including oral clefts, urinary malformations, and male genital malformations (Garlantezec et al., 2009). Similarly, a study of births from 1968-1980 reported that women who worked as nurses had a higher risk of offspring with anencephaly/spina bifida, coarctation of aorta, genital and urinary system defects (Matte et al., 1993). Mexican-American healthcare workers have also been shown to have an elevated risk of neural tube defects (Brender et al., 2002). A Danish study found an increased risk for ‘major’ malformations among laboratory workers who worked with radioimmunoassays, radiolabelling, and organic solvents (Zhu et al., 2006).

Few studies have had an adequate sample size to use precisely defined birth defects and more specific occupational categories. Furthermore, the occupational characteristics such as number of jobs, work hours, and the demographic/ life styles related to these occupations with potentially high risk have not been studied. In addition, many studies did not report adjusted effect measure estimates. Older studies were not able to take into consideration more recent changes in the job place such as use of personal protective equipment, chemical exposures, and the integration of women into jobs once held by men (Matte et al., 1993; Zhang et al., 1992; Savitz et al., 1996; Hemminki et al., 1981). Although folic acid supplementation prior to and during pregnancy has been shown to be protective against NTDs, cleft lip with/without cleft palate, and possibly other birth defects, its potential interactive effect with occupation has not been explored (MRC Vitamin Study Research Group, 1991; van Rooij et al., 2004; Wilcox et al., 2007).

The purpose of this analysis is to address these limitations and expand our recent case-control analysis. Previously, we used National Birth Defects Prevention Study (NBDPS) data including over 12,000 working women and looked at 24 maternal occupations and 45 birth defect outcomes within 9 organ systems for births between 1997 and 2003 (Herdt-Losavio, et al., 2010). Results for five maternal occupational groups from that study were of considerable interest because they were large groups and each was associated with several birth defects. Using the same national dataset with one more year of interview data, the objective of this subsequent in-depth analysis is to further evaluate the association between these five maternal occupational groups, including subgroups of healthcare workers, cleaners, scientists, personal service workers, and teachers, and specific birth defects. In addition, these associations were examined for effect measure modification by folic acid. A dose response relationship for work hours and number of jobs held was explored, and socio-demographic/life style characteristics related to these jobs were described.

Materials and Methods

Design and study population

The current analysis used data from the NBDPS, which is an ongoing, multi-center, case-control study (Yoon et al., 2001). Birth defects with known etiologies, such as single-gene conditions or chromosomal abnormalities, were excluded from the NBDPS. A total of ten centers (California, Iowa, Massachusetts, New Jersey, New York, Texas, CDC/Atlanta, North Carolina, Arkansas, and Utah) contributed data for infants with estimated delivery dates between October 1, 1997 and December 31, 2004. Each study site obtained institutional review board approval for the NBDPS. The methods used by the NBDPS have been previously described (Herdt-Losavio, et al., 2010; Yoon et al., 2001).

Isolated (1 defect only) and multiple (2 or more unrelated defects in an infant) cases were considered eligible for this analysis. Isolated and multiple cases were combined to increase power. The ratio of cases to controls in the NBDPS is approximately 3 to 1. Controls were live births without defects randomly selected from birth certificates and hospital records at the same time and within the same source population as the cases. Because some case data was collected for limited years at certain centers, only controls from corresponding years at those centers were included in those analyses.

Data collection

Mothers of cases and controls completed a computer-assisted telephone interview between six weeks and two years after their estimated date of delivery. This window was necessary to allow sufficient time for the ascertainment of cases. Participants were enrolled using a standard procedure (Yoon et al., 2001). Interview questions relating to the mother's occupational history from three months preconception through delivery were asked as well as information on a wide variety of topics including family demographics, pregnancy and medication history, vitamin intake, tobacco and alcohol use, and environmental exposures. To aid mothers in their recall of exposures, a pregnancy calendar was used so that the mother could specify timing by date, month of pregnancy, or trimester.

Outcomes

A total of 45 birth defects were analyzed. Descriptive analyses and results of the examination of the association between the 45 birth defects and 24 occupational groups were presented in a previous paper (Herdt-Losavio, et al., 2010). Among the 45 defects, some birth defects included subgroups that were also analyzed separately: NTDs included anencephaly/cranioraschischisis, encephalocele, and spina bifida; limb deficiencies included intercalary, longitudinal, preaxial, transverse and not otherwise specified; and oral clefts included cleft palate and cleft lip with or without cleft palate (CL/P). Only exposures with at least 5 exposed cases of a specific defect were analyzed to increase precision.

Exposure

Occupational groups were created by two occupational epidemiologists and two industrial hygienists using occupational information from the interview. Mother's job title, job duties, and what the company makes or does, were used to assign 2000 Standard Occupational Classification (SOC) System codes for occupations and 1997 North American Industry Classification System (NAICS) codes for industry. . The NBDPS allowed the reporting of up to 6 jobs, but only the job at which the mother worked the most hours in during the critical period (one month before conception through the end of the third pregnancy month) was included in this analysis. If the mother worked in more than one job for the same number of hours, then the first job that she reported was chosen. The usual number of hours worked per week was calculated by multiplying the self-reported usual hours worked per day by the days per week. This information was not provided for approximately 0.5% of jobs; for these jobs, 8 hours/day and/or 5 days/week were assumed.

Of the 14,922 women who held jobs during the critical period, 4,132 case and control women held their primary job in one of the five occupational groups of interest. The five occupational groups selected were broken into more specific job categories: healthcare workers were divided into doctors, dentists, and nurses; cleaners were divided into maids/housekeepers and janitors, which included building cleaning workers, janitors and cleaners, and cleaners of vehicles and equipment. Scientists were broken into biological scientists, chemical scientists/pharmacists, and engineers; teachers were divided into preschool teachers and those that did not teach preschool. Personal service workers were divided into child care workers and entertainers/athletes. Other personal service workers were not further analyzed because they were a very heterogeneous group, such as athletes, crossing guards, funeral attendants, gaming dealers, tour guides, and ushers, and each of these groups had very small numbers. The comparison group for each specific occupation studied was all other occupations combined including those not specifically studied here, consistent with the previous study (Herdt-Losavio, et al., 2010). Although the groups change for each comparison, the comparison group changes by less than 10% each time, which does not have a material impact on results.

Potential confounders and statistical analysis

Ten covariates were selected a priori based on literature review and previous analyses: mother's age at delivery, maternal education, maternal race/ethnicity, maternal pre-pregnancy body mass index, parity, study center, maternal pre-gestational diabetes status, folic acid intake, smoking status, and alcohol use. The latter two covariates were defined for use in the critical developmental period (one month onth before conception through the end of the third pregnancy month). Folic acid was specific to the period one month before pregnancy through the first month of pregnancy. Using the month before pregnancy through the first month of pregnancy is a good indicator of the woman's folic acid status at the start of embryologic development. All variables except for age, body mass index, and education were defined as yes/no dichotomized variables.

Logistic regression models were used to examine the association between the selected occupations and 45 specific birth defects while adjusting for the potential confounders described above. In addition, each model was stratified separately by folic acid use and full-time/part-time work status (<40 hours, >=40 hours per week) in that occupation. In addition to the logistic regression models, a Bayesian analysis was conducted to allow for further stability of the effect estimates. Since many exposure/outcome analyses had small numbers, and since multiple comparisons were conducted, Bayesian methods were used to shrink the odds ratios closer to the null, which would minimize type 1 errors. The specific Bayesian methods used were based on those described by Greenland (2006, 2007) and were the same as those used in the previous analysis (Herdt-Losavio, et al., 2010). Priors were conservatively set to 1 for all covariates except for mothers who smoked, used alcohol, or who were older than 35; these were set to 2. The specified variance set to 1.125 was unrestrictive and wide and a rescale factor of 10 was incorporated (Greenland, 2007). Finally, to reduce potential bias due to multiple jobs a sensitivity analysis was performed in which we reran the analysis, excluding mothers who reported more than one job (data not shown). Results were similar; thus, we have displayed results using the whole working mother sample.

Results

The response proportions of the telephone interview were 69% for the cases and 65% for the controls, respectively. At the time of interview, about 72% of the mothers (both the cases and the controls) reported being employed. There were significant differences between all case mothers combined and control mothers in terms of age, body mass index, education, parity, pre-pregnancy diabetes, smoking and study site (Herdt-Losavio, et al., 2010). These factors were controlled in the multivariable analysis.

The descriptive analysis of demographic and life-style factors reported by the participating women in these occupations are explored in Table 1. Women working as janitors/maids and child caretakers were younger than women employed in other occupations. The proportions of non-white (about 57%) or Hispanic (about 40%) were significantly higher among janitors/maids than other occupations. In addition, janitors/maids reported the lowest proportion of folic acid use (approximately 31%), compared to other occupations (52%-83%). In terms of lifestyle, mothers working as janitors, nurses, preschool teachers, and child caretakers had a higher proportion of obesity (> 20%), while entertainers/athletes and doctors had the lowest (3%-5%). Maids and entertainers/athletes had the highest proportion of smokers. Doctors, engineers, and chemists had the lowest smoking rates. Healthcare workers, scientists and entertainers/athletes had the highest proportion of drinking (43%-60%). Less than 2% of chemists and entertainers/athletes reported having diabetes.

Table 2 summarizes results of the associations between the specific occupation subgroups and a spectrum of birth defects using both logistic regression and Bayesian analyses where there were at least five exposed cases and the results were statistically significant ($p < 0.05$). Because Bayesian results are considered more stable, we will refer here to Bayesian results only. Maternal occupation as a maid or janitor was positively associated with a total of 9 different birth defects, including NTDs, oral clefts, and gastrointestinal defects, among others (OR range: 1.72-3.99), which is more than any other occupation. Most of the increased odds ratios for the birth defects associated with maternal occupation as a janitor were over 2. The highest odds ratio was for the association of esophageal atresia with janitors (OR=3.99, 95%CI: 1.58, 10.08). Among the health care worker group, female nurses were the only occupation found to be associated with increased odds ratios for hydrocephalus (OR=1.87, 95% CI: 1.25, 2.81) and left ventricular outflow tract heart defects (LVOTO) (OR=1.35, 95% CI: 1.03, 1.77). Maternal occupation as a doctor or dentist was not significantly associated with any major birth defects (data not shown). Other positive associations included chemical scientists and conotruncal heart defects or neural tube defects; engineers and conotruncal heart defects; and entertainers/athletes and gastroschisis. Preschool teachers had an increased risk for having a child with cataracts or CL/P. Teachers who did not teach preschool had significantly reduced risks of oral clefts, CL/P, , and gastroschisis in their offspring.

Table 3 displays adjusted odds ratios for the association between maternal occupation and birth defects, stratified by folic acid use, for maternal occupation-defect associations identified in Table 2. Only these occupation-defect combinations were chosen for additional analysis in this manuscript because a significant association was seen and for continuity of presentation. In general, there was a suggestion that the risk of defects of the central nervous system was lower among mothers with many different occupations studied who used folic acid during the critical period than among those mothers who did not use folic acid. For example, non-folic acid users in the following occupations were at an increased risk of having children with a central nervous system defect: hydrocephalus among nurses, NTDs or anencephaly among maids, and NTDs among chemists than those folic acid users, although these differences may not be statistically significant. A suggestive pattern of lower risk for maternal folic acid users for cleft lip with/without cleft palate were also found for janitors and preschool teachers. There were no consistent patterns in terms of effect modification of maternal folic acid use on occupational exposure or its protective effects on other birth defects.

We also examined maternal occupations stratified by hours worked (40 or more hours per week (52.8%) versus less than 40 hours per week (47.2%)), for maternal occupation-defect associations identified in Table 2. Mothers working full-time as scientists, including engineers, biological scientists, and chemical scientists, seemed to have trends of increased risks of conotruncal or NTD defects in their offspring (OR range: 2.00-3.65) compared to mothers working part-time in these occupations (OR range: 1.49-1.78). Similarly, full-time non-preschool teachers also showed a greater reduction in risk for gastroschisis in their children (OR=0.34) compared to part-time teachers (OR=0.77). Mixed results or no clear dose-response relationships were observed for other maternal occupations such as cleaners, nurses, and personal service workers (data not shown).

Job characteristics including number of jobs held, number of days worked per week, and number of hours worked per day were compared between cases and controls for the occupations studied. Among these selected occupations, a total of 89% of women had one job, 10% had two jobs, and 1.0% had more ore than 2 jobs during the critical period in this study. Among the non-preschool teachers, case mothers reported a lower proportion of having 2 or more jobs (5.84%) than the control mothers (10.57%), but there were no differences in terms of number of days worked per week and number of hours worked per day by mothers between the cases and controls. Among mothers working as engineers, mothers of cases worked significantly more days per week (4.93 days/week) than mothers of the controls (4.10 days/week). However, there were no significant differences between cases and controls in terms of days worked per week and hours worked per day for other maternal occupations (data not shown).

Discussion

This study found that maternal occupation as a nurse was positively associated with an increase in hydrocephalus and LVOTO. However, women having other health care occupations such as physicians and dentists were not positively associated with any birth defects. Although the evidence was not consistent in all previous studies, our findings for nurses were consistent with previous studies of maternal occupation as a nurse and hydrocephalus or other central nervous system defects (Brender et al., 2002; Matte et al., 1993). Cytostatic drugs and anesthetic gases are two long-known hazards for nurses (Matte et al., 1993; Hemminki et al., 1985). Hemminki et al. (1985) found that handling of cytostatic drugs was associated with malformation in the offspring (OR: 4.7, P=0.02) based on eight cases from the Finland Registry data. Matte et al. (1993) found that nurses exposed to anesthetic gases had an increased risk of having a child with spina bifida.

The current study also found that occupation as a janitor/cleaner was associated with 9 types of birth defects, the most among all occupations. These defects include oral clefts, NTDs, esophageal atresia, and anorectal atresia. The magnitudes of the odds ratios were also consistently strong (OR range: 1.72-3.99). Janitors in this study consisted of building cleaning workers, cleaners, and cleaners of vehicles and equipment. Brender et al. (2002) also found that mothers of infants with NTDs were more likely to have worked in cleaning jobs compared to controls (OR: 9.5, 95%CI: 1.1-82.2). By using data from 6 congenital malformation registries, Lorente et al. (2000) reported that cleft palate only was significantly associated with housekeeping after controlling for confounders (OR: 2.8, 95%CI: 1.1-7.2). Similarly, a Brazilian study found that the occupation of domestic services (janitors, baby-sitters, etc) was at greater than 2 fold increased risk of oral clefts (Leite et al., 2002). The magnitudes of the odds ratios in our study were also consistent with those reported by other studies. None of the prior research had examined gastrointestinal defects.

Maternal occupation in child care and entertainment were found to be associated with encephalocele and gastroschisis, respectively. To our knowledge, there has only been one other study looking specifically at child care workers. A Finnish study concluded that daycare employees did not generally have an increased risk of major birth defects overall (Riipinen et al., 2010). However, this study used healthcare workers as a reference group, which may also have an increased risk of some birth defects. Therefore, any risk for daycare workers could have been under-estimated. An older study found that more child care workers had birth defects among their children than expected (McDonald et al., 1987). Both of these studies grouped all defects.

Our study also found that mothers who worked as scientists including biological or chemical scientists and engineers had increased risks of NTDs, spina bifida, and conotruncal defects. A study conducted by Zhu et al. (2006) reported a borderline significantly increased risk of major malformations (OR=2.1, 95%CI: 1.0-4.7) among mothers working with radioimmunoassays as laboratory technicians.

A new finding from our study is the differential effect on birth defects between preschool teachers and other teachers. While mothers working in a preschool setting had increased risks of CL/P and cataract, mothers working as non-preschool teachers showed consistent and significant reduced odds in relation to oral clefts, CL/P and gastroschisis. Few studies assessed adverse reproductive outcomes among teachers and there was no research examining subgroups of teachers as we did in this study. Similar to our study, Lorente et al. (2000) also found a reduced risk of CL/P or CP among teachers using multiple registries in Europe, although the sample size was too small to detect a statistically significant difference. In a case-control study in Norway, Nguyen et al. (2007) found a non-significant near null association between teachers and isolated clefts. The reason why two subgroups of teachers had opposite effects on birth defects is unknown. A possible explanation may be that preschool teachers are often exposed to a variety of viral and bacterial agents from young children and they have higher physical demands such as bending and lifting compared to other teachers. These two types of exposures have been associated with birth defects previously, including defects associated in this study (Lin et al., 1998).

The current study did not show consistent evidence of a dose-response relationship between maternal work hours for most occupations and most birth defects studied. However, the analyses comparing full-time versus part-time, number of jobs held, and different hours worked with various defects demonstrated a potential trend of higher risk with more work among scientists, especially engineers. Consistent with many previous studies demonstrating a protective effect of folic acid against NTDs and oral clefts, CL/P in particular, maternal folic acid users showed a suggestive interactive effect with various maternal occupational exposures on NTD and CL/P (MRC Vitamin Study Research Group, 1991; van Rooij et al., 2004; Wilcox et al., 2007). In other words, women who did not take folic acid and who worked as a nurse, janitor, scientist or preschool teacher had increased risks of NTDs or CL/P.

While comparing demographic and behavior patterns among these occupations, we found that janitors, the group with an increased risk for several birth defects and for which we observed the highest risk estimates of birth defects, were younger, had a lower proportion of whites, higher proportions of Hispanic ethnicity, smoking, obesity and diabetes, and the lowest proportion of folic acid use during pregnancy. Most of these factors are known risk factors for some birth defects (Brender et al., 2002; Nguyen et al., 2007) and appear to differ by occupation. One interesting finding is that nurses reported a high proportion of smoking (over 20%), while doctors reported one of the lowest proportions of smokers. Approximately half of the women working in health care, entertainment and as scientists reported alcohol drinking during a critical developmental period. No prior research is available to compare to our findings.

The associations we found may be biologically plausible and could be explained by different levels of chemicals or hazards at work. Lorente et al. (2000) described and compared the proportions of women exposed to seven substances potentially associated with oral clefts among multiple maternal occupations. Their study found that nurses or nurses' aides had higher exposure to biocides, antineoplastic ineoplastic drugs, and aliphatic aldehydes. Housekeepers were exposed to aliphatic aldehydes, biocides, and glycol ethers. Teachers showed low or very low exposure to lead compounds, aliphatic acids, biocides, and glycol ethers and no exposure to trichloroethylene, antineoplastic drugs and aliphatic aldehydes (Lorente et al., 2000). These exposure patterns were consistent with the risks of various occupations in our study.

By using data from 10 study centers throughout the U.S., this is one of the largest population-based studies and examined 45 birth defects. The large sample size for these rare endpoints was ideal to describe multiple occupations and multiple defects as well as generate hypotheses. All defect cases were reviewed and confirmed by experienced clinicians based on a standardized protocol (Rasmussen et al., 2003). Large amounts of maternal/infant information collected from the telephone interview provided a wide range of detailed information including potential confounders.

To further explore our previous findings, this analysis assessed the risk among subgroups of five large occupational groups identified with the highest or largest number of risks. Although job title was used as an exposure proxy in this study, this was supplemented with several job characteristics including full- or part-time, number of jobs held, number of working days per week and number of working hours per day. Differing from some prior studies in which non-working women were used as a comparison group, we used all other occupations as the comparison to avoid bias due to the healthy worker effect. Since some of the “other occupations” in the comparison group were associated with increased risks of certain birth defects, the associations found in this study may have been under-estimated. Because multiple comparisons, correlated jobs, and imprecision were of concern for this analysis, we employed a Bayesian method as the primary analytic approach. To improve exposure assessment, all job titles were categorized by industrial hygienists and occupational epidemiologists to ensure appropriate grouping.

The primary deficiency of this study is lack of information on specific hazard exposures in the work setting since job titles have inherent limitations as markers of occupational exposure. In addition, information on socio-economic status (SES) of study participants was limited. Recall bias, especially for those women with multiple jobs, is usually a major concern for a case-control study. To minimize recall bias, we limited our main analysis to the primary job since the proportion of women with multiple jobs s (>= 3) was low (1.0%). Several strategies to reduce recall or reporting bias were used by the NBDPS, including use of a pregnancy calendar to aid recall, using many closed-ended questions and asking about specific exposures, frequency, and timing for each exposure. Furthermore, the exposure variable, job title, is generally well-reported (Teschke et al., 2002) and was not affected by the women’s knowledge of their child’s case/control status. Finally, although the overall size of the study is large, the number of infants with specific birth defects born to mothers in specific occupations was relatively small. This limitation reduced our power to detect associations especially in stratified analyses.

This study found that maternal occupations as cleaners, scientists, nurses, certain personal service workers and preschool teachers were associated with increased risks of several birth defects, but maternal occupation as non-preschool teachers was associated with significantly lower risks of oral clefts and gastroschisis. Maternal occupation as cleaners had the highest risks of birth defects among their offspring and increased risks were observed for more types of defects than other occupations. Maternal folic acid use had interactive effects with occupations to lower the risk of NTDs and CL/P. Different occupational groups reported different maternal behavior patterns during pregnancy, which will be studied in more detail in future projects using the NBDPS data. This hypothesis-generating study will provide information for future studies with better exposure data including a more comprehensive collection of data on work environments, specific hazard exposures, maternal life style and SES across different specific occupational groups.

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Table 1

Demographic characteristics* of women who worked during the critical period§ (by occupation) who participated in the National Births Defects Prevention Study, 1997-2004.

Occupation	N‡	Mother's age(mean)	White (%)	Hispanic (%)	Folic Acid Use (%)	Obese (%)	Smoker (%)	Drinking (%)	Pre-Preg Diabetes (%)
Healthcare									
Doctors	113	33.12	76.99	5.31	76.11	5.31	3.54	54.46	2.65
Dentists	100	29.56	79.00	15.00	59.00	12.12	17.00	48.00	4.00
Nurses	1544	28.84	69.82	10.75	60.56	20.16	21.31	44.57	4.21
Cleaners									
Janitors	101	25.97	43.56	35.64	30.69	27.37	21.78	28.28	6.93
Maids	406	25.91	42.36	39.90	31.77	18.28	28.08	28.89	5.67
Scientists									
Biological	149	29.37	79.19	4.03	69.13	9.40	22.15	58.78	2.01
Chemical	59	30.24	66.10	6.78	76.27	11.86	1.69	43.10	1.69
Engineers	52	31.96	75.00	5.77	82.69	9.62	3.85	59.62	3.85
Teachers									
Preschool	194	28.55	73.71	9.79	65.46	24.74	9.28	34.02	6.70
Non-preschool	987	30.31	77.51	10.13	69.60	15.71	5.88	39.06	2.43
Personal service									
Child care	353	26.00	69.12	16.71	51.56	21.10	21.53	32.29	3.12
Entertainment	74	28.35	86.49	4.05	71.62	2.70	31.08	52.70	1.35

*Demographic characteristics except for age were defined as Yes/No dichotomized variables.

§Critical period= one month prior through the end of the third pregnancy month

‡N included both the cases and the controls

Table 2

Odds ratios for logistic regression and the Bayesian logistic regression for maternal occupations during the critical period[#] significantly associated with birth defects with at least 5 exposed cases, National Birth Defects Prevention Study, 1997-2004.

Occupation	Exposed cases [*]	Exposed controls[§]	Birth Defect	Logistic Regression aOR (95%CI)[‡]	Bayesian aOR (95%CI)[‡]
Healthcare					
Nurses	31	415	Hydrocephalus	**1.92 (1.27, 2.90)**	**1.87 (1.25, 2.81)**
	73		LVOTO	**1.36 (1.03, 1.78)**	**1.35 (1.03, 1.77)**
	34		Transverse limb deficiency	1.47 (1.00, 2.16)	1.45 (0.99, 2.11)
Cleaners					
Janitors	7	19	Anorectal atresia	**3.75 (1.51, 9.31)**	**3.02 (1.27, 7.16)**
	22		Oral clefts	**2.72 (1.44, 5.14)**	**2.50 (1.36, 4.58)**
	14		Cleft lip w/wo cleft palate	**2.51 (1.23, 5.15)**	**2.28 (1.15, 4.50)**
	8		Cleft palate	**3.26 (1.39, 7.65)**	**2.64 (1.18, 5.91)**
	6		Esophageal atresia	**5.49 (2.10, 14.32)**	**3.99 (1.58, 10.08)**
	15		Septal defects	**2.40 (1.16, 4.97)**	**2.19 (1.10, 4.36)**
Maids	28	89	Neural tube defects	**1.77 (1.13, 2.77)**	**1.72 (1.10, 2.67)**
	12		Anencephaly	**2.73 (1.41, 5.28)**	**2.44 (1.29, 4.63)**
	16		Anotia/Microtia	**2.84 (1.56, 5.16)**	**2.62 (1.46, 4.69)**
	20		Cleft palate	**1.85 (1.09, 3.14)**	**1.77 (1.06, 2.97)**
	11		Esophageal atresia	**2.21 (1.13, 4.30)**	**2.04 (1.07, 3.90)**
Scientists					
Biological	8	41	Spina bifida	**2.22 (1.02, 4.84)**	2.00 (0.95, 4.24)
Chemical	7	12	Conotruncal defects	**2.96 (1.14, 7.67)**	**2.44 (1.01, 5.91)**
	6		Neural tube defects	**3.25 (1.19, 8.86)**	**2.56 (1.01, 6.55)**
Engineers	8	10	Conotruncal defects	**4.55 (1.76, 11.75)**	**3.48 (1.45, 8.37)**
Teachers					
Preschool	5	39	Cataract	**3.44 (1.29, 9.19)**	**2.70 (1.05, 6.94)**
	21		Cleft lip w/wo cleft palate	**1.73 (1.02, 2.94)**	1.68 (1.00, 2.81)
Non-preschool	85	293	Oral clefts	**0.76 (0.59, 0.98)**	**0.76 (0.59, 0.98)**
	49		Cleft lip w/wo cleft palate	**0.68 (0.49, 0.93)**	**0.66 (0.50, 0.94)**
	10		Gastroschisis	**0.50 (0.25, 0.97)**	**0.53 (0.29, 0.99)**

Occupation	Exposed cases *	Exposed controls§	Birth Defect	Logistic Regression aOR (95%CI)‡	Bayesian aOR (95%CI)‡
Personal service					
Child care	5	96	Encephalocele	**2.99 (1.15, 7.82)**	2.48 (0.99, 6.24)
Entertainment	6	14	Gastroschisis	**4.50 (1.58, 12.79)**	**3.30 (1.25, 8.70)**

Abbreviations: aOR=adjusted odds ratio; 95%CI= 95% confidence interval; LVOTO= left ventricular outflow tract heart defects; w/wo=with or without

#Critical period= one month prior through the end of the third pregnancy month

*Only cases associated with at least 5 exposures are presented

§For each occupational group, the number of controls is the same across all defect analyses.

‡Adjusted for mother's age at delivery, maternal education, maternal race/ethnicity, maternal pre-pregnancy body mass index, parity, study center, maternal pre-gestational diabetes status, folic acid intake, smoking status, and alcohol use

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Table 3

Adjusted odds ratios for birth defects using standard logistic regression and Bayesian logistic regression, stratified by folic acid use and occupation during the critical period#, National Birth Defects Prevention Study, 1997-2004*.

		Without Folic Acid			With Folic Acid		
Occupation	**Birth Defect**	**Exposed cases**	**Logistic Regression aOR (95%CI)‡**	**Bayesian aOR (95%CI)‡**	**Exposed cases**	**Logistic Regression aOR (95%CI)‡**	**Bayesian aOR (95%CI)‡**
Healthcare							
Nurses	Hydrocephalus	16	**2.04 (1.12, 3.69)**	**1.93 (1.09, 3.43)**	15	1.77 (0.98, 3.19)	1.70 (0.96, 3.00)
	LVOTO	47	1.23 (0.78, 1.93)	1.22 (0.78, 1.90)	26	**1.47 (1.04, 2.08)**	**1.45 (1.03, 2.04)**
	Transverse limb deficiencies	12	1.13 (0.59, 2.14)	1.12 (0.61, 2.06)	22	**1.76 (1.08, 2.87)**	**1.69 (1.05, 2.73)**
Cleaners							
Janitors	Anorectal atresia	5	**3.41 (1.13, 10.28)**	2.52 (0.92, 6.86)	2	4.97 (0.86, 28.75)	2.45 (0.57,10.50)
	Oral clefts	15	**2.34 (1.11, 4.95)**	**2.12 (1.11, 4.30)**	7	**4.03 (1.16, 14.01)**	2.82 (0.99, 8.02)
	Cleft lip w/wo cleft palate	11	**2.43 (1.07, 5.51)**	2.15 (1.00, 4.63)	3	2.57 (0.56, 11.77)	1.84 (0.52, 6.47)
	Cleft palate	4	2.22 (0.70, 7.00)	1.83 (0.65, 5.20)	4	**6.58 (1.57, 27.61)**	**3.57 (1.06, 11.99)**
	Esophageal atresia	4	**4.32 (1.32, 14.10)**	2.96 (0.99, 8.90)	2	**11.65 (1.92, 70.87)**	3.53 (0.75, 16.66)
	Septal defects	10	2.07 (0.86, 4.95)	1.87 (0.83, 4.20)	5	3.89 (0.99, 15.22)	2.58 (0.83, 8.03)
Maids	Neural tube defects	20	**1.90 (1.11, 3.26)**	**1.82 (1.08, 3.07)**	8	1.52 (0.66, 3.50)	1.43 (0.65, 3.11)
	Anencephaly	10	**3.61 (1.69, 7.73)**	**2.99 (1.45, 6.19)**	2	1.21 (0.27, 5.49)	1.13 (0.33, 3.90)
	Anotia/Microtia	11	**2.67 (1.30, 5.51)**	**2.40 (1.20, 4.80)**	5	**3.14 (1.05, 9.42)**	2.41 (0.88, 6.59)
	Cleft palate	16	**2.34 (1.26, 4.34)**	**2.14 (1.18, 3.89)**	4	1.15 (0.38, 3.41)	1.11 (0.42, 2.93)
	Esophageal atresia	11	**3.90 (1.91, 7.96)**	**3.30 (1.66, 6.59)**	0	---------	---------
Scientists							
Biological	Spina bifida	2	2.93 (0.61, 13.99)	1.91 (0.49, 7.38)	6	2.03 (0.82, 5.01)	1.80 (0.77, 4.24)
Chemical	Conotruncal defects	3	**11.08 (1.10, 111.49)**	3.30 (0.78, 14.04)	4	1.85 (0.57, 6.01)	1.59 (0.56, 4.55)
	Neural Tube defects	3	**30.21 (3.08, 297.88)**	**5.57 (1.29, 24.11)**	3	1.56 (0.43, 5.73)	1.37 (0.44, 4.25)
Engineers	Conotruncal defects	1	2.56 (0.24, 26.76)	1.44 (0.28, 7.45)	7	**5.03 (1.73, 14.63)**	**3.58 (1.37, 9.34)**
Teachers							
Preschool	Cataract	2	**12.24 (2.22, 67.57)**	3.57 (0.77, 16.54)	3	2.57 (0.72, 9.16)	1.93 (0.61, 6.06)
	Cleft lip w/wo cleft palate	7	2.39 (0.90, 6.32)	2.05 (0.84, 5.02)	14	1.54 (0.82, 2.91)	1.49 (0.81, 2.75)
Non-preschool	Oral clefts	26	0.73 (0.46, 1.16)	0.74 (0.48, 1.16)	59	0.77 (0.56, 1.05)	0.78 (0.57, 1.06)

		Without Folic Acid			With Folic Acid		
Occupation	**Birth Defect**	**Exposed cases**	**Logistic Regression aOR (95%CI)‡**	**Bayesian aOR (95%CI)‡**	**Exposed cases**	**Logistic Regression aOR (95%CI)‡**	**Bayesian aOR (95%CI)‡**
	Cleft lip w/wo cleft palate	16	0.68 (0.39, 1.19)	0.70 (0.41, 1.19)	33	**0.66 (0.45, 0.98)**	**0.68 (0.46, 0.99)**
	Gastroschisis	7	0.73 (0.32, 1.68)	0.78 (0.36, 1.66)	3	**0.30 (0.09, 0.99)**	0.40 (0.15, 1.02)
Personal service							
Child care	Encephalocele	2	2.59 (0.55, 12.13)	1.86 (0.49, 7.02)	3	3.47 (0.98, 12.31)	2.44 (0.76, 7.86)
Entertainment	Gastroschisis	3	**7.94 (1.24, 51.01)**	3.27 (0.82, 13.10)	3	3.11 (0.75, 12.87)	2.12 (0.61, 7.30)

Abbreviations: aOR=adjusted odds ratio; 95%CI= 95% confidence interval; LVOTO= left ventricular outflow tract heart defects; w/wo=with or without

#Critical period= one month prior through the end of the third pregnancy month

*Only associations presented in Table 1 were further analyzed

‡Adjusted for mother's age at delivery, maternal education, maternal race/ethnicity, maternal pre-pregnancy body mass index, parity, study center, maternal prepregnancy diabetes status, smoking status, and alcohol use