Maternal Smoking and Birth Defects: Validity of Birth Certificate Data for Effect Estimation

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SYNOPSIS

Objectives. The authors sought to assess the validity of birth certificate data for estimating the association between maternal smoking and birth defects. The US standard birth certificate includes check boxes for maternal smoking and for 21 congenital anomalies. The sensitivity and specificity of birth certificate data have been studied, but previous studies have not addressed the validity of these data for estimating the association between birth defects and maternal smoking or other risk factors.

Methods. US public-use natality data (1997–1998) were used to calculate the prevalence ratio (adjusted for maternal age, race/ethnicity, and education) for the association between maternal smoking and 13 defects/defect categories. All analyses were restricted to 45 states, New York City, and the District of Columbia because they collect both maternal smoking and birth defect data.

Results. Maternal smoking was associated with an increased prevalence of hydrocephaly (adjusted prevalence ratio [PR] = 1.24; 95% confidence interval [CI] = 1.08,1.43), microcephaly (PR 1.47; 95% CI 1.15,1.88), omphalocele/gastroschisis (PR 1.37; 95% CI 1.22,1.53), cleft lip/palate (PR 1.35; 95% CI 1.25,1.45), clubfoot (PR 1.62; 95% CI 1.49,1.75), and polydactyly/syndactyly/adactyly (PR 1.33; 95% CI 1.23,1.43). Previous studies have indicated an association between maternal smoking and gastroschisis, oral clefts, and clubfoot with effect estimates of similar magnitude to this study.

Conclusions. These findings suggest that birth certificate data may be useful for exploratory or corroborative studies estimating the association between birth defects and some risk factors recorded on birth certificates.

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Birth certificates are completed for all live-born infants in the US. The US standard birth certificate collects data on many factors, including presence of defects at birth. Although limitations to the quality of birth defect data from birth certificates have been noted, birth certificates are a stable data source that have both some exposures of interest and birth defect outcome information for approximately four million births per year.[1–3] The validity of using birth certificate data to support or refute findings from earlier studies and to identify possible etiologic risk factors for birth defects has not been assessed.

To test the validity of birth certificate data, we examined the relationship between maternal smoking and birth defects in these data. In 1997 and 1998, maternal smoking data and birth defect data were collected on birth certificates by 45 states, New York City, and the District of Columbia; therefore, data on more than three million births per year were available for this analysis. Maternal smoking has diverse, well-recognized adverse effects on the fetus, but information about its association with major malformations is limited and controversial.[4,5] Because approximately 24% of 18- to 44-year-old US women are current smokers, further elucidating a role of maternal smoking in major malformations is important.[6]

METHODS

We used public-use natality data tapes (National Vital Statistics System, National Center for Health Statistics) for all live-born infants to residents of 45 states, New York City, and the District of Columbia born in the US during 1997 and 1998. We restricted the analysis to 13 defects/defect categories from the birth certificate that are likely to be observable at birth and that are relatively well-defined categories of defect: anencephaly, spina bifida, hydrocephaly, microcephaly, rectal atresia/stenosis, tracheo-esophageal fistula/esophageal atresia, omphalocele/gastroschisis, cleft lip/cleft palate, clubfoot, polydactyly/syndactyly/adactyly, congenital diaphragmatic hernia, renal agenesis, and Down syndrome. We excluded malformed genitalia, other central nervous system anomalies, other gastrointestinal anomalies, other urogenital anomalies, heart malformations, other circulatory/respiratory anomalies, and other musculoskeletal/integumental anomalies because the range of defects that may be included in these broad categories is not clear, making any meaningful comparison with the literature difficult. Because individual defects are rare events, any infant whose birth certificate did not indicate the presence of a specific defect was assumed, for analytic purposes, not to have that defect. No attempt was made to control for multiple defects. We excluded birth certificates for residents of New Mexico because New Mexico does not require reporting of congenital anomalies on the birth certificate.

Maternal smoking during pregnancy was ascertained from the yes/no question on the birth certificate. We excluded from this analysis infants with birth certificates on which the maternal smoking information was left blank or was coded as unknown. We excluded birth certificates for residents of California, New York State (except for New York City), Indiana, and South Dakota because those states do not require reporting of maternal smoking in the standard format on the birth certificate. Birth certificates record the number of cigarettes smoked per day, but they do not contain information about the timing of smoking during pregnancy. We analyzed smoking dose in four exposure categories: ≥21 cigarettes per day, 11 to 20 cigarettes per day, six to 10 cigarettes per day, and one to five cigarettes per day. All exposure levels were compared to the referent (nonsmokers).

We calculated the prevalence ratio for the association between maternal smoking and selected defects. Because demographic variables may confound this relationship, we adjusted for maternal age (< 30 years, ≥30 years), maternal race/ethnicity (Hispanic, non-Hispanic black, non-Hispanic white, other), and maternal education (0 to 11 years, ≥ 12 years). The adjusted prevalence ratios and 95% confidence intervals were calculated using the test-based Mantel-Haenszel method with SAS software (version 6.09). We calculated prevalence ratios for all infants and by gender of the infant, because some evidence suggests that the male fetus may be more susceptible to the effects of tobacco.[7,8]

We compared the effect estimates using birth certificate data with published studies on smoking and birth defects. We identified previous studies by searching the MEDLINE database for publications from 1966 to early 2000 on smoking and each of the selected defects (by subject heading and keyword), and by tracing references in identified studies. We excluded studies that did not include either comparable measures of association (odds ratios, risk ratios, or prevalence ratios) between maternal smoking and the defect or adequate data to calculate an effect estimate. We excluded previous studies based solely on birth certificate data from this comparison. Both the direction and strength of the effect estimate were considered in this comparison.

RESULTS

There were 3,051,349 live births in 1997 and 3,110,157 live births in 1998 to residents of 45 US states, the District of Columbia, and New York City. Six of the 13 defects analyzed had statistically significant positive associations with maternal smoking in 1997–1998 birth certificate data: hydrocephaly (adjusted prevalence ratio [PR] = 1.24; 95% confidence interval [CI] = 1.08, 1.43), microcephaly (PR 1.47; 95% CI 1.15, 1.88), omphalocele/gastroschisis (PR 1.37; 95% CI 1.22, 1.53), cleft lip/palate (PR 1.35; 95% CI 1.25, 1.45), clubfoot (PR 1.62; 95% CI 1.49, 1.75), and polydactyly/syndactyly/adactyly (PR 1.33; 95% CI 1.23, 1.43) (Table 1). Most of these had consistent effect estimates for 1997 and 1998; microcephaly was an exception, with a strong association with maternal smoking in 1998 and no apparent association with maternal smoking in 1997.

Four of these defects (omphalocele/gastroschisis, oral clefts, polydactyly/syndactyly/adactyly, and clubfoot) were positively associated with maternal smoking among both male and female infants (Table 2). For infants with each of these four defects, the adjusted prevalence ratio was higher for male infants than for female infants. Microcephaly, hydrocephaly, and congenital diaphragmatic hernia showed a stronger association with maternal smoking for females than for males. The 95% confidence intervals for both microcephaly and hydrocephaly included the null value for males, and the 95% confidence intervals for congenital diaphragmatic hernia included the null value for both males and females.

Although there was no clear dose-response effect, there was an indication of a stronger association between heavy maternal smoking (≥20 cigarettes per day) and infants with clubfoot, hydrocephaly, or oral clefts (Table 3). No dose-response effect of maternal smoking was observed for infants with omphalocele/gastroschisis, microcephaly, or polydactyly/syndactyly/adactyly. Renal agenesis increased nearly twofold among infants whose mothers smoked more than 20 cigarettes per day, but the association was not statistically significant.

DISCUSSION

Using US birth certificate data for 1997–1998, we found a positive association between reported maternal smoking and hydrocephaly, microcephaly, omphalocele/gastroschisis, oral clefts, polydactyly/syndactyly/adactyly, and clubfoot. There was a stronger positive association observed among male infants than female infants for omphalocele/gastroschisis, oral clefts, polydactyly/syndactyly/adactyly, and clubfoot, and a stron-

Table 1. Number of infants with selected birth defects and the prevalence ratio for the association between maternal smoking and these defects using birth certificate data from 45 states, the District of Columbia, and New York City, 1997–1998

	1997[a]		*1998*[b]		*1997–1998*
Defect	*Number*	*Adj.PR*[c]*; 95% CI*	*Number*	*Adj.PR*[c]*; 95% CI*	*Adj.PR*[c]*; 95% CI*
Anencephaly	407	0.89; 0.65, 1.24	340	0.70; 0.49, 1.02	0.80; 0.63, 1.03
Spina bifida	820	0.90; 0.73, 1.11	743	1.17; 0.94, 1.45	1.02; 0.88, 1.19
Hydrocephaly	844	1.18; 0.97, 1.43	791	1.32; 1.08, 1.61	1.24; 1.08, 1.43
Microcephaly	220	1.11; 0.76, 1.61	187	1.95; 1.40, 2.70	1.47; 1.15, 1.88
Rectal atresia/stenosis	272	1.18; 0.85, 1.66	292	1.19; 0.86, 1.64	1.19; 0.94, 1.50
Tracheo-esophageal fistula/ esophageal atresia	411	0.83; 0.61, 1.13	337	1.00; 0.72, 1.38	0.90; 0.72, 1.13
Omphalocele/gastroschisis	948	1.46; 1.24, 1.72	1024	1.28; 1.09, 1.51	1.37; 1.22, 1.53
Renal agenesis	422	1.10; 0.82, 1.46	397	1.19; 0.90, 1.58	1.14; 0.93, 1.39
Oral clefts	2,632	1.32; 1.19, 1.46	2606	1.38; 1.24, 1.53	1.35; 1.25, 1.45
Polydactyly/syndactyly/adactyly	2,748	1.37; 1.23, 1.52	2825	1.29; 1.16, 1.44	1.33; 1.23, 1.43
Clubfoot	1,958	1.62; 1.45, 1.81	1936	1.61; 1.44, 1.80	1.62; 1.49, 1.75
Congenital diaphragmatic hernia	394	1.12; 0.84, 1.50	460	1.15; 0.87, 1.52	1.13; 0.93, 1.39
Down syndrome	1,346	1.11; 0.95, 1.31	1373	1.02; 0.86, 1.20	1.07; 0.95, 1.20

[a]3,051,349 live births in the 45 states, the District of Columbia, and New York City in 1997

[b]3,110,157 live births in the 45 states, the District of Columbia, and New York City in 1998

[c]Adjusted prevalence ratio, adjusted for maternal age, education, and race/ethnicity

Table 2. Effect estimates for the association between maternal smoking and birth defects by gender of the infant using birth certificate data from 45 states, the District of Columbia, and New York City, 1997–1998

	Male		Female	
Defect	*Number*[a]	*Adj. PR*[b]*; 95% CI*	*Number*[a]	*Adj.PR*[b]*; 95% CI*
Anencephaly	359	0.62; 0.42, 0.93	388	0.97; 0.71, 1.31
Spina bifida	822	1.05; 0.86, 1.29	741	0.98; 0.78, 1.23
Hydrocephaly	881	1.20; 0.99, 1.45	754	1.30; 1.06, 1.60
Microcephaly	177	1.22; 0.83, 1.81	230	1.67; 1.21, 2.29
Rectal atresia/stenosis	323	1.26; 0.94, 1.71	241	1.08; 0.75, 1.57
Tracheo-esophageal fistula/esophageal atresia	414	0.79; 0.58, 1.09	334	1.05; 0.76, 1.45
Omphalocele/gastroschisis	992	1.39; 1.19, 1.63	980	1.34; 1.14, 1.58
Renal agenesis	529	1.19; 0.93, 1.52	290	1.05; 0.74, 1.49
Oral clefts	3035	1.45; 1.32, 1.59	2203	1.22; 1.09, 1.37
Polydactyly/syndactyly/adactyly	3275	1.40; 1.27, 1.54	2298	1.24; 1.10, 1.39
Clubfoot	2421	1.78; 1.61, 1.96	1473	1.36; 1.19, 1.57
Congenital diaphragmatic hernia	510	1.01; 0.77, 1.32	344	1.34; 0.99, 1.82
Down syndrome	1396	1.01; 0.86, 1.19	1323	1.12; 0.96, 1.32

[a]3,153,486 male live births and 3,008,020 female live births in 1997–1998.

[b]Adjusted prevalence ratio, adjusted for maternal age, education, and race/ethnicity.

ger association for hydrocephaly and microcephaly among female infants than among male infants.

To assess the validity of birth certificate data for identifying birth defect risk factors, we compared the estimates from our analysis with previous studies of maternal smoking and birth defects (Table 4). We excluded literature based solely on birth certificate data from this table.

Our results of a borderline protective effect for anencephaly and no effect for spina bifida were consistent with the previous literature, which has shown a possible protective effect or no effect of maternal smoking.[9–12] Although some early small studies showed an increased risk of neural tube defects associated with maternal smoking,[13] this finding has not been supported by more recent studies. Pregnancies affected

Table 3. Effect estimates for the association between number of cigarettes smoked per day and selected birth defects using birth certificate data from 45 states, the District of Columbia, and New York City, 1997–1998

Defect	*≥21 cigarettes/day Adj. PR*[a]*; 95% CI*	*11–20 cigarettes/day Adj. PR*[a]*; 95% CI*	*6–10 cigarettes/day Adj. PR*[a]*; 95% CI*	*1–5 cigarettes/day Adj. PR*[a]*; 95% CI*
Anencephaly	0.54; 0.14, 2.09	0.79; 0.51, 1.24	0.68; 0.46, 1.02	0.92; 0.60, 1.39
Spina bifida	1.49; 0.83, 2.67	1.27; 0.99, 1.62	0.95; 0.75, 1.21	0.84; 0.62, 1.13
Hydrocephaly	2.45; 1.56, 3.86	1.36; 1.07, 1.73	1.20; 0.97, 1.48	1.02; 0.78, 1.33
Microcephaly	1.31; 0.41, 4.19	1.99; 1.37, 2.89	0.84; 0.52, 1.33	1.29; 0.81, 2.05
Rectal atresia/stenosis	0.94; 0.29, 2.98	1.19; 0.80, 1.79	1.38; 1.00, 1.90	0.95; 0.60, 1.50
Tracheo-esophageal fistula/ esophageal atresia	0.50; 0.13, 1.95	0.83; 0.55, 1.25	1.03; 0.75, 1.42	0.81; 0.52, 1.26
Omphalocele/gastroschisis	1.18; 0.68, 2.06	1.34; 1.09, 1.64	1.33; 1.13, 1.58	1.34; 1.10, 1.64
Renal agenesis	1.91; 0.96, 3.78	0.92; 0.63, 1.36	1.20; 0.89, 1.60	1.16; 0.81, 1.66
Oral clefts	1.69; 1.28, 2.25	1.38; 1.22, 1.57	1.28; 1.14, 1.42	1.27; 1.10, 1.45
Polydactyly/syndactyly/adactyly	1.28; 0.89, 1.86	1.38; 1.21, 1.59	1.28; 1.15, 1.44	1.27; 1.12, 1.45
Clubfoot	2.33; 1.76, 3.08	1.55; 1.35, 1.78	1.64; 1.46, 1.83	1.51;(1.30,1.74
Congenital diaphragmatic hernia	1.19; 0.49, 2.88	1.23; 0.87, 1.73	1.16; 0.86, 1.56	1.00; 0.68, 1.47
Down syndrome	1.12; 0.70, 1.81	0.97; 0.78, 1.19	1.02; 0.85, 1.22	1.15; 0.93, 1.41

[a]Adjusted prevalence ratio, adjusted for maternal age, education, and race/ethnicity; all four exposure categories compared with nonsmokers (referent).

Table 4. Comparison of the effect estimates for the association between maternal smoking and selected birth defects from birth certificate data for 1997–1998 [this analysis] and other studies reported in the literature

Defect	*Birth certificates 1997–1998 (this analysis)[a]; 95% CI*	*Literature (effect estimates, 95% CI, source)*
Anencephaly	0.80; 0.63, 1.03	0.49; 0.28, 0.85[9] 0.77; 0.44, 1.36[10] 0.77[c]; 0.45, 1.29[11] 1.30; 0.93, 1.83[12]
Spina bifida	1.02; 0.88, 1.19	0.76; 0.61, 0.95[9] 0.73; 0.43, 1.21[11] 0.99; 0.74, 1.34[12]
Hydrocephaly	1.24; 1.08, 1.43	0.8; 0.3, 2.2[14]
Microcephaly	1.47; 1.15, 1.88	1.1; 0.3, 3.6[14]
Rectal atresia/ stenosis	1.19; 0.94, 1.50	Anal atresia: 1.4; 0.5, 3.6[16] 0.4; 0.1, 1.9[14] Atresia of rectum, anal canal, large intestine: 2.24; 1.15, 4.16[17]
Tracheo-esophageal fistula/ esophageal atresia	0.90; 0.72, 1.13	Esophageal atresia: 0.5; 0.1, 4.3[14]
Omphalocele/ gastroschisis	1.37; 1.22, 1.53	Omphalocele: 3.8; 0.6, 22.7[14] Gastroschisis: 1.81; $P < 0.07$[18] 1.5; 0.6, 3.7 [>1 pack/day]; 1.5; 0.9, 2.5 [<1 pack/day][19] 2.1; 0.9, 4.8[20]
Renal agenesis	1.14; 0.93, 1.39	Renal agenesis/hypoplasia: 1.32; 0.96, 1.80[21] 1.1; 0.3, 3.6[14] All urinary tract defects combined: 2.3; 1.2, 4.5[22] No association [internal defects only][23]
Polydactyly/syndactyly/ adactyly	1.33; 1.23, 1.43	Polydactyly: 1.0; 0.6, 1.6[14] Syndactyly: 0.7; 0.3, 1.5[14]
Clubfoot	1.62; 1.49, 1.75	Clubfoot/talipes equinovarus: 1.34[b]; 1.04, 1.72[b, 25] 1.92; 1.29, 2.86[c, 26] 1.02; 0.88, 1.17[10] 0.7; 0.6, 0.9[14] Foot deformities (including clubfoot): 1.21; 1.14, 1.29[24] 1.73; 1.27, 2.34[17]
Congenital diaphragmatic hernia	1.13; 0.93, 1.39	0.8; 0.1, 8.1[14]
Down syndrome	1.07; 0.95, 1.20	No effect overall[29] No effect overall, slight reduction in risk among heavy smoking primiparas[28] 0.2; 0.1, 0.9[14] 0.58; 0.34, 0.98[27]

(continued)

Table 4 (*continued*). Comparison of the effect estimates for the association between maternal smoking and selected birth defects from birth certificate data for 1997–1998 [this analysis] and other studies reported in the literature

Defect	*Birth certificates 1997–98 (this analysis)[a]; 95% CI*	*Literature (effect estimates, 95% CI, source)*
Cleft lip/palate	1.35; 1.25, 1.45	Oral clefts: 1.75; 1.01, 3.02[35] 1.28 (P>0.10)[40] Cleft lip with cleft palate: 1.24; 1.0, 1.54[d]; 1.45; 1.02, 2.07[e, 33] Cleft lip with or without cleft palate: 1.79; 1.07, 3.04[31] 1.3; 0.7, 2.3 [≥10 cig/day]; 1.2; 0.6, 2.1 [1–9 cig/day][32] 1.40; 0.99, 2.00[34] 1.16; 1.02, 1.32[36] 2.1; 1.3, 3.6[d] [>20 cig/day]; 1.6; 1.2, 2.3[d] [1–19 cig/day][37] 0.7; 0.3, 1.6) [≥25 cig/day]; 1.4; 1.0, 2.1 [15–24 cig/day][39] 1.47; 1.09, 1.97[38] 1.1; 0.5, 2.4[14] Cleft palate alone: 0.86; 0.40, 1.87[31] 2.3; 1.1, 4.6 [≥10 cig/day]; 1.5; 0.6, 3.3[32] 0.87; 0.50, 1.52[34] 1.29; 1.08, 1.54[36] 2.2; 1.1, 4.5[d] [>20 cig/day]; 1.4; 0.9, 2.3[d] [1–19 cig/day][37] 0.8; 0.3, 2.2 [≥25 cig/day]; 0.9; 0.5, 1.5 [15–24 cig/day][39] 1.50; 0.97, 2.32[38] 0.7; 0.3, 1.8[14]

[a]Adjusted prevalence ratio, adjusted for maternal age, education, and race/ethnicity

[b]Among infants with no family history of clubfoot

[c]Crude odds ratio calculated from data in paper.

[d]Infants with isolated defects

[e]Infants with multiple defects

by either anencephaly or spina bifida have high rates of spontaneous abortion, and the likelihood of spontaneous abortion of affected fetuses may be increased among women who smoke. Pregnancies affected by these two defects may also be terminated after a prenatal diagnosis, but this seems unlikely to vary by smoking status of the mother. The borderline protective effect observed here for anencep-haly could perhaps result from under-ascertainment of maternal smoking on the birth certificate when the infant has a lethal defect.

Maternal smoking was positively associated with both hydrocephaly and microcephaly, but this association is not supported by the literature.[14] Little has been published about maternal smoking with these two defects, and some possible diagnostic issues exist. For example, microcephaly may be over-ascertained for low birthweight infants who have reductions in all growth parameters, not just head circumference. In addition, one study found that the sensitivity of birth certificate data on maternal smoking was higher among infants with low birthweight,[15] which may contribute to the observation of a positive association. Also, the association between maternal smoking and low birthweight is well established, and the outcome of low birthweight may prompt additional probing for maternal smoking.[4]

Maternal smoking was positively associated with rectal atresia/stenosis, although this relationship was not statistically significant. This is consistent with two literature reports showing an association;[16,17] one earlier study did not find an association.[14] Our findings for tracheo-esophageal fistula/esophageal atresia were also consistent with the only literature report located, which found no association for maternal smoking.[14]

Maternal smoking was positively associated with the defect category of omphalocele and gastroschisis in this study. Omphalocele and gastroschisis are etiologically distinct, making this finding difficult to interpret

with only the combined category available from birth certificate data. However, there are literature reports linking maternal smoking to both omphalocele[14] and gastroschisis.[18–20]

We observed an association only between the heaviest exposure to maternal smoking (≥20 cigarettes per day) and renal agenesis, although this was not statistically significant; one literature report showed a modest (not statistically significant) association with renal agenesis,[21] and another showed no association.[14] It is important to note that renal agenesis detected at birth and reported on the birth certificate is most likely to be bilateral. We also found two literature reports for all urinary tract defects combined; one report showed a positive association with maternal smoking[22] and one showed no association with maternal smoking.[23]

Maternal smoking was positively associated with the defect category of polydactyly/syndactyly/adactyly in our study, but we did not locate any reports to support this finding. We are unable to separate the defects included in this check box on the birth certificate, and each of these may be etiologically distinct. One study assessed the association between maternal smoking and polydactyly and syndactyly separately and did not show an association.[14]

Maternal smoking was positively associated with clubfoot, which is consistent with the literature. Two studies showed an association between all foot deformities and maternal smoking,[17,24] and two studies showed an association between clubfoot and maternal smoking.[25,26] The two studies of clubfoot also found a stronger effect in male infants than in female infants, which is consistent with the results of our analysis. Two early studies of clubfoot did not report any association between clubfoot and maternal smoking.[10,14]

No association was observed between maternal smoking and congenital diaphragmatic hernia, which is consistent with the one literature report located.[14] We also did not observe an association between maternal smoking and Down syndrome, although two literature reports have shown a possible protective effect of maternal smoking on Down syndrome[14,27] and one other report showed a protective effect among heavy smoking primiparas.[28] One recent report showed a positive association between maternal smoking and Down syndrome only for a subset of meiotically derived cases among young mothers.[29] Maternal smoking has also been associated with cardiac defects among infants with Down syndrome,[30] and Down syndrome could be better ascertained on the birth certificate when associated defects are present.

Oral clefts have the most extensive literature of any birth defect supporting an association with maternal smoking.[31–38] Reports have classified oral clefts in many different ways, but nearly all have shown a positive association with maternal smoking, with only a few reports not observing this association,[14,39,40] and one report not observing this association for cleft palate alone.[34] The magnitude of the effect estimate observed in our study also is similar to that reported from the wide array of previous studies.

In summary, the effect estimates for maternal smoking using birth certificate data were consistent with previous studies for anencephaly, spina bifida, rectal atresia, tracheo-esophageal fistula/esophageal atresia, omphalocele/gastroschisis, renal agenesis, congenital diaphragmatic hernia, clubfoot, Down syndrome, and oral clefts. The estimates obtained from birth certificate data for microcephaly, hydrocephaly, and polydactyly/syndactyly/adactyly were not consistent with the one previous study identified that assessed the impact of maternal smoking on these defects.[14]

Birth defect data from birth certificates has not been widely used because studies have demonstrated low overall sensitivity; however, sensitivity is better for more severe defects such as those selected for this study, and the positive predictive value of birth defect data from the birth certificate is high.[1,2] Given that birth defects are rare, false negatives should not have much impact on the effect estimates as long as the recording of defects is not related to the exposure, e.g., maternal smoking. Nondifferential misclassification of the outcome will usually result in bias toward the null value, but prevalence ratio estimates will not be biased when specificity is 100%.[41]

Although birth certificates are commonly used to monitor trends in maternal smoking in the US, they underestimate the true prevalence of smoking during pregnancy. A recent capture-recapture study in six US states found that birth certificates ascertained 70.6%–82.0% of maternal smoking, and confidential questionnaires ascertained 86.2%–90.3% of maternal smoking.[15] This result was similar to an earlier study that used the medical record as the "gold standard" and estimated that birth certificates had a sensitivity of 73.5% for maternal smoking.[2] It is important to recognize that even confidential questionnaires typically used for case-control studies of birth defects do not ascertain all maternal smoking. If maternal smoking is under-reported nondifferentially with respect to birth defect outcome, then under-reporting should bias the effect estimates toward the null. If, however, the sensitivity of reporting maternal smoking is better in the presence of a major birth defect, then the effect estimates could be inflated.

Although biases in exposure ascertainment are pos-

sible, they are unlikely to account for the results of this study. We examined 13 categories of major birth defects and found positive associations with maternal smoking for only six of these defects. Smoking exposure information on birth certificates is usually completed either by mothers or from prenatal records that are completed before the outcome of the pregnancy is known. Whereas mothers are likely to know that smoking adversely affects health in many ways, they are unlikely to be aware of the existing literature on birth defects and smoking. In addition, recording of exposure is unlikely to vary by the gender of the infant; all four defects that showed an association with maternal smoking for both males and females had a stronger effect among male infants than among female infants. The stronger effect of maternal smoking on oral clefts and clubfoot among male infants is consistent with previous literature and is supported by the fact that the impact of maternal smoking on birthweight and fetal growth has been reported to be stronger for male infants than for female infants.[7,8] Also, some evidence existed for a dose-response effect of maternal smoking, and this outcome would not be predicted if the effect estimates were due only to misclassification of exposure.

It is both a strength and a limitation of this study that over six million births were used in the analysis. The large numbers allow examination of exposure-outcomes relationships for rare outcomes and subanalyses by gender of the infant and dose of maternal smoking. They may, however, increase the likelihood of attaining statistical significance for even small differences in exposures between those with birth defects and the total population.

The consistency between published studies and our findings for the association between maternal smoking and selected birth defects indicates that birth certificate data may be very useful for identifying possible risk factors for the birth defects examined in this study. This data source may also provide important information to support or refute earlier studies. The utility of this data source for assessing maternal smoking may be further enhanced when the next revision of the US standard birth certificate is adopted because the proposed revision includes more detailed questions on the timing of smoking during pregnancy.[42,43] Although smoking is an example of a risk factor that most states collect on birth certificates, many other variables of potential interest are also collected. Some other potential risk factors ascertained using the US standard birth certificate include anemia, diabetes, hypertension, previous preterm birth, alcohol use during pregnancy, and weight gained during pregnancy. The sensitivity with which risk factor variables are ascertained by the birth certificate vary considerably, and this should be considered when using birth certificate data to assess exposure-outcome associations. Given the existing limitations, studies using birth certificate data are not an adequate substitute for well-designed and conducted case-control studies of birth defects that include extensive interview data and, often, biological samples; however, birth certificates are a potentially valuable data source for exploratory or corroborative studies and they merit more widespread use.

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