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Association of Maternal Smoking during Pregnancy with Infant Hospitalization and Mortality Due to Infectious Diseases

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Abstract

Background—Maternal smoking is associated with infant respiratory infections and with increased risk of low birthweight (LBW) infants and preterm birth. This study assesses the association of maternal smoking during pregnancy with both respiratory and non-respiratory infectious disease (ID) morbidity and mortality in infants.

Methods—We conducted two retrospective case-control analyses of infants born in Washington State from 1987–2004 using linked birth certificate, death certificate, and hospital discharge records. One assessed morbidity—infants hospitalized due to ID within one year of birth (47,404 cases/48,233 controls). The second assessed mortality—infants who died within one year due to ID (627 cases/2,730 controls).

Results—Maternal smoking was associated with both hospitalization (Adjusted Odds Ratio (AOR)=1.52; 95%CI: 1.46, 1.58) and mortality (AOR=1.51; 95%CI: 1.17, 1.96) due to any ID. In subgroup analyses, maternal smoking was associated with hospitalization due to a broad range of ID including both respiratory (AOR=1.69; 95%CI: 1.63, 1.76) and non-respiratory ID (AOR=1.27; 95%CI: 1.20, 1.34). Further stratification by birthweight and gestational age did not appreciably change these estimates. In contrast, there was no association of maternal smoking with ID infant mortality when only LBW infants were considered.

Conclusions—Maternal smoking was associated with a broad range of both respiratory and non-respiratory ID outcomes. Despite attenuation of the mortality association among LBW infants, ID hospitalization was found to be independent of both birthweight and gestational age. These findings suggest that full-term infants of normal weight whose mothers smoked may suffer an increased risk of serious ID morbidity and mortality.

Keywords

infant; infectious disease; prenatal exposure; maternal smoking

INTRODUCTION

Infectious disease (ID) morbidity and mortality in the United States (US) has decreased over the past century (1), but remain a serious public health concern, especially for infants. In the US, 43% of all infant hospitalizations in 2003 were due to ID (2), and childhood mortality

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CONFLICTS OF INTEREST

The authors report no conflicts of interest.

due to ID has not substantively declined since the 1980s (3). Maternal smoking is associated with multiple adverse infant outcomes including low birthweight, preterm birth, and impaired lung growth (4–6), and maternal smoking both before and after birth has been shown to increase risk of respiratory ID in infants (4, 7–12). Despite a marked decrease in the percentage of mothers who smoke during pregnancy from—18.4% in 1990 to 9.7% in 2008 in the US (13), and from 20.1% to 10.3% in the state of Washington (14)—maternal smoking continues to pose significant risks for infant health. Additionally, studies suggest that maternal smoking is associated with some specific infections that are not limited to the lung. In particular, smoking during pregnancy has been associated with infant otitis media (4, 9, 15), bacterial meningitis (16, 17), necrotizing enterocolitis (18), and increased risk of vertical HIV transmission (19, 20). In children over 6 months of age (21), Yuan *et al.* reported an association between maternal smoking and ID that included both respiratory and non-respiratory infections, and exposure to environmental tobacco smoke (ETS) was associated with gastroenteritis in children under 36 months of age (22).

Despite these suggestive findings, no studies to date have systematically investigated the effects of maternal smoking on a broad range of respiratory and non-respiratory ID in infancy. We examined the association between maternal smoking during pregnancy and any ID hospitalization and mortality in infants, using administrative databases and systematically identifying ID based on *International Classification of Diseases* (ICD) codes. Two alternative causal models may explain the hypothesized association between maternal smoking and infant ID, (1) maternal smoking may cause low infant birthweight and early gestational age, and these conditions may cause an increased risk of ID, or (2) maternal smoking may cause an increased risk of ID through some other mechanism. We therefore assessed dependence of the observed associations on birthweight and gestational age.

MATERIALS AND METHODS

Study design

Washington State birth certificate data linked to infant death certificate data and the Washington State inpatient hospital discharge records database (Comprehensive Hospital Abstract Reporting System, CHARS) were used to conduct two independent case-control analyses. In one analysis, the outcome was infant hospitalization; in the other, infant mortality. Eligible subjects were infants born in Washington State between 1987 and 2004, excluding those with any congenital abnormality recorded on the birth certificate (or with missing data regarding congenital abnormality). Maternal smoking was determined by self-report of smoking during pregnancy on infant birth certificates (reported both as a binary variable and as the number of cigarettes smoked per day).

In the hospitalization analyses, cases were defined as all infants hospitalized within one year of birth for an ID, determined by the primary *ICD, Ninth Edition, Clinical Modification* (ICD9-CM) diagnosis code in the hospitalization inpatient discharge records (excluding the birth hospitalization). Controls consisted of a randomly selected subset of all infants who were not hospitalized for an ID within one year of birth, chosen at a 1:1 ratio and frequency matched by year of birth (47,404 cases/48,233 controls).

In the mortality analyses, cases were defined as all infants who died within one year of birth due to an ID (determined by ICD9 and ICD10 codes recorded as either the underlying cause or any contributing cause of death on the death certificate). Controls were randomly selected from all infants who did not die due to an ID within one year of birth. We adopted a 4:1 ratio of controls to cases (frequency matched by year of birth) to increase statistical power, given the relatively small number of cases (627 cases/2,730 controls).

The ICD codes comprising the ID case definition were based on prior studies of ID trends in the US employing ICD9-CM codes (23, 24) and a total of 1,161 ICD9/ICD9-CM codes and 1,205 ICD10 codes were used. We also created and evaluated subgroups, broadly categorizing ID as respiratory and non-respiratory, as well as creating subgroups based on the site of infection or etiology (case definitions available on request). For the hospitalization analyses, all available diagnosis codes were used from any hospitalization that fit the case definition within the first year of life, but each subject was counted as a single case, regardless of the number of hospitalizations. For the mortality analyses, the underlying cause of death and all contributing causes of death were used to classify subgroups.

The use of data from human subjects in this study was conducted under the 98–7712-E/G 10 Data Sharing Agreement between the Washington State Department of Health and the University of Washington. All analyses were approved by the Institutional Review Board.

Data analysis

We conducted Mantel-Haenszel analyses to estimate Adjusted Odds Ratios (AOR) and 95% Confidence Intervals (CI) describing the association between maternal smoking and both infant hospitalization and mortality using STATA 9 (StataCorp, College Station, Texas, USA). A Bonferroni adjustment for multiple comparisons was used to determine statistical significance in subgroup analyses (the *P* value significance level was adjusted to 0.05/20 for the analysis of the 20 subgroups).

We assessed the following as potential confounding factors: marital status, income below the median, maternal race (white vs. non-white), infant sex, maternal age, hypertension, gestational diabetes, maternal alcohol consumption during pregnancy (self-reported on birth certificate), birth year, parity, and number of infants at birth (singleton vs. multiple). Income data from the hospitalization control population were used to determine thresholds for annual income quartiles. Missing data for clinically estimated gestational age were imputed using last menstrual period when available. Variables were considered confounders if they were significantly associated with both case status and maternal smoking, and if adjustment altered the OR for maternal smoking by greater than 5%. Birthweight and gestational age potentially lie in the causal pathway of the hypothesized effect of maternal smoking on infant ID and were assessed separately.

RESULTS

Study demographics and pregnancy characteristics

The hospitalization case and control populations were similar with regard to singleton birth, as well as maternal gestational diabetes, preeclampsia, hypertension, and demographic factors. However, mothers of case infants were more likely to have used government payment, to have less than 12 years of education and income below the median, to be unmarried, non-white, and under 18 years of age (Table 1). More ID hospitalization and mortality cases were low birthweight (LBW, <2,500 g), very low birthweight (VLBW, <1,500 g), or preterm (<37 weeks), but the difference was more dramatic for mortality (62.1% of mortality cases were LBW, compared to 8.4% of hospitalization cases, and 5.0% of controls).

Hospitalization due to infectious disease

Hospital admissions due to ID represented significant morbidity, with 10% of case infants being hospitalized more than once, and over half (52%) of the hospitalizations lasting greater than one week (Table 2). Maternal smoking was associated with hospitalization for

any ID (AOR = 1.52; 95% CI: 1.46, 1.58), adjusting for marital status, income below the median, and maternal race. In subgroup analyses, maternal smoking was associated with hospitalization for both respiratory (AOR = 1.69; 95% CI: 1.63, 1.76) and non-respiratory infection (AOR = 1.27; 95% CI: 1.20, 1.34), although the association with respiratory infection was stronger (Table 3). More specific subgroup analyses demonstrated significant associations between maternal smoking and nearly all types of respiratory infections. AORs for each type of respiratory infection were roughly similar to the aggregate AOR, although respiratory syncytial virus (RSV) and acute upper respiratory infections (AURI) had weaker associations with maternal smoking than pneumonia/influenza, bronchitis/bronchiolitis, and otitis media. The exception was croup, which was not associated with maternal smoking (AOR = 1.03; 95% CI: 0.90, 1.19; n cases = 1,545).

Non-respiratory infections showed a similar pattern; the relationships between specific non-respiratory infections and maternal smoking were generally similar to all non-respiratory infections combined. The exception was the lack of an association with urinary tract infections (UTI). Also notable were skin infections and conjunctivitis, which were more strongly associated with maternal smoking than the overall non-respiratory infection subgroup (AOR = 1.57; 95% CI: 1.40, 1.78; and AOR = 1.71; 95% CI: 1.44, 2.04, respectively).

Although viral/chlamydial and bacterial infections were each associated with maternal smoking, the strongest associations were with mycotic and parasitic/protozoic infections. Despite the small number of cases (1,935 and 69 respectively), the relationships were strong (AOR = 2.02; 95% CI: 1.81, 2.25; and AOR = 2.73; 95% CI: 1.59, 4.68).

We found that the associations between maternal smoking and ID morbidity increased with the number of cigarettes smoked per day. For infants of mothers who smoked 1–9 cigarettes/day, 10–19, and 20+, the AORs were 1.42 (95% CI: 1.33, 1.50), 1.51 (95% CI: 1.42, 1.60), and 1.60 (95% CI: 1.48, 1.74), respectively. This dose-response relationship was also observed for both respiratory and non-respiratory ID hospitalizations (Table 4).

Additionally, when cases were stratified by infant age at first ID hospital admission, the association with maternal smoking increased throughout the first 6 months of life, and declined during the second half of the first year (Table 5).

Finally, we assessed the role of birthweight and gestational age in the observed associations. The association between maternal smoking and ID hospitalization was not substantially different between LBW and normal weight infants, or between preterm or full term infants (Table 5). This suggests that the associations we observed between maternal smoking and hospitalizations due to both respiratory and non-respiratory ID were largely independent of birthweight and gestational age throughout the first year of life.

Mortality due to infectious disease

In contrast to the hospitalization analysis, where less than 1% of ID cases were admitted within the first two days of life, a large proportion (32.4%) of deaths occurred within the first two days (Table 2). Maternal smoking was significantly associated with ID-related mortality (AOR = 1.51, 95% CI: 1.17, 1.96), adjusting for marital status, income, and maternal race (Table 3). Subgroup analyses of maternal smoking and mortality due to specific infections were limited by small sample sizes. Consistent with the analyses of hospitalization, ORs were elevated, although none attained statistical significance after taking into account multiple subgroup comparisons. Stratification of cases by age at death revealed that the magnitude of the association with maternal smoking peaked at 31–90 days

(AOR = 2.47; 95% CI: 1.52, 4.03) and then dropped, with no relationship observed after 6 months (Table 5).

The separation of infants into preterm and full term did not greatly alter the magnitude of the association between maternal smoking and ID mortality (Table 5). The association also remained significant with infants of normal birthweight (>2,500 g; AOR = 1.60; 95% CI: 1.09, 2.35). In contrast, there was no association of maternal smoking with ID infant mortality when only LBW infants were considered. Thus, the association between maternal smoking and infant mortality due to ID is largely independent of gestational age, but linked to birthweight.

DISCUSSION

In this population-based study, infants who were hospitalized or died due to infections during the first year of life were 50% more likely to have had mothers who smoked than control infants. Although the association of maternal smoking was stronger with respiratory infections, it was present with both respiratory and non-respiratory infant infections. Previous investigations of the effects of maternal smoking on infectious disease only evaluated hospitalizations after 6 months of age (21), while we found that the effects of maternal smoking were apparent at much younger ages. In fact, the strongest association with ID hospitalization was observed from 3 to 6 months of life and, with ID mortality, during months 2 and 3.

The “Birthweight Paradox” is a common epidemiological phenomenon, in which infants of low birthweight appear to have a decreased risk of death if their mothers smoked (25,26). Controlling for an intermediate factor (e.g., infant birthweight) can lead to a biased association if there is an unmeasured confounder that increases the risk of both LBW and infant mortality (27,28). Despite the potential biases of unmeasured confounders, stratification by birthweight and gestational age may help to understand the role of these factors in the causal pathway linking maternal smoking with ID morbidity and mortality. The association of maternal smoking with hospitalization due to ID was present in both infants of normal weight and LBW infants. Therefore, the relationship is largely independent of these factors, which suggests there may be an alternative mechanism by which maternal smoking affects infant ID morbidity. The lack of an association with ID mortality in LBW infants may reflect either dependence on birthweight or bias due to an unmeasured confounder, as in the birthweight paradox. The observation of an association with ID mortality within infants of normal birthweight suggests that the relationship may be at least partially independent of birthweight.

The finding of a birthweight- and gestational age-independent association of maternal smoking with ID morbidity is clinically relevant, for even if an infant whose mother smoked is of normal weight and gestational age, exposure to maternal smoking appears to carry an increased risk of most types of infection as well as ID mortality. This again suggests an alternative causal mechanism, and an adverse effect of *in utero* smoke exposure on the infant immune system is a plausible explanation. Studies analyzing cord-blood of infants (29–31) and exposure of primates (32) have shown that infant immune systems can be modified by exposure to tobacco smoke; however, further research is needed to understand the biological mechanisms for this.

While other studies have characterized the association of maternal smoking during pregnancy and ETS exposure after birth with certain respiratory infections (4, 7–12, 33), this study expands on these findings, demonstrating for the first time that a broad range of both respiratory and non-respiratory infections in infants are associated with maternal smoking.

The observation of a dose-response relationship for the number of cigarettes with both respiratory and non-respiratory ID hospitalizations further supports a causal relationship. We identified associations between maternal smoking and specific infant infectious diseases that had not been previously reported, including bacteremia/sepsis, mycosis, and parasitic/protozoic infections. Further prospective studies on these newly identified associations are warranted both to confirm the findings and to assess their occurrence and potential impact in other populations.

The observation of a strong association with parasitic and protozoic infections is intriguing, although unmeasured confounders may be involved and, given the small numbers of cases, these results should be interpreted with caution. If confirmed, the impact of maternal smoking (and/or exposure to ETS) may have even greater clinical relevance in developing countries where parasitic and protozoic infections impose a greater health burden on the population, and where laws protecting children from ETS exposure are largely absent (34). The use of ICD codes, while integral to this study, brings with it several limitations: First, ID conditions may be incorrectly diagnosed or coded; Second, some ICD codes allow for ambiguity regarding the etiology or site of infection; Third, both ICD9 and ICD10 codes were used in our mortality analyses (Washington State switched from ICD9 to ICD10 for death certificates in January 1999). Although most ICD9 codes had a direct corollary in the ICD10 system, there may be inherent differences between the two types of codes.

An additional consideration is that the CHARS database is limited to inpatient hospitalizations, and does not include medical clinic and emergency room visits. Thus, our analyses included only cases of severe illness and do not represent the burden of outpatient-treated infectious diseases in this population. While analyses of hospitalization may have excluded individuals with reduced access to care, this would not influence mortality outcomes. Infants who moved out of Washington State within the first year of life may also have been excluded and potentially misclassified as controls, but moving out of the state is unlikely to be associated with maternal smoking status or infectious disease.

As maternal smoking status was obtained by self-report, smoking is likely to have been underreported due to social stigma (35), and our findings would thus underestimate the true prevalence of infant exposure. We were also unable to assess exposure to ETS. Since maternal smoking during pregnancy is highly correlated with continued smoking after pregnancy and having a partner who smokes, the observed associations may be due in part to post-natal exposure to ETS. However, the association with ID hospitalization within the first month of life suggests that long-term post-natal ETS exposure is not required for adverse ID outcomes, and the birthweight- and gestational age-dependent associations with ID mortality are due to pre-natal exposure. Finally, restricting our study population to infants born before 2005 prevented potential confounding from the implementation of an amended Clear Indoor Air Act in Washington State in December of 2005, which drastically reduced environmental tobacco smoke exposure in public places (Revised Code of Washington, Chapter 70.160).

In summary, we observed consistent associations between maternal smoking and nearly all types of infant infectious disease hospitalization and mortality while confirming the established link with respiratory infections. Our findings strengthen the argument that exposure to maternal smoking may adversely affect infant immune responses more broadly, in addition to well-known harms caused to the pediatric respiratory system. This hypothesis is further supported by our finding that the relationship between maternal smoking and hospitalization due to ID was independent of birthweight and gestational age. Clearly, maternal smoking has detrimental effects on infant health, and those effects are more wide-

ranging than previously suspected. More intensive efforts to decrease maternal smoking will be essential to reduce infant morbidity and mortality.

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TABLE 1

Maternal and Infant Characteristics of Infant ID Cases and Controls, Washington State, 1987–2004.^d

	Hospitalization				Mortality			
	Cases		Controls		Cases		Controls	
	n	%	n	%	n	%	n	%
Total number	47,404		48,233		627		2,730	
Mother smoked during pregnancy	10,709	23.4	7,297	15.7	135	23.5	424	16.2
Infant sex								
Male	26,645	56.2	24,541	50.9	359	57.3	1,337	49.0
Birth-weight (g)								
25th Q-tile	3,005		3,118		649		3,090	
Median	3,374		3,458		1,355		3,458	
75th Q-tile	3,718		3,798		3,116		3,798	
Low birth-weight (<2,500 g)	3,970	8.4	2,381	5.0	377	62.1	140	5.1
Very low birth-weight (<1,500 g)	812	1.7	344	0.7	312	51.4	19	0.7
Small for gestational age	5,168	11.5	4,262	9.2	81	16.2	234	8.9
Large for gestational age	4,096	9.1	4,586	9.9	30	6.0	254	9.7
Preterm (<37 weeks)	5,267	11.3	3,328	7.0	390	63.9	209	7.7
Singleton birth	46,097	97.2	47,063	97.6	565	90.1	2,663	97.5
Source of payment								
Government aid	22,948	50.4	15,098	35.5	264	51.0	880	36.1
Parity								
0	15,150	32.5	19,495	41.1	258	42.7	1,096	40.9
1	15,852	34.0	15,491	32.7	161	26.7	863	32.2
2 or more	15,617	33.5	12,402	26.2	185	30.6	722	26.9
Prenatal care began								
1st trimester	34,312	78.3	36,646	81.5	392	76.7	2,055	81.4
2nd trimester	7,828	17.9	6,976	15.5	103	20.2	401	15.9
3rd trimester	1,667	3.8	1,358	3.0	16	3.1	70	2.8
Gestational diabetes	1,377	3.0	1,372	2.9	20	3.2	78	2.9
Preeclampsia	2,272	4.9	2,304	4.9	26	4.2	132	5.0
Maternal hypertension	414	1.0	445	1.1	8	1.5	21	0.9
Maternal infection ^b	396	7.5	313	5.9	11	13.8	22	6.4
Maternal age (years)								
<18	2,684	5.7	1,650	3.4	45	7.2	84	3.1
18–34	40,456	85.4	40,454	83.9	493	78.9	2,312	84.7

	Hospitalization				Mortality			
	Cases		Controls		Cases		Controls	
	n	%	n	%	n	%	n	%
35 and over	4,230	8.9	6,090	12.6	87	13.9	333	12.2
Maternal education (years) ^c								
<12	^a 9,933	30.4	^a 6,018	17.8	^a 110	28.8	^a 341	18.3
Maternal alcohol consumption								
	^a 1,040	3.0	^a 922	2.6	^a 21	4.8	^a 49	2.5
Maternal race								
White	32,657	70.7	36,571	77.9	392	65.7	2,072	78.4
Black	1,778	3.8	1,696	3.6	50	8.4	100	3.8
Native American	2,192	4.7	1,040	2.2	43	7.2	63	2.4
Asian/Pacific								
Islander	2,577	5.6	3,097	6.6	35	5.9	167	6.3
Hispanic	6,989	15.1	4,554	9.7	77	12.9	241	9.1
Other	20	0.0	11	0.0	0	0.0	1	0.0
Married	29,436	62.3	35,687	74.2	368	59.3	2,001	73.5
Income quartile								
0–24%	14,553	33.2	11,154	24.9	^a 192	34.8	627	24.8
25–49%	11,696	26.7	11,187	25.0	^a 135	24.5	633	25.0
50–74%	9,423	21.5	11,175	25.0	^a 120	21.7	631	25.0
75–100%	8,206	18.7	11,207	25.1	^a 105	19.0	638	25.2
Enrolled in Women, Infants and Children ^b	^a 2,700	59.3	^a 1,934	41.8	^a 23	36.5	^a 118	39.3
Rural v. urban	10,244	23.9	10,600	24.3	^a 138	25.7	600	24.3
Foreign born mother ^c	^a 7,578	22.8	^a 6,817	20.2	^a 87	21.5	^a 361	19.7

^a missing values in >10% of total cases or controls

^b available '02-'04 only

^c available '91-'04 only

^d % represents % of all non-missing values

Table 2

Table 2a. Outcome Characteristics of Infant ID Hospitalizations Cases, Washington State, 1987–2004.			
Hospitalization		n	%^a
All cases		47,404	
ID admissions per subject	1	42,606	89.9
	2	3,964	8.4
	3	627	1.3
	4	153	0.3
	5	37	0.1
	6	10	0.0
	7	4	0.0
	8	3	0.0
Based on 1st admission only:			
Month of admission	Dec–Feb	17,940	37.8
	Mar–May	14,239	30.0
	Jun–Aug	7,002	14.8
	Sep–Nov	8,223	17.3
Age at admission (days)	1–2	361	0.8
	3–30	8,853	18.7
	31–90	15,192	32.0
	91–180	10,141	21.4
Length of hospitalization (days)	180+	12,857	27.1
	0–7	22,423	48.0
	8–90	21,857	46.8
	91–365	2,413	5.2

Table 2b. Outcome Characteristics of Infant ID Mortality Cases, Washington State, 1987–2004.

Mortality		n	%^a
All cases		627	
Day of death	1–2	202	32.4
	3–30	173	27.7
	31–90	108	17.3
	91–180	68	10.9
	180+	73	11.7
Month of death	Dec–Feb	161	25.7
	Mar–May	159	25.4
	Jun–Aug	147	23.4
	Sep–Nov	160	25.5
N with ID code listed in	ucodID	407	64.9
	ccod1ID	388	61.9
	ccod2ID	186	29.7

Table 2b. Outcome Characteristics of Infant ID Mortality Cases, Washington State, 1987–2004.

Mortality	n	%^a
ccod3ID	77	12.3
ccod4ID	20	3.2
ccod5ID	5	0.8
ccod6ID	1	0.2

^a% excludes missing^a% excludes missing

Association of Maternal Smoking With Infant Infectious Disease, Washington State, 1987–2004. (Controlling for Marital Status, Below Median Income, and Maternal Race)

TABLE 3

	Hospitalization				Mortality			
	n ^a	AOR	95% CI	P value	n ^a	AOR	95% CI	P value
All	41,215	1.52	1.46, 1.58	<0.0001 *	480	1.51	1.17, 1.96	0.0015 *
Respiratory								
All respiratory	28,155	1.69	1.63, 1.76	<0.0001 *	136	1.53	0.98, 2.38	0.06
Pneumonia and/or flu	9,330	1.72	1.62, 1.82	<0.0001 *	118	1.45	0.90, 2.34	0.13
Bronchitis/bronchiolitis	16,698	1.81	1.73, 1.90	<0.0001 *	11	ND		
Pertussis	570	1.38	1.12, 1.69	0.0027	4	ND		
Croup	1,545	1.03	0.90, 1.19	0.65	0	ND		
RSV	8,113	1.41	1.33, 1.50	<0.0001 *	5	ND		
AURI	4,672	1.41	1.30, 1.52	<0.0001 *	3	ND		
Otitis media	8,438	1.88	1.77, 1.99	<0.0001 *	3	ND		
Non-respiratory								
All non-respiratory	12,538	1.27	1.20, 1.34	<0.0001 *	254	1.32	0.93, 1.88	0.12
GI infection	2,744	1.27	1.15, 1.41	<0.0001 *	16	ND		
CNS inflamm/infection	1,721	1.47	1.30, 1.66	<0.0001 *	21	ND		
UTI	4,478	0.99	0.90, 1.08	0.76	0	ND		
Skin infection	1,728	1.57	1.40, 1.78	<0.0001 *	3	ND		
Bacteremia/sepsis	2,308	1.33	1.19, 1.48	<0.0001 *	126	1.10	0.67, 1.82	0.69
Abcess and/or cellulitis	1,144	1.26	1.07, 1.47	0.0042	2	ND		
Conjunctivitis	756	1.71	1.44, 2.04	<0.0001 *	0	ND		
Etiology								
Bacterial	8,636	1.36	1.28, 1.45	<0.0001 *	177	1.31	0.87, 1.96	0.19
Viral or chlamydial	20,681	1.54	1.48, 1.61	<0.0001 *	41	2.18	1.00, 4.76	0.04
Mycosis	1,935	2.02	1.81, 2.25	<0.0001 *	16	ND		

	Hospitalization				Mortality		
	n ^a	AOR	95% CI	P value	n ^a	AOR	95% CI P value
Parasitic/protozoic	69	2.73	1.59, 4.68	0.0001 [*]	0	ND	

Abbreviations used: RSV, Respiratory Syncytial Virus; AURI, acute upper respiratory infection; GI, gastrointestinal; CNS, central nervous system; UTI, urinary tract infection; ND, not done

^{*} Significant *P*value (<0.05 for all cases, <0.0025 for subgroup analysis)

^aExcluding cases with missing data for maternal smoking and confounding variables

Associations of Increasing Doses of Maternal Smoking Exposure with Infant ID Hospitalization, Washington State, 1987–2004. (Controlling for Marital Status, Below Median Income, and Maternal Race)

Table 4

	Cigs/Day	n cases	n controls	AOR	95%CI	P value
All cases	0	34,991	39,245	1.00		
	1–9	3,202	2,237	1.42	1.33, 1.50	<0.0001
	10–19	3,418	2,335	1.51	1.42, 1.60	<0.0001
	20+	1,838	1,241	1.60	1.48, 1.74	<0.0001
Respiratory	0	23,324		1.00		
	1–9	2,425		1.59	1.48, 1.68	<0.0001
	10–19	2,592		1.67	1.57, 1.78	<0.0001
	20+	1,427		1.81	1.67, 1.97	<0.0001
Non-respiratory	0	10,991		1.00		
	1–9	851		1.20	1.10, 1.31	<0.0001
	10–19	875		1.22	1.11, 1.33	<0.0001
	20+	468		1.34	1.19, 1.50	<0.0001

TABLE 5
Role of Birthweight and Gestational Age on the Association of Maternal Smoking With Infant Infectious Disease, Washington State, 1987–2004.
(Controlling for Marital Status, Below Median Income, and Maternal Race)

	Hospitalization				Mortality			
	n ^a	AOR	95% CI	P value	n ^a	AOR	95% CI	P value
Stratification by birthweight								
all	41,215	1.52	1.46, 1.58	<0.0001*	480	1.51	1.17, 1.96	0.0015*
normal (>2,500 g)	37,791	1.50	1.45, 1.56	<0.0001*	189	1.60	1.09, 2.35	0.015*
LBW (<2,500 g)	3,308	1.35	1.18, 1.54	<0.0001*	279	0.85	0.50, 1.44	0.54
VLBW (<1,500 g)	660	1.84	1.25, 2.73	0.0019*	224	2.21	0.33, 14.97	0.40
Logistic regression model								
including confounding variables only	41,215	1.51	1.46, 1.57	<0.0001*	480	1.52	1.18, 1.96	0.0010*
+ birthweight	41,099	1.45	1.40, 1.51	<0.0001*	468	1.12	0.81, 1.55	0.50
+ gestational age	41,609	1.50	1.45, 1.56	<0.0001*	365	1.40	1.00, 1.96	0.05

* Significant P value

^a Excluding cases with missing data for maternal smoking, and confounding variables (and birthweight and gestational age, when included in the analysis)