Published in final edited form as:

Pediatrics. 2008 July ; 122(1): 58–64. doi:10.1542/peds.2007-2087.

The Increasing Burden and Risk Factors for Bronchiolitis-related Medical Visits in Infants Enrolled in a State Healthcare Insurance Plan

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Abstract

OBJECTIVE—To estimate the year-round burden of healthcare visits attributable to bronchiolitis and identify risk factors for bronchiolitis in term, healthy infants.

PATIENTS AND METHODS—We conducted a population-based, retrospective cohort study of 103,670 term, non-low birth weight infants enrolled in Tennessee Medicaid, 1995 to 2003. We followed infants through the first year of life. Risk factors for bronchiolitis during infancy and rates of inpatient, emergency department, and outpatient visits during the study period were calculated using claims data.

RESULTS—Over the 9 study years, rates of bronchiolitis visits per 1000 infant years were: 238 (outpatient), 77 (emergency department), and 71 (hospitalization). Average annual rates of bronchiolitis visits increased 41% from 188 to 265/1000 infant years from 1996-1997 to 2002-2003 (test of trend, $p < .001$). Analysis of the linear trend in 500 gram increments demonstrated a negative association between increasing birth weight and bronchiolitis diagnosis ($p < 0.0001$). There was a significant, negative trend between maternal age and infant bronchiolitis diagnosis. Compared to infants of mothers aged 20-29 years, infants of mothers aged 15-19 had a small increase in risk of

having a bronchiolitis visit (Hazard ratio 1.05, 95% Confidence Interval 1.01-1.09), while infants of older mothers were less likely to have a visit including women aged 30-39 (Hazard ratio 0.76, 95% Confidence Interval 0.72-0.79) and 40-44 (Hazard ratio 0.54, 95% CI 0.43-0.68).

CONCLUSIONS—The disease burden of bronchiolitis is substantial with increasing rates of all types of visits among term, otherwise healthy infants enrolled in Tennessee Medicaid from 1995 to 2003. Protective factors in this cohort of term infants included higher birth weight and older maternal age.

Keywords

bronchiolitis; risk factors; trends

Introduction

Bronchiolitis is a disease of the lower respiratory tract characterized clinically by cough, tachypnea, wheezing and/or rales.¹ Yearly, up to 3% of healthy infants in the United States are hospitalized for bronchiolitis resulting in an estimated 120,000 hospitalizations with report of increasing hospitalization rates between 1988 and 1996.^{2,3} Several viruses cause bronchiolitis, including respiratory syncytial virus (RSV), influenza virus, human rhinovirus, and human metapneumovirus.⁴⁻⁶ RSV infects most children in the first year of life, and typically causes yearly epidemics of bronchiolitis between November and April resulting in an estimated 80,000 infant hospitalizations yearly.^{3,7} Although children with chronic lung disease, cardiac disease, or those born prematurely are at increased risk of developing severe RSV bronchiolitis, the majority of illness occurs in term, other-wise healthy infants. Efforts to develop a vaccine for RSV have been on-going over the past several decades with challenges in developing a safe and effective vaccine.⁸ Although national estimates for bronchiolitis visits exist,⁹⁻¹² there have been no population-based studies examining the full spectrum of the health care burden of bronchiolitis in term infants by examining outpatient and inpatient visits for bronchiolitis during both RSV and non-RSV peaks.

Using a large population-based administrative database linked with vital records, we examined outpatient and inpatient visits for bronchiolitis among term infants enrolled in the Tennessee Medicaid Program. To investigate risk factors associated with bronchiolitis, we assembled a cohort of term otherwise healthy infants, to avoid potential confounders such as chronic lung disease and prematurity. The objectives of this study were to estimate the year round burden of healthcare visits attributable to bronchiolitis, determine if rates are continuing to increase since the last report on hospitalization trends (1988 – 1996),^{3,13} and estimate risk factors for bronchiolitis diagnoses in term, healthy infants. These data are important to establish the burden and trends in disease for both outpatient and inpatient visits, to establish potentially modifiable risk factors for term otherwise healthy infants, and to inform biologic research on the mechanisms of disease.

Patients and Methods

We conducted a population-based retrospective cohort study of over 100,000 term, otherwise healthy infants enrolled in the Tennessee Medicaid Program, during 1995-2003. Approximately 50% of infants born in Tennessee are enrolled in the Tennessee Medicaid Program. Using previously described methods, we obtained study data from linked Tennessee Medicaid administrative data files and Tennessee State vital records.^{14,15} The protocol was approved by the Institutional Review Boards of Vanderbilt University and the Tennessee Department of Health.

Eligible infants were ≥ 37 weeks estimated gestational age (EGA), weighed ≥ 2500 grams at birth, and were born to women who were continuously enrolled in the Tennessee Medicaid program. Continuous maternal enrollment was defined as no more than 45 days of non-enrollment during the year prior to pregnancy (last menstrual period minus 365 days) through delivery. In order to investigate risk factors for bronchiolitis in infants without the confounding of chronic disease, we excluded infants with any of the following during the first three months of life (3.11%): an International Classification of Diseases, Ninth Revision (ICD-9) code for congenital heart disease, chronic lung disease, or congenital anomaly of the airway, a Current Procedural Terminology (CPT) code indicating surgery for congenital heart disease, or receipt of one or more doses of RSV immune globulin. Infant EGA was determined using the date of last menstrual period on the birth certificate (91.7%), calculated based on the median gestational period in weeks for the infant's race, birth weight, and birth year (8.22%) or assigned last menstrual period as 270 days prior to birth (0.04%).^{16;17}

We determined infant healthcare visits for bronchiolitis using ICD-9 codes for bronchiolitis (466.1) and/or RSV pneumonia (480.1). To investigate the full-spectrum of the health care burden of bronchiolitis in term infants we examined outpatient and inpatient visits for bronchiolitis year-round. During the first few months of life, infant Medicaid visits may be billed to the infant's mother. Therefore we attributed bronchiolitis visits in the mother's record to the infant, as bronchiolitis is a rare diagnosis in women of child bearing age.

To illustrate the pattern of the monthly distribution of bronchiolitis diagnoses, we captured all diagnoses by month from 1995 to 2003. All infants in the study cohort were followed until one year of age, until they had more than 21 days of non-enrollment in Tennessee Medicaid, or death. We determined the rate of bronchiolitis associated outpatient visits (not associated with a same day hospitalization or emergency department visit), emergency department visits (not associated with a same day 23 hour observation or hospitalization), and combined 23 hour observations and hospitalizations per 1,000 infant years. To examine trends in bronchiolitis rates, we studied years 1996 to 2003 only. During this time period, we determined the first and all ICD-9 diagnoses for all bronchiolitis visit types. The numerator consisted of bronchiolitis diagnoses. To estimate the denominator for each year we determined the total number of infants who were less than 12 months of age on July 1 for each year 1996 to 2003. We applied Poisson regression to assess temporal trends in the rates.¹⁸

In this large cohort of term infants, we estimated the association between bronchiolitis during infancy and available demographic variables, including infant birth weight and maternal age at delivery.^{2;19-22} From infant birth certificate data we identified infant birth weight, maternal age at delivery, infant sex, siblings (none, one, two or more based on birth certificate report of number of prior live births), self-reported maternal smoking during pregnancy, maternal education level, and marital status. We identified infant race and region of residence (urban, suburban, rural) from Tennessee Medicaid enrollment files. We identified mothers with asthma by capturing asthma-specific health care visits and medication as previously described.¹⁷ To estimate independent predictors of at least one bronchiolitis healthcare visit during infancy, we included the above variables in a Cox proportional hazard model with age as the time dependent variable. As a measure of severe bronchiolitis, we also estimated predictors of a bronchiolitis hospitalization. We calculated linear test of trend of the effects of infant birth weight, maternal age at delivery, number of cigarettes smoked during pregnancy, and number of siblings as ordered continuous variables using Cox proportional hazards models. We tested for interaction between maternal age and infant sex on bronchiolitis incidence.

Results

Among 103,670 term infants there were 23,306 outpatient visits, 7,511 emergency department visits, and 6,936 hospitalizations for bronchiolitis. Overall, 20% of infants had at least one bronchiolitis visit, and 8.8 % of infants had more than one healthcare visit for bronchiolitis during infancy. During the first year of life, 13.3% of infants had a clinic visit, 6.2% had an emergency department visit, and 5.5% of infants had a 23 hour observation or hospitalization. Bronchiolitis visits peaked December through February, which parallels the known epidemiology of RSV (Figure 1), with 80% of visits occurring during the winter virus season between November and April.²³ There were 98,080 eligible infant-years during the study with 238 bronchiolitis outpatient visits, 77 emergency department visits, and 71 hospitalizations per 1000 infant years.

Figure 2, demonstrates an overall increase in yearly bronchiolitis rates, 1996-2003, for infants with at least one visit for bronchiolitis (first visit during infancy, combined inpatient and outpatient), and the rates stratified by visit type. Comparing the average of years 1996 and 1997 to that of years 2002 and 2003, the rates of infants having any bronchiolitis diagnosis increased 41% from 188/1000 to 265/1000 infants. There was a positive trend in increased rates of bronchiolitis 1996 to 2003 (test of trend, $p<0.001$). The average rates of having at least one hospitalization for bronchiolitis increased from 5.5% to 6.4% comparing the same time periods. We also estimated the total burden of all visits for bronchiolitis (repeat visits included), 1996 through 2003. The average burden of all visits for bronchiolitis increased 48% from 304/1000 infants in 1996-1997 to 449/1000 infants in 2002-2003.

Differences in rates of outpatient visits, emergency department visits, and hospitalizations by sociodemographic factors are listed in Table 1. In a multivariable analysis, we compared the risk of having a visit for bronchiolitis by sociodemographic factors (Table 2). As illustrated in Table 2 and figure 3, analysis of the linear trend in 500 gram increments demonstrated a significant negative association with bronchiolitis risk ($p<0.0001$). In addition, there was a significant and negative relationship between maternal age and infant bronchiolitis diagnosis (Test of trend, $p<0.0001$). Compared to infants of mothers who were 20-29 years at the time of delivery, infants of younger mothers had a small increase in risk of bronchiolitis diagnosis while infants of older mothers were much less likely to have a bronchiolitis diagnosis (Table 2). Similar to results for any bronchiolitis health care visit, a negative linear relationship was found between maternal age at delivery and risk of a bronchiolitis hospitalization (data not shown). Adjusted for other factors, females and African-Americans remained less likely to have a visit for bronchiolitis in the first year of life compared to males and whites, respectively (Table 2). Although female infants have a lower bronchiolitis risk than males, increasing maternal age is protective in both sexes (Figure 4). Statistically significant differences in the rate of visits for bronchiolitis were not seen by maternal education level. Infants whose mothers have asthma were more likely to have a bronchiolitis diagnosis than infants whose mothers did not have asthma (HR 1.35, 95% CI 1.28-1.41). There was a significant dose-response relationship between number of cigarettes smoked and bronchiolitis incidence (Test of trend, $p<0.001$). In analyses stratifying infants by their maternal asthma and smoking history, infants of women with asthma and who smoked 10 or more cigarettes daily had the highest risk of bronchiolitis. In addition, there was a significant graded association with number of siblings and bronchiolitis (Test of trend, $p<0.0001$). Infants with siblings were 20% (one sibling) to 30% (≥ 2 siblings) more likely to have a bronchiolitis diagnosis than infants without a sibling. Infants in rural and suburban areas were more likely to have a bronchiolitis diagnosis than infants in urban areas. In addition, as indicated in Table 2, factors such as higher birth weight, older maternal age, residing in an urban area, and having no siblings were also associated with a decreased risk, or tended to have a decreased risk, of a bronchiolitis hospitalization in term infants.

Discussion

This population of term, otherwise healthy, low-income children experienced high rates of bronchiolitis diagnoses with rates for outpatient visits of 238/1000 infant years and hospitalizations of 71/1000 infant years during the first year of life. Overall, 20% had a healthcare claim for bronchiolitis, with 13.3 % having an outpatient visit, 6.2% an emergency department visit, and 5.5% requiring hospitalization. Additionally, overall rates of having at least one bronchiolitis visit have increased by 41% from 1996 – 2003.

Previous studies have reported increases in hospitalizations for bronchiolitis through the 1990s.³ The reasons for the increase in hospitalizations are unclear. Increases in the rates of bronchiolitis visits over time could reflect true increases in disease incidence and severity or non-biologic factors such as improved access to medical care or changes in how physicians code for visits for lower respiratory tract illnesses. It is debated whether increased use of pulse oximetry has influenced hospital admissions for bronchiolitis although several studies have not found increasing rates of hospitalizations during infancy over time for other respiratory illnesses in which pulse oximetry is routinely used.^{3;24;25} Furthermore, we estimated trends in rates of all bronchiolitis diagnoses, not solely hospitalizations, and found that rates of both outpatient and inpatient bronchiolitis diagnoses are substantial and increasing.

We also determined risk factors for a bronchiolitis healthcare visit in the first year of life. Even among infants who were normal birth weight, higher birth weight was protective for bronchiolitis and severe bronchiolitis. Hoo et al. found that low birth weight for gestational age is associated with lower lung function in infancy and lower lung function during early infancy has been associated with other respiratory illnesses later in life.²⁶⁻²⁸ There has been an increasing trend in the rates of elective induction of labor prior to full term birth.^{29;30} This practice may impact the birth weight of infants and therefore decrease the protection that higher birth weight confers on bronchiolitis risk. Elective induction of labor before full term delivery may have important implications particularly for infants with the highest risks of developing asthma, those born to mothers with asthma. Infants whose mothers have asthma are known to have lower birth weights corrected for gestational age, than infants whose mothers do not have asthma.³¹

Across the age continuum, infants born to younger women are at increased risk of bronchiolitis compared to infants of older women, even after adjustment for number of living siblings, infant birth weight, infant race, region of residence, and maternal education level. Further supporting this association is that older maternal age was also protective against severe bronchiolitis as indicated by the negative linear relationship across the age continuum. The association of younger maternal age and increased risk of wheezing lower respiratory illnesses during infancy, particularly in male infants, has been described in a prospective cohort of middle-class women and their infants.¹⁹ In our larger cohort of lower-income families, the increased risk of bronchiolitis in infants of younger women was detected in both male and female infants. It is unclear whether differences in bronchiolitis risk are due to protective factors associated with the *in utero* environment of older women or due to differences in sociodemographic factors such as health care seeking behaviors, breastfeeding, or day care use.^{32;33} For example, it is possible that less experienced teenage mothers would be more likely to take their infants in for medical care or that physicians would be more likely to admit infants of teenagers for social reasons. However, as illustrated in Figure 4, the decreased likelihood of a bronchiolitis visit was seen across the continuum of maternal age, not simply when comparing the youngest women to the oldest. For example, when comparing women in the 40 to 44 year age group to the 30 to 39 year age group, women in their 30s had a 40% increased risk of having a bronchiolitis diagnosis than women in their 40s (data not shown). Furthermore, Martinez et al. found decreased risk of wheezing lower respiratory illnesses in infants of older women even

after adjustment for day care exposure and infant feeding method.¹⁹ Interesting work of others may provide further insights into the association of familial and environmental antenatal exposures and the developing immune system that might explain this association.^{32;34}

Previous findings in the Tennessee Medicaid population suggested that white infants were more likely to be hospitalized for bronchiolitis than African-Americans and we found that white infants were more likely to have a bronchiolitis diagnosis overall.² The decreased incidence may reflect differences in illness incidence, health seeking behavior, or access to care. In analyses by visit type, African-American and Latino infants were more likely to have emergency department visits for bronchiolitis than white infants, suggesting differential use of services. In a previous investigation, we addressed the primary question of whether there was an association between a familial predisposition to develop asthma and maternal smoking with the incidence and severity of bronchiolitis during infancy.³⁵ We found that infants with maternal asthma or maternal smoking during pregnancy were more likely to have a bronchiolitis diagnosis than infants without either respective maternal risk factor.³⁵ In this current study, there was a dose-response relationship between maternal smoking during pregnancy and infants having at least one bronchiolitis diagnosis or more severe bronchiolitis. In addition, infants with siblings were 20% to 30% more likely to have a bronchiolitis diagnosis than infants without a sibling likely explained by the greater likelihood for viral exposure and infection among infants with a sibling. Infants in rural and suburban areas were more likely to have a bronchiolitis diagnosis than infants in urban areas, an interesting and unexplained finding. Maternal smoking during pregnancy, having siblings, and living in a rural residence were associated with increased risk of severe bronchiolitis compared to infants without maternal smoking, no siblings, or living in an urban region of the state, respectively.

There are several potential limitations of this work which should be considered. In this retrospective cohort study using existing data to categorize study variables, misclassification of the predictor variables is possible. However, as all predictors were measured before the infant outcome of bronchiolitis, it is likely that any misclassification would be non-differential. If non-differential misclassification occurred this would bias results toward the null which would conservatively lead to an underestimation of the association of the predictor variables and the bronchiolitis outcome. In addition, the cases of bronchiolitis may be over or under-detected. However, ICD-9 diagnoses of bronchiolitis represent objective physician characterized outcomes at the time of illness that would not be influenced by recall bias. Hospitalization for bronchiolitis has been used in epidemiologic investigations as a measure of severity for decades, however it is possible that social factors may have influenced providers' decisions to hospitalize infants.³⁶⁻⁴⁰ Due to the retrospective nature of this cohort it is also possible that study findings were influenced by other unmeasured factors. Therefore, while we determined risk factors for bronchiolitis, we can not conclude that these factors are causal. We conducted our study in the Medicaid population in which approximately half of infants born in Tennessee are enrolled. Population-based cohort investigations in non-Medicaid populations would provide further insight into the disease burden in different socioeconomic populations. Although, results may not be generalizable to the non-Medicaid population, this study cohort represents a substantial portion of children born in the state and in other areas in the United States.

Conclusion

Health care visits for bronchiolitis during infancy are substantial with one in five infants having at least one health care visit for bronchiolitis during infancy. In addition, rates of clinic visits, emergency department visits, and bronchiolitis hospitalizations are all increasing in this otherwise healthy, term, low-income cohort of infants. Protective factors in this cohort of term infants included older maternal age and higher birth weight. These data reinforce the

importance of determining why bronchiolitis rates are increasing and acting to prevent or lessen the severity of this cause of significant of infant morbidity.

Acknowledgements

The authors are indebted to the Tennessee Bureau of TennCare of the Department of Finance and Administration, and the Tennessee Department of Health, Office of Policy, Planning & Assessment, for providing the data. The authors are grateful to Fernando Martinez, M.D., The University of Arizona College of Medicine, for his critical review of the manuscript.

This study was supported by grants from the following sources: National Institutes of Health (U01 HL 72471, MO1 RR00095, KO8 AI01582, K12 RR17697); The Agency for Healthcare Research and Quality, Centers for Education and Research (U18-HS10384); The Geriatric Research Education and Clinical Center, Department of Veterans Affairs; and the Thrasher Research Fund.

Dr. Griffin reports receiving investigator initiated grant support from MedImmune.

Abbreviations

(RSV), Respiratory syncytial virus; (EGA), Estimated gestational age; (ICD-9), International Classification of Diseases, Ninth Revision; (CPT), Current Procedural Terminology; (ED), Emergency department; (HR), Hazard ratio.

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Figure 1.
Monthly Cumulative Frequency of Bronchiolitis Diagnoses Among Term Infants Enrolled in Tennessee Medicaid, 1995-2003

Figure 2.
Trends in Rates of Bronchiolitis Diagnoses Among Term Infants Enrolled in Tennessee Medicaid, 1995-2003

Figure 3. Relative Risk, including 95% Confidence Intervals (dashed lines), of Bronchiolitis Diagnoses by Birth Weight Among Term Infants Enrolled in Tennessee Medicaid 1995-2003

Figure 4. Relative Risk, including 95% Confidence Intervals (dashed lines), of Bronchiolitis Diagnoses in Males and Females by Maternal Age at Delivery Among Term Infants Enrolled in Tennessee Medicaid 1995-2003

Table 1

Rates of Bronchiolitis Visits Among 103,670 Term Infants Enrolled in Tennessee Medicaid 1995-2003, by Maternal and Infant Characteristics

Characteristic	Child years	Outpatient visits	Outpatient visits/1000 child years	ED Visits	ED visits/1000 child years	Hospital visits	Hospital visits/1000 child years
Birth Weight							
2500 to 3000 grams	98080	23306	238	7511	77	6936	71
3001 to 3500 grams	23449	5725	244	2013	86	1883	80
3501 to 4000 grams	43238	10040	232	3245	75	3019	70
4001 to 4500 grams	24749	6084	246	1839	74	1636	66
4501 to 5000 grams	5636	1248	221	371	66	353	63
	1008	209	207	43	43	45	45
Maternal Age *							
15-19	25137	5592	222	2074	83	1801	72
20-29	61272	15310	250	4804	78	4550	74
30-39	11076	2311	209	608	55	566	51
40-44	594	93	157	25	42	19	32
Infant Sex							
Male	50324	13927	277	4485	89	4062	81
Female	47756	9379	196	3026	63	2874	60
Infant Race							
White	54048	16599	307	3788	70	4889	90
African-American	40648	5919	146	3445	85	1730	43
Latino	978	223	228	91	93	69	71
Maternal Education							
<12 Years	41616	9809	236	3609	87	3372	81
12 Years	43529	10479	241	3145	72	2849	65
>12 Years	12727	2975	234	746	59	698	55

Characteristic	Child years	Outpatient visits	Outpatient visits/1000 child years	ED Visits	ED visits/1000 child years	Hospital visits	Hospital visits/1000 child years
Maternal Asthma							
No	91473	21179	232	6708	73	6224	68
Yes	6607	2127	322	803	122	712	108
Maternal Smoking[†]							
Non-smoker	71107	15207	214	5180	73	4236	60
1 - 9 cigarettes/day	6078	1518	250	519	85	479	79
≥ 10 cigarettes/day	20261	6404	316	1772	87	2167	107
Number of Siblings							
No Siblings	28419	6447	227	2026	71	1699	60
One sibling	35830	9199	257	2725	76	2694	75
Two or more siblings	33751	7637	226	2756	82	2534	75
Residence							
Metropolitan	44009	6477	147	4163	95	1907	43
Suburban	21945	6343	289	1486	68	1535	70
Rural	32034	10475	327	1855	58	3488	109

* maternal age at delivery

[†] maternal smoking during pregnancy

Table 2

Risk Factors for Any Type of Bronchiolitis Visit or Hospitalization* Among Term Infants Enrolled in Tennessee Medicaid, 1995-2003

Characteristic	Any Visit HR (95% CI)	Hospitalization HR (95% CI)
Birth Weight		
2500 to 3000 grams	1	1
3001 to 3500 grams	0.92 (0.89-0.96)	0.86 (0.81-0.92)
3501 to 4000 grams	0.90 (0.86-0.94)	0.80 (0.75-0.87)
4001 to 4500 grams	0.80 (0.75-0.85)	0.76 (0.67-0.86)
4501 to 5000 grams	0.72 (0.61-0.83)	0.57 (0.41-0.78)
Maternal Age[†]		
15-19	1.05 (1.01-1.09)	1.15 (1.06-1.23)
20-29	1	1
30-39	0.76 (0.72-0.79)	0.66 (0.60-0.73)
40-44	0.54 (0.43-0.68)	0.43 (0.26-0.69)
Infant Sex		
Female	1	1
Male	1.35 (1.31-1.39)	1.33 (1.26-1.41)
Infant Race		
White	1	1
African-American	0.73 (0.70-0.76)	0.66 (0.61-0.71)
Latino	0.88 (0.77-1.02)	0.87 (0.67-1.13)
Maternal Education		
<12 Years	1.03 (0.99-1.08)	1.15 (1.04-1.26)
12 Years	1.01 (0.97-1.06)	1.02 (0.93-1.11)
>12 Years	1	1
Maternal Asthma		
No	1	1
Yes	1.35 (1.28-1.41)	1.45 (1.33-1.59)
Maternal Smoking[‡]		
Non-smoker	1	1
1 - 9 cigarettes/day	1.09 (1.03-1.15)	1.14 (1.03-1.27)
≥10 cigarettes/day	1.17 (1.13-1.22)	1.28 (1.20-1.36)
Number of Siblings		
0	1	1
1	1.21 (1.17-1.26)	1.38 (1.29-1.49)

Characteristic	Any Visit HR (95% CI)	Hospitalization HR (95% CI)
≥ 2	1.31 (1.25-1.36)	1.64 (1.51-1.78)
Residence		
Urban	1	1
Suburban	1.17 (1.12-1.21)	1.28 (1.18-1.39)
Rural	1.23 (1.19-1.28)	1.87 (1.74-2.02)

* Includes 23 hour observations

[†] maternal age at delivery

[‡] maternal smoking during pregnancy