Impact of Low Birth Weight on Early Childhood Asthma in the United States

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Objective: To estimate the independent contribution of birth weight to asthma prevalence among children younger than 4 years in the United States and to compare the magnitude of its effect on asthma between African American and white children.


Setting: United States.

Patients: Eight thousand seventy-one subjects, selected from a randomized, systematic population-based sample and weighted to be nationally representative, who completed both initial and longitudinal follow-up surveys and reported information on asthma diagnosis.

Main Outcome Measures: Birth weight and other sociodemographic factors linked to birth outcome were analyzed for independent association with physician-diagnosed asthma by age 3 years.

Results: The prevalence of asthma varied by birth weight category: 6.7% in children 2500 g or more at birth, 10.9% in children 1500 to 2499 g at birth, and 21.9% in children less than 1500 g at birth (very low birth weight [VLBW]) (P<.001). Some of the characteristics shown to be independently associated with asthma included: VLBW (odds ratio [OR], 2.9; 95% confidence interval [CI], 2.3-3.6), moderately low birth weight (OR, 1.4; 95% CI, 1.1-1.8), and African American race (OR, 1.9; 95% CI, 1.6-2.4). In stratified analyses, the independent association between VLBW and asthma in white and African American populations was: ORwhite, 3.1 (95% CI, 2.2-4.3) and ORAfrican American, 2.5 (95% CI, 2.0-3.3). The prevalence of VLBW, however, was tripled in African American compared with white children (1.8% vs 0.6%).

Conclusions: These data confirm findings of other studies that identify a strong independent association between low birth weight and asthma. For this 1988 national birth cohort, an estimated 4000 excess asthma cases were attributable to birth weight less than 2500 g. Although the strength of the independent association between VLBW and asthma was smaller in the African American population, the substantially increased prevalence of VLBW in this community may contribute to the disproportionately increased prevalence of asthma among African American children.


The burden of asthma in very young children has increased markedly in this country during the past 2 decades. In children 0 to 4 years old, asthma prevalence has risen 164% (from 2.2% in 1980 to 5.8% in 1994).1 Similarly, the cost of asthma-related health care is disproportionately higher in very young children compared with other age categories. Although children 4 years or younger represent less than 30% of the pediatric asthma population nationally, they account for nearly 50% of total direct asthma costs.2 Identifying individual risk factors that contribute to the burden of asthma in this age group is useful for generating pathophysiologic hypotheses for these disturbing trends and for directing public health resources.

Although many small studies have demonstrated an association between low birth weight (LBW) and asthma throughout childhood,3-7 to our knowledge, none have described the extent to which LBW contributes to the “epidemic” of asthma in very young children. On the individual level, the effects of LBW on lung function and respiratory health appear to be most pronounced in the first few years of life.8-15 The impact of LBW on asthma prevalence, therefore, may be most noticeable in early childhood. Nationally, the prevalence of both LBW11 and asthma1 has been increasing during the past 2 de-
American children have a greater risk for asthma and between white and African American children. African help to explain some of the disparity in asthma burden asthma.

These points suggest that LBW may have a role in the trends of increasing asthma burden in early childhood. There has also been a significant increase in the use of neonatal respiratory support modalities, which may contribute to disturbances in pulmonary function. These points suggest that LBW may have a role in the trends of increasing asthma burden in early childhood asthma.

Understanding differential trends in LBW may also help to explain some of the disparity in asthma burden between white and African American children. African American children have a greater risk for asthma and frequent wheeze than white children. Low birth weight is also more prevalent in African American populations. The increased numbers of children with LBW may simply translate to an increased contribution of LBW to asthma prevalence in the African American population. Pulmonary development and/or physiologic responses to perinatal respiratory interventions appears to differ between races because African American race is associated with decreased risk for oxygen dependence and chronic lung disease (CLD), even after gestational age and birth weight are controlled for. The independent association between LBW and asthma, therefore, is not necessarily the same between African American and white populations.

This article describes the contribution of LBW to early childhood asthma prevalence. We used a nationally representative sample to estimate the strength of the association between LBW and asthma (relative risk) as

**METHODS**

Data from the 1988 National Maternal-Infant Health Survey (NMIHS) and the 1991 Longitudinal Follow-up Survey were analyzed for this study. The NMIHS was conducted by the National Center for Health Statistics and represents a randomized, systematic sample drawn from civilian, noninstitutionalized vital records in the United States and the District of Columbia. African American and LBW infants were oversampled, so that the final sample composition was approximately 50% African American and 30% LBW infants. All data were subsequently weighted to be nationally representative. The child’s primary caretaker, in most cases the mother, was questioned. The sample of caretakers contacted totaled 13,417; 74% returned the original questionnaire. The initial survey contained sociodemographic information, prenatal history, and delivery outcomes.

Caretakers responding to the first survey were recontacted in their child’s third year of life for the Longitudinal Follow-up Survey. The longitudinal follow-up included all women who completed the baseline survey (except for those who said they did not want to be recontacted) and whose child was alive in 1991. There was an 88% completion rate. Of the 8145 subjects who completed the longitudinal survey, 8071 answered the question on physician-diagnosed asthma and were included in this analysis. The follow-up survey questioned caretakers on the child’s developmental, medical, and social history during the 3 years since birth. Although abstracted information from clinician and hospital medical records were included in the original data set, this information was not included in the analyses reported in this article because a substantial amount of data was missing.

Independent variables included potential confounders of the relationship between LBW and asthma available from the NMIHS, such as sex of the child, maternal age at the child’s birth, race, maternal education and socioeconomic status, gestational age and birth weight, and history of maternal smoking of tobacco products before, after, and/or during the pregnancy. A poverty status variable was developed by means of report of family income and number of members in the household and categorized according to standard national poverty levels. Birth weight, extracted from the child’s birth certificate, was also obtained from the NMIHS. Standard limits for moderately low birth weight (MLBW) (1500-2499 g) and very low birth weight (VLBW) (<1500 g) were used to categorize children. Racial categories in the NMIHS included white, African American, and other. A final variable in the analysis, history of CLD, was identified in the Longitudinal Follow-up Survey by the question: “. . . have [you] ever been told by a doctor, nurse, or other health care provider that [child’s name] has any other chronic respiratory, lung, or breathing condition?” In the child with LBW, this question could be expected to identify those with a history of CLD of prematurity.

The sole outcome measure in this study was physician-diagnosed asthma in the first 3 years of life. Children were categorized as having asthma if there was a positive response to the question in the Longitudinal Follow-up Survey: “. . . ever been told by a doctor, nurse, or other health care provider that [child’s name] has asthma?”

Analyses were performed on SUDAAN software to account for the complex sampling design, and χ2 tests were used for determining differences in proportions. Variables were tested individually for an association with history of asthma in the entire population and African American and white subpopulations separately. Factors that approached statistical significance (P < .1) were entered into a forced logistic regression model to investigate independent associations.

Prevalence and attributable risk calculations were performed on the basis of nationally weighted sample sizes. Attributable risk estimates included an estimate of the percentage reduction in a given outcome that would occur if the risk factor were eliminated from the general population (population attributable risk percentage) and an estimate of the proportion of an outcome that is explained by exposure to the risk factor alone (attributable risk percentage). These calculations were based on the following formulas:

\[
\text{PAR\%} = \frac{P(E)(RR - 1)}{1 + P(E)(RR - 1)} \times 100,
\]

where PAR\% indicates population attributable risk percentage, P(E) indicates proportion of whole population exposed to risk factor, and RR indicates relative risk of disease; and

\[
\text{AR\%} = \frac{AR_{exposed} - AR_{nonexposed}}{AR_{exposed}} \times 100,
\]

where AR\% indicates attributable risk percentage and AR indicates absolute risk of disease.
well as the magnitude of population-wide impact of LBW on the number of children with asthma (attributable risk). Our objective was to test the hypothesis that LBW is independently associated with asthma development by the fourth year of life and that this association significantly affects asthma prevalence in the general population. We also assessed the association between prenatal risk factors, including LBW, and asthma in African American and white children. Our objective was to identify differences in prenatal exposures that could help to explain the disparity of early childhood asthma burden between these 2 populations.

### RESULTS

In this nationally representative, longitudinal sample of 3-year-olds, the prevalence of asthma was 7.1%. Asthma prevalence was 21.9% among VLBW children and 10.9% among MLBW children, compared with 6.7% among children with normal birth weight (P<.001).

The association between asthma and a number of sociodemographic characteristics was investigated. In the general population, birth weight, history of maternal smoking, race, sex, maternal education, maternal age at time of child’s birth, poverty status, and history of other CLD all approached statistical significance; interval since last live birth, prenatal care, and maternal weight gain during pregnancy did not. Since many of these variables are interrelated, they were included in a logistic regression analysis to estimate the independent contribution of each factor to asthma (Table 1). After other variables were accounted for, children with VLBW had nearly 3 times the risk of physician-diagnosed asthma compared with those born weighing 2500 g or more. Children in the MLBW category had a smaller but still significant risk. African American race, male sex, and maternal history of smoking were also independently associated with increased risk of early-childhood asthma in the overall population.

In this sample, a positive response to the question of other chronic respiratory diseases was the strongest independent predictor of asthma of all the variables entered into this model. Because this variable was not clearly defined, its effect on the analysis was evaluated by running the regression with and without it in the model (data not shown). The statistical conclusions were not altered with history of CLD excluded from the model. The RR for all variables, except the birth weight categories, remained the same with and without CLD in the regression analysis. The RR in the LBW categories increased with CLD excluded (MLBW, 1.39-1.45; VLBW, 2.86-3.41), suggesting a confounding relationship between birth weight, CLD, and development of asthma. In a separate analysis in children with VLBW, CLD was not an independent predictor of asthma.

Weighted sample sizes and the most conservative RR were used for attributable risk calculations. Table 2 presents the results of these calculations. The majority of the increased risk for asthma in children with VLBW (68%) was explained by their birth weight alone. Approximately 4000 excess cases of early-childhood asthma nationally could be attributed to LBW. The calculations for attributable risk in children whose mothers smoked were included for comparison.

Separate analyses were run on white and African American children. In both populations, male sex (odds ratio [OR]white, 1.8; 95% confidence interval [CI], 1.3-2.5; OR African American, 1.5; 95% CI, 1.2-1.9) and CLD (ORwhite, 3.9; 95% CI, 2.4-6.1; OR African American, 2.8; 95% CI, 2.0-3.9) were independently associated with asthma. Maternal education, maternal age at delivery, and poverty status were not independent contributors to asthma prevalence in both white and African American children. Interestingly, a history of maternal smoking was not independently associated with increased risk for asthma in African American children (OR, 1.2; 95% CI, 0.9-1.6); it was significant in the white population (OR, 1.7; 95% CI, 1.3-2.4). Odds ratios for both VLBW and MLBW were slightly higher for white children (OR, 3.1; 95% CI, 2.2-4.3; and OR, 1.7; 95% CI, 1.2-2.3, respectively) compared with African American children (OR, 2.5; 95% CI, 2.0-3.3; and OR, 1.1; 95% CI, 0.8-1.4, respectively). The contribution of VLBW to asthma was greater in the African American population, however, because of the increased prevalence of VLBW (population attributable risk percentage, 2.7%).

### Table 1. Reported Asthma Prevalence and Independent Associations for Asthma Diagnosis in Selected Characteristics: 1988 National Maternal-Infant Health Survey and 1991 Longitudinal Follow-up Survey

<table>
<thead>
<tr>
<th>Characteristics</th>
<th>% With Asthma</th>
<th>OR 95% CI</th>
</tr>
</thead>
<tbody>
<tr>
<td>Overall</td>
<td>7.1</td>
<td></td>
</tr>
<tr>
<td>Birth weight, g</td>
<td></td>
<td></td>
</tr>
<tr>
<td>&lt;1500</td>
<td>21.9</td>
<td>2.9</td>
</tr>
<tr>
<td>1500-2499</td>
<td>10.9</td>
<td>1.4</td>
</tr>
<tr>
<td>≥2500</td>
<td>6.7</td>
<td>Referent</td>
</tr>
<tr>
<td>Smoking status</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Yes</td>
<td>9.3</td>
<td>1.6</td>
</tr>
<tr>
<td>No</td>
<td>6.2</td>
<td>Referent</td>
</tr>
<tr>
<td>Maternal race</td>
<td></td>
<td></td>
</tr>
<tr>
<td>African American</td>
<td>12.0</td>
<td>1.9</td>
</tr>
<tr>
<td>Other</td>
<td>8.0</td>
<td>1.6</td>
</tr>
<tr>
<td>White</td>
<td>6.0</td>
<td>Referent</td>
</tr>
<tr>
<td>Sex</td>
<td></td>
<td></td>
</tr>
<tr>
<td>M</td>
<td>8.4</td>
<td>1.6</td>
</tr>
<tr>
<td>F</td>
<td>5.5</td>
<td>Referent</td>
</tr>
<tr>
<td>Maternal education</td>
<td></td>
<td></td>
</tr>
<tr>
<td>&lt;High school</td>
<td>8.4</td>
<td>0.9</td>
</tr>
<tr>
<td>High school</td>
<td>7.6</td>
<td>1.0</td>
</tr>
<tr>
<td>&gt;High school</td>
<td>6.1</td>
<td>Referent</td>
</tr>
<tr>
<td>Maternal age at child’s birth, y</td>
<td></td>
<td></td>
</tr>
<tr>
<td>&lt;20</td>
<td>9.0</td>
<td>1.1</td>
</tr>
<tr>
<td>&gt;30</td>
<td>5.3</td>
<td>0.8</td>
</tr>
<tr>
<td>20-30</td>
<td>7.3</td>
<td>Referent</td>
</tr>
<tr>
<td>Poverty status, % of poverty level</td>
<td></td>
<td></td>
</tr>
<tr>
<td>&lt;100</td>
<td>9.1</td>
<td>1.2</td>
</tr>
<tr>
<td>100-150</td>
<td>8.8</td>
<td>1.4</td>
</tr>
<tr>
<td>&gt;150</td>
<td>5.6</td>
<td>Referent</td>
</tr>
<tr>
<td>Chronic lung disease (n = 8058)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Yes</td>
<td>20.4</td>
<td>3.4</td>
</tr>
<tr>
<td>No</td>
<td>6.4</td>
<td>Referent</td>
</tr>
</tbody>
</table>

*Sample size of 8071 (unless otherwise noted) was weighted to be nationally representative, OR indicates odds ratio; CI, confidence interval.

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This study identified a strong independent association between LBW and asthma in young children that was not equal across LBW categories. These data are also the first we are aware of to suggest that the impact of LBW on asthma prevalence is not uniform across ethnic groups. The increased contribution of LBW to asthma in African American populations was due to the increased prevalence of LBW in this group alone, not to an increased association between birth weight and asthma. Recognizing the elevated risk for asthma in an individual child with LBW may prove useful for explicating the pathophysiology of this disease, educating providers and parents, and focusing early intervention programs aimed at reducing asthma burden in the population as a whole and in specific ethnic communities.

The effect of birth weight on an individual child’s risk for developing asthma was substantial and most pronounced in the lowest birth weight category. Children with VLBW had nearly twice the risk of being diagnosed as having asthma compared with MLBW children and nearly 3 times that of children with normal birth weight. Although the causative factor for asthma development in the VLBW child has not been clearly identified, children born weighing less than 1500 g have patterns of reduced pulmonary function similar to those described in children at risk for transient or early-childhood wheezing.4,21,34,35,40 It may also be hypothesized that VLBW is a marker for a family or environment vulnerable to the development of asthma. Further research needs to be done to assess the potential contribution of each of these factors on asthma development in the VLBW child.

Enhancing national efforts to reduce LBW and targeting VLBW children, in particular, for programs to reduce asthma morbidity may result in reduction of early-childhood asthma burden within a given community. In the individual child with VLBW, more than half of the increased risk for asthma was explained by birth weight alone (attributable risk percentage, 68%). Methods aimed at reducing VLBW in a general population, therefore, should also have an effect on lowering asthma prevalence. Because of the low prevalence of VLBW in the average community, however, the change in the overall number of affected children with asthma can be expected to be modest. A more substantial impact on asthma prevalence would be seen within African American communities, where LBW is proportionately more common.

Reducing the incidence of VLBW also may have a noticeable effect on asthma-related utilization of medical resources. A recent assessment of asthma-related costs in a Medicaid population showed that mean per capita asthma costs were approximately 4 times higher in VLBW children than in children with normal birth weight.42 The gains achieved by targeting VLBW, therefore, may have the greatest impact on distribution of medical resources and overall dollars spent in caring for young children with asthma. Again, these gains may be most significant in African American communities.

There were few differences in independent contributors to asthma development between African American and white children. The odds for developing asthma in children with VLBW were smaller in the African American than in the white population. Confidence intervals overlapped substantially between the 2 groups, however, making it difficult to infer true difference between the groups. In addition, it is interesting that maternal smoking was not a significant independent contributor to asthma prevalence in young African American children. These data are preliminary and require further research to substantiate their veracity. If true, however, they may indirectly support the hypothesis initiated in the literature on bronchopulmonary dysplasia14-18 that pulmonary function and/or response to prenatal insults or perinatal respiratory interventions are somehow different in African American children than in white children.

A large national sample provides many advantages for studying the impact of a relatively rare event like LBW, including increased power and generalizability of results. There are limitations, however, to these data specifically. First, our ability to accurately classify children with a history of bronchopulmonary dysplasia was limited. Our purpose was to identify the contribution of LBW to asthma prevalence, regardless of any comorbid conditions that may exist. In early childhood, however, significant respiratory disease related to prematurity may obscure the diagnosis of asthma. In several small studies, an increased risk for asthma symptoms and/or diagnosis has been found in VLBW children, irrespective of history of bronchopulmonary dysplasia.4,21,36,33,40

Table 2. Asthma Prevalence and Attributable Risk Calculations Based on Weighted, National Sample Sizes: 1988 National Maternal-Infant Health Survey and 1991 Longitudinal Follow-up Survey

<table>
<thead>
<tr>
<th>Risk Factor</th>
<th>Prevalence of Risk Factor, %</th>
<th>Prevalence of Asthma, %</th>
<th>Attributable Risk, %</th>
<th>Population Attributable Risk, %</th>
<th>No. of Excess Cases of Asthma</th>
</tr>
</thead>
<tbody>
<tr>
<td>VLBW†</td>
<td>0.8</td>
<td>21.0</td>
<td>68</td>
<td>0.8</td>
<td>1881</td>
</tr>
<tr>
<td>LBW† (MLBW + VLBW)</td>
<td>7.0</td>
<td>21.0</td>
<td>46</td>
<td>1.8</td>
<td>4379</td>
</tr>
<tr>
<td>Maternal smoking†</td>
<td>31.2</td>
<td>5.0</td>
<td>36</td>
<td>16.0</td>
<td>38129</td>
</tr>
<tr>
<td>VLBW (white)‡</td>
<td>0.6</td>
<td>5.0</td>
<td>60</td>
<td>1.2</td>
<td>1943</td>
</tr>
<tr>
<td>VLBW (African American)§</td>
<td>1.8</td>
<td>12.0</td>
<td>56</td>
<td>2.7</td>
<td>1714</td>
</tr>
</tbody>
</table>

*VLBW indicates very low birth weight; LBW, low birth weight; and MLBW, moderately low birth weight.
†Calculations are based on the entire population of children included (N = 8071; weighted number of asthmatic persons nationally, 225 409).
‡Calculations are based on the white subpopulation of children (n = 3913; weighted number of asthmatic persons nationally, 161 917).
§Calculations are based on the African American subpopulation of children (n = 3884; weighted number of asthmatic persons nationally, 63 492).
also suggested in our data by the lack of independent association between CLD and asthma in the VLBW group. A history of bronchopulmonary dysplasia, therefore, may modify the strength of the independent association between VLBW and asthma, but all VLBW children share this increased risk for asthma.

A second limitation is the potential for selection bias. Identifying asthmatic children on the basis of parental report alone leaves room for error. Parental report of physician-diagnosed asthma in a questionnaire format, however, has been shown to have a high specificity and positive predictive value (95% and 54%, respectively) compared with exercise challenge and physician assessment (85% and 61%, respectively). Young children with asthma may be misclassified as normal when their symptoms are mild and less persistent. The likelihood is greater, therefore, that these prevalence values are underestimates of true disease burden.

Since no gold standard for defining asthma exists, systematic selection bias may occur if diagnostic practices are influenced by birth weight. In LBW infants without co-morbid respiratory conditions, physicians may be more or less likely to attribute wheezing in a LBW child to “asthma” depending on their belief that wheezing is expected in children born prematurely. Large national samples should provide an averaging effect by including physicians who err in both directions. Without a record of quality and quantity of symptoms, however, the direction and magnitude of any bias effect cannot be accurately assessed. We would argue, however, that the labeling and treatment of a disease process as asthma results in a measurable and valid impact on medical resource utilization even if the diagnosis itself is inaccurate. Investigations into the pathophysiological processes of recurrent wheezing in LBW children compared with children with normal birth weight are needed to clarify whether the disease processes are the same. A better understanding of physician decision-making processes also is needed to identify sources of bias in early-childhood asthma diagnosis.

These data contribute to the continued exploration of the public health impact of LBW on early childhood asthma. The modest contribution of LBW to the overall prevalence of asthma in very young children suggests that other factors are responsible for the increasing asthma prevalence in this age group. The strength of the individual association between LBW and asthma shown in this study, however, supports the need for focused intervention in this group of children. The disproportionate effect of VLBW in racial subpopulations also warrants targeted intervention programs specifically aimed at reducing the prevalence of this risk factor. Educational programs, therapeutic trials, and etiologic research specific for children with LBW may result in substantial reduction of morbidity in LBW children and improve outcomes in high-risk populations.

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Reprints not available from the authors.

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