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Predictors for Asthma at Age 7 Years for Low-Income Children Enrolled in the Childhood Asthma Prevention Study

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Abstract

Objective—To identify the predictive factors of early childhood wheezing in children of low socioeconomic status.

Study design—The Childhood Asthma Prevention Study (CAPS) enrolled 177 low-income children (9–24 months old) with frequent wheezing. At age 7 years, presence of asthma was assessed through caregiver reports of physician diagnosis of asthma (CRPDA) and corroborated by assessment of bronchial hyperresponsiveness (BHR). Lung function, inflammatory markers, and asthma symptom severity were compared for children with $\pm$ CRPDA, $\pm$ BHR, and asthma. Baseline predictors for CRPDA, BHR and asthma at 7 years of age were examined.

Results—Maternal symptom report strongly differentiated children with +CRPDA (50%) despite comparable airflow measurements ($p < 0.0001$), and spirometric lung function measurements were different for +BHR (65%) vs. –BHR ($p < 0.005$). Univariate analyses revealed different baseline predictors of +CRPDA and +BHR for children at age 7 years. Higher levels of maternal psychological resources were associated with +CRPDA, but not +BHR. Only 39% of children with a history of frequent wheezing met the conservative definition of asthma at age 7 years, with the following significant predictors found: low birth weight, baseline symptom severity and maternal psychological resources.

Conclusions—This low-income, multi-ethnic group of wheezing infants represents a unique population of children with distinct characteristics and risks for persistent asthma. Determination of asthma status at 7 years of age required objective measurement of BHR in addition to CRPDA. The association of maternal psychological resources with +CRPDA may represent a previously unrecognized factor in determination of asthma status among low-income groups.

Elevated asthma prevalence and morbidity among low-income minority children remain a significant public health problem in the U.S.(1) Low-income children with persistent wheezing have been found to have recurrent asthma symptoms since early infancy. Because most prospective studies of early asthma onset have enrolled families from middle to higher

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socioeconomic status (SES), risk factors for early childhood wheezing and persistent asthma in low-income children remain unclear, and may be quite different.

Multiple prospective birth cohort studies have shown that low birth weight is associated with higher risk for persistent wheezing in early childhood(2); however, findings are inconsistent. (3) Other variables associated with low birth weight such as prematurity, maternal smoking, and low (SES) have been implicated as risk factors for early onset of asthma symptoms, confounding the complex interrelationship between birth weight and infantile wheezing.(3, 4) Social risk variables associated with low SES have been shown to be as important as biomedical risk factors in affecting child health and health seeking behavior.(5)

The Childhood Asthma Prevention Study (CAPS) was a prospective, controlled study of wheezing infants from low-income families designed to assess the efficacy of a multifaceted nurse home visitor/environmental intervention in reducing asthma onset, morbidity and severity at 4-year and 7-year follow-ups.(6, 7) This report focuses on biomedical and psychosocial predictors from the first 2 years of life in relation to caregiver report of physician diagnosed asthma (CRPDA), quantified bronchial hyperresponsiveness (BHR), and asthma status at age 7 years. Results of the intervention will be reported separately.

METHODS

Eligible infant participants were between the age of 9 and 24 months, with medical record documentation of 3 wheezing episodes observed, and were from low-income families (Medicaid eligible, i.e. family income < 1.5 times the annualized federal poverty level [FLP]; in 1997 the FLP was \$13,330 for a 3-person family). Infants were excluded if they were <34 weeks gestation, had postnatal oxygen requirement >48 hours, or complicating medical conditions. Families were recruited from pediatric departments of local hospitals and clinics between January 1998 and March 2000. Consent forms approved by the Institutional Review Boards of participating institutions were signed by caregivers during enrollment, and by both caregivers and children at the follow-up assessment. Following baseline evaluations, families were assigned randomly to the yearlong nurse home visitor intervention or control group, and 1- and 4-year follow-up assessments have been reported. (6, 7) Data for this report were derived from a final assessment to determine the children's asthma status at age 7 years.

Baseline Evaluation at 9 to 24 months

Interviews were conducted with the infants' primary caregivers in their homes to obtain baseline demographic, medical, environmental, and psychosocial information. We obtained infant urine specimens for cotinine analysis and household dust samples to determine allergen content (cockroach, cat and dog dander). Consistent with the symptom report dimension of the NHLBI asthma severity classification available at the time of study implementation,(8) caregivers reported infantile wheezing frequency/severity for the past 6 months using a modified check-list,(9, 10, 11) with 5-point scales for daytime, nighttime, and following physical activity, and a yes/no rating for occurrence of severe breathing difficulty. Caregiver psychosocial measures that assessed mental health,(12) cognitive functioning,(13, 14) and sense of mastery,(15) were z-score standardized and combined to indicate caregivers' personal psychological resources.(16) In clinic following enrollment, infants underwent venipuncture for total serum immunoglobulin E (IgE) and prick skin testing to common indoor inhalant allergens (*D. pteronyssinus*, *D. farinae* American and German cockroach mix, cat dander, dog dander, indoor molds) and food allergens (egg, milk, soybean). Medical records were obtained and abstracted for child's birth weight, history of RSV bronchiolitis, physician documented wheezing episodes, emergency department visits and hospitalizations.

Evaluation at 7 years

Of the 177 children randomized to nurse home visitor/environmental intervention or control groups at baseline, 140 (79%) families participated in follow-up at age 7 years. 128 (72%) children were evaluated in clinic and 125 (71%) children had complete spirometric lung function measurement data for this report (Figure). 7-year evaluations took place from November 2002 through June 2006. Age at follow-up was an average of 7.15 years (SD=0.28, range = 6.7–8.3 years). During the clinic visit, caregivers were interviewed regarding child's asthma status, symptoms, medications, and health care utilization and were asked "Has a doctor told you in the past year that your child has asthma?" Interview-embedded questions included the Pediatric Asthma Symptom Scale (PASS) regarding symptoms that occurred in past four weeks(17) and the Functional Severity Scale regarding frequency and severity of symptoms over the past year.(9)

Prior to pulmonary function testing, fractional exhaled nitric oxide (FeNO) was measured using NIOX (Aerocrine, Inc, Stockholm, Sweden). Pulmonary function testing included: (1) baseline spirometry; (2) 10-minute treadmill exercise challenge with spirometry at 1, 5, and 10 minutes post-exercise; (3) followed by bronchodilator administration; and (4) post bronchodilator spirometry measurement (Jaeger MasterScreen Spirometry system, Jaeger Co. Hoechberg, Germany). Children were instructed to refrain from taking controller medication and bronchodilator medication for 24 hours and 6 hours prior to testing, respectively. Children were considered to have bronchial hyperresponsiveness (+BHR) if there was a decrease in FEV₁ of 10% from baseline to post-exercise, or an increase in FEV₁ of 12% from baseline to post-bronchodilator measurement, based on NHLBI/NAEPP guidelines.(18) BHR data were analyzed for 107 children (Figure). If the pre-post bronchodilator measurement failed to meet criteria for BHR and the exercise challenge was not conducted, data was excluded from BHR analyses (n=10; Figure). Children did not receive the exercise challenge if: (1) baseline FEV₁ values were below 80% predicted; (2) challenge was contraindicated due to asthma symptoms; or (3) caregivers declined the challenge. Because exposure to corticosteroid medication reduces airway reactivity(19), for analyses where BHR was the outcome variable, children with +CRPDA/-BHR but documented prescription of controller medication were excluded (n=8; Figure). Children underwent prick skin testing for inhalant allergens using the Colorado Panel (24 antigens, 3 mm wheal bigger than the negative saline control read as positive). The occurrence of American Thoracic Society-B (ATS-B) (20) symptoms within the past year was queried: (1) wheeze with colds; (2) wheeze without colds; (3) shortness of breath (SOB) with wheeze; (4) cough, wheeze, or SOB after exercise; or (5) persistent cough without colds. Medical records were obtained and abstracted for documentation of asthma medication prescriptions.

Outcome Measures

The primary outcome measures for this report are caregiver report of physician diagnosed asthma (CRPDA), evidence of bronchial hyperresponsiveness (BHR), and asthma at age 7 years. Asthma was defined as +CRPDA corroborated by +BHR. In addition, children with +CRPDA but negative BHR challenges (–BHR) or no BHR data (NoBHR), but who had medical record documentation of controller medication (+MR) were included in the final asthma group (Figure).

Statistical Analyses

Data with right-skewed distributions were log transformed for analyses, then back-transformed for presentation, yielding geometric means. Unadjusted comparisons of baseline predictor variables and concurrent measures of asthma and allergy in relation to age 7 years outcomes (CRPDA, BHR, asthma) were based on *chi-square* tests, two-sample *t*-tests or analyses of variance with Tukey-Kramer HDS post hoc comparisons when indicated.

Backward stepwise logistic regression was used to model the age 7 years outcome variables using multiple predictors, with the significance level to stay in the model set to 0.10. Predictor variables were initially selected for the backward stepwise regression on the basis of univariate comparisons significant at p -value <0.10 and previous research. They included dichotomous birth weight, baseline total IgE, infant wheeze pattern, baseline symptom severity, maternal education level, maternal history of asthma, maternal psychological resources, household cockroach dust level, child sex, race (African American vs. other) and ethnicity (Hispanic vs. non-Hispanic). Sex, race and sex, and ethnicity ethnicity interactions were also included in the backward selection based on preliminary significance. Although not the focus of this report, intervention group assignment was fixed in the regression models. P -values for 2-sided tests were considered in all cases, and $p<0.05$ was considered statistically significant (not including model building). SAS (version 9.1) and JMP (version 8.0.1) software was used for statistical analyses.

RESULTS

Children were 74% male. Parent-reported racial/ethnic backgrounds were: white—22%, black—22%, Hispanic—54%, and other minority—3%. Among mothers reporting Hispanic racial/ethnic background, 36% were born outside of the U.S. Mothers of 46% of the children had less than a high school education, and 54% were single parents. Median family income at baseline (1998–2001) was \$12,500 (IQR = \$6,000 – \$17,100). There were no differences for any demographic variables between subjects evaluated at age 7 years and those not followed.

At follow-up at 7 years of age, 61 of 124 (49%) caregivers reported a physician diagnosis of asthma for their child within the past year (Figure). Seventy of 115 children (60%) with BHR data demonstrated bronchial hyperresponsiveness. Table I presents clinical descriptors for $\pm$ CRPDA and $\pm$ BHR ($n=107$; Figure). Children with +CRPDA had significantly higher asthma symptom scores than –CRPDA. However, pulmonary function measures for $\pm$ CRPDA groups were not different. In contrast, children with +BHR had significantly lower levels of pulmonary functions than those with –BHR, and had only minimal differences in reports of asthma symptoms. FeNO was significantly higher for children with +CRPDA compared with –CRPDA, but comparable between +BHR and –BHR children. Neither positive skin tests nor total IgE was different for $\pm$ CRPDA or $\pm$ BHR.

Table II (available at www.jpeds.com) presents univariate comparisons for children's characteristics at baseline in relation to $\pm$ CRPDA and $\pm$ BHR status at age 7 years. Significant univariate baseline predictors for +CRPDA at age 7 years included low birth weight, infant wheezing without colds, maternal reports of wheezing severity, and a trend for higher maternal psychological resources. Significant baseline predictors for +BHR at age 7 years included low birth weight, wheezing without colds, lower gestational age, lower levels of household cockroach dust, and trends for negative maternal asthma history, presence of positive skin tests, and higher total IgE.

Forty-five children were classified as having asthma, defined as positive +CRPDA supported by evidence of +BHR ($n=35$) or confirmed prescription for asthma controller medication ($n=10$), and 71 children (61%) had no asthma. The Figure shows subjects' asthma classification.

Table III shows clinical characteristics of the asthma and no asthma groups. The children with asthma had higher symptom scores and FeNO, and more positive skin tests. However, there was no difference between groups for pulmonary function measures. Consistent with their diagnosis and our definition of asthma, 60% of the asthma group was prescribed

controller medication, and none of the children from the group without asthma had prescriptions for controller medication.

Backward stepwise logistic regression was used to construct separate predictive models for $\pm$ CRPDA, $\pm$ BHR, and asthma. Predictors for +CRPDA at age 7 years included greater symptom severity at baseline, higher maternal psychological resources and an interaction between Hispanic ethnicity and sex, with Hispanic mothers reporting +CRPDA for their male children more often than for their female children (Table IV). Significant predictors for age 7 years +BHR included regular vs. cold-induced wheezing in infancy, higher levels of total IgE and lower levels of household cockroach dust. In the final model for asthma versus no asthma groups, predictors included low birth weight, greater baseline symptom severity and higher maternal psychological resources. The asthma model was replicated using a more conservative definition of asthma, +CRPDA/+BHR (n=104), with essentially the same results (data not shown).

DISCUSSION

Children from low-income families suffer from greater asthma morbidity and remain a public health burden. Our study characterizes the outcome of early wheezing infants from low-income families and identifying predictors for persistent asthma from a broad range of demographic, environmental, medical, and psychosocial variables. The combination CRPDA and BHR provide a useful metric for the clinical diagnosis of asthma in children with early wheezing history, with one third of children having documented frequent wheezing in early childhood meeting a conservative definition of asthma. Within the CAPS cohort, different baseline variables were predictive for CRPDA and BHR at the age 7 year follow-up, and a subset of the variables were predictive for asthma. Maternal psychological resources appeared to influence reports of asthma diagnoses in a manner not previously described.

For the CAPS cohort, the ascertainment of asthma status at age 7 years required assessment of both CRPDA and BHR. Caregiver report of asthma (+CRPDA) at age 7 years was associated with higher symptom levels, whereas pulmonary function differentiated $\pm$ BHR. When $\pm$ CRPDA status was combined with $\pm$ BHR, a clear differentiation of asthma status emerged. Compared with children without asthma, those with asthma had symptom levels in the clinical range, they had more airway inflammation (FeNO), and they were more likely to be allergic (positive skin tests). Still, spirometric measures of pulmonary function were not significantly different for the asthma and no asthma groups, with values in the normal range. This is not surprising given that conventional measures of airflow limitation among various levels of asthma severity can still be well within the normal range and that the discordance between symptom severity and lung function in children with asthma is more the rule than the exception.(21) Asthma is characterized by a reversible or variable airway obstruction in children, which can be influenced by use of medications and avoidance of triggers and environmental exposures.

Different sets of infant and caregiver baseline characteristics predicted +CRPDA and +BHR measured at age 7 years. One of the variables predicting +CRPDA at age 7 years was maternal psychological resources at baseline. High scores on maternal psychological resources reflected higher cognitive functioning, better mental health, and a greater sense of mastery.(16) This variable was assessed at baseline in the CAPS study because a series of non-medical, home visitation intervention studies with low-income families had demonstrated that mothers with fewer psychological resources showed the greatest gains in maternal emotional functioning and parent-child interaction.(16) Paradoxically, in our study of childhood asthma, mothers with greater psychological resources at baseline were more

likely to report +CRPDA and higher levels of asthma symptoms when their children were 7 years old. Maternal psychological resources may play a unique and previously unrecognized role when study outcome variables depend on access to the medical care system. +CRPDA requires physician contact, and parents with fewer psychological resources might have less access to medical care, contributing to fewer reports of +CRPDA. Maternal psychological resources might also impact +CRPDA through influences on parent perception of asthma symptoms, understanding or comfort level with an asthma diagnosis, knowledge of optimal asthma management (22), or level of engagement with the medical care system as a whole. (5) That maternal psychological resources was a significant predictor for +CRPDA, but not for BHR, suggests a specific influence on parent report of physician diagnosed asthma. It is unknown whether the relationship between maternal psychological resources and CRPDA is specific to a low-income, multi-ethnic sample such as ours. Associations with parent psychological resources could have been amplified in this unique sample because of the restricted range for family income but broad diversity in ethnic and cultural backgrounds. (10, 11) Further studies are needed to determine how parent psychological resources impact CRPDA among various socioeconomic levels and racial/ethnic groups.

Predictors for +BHR included several variables previously identified as risk factors for persistent asthma. Infant wheezing that occurs in the absence of a cold has been identified as a predictor for active asthma at school age because it distinguishes wheezing due to respiratory illness from persistent wheezing related to asthma.(23) Early indicators of atopy are known predictors for active asthma later in childhood.(24) In this study, univariate tests showed that both positive prick skin tests and total IgE were associated with +BHR at age 7 years, but elevated total IgE emerged as the stronger predictor in multivariate modeling. Some studies also have identified low birth weight as a predictor for asthma, particularly among socially disadvantaged populations similar to the CAPS sample.(25) Low birth weight is often confounded with gestational age in relation to persistent asthma, and the two variables were correlated in this study. Both were associated with +BHR at a univariate level, but the dichotomous birth weight variable emerged as the stronger predictor for +BHR and for asthma.

Elevated cockroach allergen levels and maternal asthma, variables identified in previous studies as risk factors for asthma, emerged as protective for +BHR in this study. For cockroach, the overall low levels suggest that cockroach may have functioned as a marker for a protective microbial burden or microbiome environment, conceptually consistent with the hygiene hypothesis for allergy and asthma.(26) Several U.S. studies, including studies of inner city homes (27) and a national survey study (28), found cockroaches in homes to be associated with higher home levels of bacterial endotoxin. Higher home endotoxin levels have been associated with less allergic sensitization and less allergy-associated asthma in childhood (29, 30). Cockroach frass itself can stimulate immune responses in a similar manner to microbial components, via innate immune pathways (31). Cockroaches may also provide the home inhabitants with microbes capable of stimulating immune development in a manner that reduces asthma risk. Emerging research on protective environmental microbiomes should bring further insight to our protective cockroach observation.

The trend for maternal asthma to be protective for BHR, also counter to expectations, may reflect our unique sample of wheezing infants from low-income, multi-ethnic families where rates of maternal asthma were significantly different for mothers from white, black, U.S. born Hispanic, and foreign-born Hispanic subgroups.(10) Although foreign-born Hispanic mothers reported almost no personal asthma, their children were as likely to have +BHR as other children in the sample. This is consistent with evidence that Mexican-American immigrant children have more asthma symptoms and poorer spirometric lung functions with increasing duration of U.S. residency.(33) The apparently protective role of maternal asthma

in relation to BHR at age 7 years illustrates the complex interrelationships of demographic and asthma risk factors in the CAPS study.(10)

For pediatricians providing clinical care, it is helpful to have evidence-based information, whether for estimating the probability of persistent asthma or for understanding caregivers' presentation of their children's condition. Our study provides predictive information that may assist the clinician in identifying wheezing infants and toddlers who may be at higher risk for persistent asthma later in childhood. For this sample of wheezing infants from low-income families, low birth weight and maternal report of symptom severity increased the probability of persistent asthma, even in the absence of atopic markers or parental asthma history. In addition, maternal psychological resources should be considered when treating children with respiratory problems because fewer cognitive or emotional resources may be associated with underreporting of symptom severity or even a lack of recognition of asthma status despite recurrent episodes of wheezing. For children who present with respiratory symptoms but whose caregivers deny that the child has asthma, asthma diagnosis should nevertheless be considered and diagnostic testing performed.

Our study has several limitations. The number of study participants was relatively small. Even though the proportion of children evaluated at age 7 years was high given inherent difficulties in following low-income families longitudinally, asthma status remains unknown for the 28% of the sample that was lost to follow-up. However, the followed children were demographically representative of the entire group, suggesting that results for those not followed would not be significantly different from those presented here. In addition, some children were unable to perform the exercise challenge due to low baseline lung functions, further reducing the number evaluated and possibly biasing the reported outcomes toward an underreport of asthma or poor lung function. Although a number of these children were included in the final asthma group on the basis of medical record documentation, some children without documentation may have been incorrectly classified. These potential biases could affect our ability to generalize the associations reported here to other groups of children from low-income families. Nevertheless, the partial replication of previous observational studies of predictors for asthma supports the validity of our findings.

This study adds to existing information in describing the clinical course of low-income infants with frequent wheezing until the age of 7 years. The use of +BHR to corroborate +CRPDA resulted in more precise identification of children with asthma than would have been possible with CRPDA alone. The separate examination of $\pm$ CRPDA elucidated the manner in which maternal psychological resources may be a determining factor for children receiving asthma diagnoses and medical care. Examination of predictors for $\pm$ BHR predictors revealed that, in addition to early wheezing severity and presence of atopy, as described in other cohort studies, low birth weight was a risk factor for persistent asthma in this low-income group. In summary, comprehensive treatment for a complex, chronic condition such as childhood asthma requires integration of empiric test results with a thorough understanding of the child's baseline medical history, as well as caregivers' cognitive and emotional resources and their level of engagement with the medical care system.

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Figure.
Flowchart depicting CAPS subjects follow-up status and classification of CRPDA, BHR, and Asthma

Clinical descriptors for caregiver report of physician diagnosis of asthma (CRPDA) and for bronchial hyperresponsiveness (BHR) at 7 years of age¹

Table 1

	-CRPDA		+CRPDA		-BHR		+BHR	
	n=63		n=61	p	n=37		n=70	p
ATS-B Symptoms:								
>= 3	12.7%		63.9%	0.0001	21.6%		38.6%	0.07
< 3	87.3%		36.1%		78.4%		61.4%	
Pediatric Asthma Symptom Scale (PASS)²								
Mean (SD)	9.3 (3.0)		14.1 (4.9)	0.0001	10.0 (3.8)		12.0 (5.0)	0.04
Functional Severity³								
Mean (SD)	2.3 (3.5)		6.3 (4.5)	0.0001	2.7 (3.2)		4.1 (4.4)	0.10
Baseline FEV₁ % Predicted:								
Mean (SD)	98.6 (15.6)		94.0 (18.5)	0.14	104.5 (14.7)		92.8 (16.4)	0.005
FEV₁/FVC:								
Mean (SD)	84.8 (9.0)		83.8 (10.1)	0.57	87.9 (7.0)		82.0 (10.2)	0.0004
FEF25-75 % Predicted:								
Mean (SD)	86.4 (28.5)		80.7 (27.5)	0.26	96.9 (23.7)		75.8 (27.9)	0.0002
FeNO:								
Geometric Mean (Geo SD)	9.9 (2.1)		13.1 (2.0)	0.04	9.3 (1.6)		11.9 (2.3)	0.10
Positive Skin Test:								
Yes	33 (52%)		40 (66%)	0.14	18 (49%)		44 (63%)	0.16
No	30 (48%)		21 (34%)		19 (51%)		26 (37%)	
Total IgE:								
Geometric Mean (Geo SD)	49.4 (4.06)		44.70 (5.47)	0.67	33.12 (4.95)		54.6 4.48)	0.12

¹ Bronchial hyperresponsiveness (+BHR) was defined by a decrease in FEV₁ of 10% from baseline to post-exercise or an increase in FEV₁ of 12% from baseline to post-bronchodilator measurement, based on NHLBI/NAEPP guidelines (18)

² Range of possible PASS scores = 7 to 32

³ Range of possible Functional Severity scores = 0 to 20

Caregiver report of physician diagnosis of asthma (CRPDA) and bronchial hyperresponsiveness (BHR) at age 7 years, by baseline demographic, illness, and exposure variables

Table 2

	-CRPDA		+CRPDA		-BHR		+BHR	
	n=63	p	n=61	p	n=37	p	n=70	p
Child Sex								
Male	44	0.26	48		29		50	0.44
Female	19		13		8		20	
Child Race								
African American (AA)	13 (21%)	0.60	15 (25%)		6 (16%)		18 (26%)	0.25
Other than AA	50 (79%)		46 (75%)		31 (84%)		52 (74%)	
Hispanic Ethnicity								
Non-Hispanic	28 (44%)	0.59	30 (49%)		14 (38%)		37 (53%)	0.14
Hispanic	35 (56%)		31 (51%)		23 (62%)		33 (47%)	
Mother's Birthplace								
Mother not foreign born	48 (76%)	0.12	53 (87%)		31 (84%)		54 (77%)	0.42
Mother foreign born	15 (24%)		8 (13%)		6 (16%)		16 (23%)	
Income*								
\$12,000	30 (48%)	0.78	31 (51%)		20 (56%)		30 (43%)	0.22
>\$12,000	32 (51%)		30 (49%)		16 (44%)		40 (57%)	
Maternal Education								
High school	31 (49%)	0.27	36 (59%)		18 (49%)		40 (57%)	0.40
< High school	32 (51%)		25 (41%)		19 (51%)		30 (43%)	
Marital Status								
Mother not single	30 (48%)	0.70	27 (44%)		16 (44%)		33 (47%)	0.70
Mother single	33 (52%)		34 (56%)		21 (56%)		37 (53%)	
Maternal Psychological Resources								
Mean (SD)	98.9 (10.6)	0.06	102.3 (9.5)		98.2 (10.8)		101.1 (9.8)	0.15
Maternal History of Asthma*								
No history of asthma	44 (72%)	0.93	43 (73%)		25 (68%)		56 (84%)	0.07
History of asthma	17 (28%)		16 (27%)		12 (32%)		11 (16%)	

	-CRPDA		+CRPDA		-BHR		+BHR	
	n=63		n=61	p	n=37		n=70	p
Child's Birth Weight*								
2500 grams	57 (92%)		48 (79%)	0.05	35 (97%)		55 (79%)	0.01
<2500 grams	5 (8%)		12 (20%)		1 (3%)		14 (20%)	
Child Gestational Age								
Mean (SD)	39.2 (1.7)		39.0 (2.1)	0.43	39.6 (1.6)		38.8 (1.9)	0.04
History of RSV Bronchiolitis (MR)[†]								
No history of RSV	46 (73%)		50 (82%)	0.23	29 (79%)		55 (79%)	0.98
History of RSV	17 (27%)		11 (18%)		8 (21%)		15 (21%)	
Infant Wheeze Pattern (CG)								
Cold induced only	34 (54%)		21 (34%)	0.02	33 (62%)		28 (40%)	0.03
Regular wheezing	29 (46%)		40 (66%)		14 (38%)		42 (60%)	
History of Infant Eczema (CG)								
No	40 (64%)		42 (69%)	0.52	26 (70%)		48 (69%)	0.85
Yes	23 (36%)		19 (31%)		11 (30%)		22 (31%)	
History of Food Allergies (CG)								
No	54 (86%)		52 (85%)	0.76	32 (86%)		60 (86%)	0.95
Yes	8 (13%)		9 (15%)		5 (14%)		9 (13%)	
History of Allergic Rhinitis(CG):								
No	18 (29%)		14 (23%)	0.47	10 (27%)		20 (29%)	0.87
Yes	45 (71%)		47 (77%)		27 (73%)		50 (71%)	
Symptom Severity Score (CG):								
Mean (SD)	0.4 (0.6)		1.1 (0.75)	0.02	0.7 (0.7)		0.7 (0.7)	0.77
Hospitalizations (ratio of number/age) (MR):								
Mean (SD)	0.05 (0.10)		0.03 (0.06)	0.19	0.04 (0.1)		0.05 (0.07)	0.86
Prick Skin Testing*								
Negative skin test	48 (76%)		50 (82%)	0.62	33 (92%)		50 (71%)	0.06
1 Positive skin test	11 (18%)		9 (15%)		3 (8%)		15 (21%)	
Total IgE*								
Geometric mean (Geo SD)	14.3 (3.5, 59.1)		13.7 (3.8, 49.4)	0.87	10.4 (1.7, 4.1)		17.5 (5.3, 57.9)	0.06

	-CRPDA	+CRPDA	-BHR	+BHR	p
	n=63	n=61	n=37	n=70	
Maternal prenatal smoke (CG)*					
No maternal smoking	42 (67%)	44 (73%)	26 (70%)	45 (64%)	0.60
Maternal Smoking	21 (33%)	16 (27%)	11 (30%)	24 (34%)	
Smokers in Home (CG)					
No smokers in the home	40 (64%)	36 (59%)	22 (60%)	44 (63%)	0.73
Yes smokers in the home	23 (36%)	25 (41%)	15 (40%)	26 (37%)	
Infant Urinary Cotinine*					
Geometric mean (Geo SD)	8.8 (1.0, 73.7)	11.0 (1.3, 91.8)	11.8 (1.3, 104.6)	9.9 (1.2, 82.3)	0.69
Cockroach Dust*					
Geometric mean (Geo SD)	0.5 (0.9)	0.4 (0.5)	0.7 (1.2)	0.3 (0.5)	0.02
Dog dander*					
Mean (SD)	6.0 (3.6)	6.8 (3.1)	6.0 (3.3)	6.6 (3.1)	0.35
Cat Dander*					
Mean (SD)	6.1 (2.7)	6.6 (2.7)	6.4 (2.7)	6.2 (2.5)	0.71

* n reflects missing data: total IgE, n=110; infant urinary cotinine, n=123; cockroach dust, n=124; dog dander, n=124; cat dander, n=124

† Source of data: MR = medical record; CG = caregiver report

Table 3clinical characteristics for Asthma¹ and No Asthma groups at 7 years of age

	Asthma	No Asthma	
	n = 45	n = 71	p
ATS-B Symptoms			
≥ 3	71.1%	15.5%	<0.0001
< 3	28.9%	84.5%	
Pediatric Asthma Symptom Scale (PASS)²			
Mean (SD)	14.5 (5.2)	9.70 (3.3)	<0.0001
Functional Severity Scale³			
Mean (SD)	6.8 (4.8)	2.5 (3.2)	<0.0001
FEV₁ % Predicted			
Mean (SD)	94.6 (19.3)	98.8 (15.2)	0.19
FEV₁/FVC			
Mean (SD)	83.2 (10.7)	85.2 (8.7)	0.29
FEF 25–75 % Predicted			
Mean (SD)	80.7 (29.3)	87.0 (27.6)	0.25
FeNO			
Geometric Mean (Geo SD)	14.0 (2.1)	9.8 (1.7)	0.01
Positive Skin Test			
Yes	33 (73%)	36 (51%)	0.02
No	12 (27%)	35 (49%)	
Total IgE			
Geometric Mean (Geo SD)	60.3 (5.5)	40.5 (4.1)	0.17

¹ Asthma was defined by caregiver reported physician diagnosed asthma (+CRPDA) corroborated by laboratory evidence of bronchial hyperresponsiveness (+BHR) or confirmed prescription of controller medication (+MR).

² Range of possible PASS scores = 7 – 32

³ Range of possible Functional Severity scores = 0 – 20

Baseline predictors to asthma indicators at 7 years of age: Caregiver Report Physician Diagnosed Asthma (CRPDA), Bronchial hyperresponsiveness (BHR) and Asthma

Table 4

Predictor ²	Outcome					
	CRPDA (n=124)			BHR (n=92)		
	Odds ratio	CI	p	Odds ratio	CI	p
Low birth weight (<2500 g)				6.7	0.8–59.5	0.09
Regular vs. cold-induced wheeze pattern				3.2	1.1–9.3	0.03
Symptom severity score	1.7	1.1–2.7	0.02			
Total IgE (ln scale)				1.7	1.1–2.6	0.02
Cockroach				0.5	0.2–0.9	0.02
Maternal psychological resources	1.04	1.00–1.09	0.04			
Maternal asthma				0.4	0.1–1.2	0.08
Hispanic Ethnicity by Sex						
Hispanic: M vs. F	4.8	1.1–20.1	0.03			
Non-Hispanic: M vs. F	0.5	0.1–1.7	0.25			
Asthma vs. No Asthma				1.07	1.03–1.12	0.002

¹ Asthma vs. No Asthma

² Maternal education, race (African American vs. other), and baseline skin testing were not retained for any final