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# Relationship between maternal demoralization, wheeze, and immunoglobulin E among inner-city children

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**Background:** Prior research has linked maternal prenatal and postnatal mental health with the subsequent development of asthma in children. However, this relationship has not been examined in inner-city African Americans and Hispanics, populations at high risk for asthma.

**Objective:** To determine the relationship of maternal demoralization with wheeze, specific wheeze phenotypes, and seroatopy among children living in a low-income, urban community.

**Methods:** African American and Dominican women aged 18 to 35 years residing in New York City (the Bronx and Northern Manhattan) were recruited during pregnancy (n = 279). Maternal demoralization (ie, psychological distress) was measured both prenatally and postnatally by validated questionnaire. Outcomes included wheeze, transient (birth to 2.5 years of age), late onset (3–5 years), and persistent (birth to 5 years of age), evaluated via questionnaire and total and indoor allergen specific IgE (at birth and ages 2, 3, and 5 years). Logistic regression with generalized estimating equations assessed the association of demoralization with wheeze and atopy. Multinomial regression explored associations between demoralization and specific wheeze phenotypes.

**Results:** Prenatal demoralization significantly predicted overall wheeze (adjusted odds ratio OR, 1.66; 95% confidence interval [CI], 1.29–2.14), transient wheeze (OR, 2.25; 95% CI, 1.34–3.76), and persistent wheeze (OR, 2.69; 95% CI, 1.52–4.77). No association was found between demoralization and IgE after adjustment (total IgE: OR, 1.04; 95% CI, 0.74–1.45; any specific IgE: OR, 0.96; 95% CI, 0.57–1.60).

**Conclusions:** In this inner-city cohort, prenatal demoralization was associated with transient and persistent wheeze. Understanding how maternal demoralization influences children's respiratory health may be important for developing effective interventions among disadvantaged populations.

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## INTRODUCTION

Maternal mental health may be an important risk factor for the development of asthma and/or allergy in children.<sup>1–4</sup> For example, a cross-sectional study comparing asthmatic and nonasthmatic children aged 2 to 11 years found a significant positive relationship between concurrent maternal depression and childhood asthma.<sup>1</sup> In a longitudinal birth cohort study, mothers who self-reported anxiety during pregnancy were more likely to have children who developed asthma by the age of 7 years.<sup>2</sup> Furthermore, stress reported during pregnancy exacerbated the effects of traffic-related air pollution on asthma-related outcomes in children.<sup>5</sup> These findings suggest that the prenatal period may be a time when children are particularly susceptible to asthma-related risks.

Previous research on prenatal environmental exposures, including stress, on asthma-related outcomes in childhood has neglected to consider the development of specific wheeze phenotypes. Although respiratory symptoms such as wheeze emerge during infancy and early childhood, the triggers that induce transient, late-onset, vs persistent wheeze are not clearly understood.<sup>6–8</sup> Experimental studies have suggested that stress-induced production of proallergic cytokines during pregnancy, possibly associated with transplacental passage to

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the fetus, may operate as an underlying mechanism that promotes  $T_H2$  proinflammation.<sup>9–14</sup> To date, the association between maternal mental health, specifically during pregnancy, and childhood seroatopy has not been determined.

Inner-city, minority populations face multiple stressors that may provoke anxiety, depression, and stress.<sup>15–17</sup> Such populations also report higher rates of asthma compared with other racial groups.<sup>18,19</sup> However, the association between impaired maternal mental health and asthma among these disadvantaged groups has not been explored. In addition, tools that assess maternal distress within inner-city, minority populations have also not been well tested. Our approach was to assess prospectively links between prenatal maternal demoralization and childhood asthma-related symptoms, using the Psychiatric Epidemiology Research Instrument–Demoralization (PERI-D) scale. Demoralization denotes nonspecific psychological distress, with high demoralization indicating an individual's inability to cope with stressful situations.<sup>20,21</sup> The scale is a validated indicator of emotional well-being and burden of stress among minority and immigrant populations.<sup>22,23</sup> Children from a New York City cohort of African American and Dominican families were assessed during the first 5 years of life for risk of childhood asthma-related symptoms, including specific wheeze phenotypes and IgE levels. We hypothesized that prenatal demoralization would be associated positively with (1) persistent childhood wheeze through the age of 5 years and/or (2) elevated IgE, after controlling for potential confounders and covariates.

## METHODS

### *Participants*

All participants are part of an ongoing birth cohort study being conducted by the Columbia Center for Children's Environmental Health (CCCEH). Self-identified African American and Dominican women residing in Washington Heights, Harlem, and the Bronx in New York City were recruited during pregnancy from 1998 through 2006 and delivered at New York Presbyterian Hospital or Harlem Hospital Center; as described previously, atopy or asthma predisposition was not a selection criterion.<sup>24–26</sup> Written informed consent was obtained from all study participants, and institutional review board approvals were obtained.

Home and/or office visits were conducted during the third trimester of pregnancy and when the child was 6 months and 1, 2, 3, and 5 years of age. At each visit, a bilingual (English and Spanish) research worker interviewed the participants about sociodemographic and demographic information, residential history, living conditions during the current pregnancy (including housing quality and material hardship), history of exposure to active and passive smoking, alcohol, and drugs.

### *Maternal Demoralization*

Maternal demoralization was measured by the 27-item PERI-D scale at every visit (5 repeated measures). The PERI-D is a composite of 8 domains (perceived physical

health, sadness, poor self-esteem, dread, anxiety, confused thinking, hopelessness/helplessness, and psychophysiological symptoms) encompassing the single construct of demoralization.<sup>21,27</sup> Each question was rated on a 5-point Likert scale (scored 0 to 4), where a higher score indicated greater psychological distress, and queried about symptoms within the last year. Developed for epidemiologic research in community samples and validated in a New York City sample, the PERI-D demonstrates adequate internal consistency in minority and Spanish-speaking immigrant populations (Cronbach  $\alpha$  of 0.91 for African Americans, 0.93 for English-speaking Mexican Americans, and 0.95 for Spanish-speaking Mexican Americans).<sup>22,27</sup> Pearson correlations of the PERI-D with the Center for Epidemiologic Studies–Depression scale and the Bradburn Negative Affect Scale were 0.69 and 0.63 in African Americans, 0.66 and 0.61 in English-speaking Mexican Americans, and 0.85 and 0.63 in Spanish-speaking Mexican Americans, respectively.

### *Wheeze and IgE*

A short questionnaire was administered every 3 months after the birth of the child through 2 years of age and every 6 months thereafter. The questionnaires asked the mother/caregiver about the child's respiratory symptoms and illnesses in the previous 3 months. A binary (yes/no) variable was derived from the question, "In the last 3 months has your child had wheezing or whistling in the chest?" The outcome, wheeze, was determined at 14 time points (3, 6, 9, 12, 15, 18, 21, 24, 30, 36, 42, 48, 54, and 60 months).

Transient wheezers were defined as those children with 1 or more reports of wheeze from 3 to 30 months of age and no reports of wheeze from 3 to 5 years of age. Late-onset wheezers were defined as those children with no reports of wheeze between 3 and 30 months of age and at least 1 report of wheeze from 3 to 5 years. The persistent wheeze group had at least 1 report of wheeze between 3 and 30 months of age and at least 1 report of wheeze from 3 to 5 years, as described.<sup>8</sup>

Umbilical cord blood samples were collected at delivery, and serum blood samples were collected at ages 2, 3, and 5 years. Total IgE was measured either by immunoradiometric assay (Diagnostics Products Corp, Los Angeles, California) or ImmunoCAP (Phadia, Uppsala, Sweden).<sup>28,29</sup> Anticockroach, antimouse, and anti-*Dermatophagoides farinae* IgE levels were measured in duplicate using the fluorescence allergosorbent test (Bio Whittaker, Walkersville, Maryland) until August 2002. Subsequently, all samples (including all 5-year-old samples) were measured by ImmunoCAP. During the transition between these validated methods, a subset of samples was analyzed using both methods and demonstrated agreement.<sup>28</sup>

### *Covariates*

Exposure to secondary smoke was ascertained by maternal interview at each visit. A binary variable was derived from the question, "Has your child been exposed in your home/

apartment or outside of your home/apartment (once or more a month) to smoke from cigarettes, pipes, marijuana, or cigars?" Children exposed to smoke either prenatally or postnatally were classified as exposed to secondary smoke. Maternal report of physician-diagnosed asthma in the mother (past and current) was assessed in the prenatal, 3- and 6-month, and 1-, 2-, and 3-year questionnaires. Mothers were classified as asthmatic if they reported a history of asthma on any questionnaire. At delivery, maternal blood samples were collected and serum was measured as described above. A variable indicating cold or influenza (flu) season, previously associated with transient wheeze in this cohort, was constructed as described by Patel et al.<sup>30</sup>

### Statistical Analysis

To assess the stability of maternal distress during a 5-year period, nonparametric correlations were calculated among maternal demoralization scores (continuous variables) measured prenatally and postnatally. Participants who scored high in prenatal demoralization (predetermined cut point of  $>1.55$ ) vs low were compared on the covariates or confounders used in the analysis to assess factors of distress.<sup>31</sup> For maternal IgE, a binary variable was computed using a cut point of greater than 100 IU IgE/mL for high values.<sup>32</sup> Symptoms were categorized as being within the cold and flu season if most of the interval ( $>45$  days) queried fell between September 1 and March 31, as described.<sup>30</sup> For total IgE, the values within the upper 25% (sensitization) of the distribution were compared with the values within the lower 75% of the distribution (no sensitization).<sup>29</sup> Any sensitization (values  $>0.35$  IU/mL) of specific IgE to cockroach, dust mite, and mouse allergen, measured at the ages of 2, 3, and 5 years, was compared to no sensitization.<sup>28,33</sup>

Logistic regression with generalized estimating equations was used to model the effects of prenatal demoralization (continuous variable) on wheeze (yes/no) and child IgE (total and specific) sensitization; the parameters were the logit link function and the exchangeable correlation matrix. In assessing the relationship between prenatal demoralization and total IgE, 4 time points were modeled (birth and 2, 3, and 5 years). For any specific IgE, 3 time points were modeled (2, 3, and 5 years). Age of the child (in months) at the time of questionnaire/sample collection was the clustering variable for all generalized estimating equation analyses. The relationship between prenatal demoralization and wheeze phenotypes (transient, late onset, or persistent) was explored using a multinomial regression.

Covariates in the final model included multiple maternal (prenatal demoralization, age at pregnancy, ethnicity, education, history of asthma, and IgE) and child characteristics (exposure to secondhand smoke, sex, and wheeze reported during the cold and flu season). All statistical tests were 2-sided tests, with  $P < .05$  considered statistically significant. Data were analyzed using SPSS statistical software, version 18.0 (SPSS Inc, Chicago, Illinois).

## RESULTS

### Sample Characteristics

Among the 727 fully enrolled participants, 465 had a child who had reached the age of 56 months at the time of analysis and was thus considered eligible. Within those eligible, 279 (ie, 60% of eligible) had complete data for the outcome of wheeze (defined as at least 1 respiratory questionnaire for each year of follow-up through the age of 56 months). Data for total IgE were available for 288 participants (62%) and for specific IgE (ie, sensitization to cockroach, mouse, and/or dust mite) for 294 (63%). Except for maternal ethnicity and education, demographic characteristics for the 279 study participants included in the analysis were similar to those of the remaining 488 subjects in the CCCEH cohort (Table 1). Participants were predominantly Dominican, with an annual reported income ranging from \$10,000 to \$30,000, and most had achieved at least a high school diploma. Approximately 59% (167/279) of mothers reported that their child had wheezed within the first 5 years of life.

### PERI-D

In the current sample, the Cronbach coefficient for the prenatal PERI-D was 0.90 for both African Americans and Dominicans, examined separately. Factor analysis of the PERI-D revealed that 32% of the total variance was explained by one component (construct of demoralization), whereas 72.8% of the total variance was explained by 8 components (8 domains of the scale) (data not shown). Prenatal maternal demoralization was associated significantly with postnatal maternal demoralization illustrating that demoralization is a stable trait in this cohort (eTable 1). A total of 81 women (29%) scored high in prenatal demoralization.<sup>31</sup> No significant differences were found in the variables used as covariates or confounders in the women who scored high vs low in prenatal demoralization except for the wheeze phenotypes (Table 2).

### Association of Prenatal Demoralization With Wheeze and IgE

In the univariate regression model, prenatal demoralization was associated with maternal report of wheeze in the child (Table 3). Adjusted analysis showed that the odds ratio (OR) for wheeze in the child was 1.66 (95% confidence interval [CI], 1.29–2.14) for each additional unit increase in maternal demoralization score. No association was found between prenatal demoralization and total IgE levels in the child in univariate analysis or after adjustment (OR, 1.04; 95% CI, 0.74–1.45; data not shown). The association between prenatal demoralization and sensitization to any specific indoor allergens (cockroach, dust mite, or mouse) also was not significant after adjustment (OR, 0.96; 95% CI, 0.57–1.60). We tested postnatal demoralization as a covariate in the model to isolate the effects of prenatal demoralization on wheeze; however, the high correlations of maternal demoralization scores over time made separating the influences difficult (eTable 1).

Table 1. Demographic Distribution of Participants Included Compared With Those Excluded for the Analyses of the Wheeze Outcomes<sup>a</sup>

Predictor variables	Prenatal demoralization scores		P value <sup>b</sup>
	Included (n = 279)	Excluded (n = 448)	
Mother's age at pregnancy, mean ± SD <sup>c</sup>	24.99 ± 4.91	25.40 ± 4.92	.15
Prenatal demoralization, mean ± SD <sup>c</sup>	1.15 ± 0.64	1.15 ± 0.63	.83
Ethnicity <sup>d</sup>			
Dominican	166 (59)	307 (68)	.02
African American	113 (41)	141 (32)	
Maternal education <sup>e</sup>			
Less than high school	94 (34)	192 (43)	<.01 <sup>f</sup>
High school diploma	90 (32)	139 (32)	.18 <sup>f</sup>
Some college	95 (34)	113 (25)	
Positive maternal history of asthma <sup>d</sup>	84 (30)	140 (31)	.80
Maternal IgE >100 IU IgE/mL <sup>d</sup>	81 (29)	54 (31)	.75
Child exposed to secondhand smoke <sup>d</sup>	105 (38)	140 (31)	.09
Child's sex: male <sup>d</sup>	131 (47)	133 (46)	.59
Wheeze phenotypes at the age of 5 years <sup>e</sup>			
Transient	76 (27)	71 (34)	.47 <sup>f</sup>
Late onset	21 (8)	9 (4)	.14 <sup>f</sup>
Persistent	67 (24)	38 (18)	.16 <sup>f</sup>
Nonwheeze	115 (41)	92 (44)	

<sup>a</sup> Data are presented as number (percentage) of participants unless otherwise specified.

<sup>b</sup> P values refer to the difference between the participants selected for the analyses and those not selected. Similar findings were observed between included vs excluded for the analyses of total and specific IgE outcomes.

<sup>c</sup> P value assessed by Mann-Whitney test.

<sup>d</sup> P value assessed via a Pearson  $\chi^2$  test.

<sup>e</sup> P value assessed via a nominal regression.

<sup>f</sup> Reference group was having completed some college and no wheeze, respectively.

Table 2. Demographic Distribution of Participants Who Scored High vs Low in Prenatal Demoralization<sup>a</sup>

Predictor variable	Prenatal demoralization scores		P value <sup>c</sup>
	High <sup>b</sup> (n = 81)	Low (n = 198)	
Mother's age at pregnancy (mean ± SD) <sup>d</sup>	25.81 ± 4.78	25.37 ± 5.05	.36
Ethnicity <sup>e</sup>			.14
Dominican	27 (33)	86 (43)	
African American	54 (67)	112 (57)	
Maternal education <sup>f</sup>			
Less than high school	27 (33)	67 (34)	.96 <sup>g</sup>
High school diploma	27 (33)	53 (32)	.81 <sup>g</sup>
Some college	27 (33)	68 (34)	
Positive for maternal history of asthma <sup>e</sup>	28 (35)	56 (28)	.32
Maternal IgE > 100 IU IgE/mL <sup>e</sup>	30 (37)	51 (26)	.08
Child exposed to secondhand smoke <sup>e</sup>	32 (40)	73 (37)	.69
Child of male sex <sup>e</sup>	37 (46)	94 (48)	.79
Wheeze phenotypes at the age of 5 years <sup>f</sup>			
Transient	26 (32)	50 (25)	.04 <sup>g</sup>
Late onset	8 (10)	13 (7)	.09
Persistent	23 (28)	44 (22)	.05
Nonwheeze	24 (30)	91 (46)	

<sup>a</sup> Data are presented as number (percentage) of participants unless otherwise specified.

<sup>b</sup> High demoralization is a score greater than 1.55, as reported in the literature.<sup>31</sup>

<sup>c</sup> P values compare high vs low scores on the prenatal demoralization scale.

<sup>d</sup> P value assessed by Mann-Whitney test.

<sup>e</sup> P value assessed via a Pearson  $\chi^2$  test.

<sup>f</sup> P value assessed via a nominal regression.

<sup>g</sup> Reference group was having completed some college and no wheeze, respectively.



Table 3. Logistic Regression Using Generalized Estimating Equations for the Association of Prenatal Maternal Demoralization and Childhood Wheeze Through the Age of 5 Years

Predictor variable	OR (95% CI) for outcome of wheeze	
	Univariate	Multivariate
Prenatal demoralization score	1.60 (1.24–2.06)	1.66 (1.29–2.14)
Mother's age at pregnancy	0.99 (0.96–1.02)	1.01 (0.98–1.05)
Maternal ethnicity: African American vs Dominican	0.99 (0.69–1.41)	1.08 (0.74–1.57)
Maternal education at pregnancy		
Less than high school vs some college	1.10 (0.73–1.66)	0.93 (0.61–1.43)
High school diploma vs some college	0.86 (0.57–1.31)	0.79 (0.51–1.21)
Maternal history of asthma (yes/no)	2.28 (1.62–3.23)	2.23 (1.55–3.21)
Maternal IgE (>100 vs ≤100 IU/mL) <sup>a</sup>	1.14 (0.78–1.66)	0.96 (0.67–1.38)
Child exposed to secondhand smoke (yes/no)	1.16 (0.82–1.65)	1.00 (0.69–1.43)
Child of male sex vs. female	2.17 (1.56–3.01)	2.37 (1.69–3.30)
Wheeze within cold and flu season <sup>b</sup> (yes/no)	1.72 (1.42–2.09)	1.77 (1.44–2.17)

Abbreviations: CI, confidence interval; OR, odds ratio.

<sup>a</sup> For maternal IgE, a cut point of greater than 100 IU IgE/mL was used for analysis, as used previously.<sup>32</sup>

<sup>b</sup> Cold and influenza season was defined as symptoms occurring within September 1 to March 31.<sup>30</sup>

### Associations of Prenatal Demoralization With Wheeze Phenotypes

Mean prenatal demoralization scores were higher among mothers of children with transient and persistent wheeze compared with late-onset wheeze or no reported wheeze (Fig 1). Mother's demoralization significantly predicted transient and persistent wheeze in the child through the age of 5 years

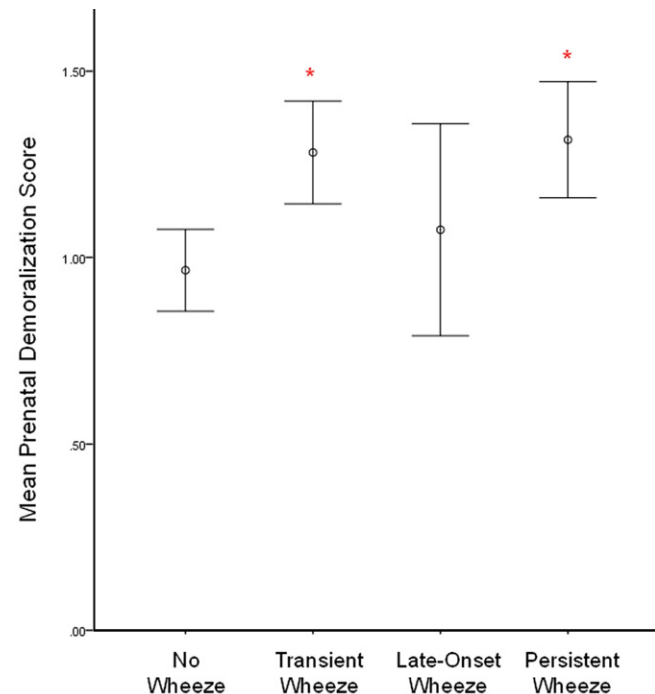


Figure 1. Mean prenatal demoralization on wheeze presentations within the first 5 years of a child's life. Error bars show 95% confidence interval of the mean; circle markers show the mean. Asterisks show significance ( $P < .05$ ).

(Table 4). In the multivariate model, compared with children with no reported wheeze, each additional unit of maternal prenatal demoralization was associated with an OR of 2.25 (95% CI, 1.34–3.76) for transient wheeze and an OR of 2.69 (95% CI, 1.52–4.77) for persistent wheeze.

### DISCUSSION

In an inner-city, minority population, high levels of prenatal maternal demoralization were associated significantly with subsequent childhood wheeze, after adjustment for multiple maternal variables (age at pregnancy, ethnicity, education, history of asthma, and IgE) and child characteristics (exposure to secondhand smoke, sex, and wheeze reported during the cold and flu season). The substantial effect of maternal demoralization on childhood wheeze is consistent with previous reports of associations between prenatal and postnatal caregiver stress and wheeze in nonminority samples.<sup>3,4</sup> These novel findings, determined prospectively, underscore the influence of prenatal mental health on asthma-related outcomes among inner-city, minority children.

Our exploration of the impact of maternal demoralization on wheeze phenotypes found a doubling of the OR for transient wheeze with each additional unit on the mother's prenatal demoralization score. We also found an almost 3-fold increase in the OR for persistent wheeze. These findings are consistent with the clinical observation that the phenotypes of transient, late-onset, and persistent wheeze are divergent entities and with distinct pathogeneses.<sup>8,34,35</sup> Moreover, prenatal demoralization was predictive of persistent wheeze in the child, a phenotype associated with clinical asthma. Evidence suggests that children with persistent wheeze from an early age use more inhaled bronchodilators and corticosteroids and have a higher prevalence of physician diagnosis of asthma, reduced lung function, elevated serum IgE levels, and atopic dermatitis early in life compared with children with transient or no wheeze, making our findings clinically relevant.<sup>7,35</sup> The

Table 4. Prenatal Demoralization Predicted Childhood Wheeze Phenotypes in the First 5 Years of Life

Predictor variable	OR (95% CI) for outcome of wheeze phenotypes <sup>a</sup>		
	Transient	Late onset	Persistent
Prenatal demoralization score	2.25 (1.34–3.76)	1.39 (0.61–3.17)	2.69 (1.52–4.76)
Mother's age <sup>b</sup>	0.98 (0.91–1.05)	1.07 (0.97–1.19)	1.07 (0.99–1.15)
Maternal ethnicity: African American vs Dominican	0.46 (0.23–0.91)	0.51 (0.17–1.53)	1.06 (0.52–2.18)
Maternal education <sup>b</sup>			
Less than high school vs some college	0.69 (0.31–1.54)	0.89 (0.24–3.28)	0.83 (0.36–1.92)
High school diploma vs some college	0.86 (0.41–1.83)	1.23 (0.38–3.99)	0.61 (0.26–1.43)
Maternal history of asthma (yes/no)	1.38 (0.64–2.94)	3.62 (1.23–10.59)	5.43 (2.52–11.68)
Maternal IgE (>100 vs ≤100 IU/mL) <sup>c</sup>	0.86 (0.43–1.72)	1.17 (0.42–3.29)	0.63 (0.30–1.36)
Child exposed to secondhand smoke (yes/no)	1.16 (0.59–2.27)	1.37 (0.48–3.93)	0.77 (0.37–1.64)
Child of male sex vs female	1.53 (0.83–2.83)	1.36 (0.52–3.61)	3.62 (1.82–7.17)

Abbreviations: CI, confidence interval; OR, odds ratio.

<sup>a</sup> No report of wheeze was the reference group.

<sup>b</sup> Maternal age and education were assessed at pregnancy.

<sup>c</sup> For maternal IgE, a cut point of greater than 100 IU IgE/mL was used for analysis, as used previously.<sup>32</sup>

longitudinal design of the present study permitted assessment of prenatal demoralization effects on childhood wheeze, showing that maternal demoralization preceded the development of wheeze in the child, thus reducing the potential for reverse causality (ie, having a sick child leads to demoralization in the mother). However, the chronicity of maternal demoralization over time (eTable 1) precluded the testing of hypotheses distinguishing the relative effects of prenatal and postnatal demoralization. Nonetheless, this prospective study suggests that maternal mental health during gestation may be a key determinant in the characterization of specific wheeze phenotypes.

It has been hypothesized that maternal effects of stress on offspring promote a transplacental transfer, or fetal production, of proallergic T<sub>H</sub>2 cytokines, which lead to atopy in offspring.<sup>13,36</sup> The absence of an association between prenatal maternal demoralization and childhood IgE in this study contrasts with previous reports of association of stress, IgE, and cytokine production with childhood wheezing.<sup>11,37</sup> These differences may be due to subject selection and differences in instrumentation.<sup>14</sup> Distinguishing features of this study with the outcome of seroatopy include the novel measurement of maternal nonspecific psychological distress for this minority population and that the selection of our participants was not contingent on parental history of asthma and/or allergy. The failure to find a significant association between prenatal demoralization and IgE may be due to insufficient statistical power to find such an effect in this cohort. Nonetheless, gaps still remain in our understanding of the roles of prenatal cytokine activity and other proallergic immune mechanisms that may explain the reported associations between maternal psychological state and development of atopy and/or asthma symptoms in children.<sup>36</sup>

Although almost one-third of the mothers in our cohort scored high for demoralization, we were not able to identify factors explaining the mothers' distress and its relationship to childhood wheeze. Inconsistent with a prior study exploring

distress in Anglos, Blacks, and Mexicans, race and education failed to explain maternal demoralization in our cohort (Table 2).<sup>38</sup> Moreover, maternal education and mental health have been associated negatively with wheeze but failed to affect the relationship between demoralization and wheeze in this study.<sup>4,17</sup> Maternal history of asthma has been recognized as a risk factor for asthma and wheeze in children, yet our results indicate that demoralization may predict childhood wheeze despite maternal history of asthma. In addition, exposure to secondhand smoke as determined by questionnaire was not a significant predictor in any of the analyses, inconsistent with previous reports.<sup>39,40</sup> However, interview during cold and influenza season was a significant predictor of wheeze, as found previously by our group.<sup>30</sup> Nonetheless, season of interview failed to explain the relationship between prenatal demoralization and report of wheeze in the child. Hence, all the covariates used in these analyses failed to affect the relationship between wheeze and maternal demoralization.

Several limitations should be acknowledged. Misclassification of the wheeze outcome could have occurred due to maternal report, missing data, and the inconsistent gaps in follow-up that occur in long-term prospective studies.<sup>7,8,34</sup> Furthermore, measures of demoralization have been associated with depression, and mothers with high levels of depression have been shown to be more likely to report illness in their children.<sup>22,41</sup> Arguably, the absence of an association with the objective IgE measure supports this possibility. Another consideration is whether maternal demoralization might affect the ability to cope and/or manage a child's health. Because of the small sample size, we were unable to control for the effects of viral and other upper respiratory tract infections and other covariates, such as breastfeeding and home endotoxin levels.<sup>39,42,43</sup> Furthermore, the study could not distinguish wheezing attributable to inadequate access to health care or compliance with a prescribed medical regimen of anti-inflammatory medications.<sup>44,45</sup> Reliance of

different assays for IgE early in the study was another limitation. Finally, because of the small sample size, it is plausible that type 2 error played a role in examining associations with IgE.

In conclusion, prenatal demoralization was predictive of wheeze among children in this urban cohort, including persistent wheeze. Low-income families experience stressors from multiple sources, such as marital discord, violent disagreements, economic hardship, and neighborhood characteristics that may contribute to a mother's demoralization, leading to adverse health outcomes in children.<sup>15,25,46,47</sup> Investigating the effects of chronic vs transient maternal demoralization throughout early childhood emphasizes the importance of assessing health outcomes in children within a multiple exposure perspective.<sup>15</sup> Understanding how maternal demoralization may influence children's health is an important step in developing effective interventions and alleviating the disproportionate burden of asthma and respiratory illness in urban minority populations.

#### SUPPLEMENTARY DATA

Supplementary data associated with this article can be found, in the online version, at doi.10.1016/j.anai.2011.03.004.

#### REFERENCES

1. Leao LL, Zhang L, Sousa PL, et al. High prevalence of depression amongst mothers of children with asthma. *J Asthma*. 2009;46:388–391.
2. Cookson H, Granell R, Joinson C, Ben-Shlomo Y, Henderson AJ. Mothers' anxiety during pregnancy is associated with asthma in their children. *J Allergy Clin Immunol*. 2009;123:847–853 e811.
3. Milam J, McConnell R, Yao L, Berhane K, Jerrett M, Richardson J. Parental stress and childhood wheeze in a prospective cohort study. *J Asthma*. 2008;45:319–323.
4. Wright RJ, Cohen S, Carey V, Weiss ST, Gold DR. Parental stress as a predictor of wheezing in infancy: a prospective birth-cohort study. *Am J Respir Crit Care Med*. 2002;165:358–365.
5. Shankardass K, McConnell R, Jerrett M, Milam J, Richardson J, Berhane K. Parental stress increases the effect of traffic-related air pollution on childhood asthma incidence. *Proc Natl Acad Sci U S A*. 2009;106:12406–12411.
6. Kuehni CE, Davis A, Brooke AM, Silverman M. Are all wheezing disorders in very young (preschool) children increasing in prevalence? *Lancet*. 2001;357:1821–1825.
7. Kurukulaaratchy RJ, Fenn MH, Waterhouse LM, Matthews SM, Holgate ST, Arshad SH. Characterization of wheezing phenotypes in the first 10 years of life. *Clin Exp Allergy*. 2003;33:573–578.
8. Matricardi PM, Illi S, Gruber C, et al. Wheezing in childhood: incidence, longitudinal patterns and factors predicting persistence. *Eur Respir J*. 2008;32:585–592.
9. Pincus-Knackstedt MK, Joachim RA, Blois SM, et al. Prenatal stress enhances susceptibility of murine adult offspring toward airway inflammation. *J Immunol*. 2006;177:8484–8492.
10. Entringer S, Kumsta R, Nelson EL, Hellhammer DH, Wadhwa PD, Wust S. Influence of prenatal psychosocial stress on cytokine production in adult women. *Dev Psychobiol*. 2008;50:579–587.
11. Kim JH, Kim KH, Woo HY, Shim JY. Maternal cytokine production during pregnancy and the development of childhood wheezing and allergic disease in offspring three years of age. *J Asthma*. 2008;45:948–952.
12. Warner JA, Warner JO. Early life events in allergic sensitisation. *Br Med Bull*. 2000;56:883–893.
13. Kumar RK, Hitchins MP, Foster PS. Epigenetic changes in childhood asthma. *Dis Model Mech*. 2009;2:549–553.
14. von Hertzen LC. Maternal stress and T-cell differentiation of the developing immune system: possible implications for the development of asthma and atopy. *J Allergy Clin Immunol*. 2002;109:923–928.
15. Evans GW, English K. The environment of poverty: multiple stressor exposure, psychophysiological stress, and socioemotional adjustment. *Child Dev*. 2002;73:1238–1248.
16. Moore CG, Probst JC, Tompkins M, Cuffe S, Martin AB. The prevalence of violent disagreements in US families: effects of residence, race/ethnicity, and parental stress. *Pediatrics*. 2007;119(suppl 1):S68–S76.
17. Horwitz SM, Briggs-Gowan MJ, Storfer-Isser A, Carter AS. Prevalence, correlates, and persistence of maternal depression. *J Womens Health (Larchmt)*. 2007;16:678–691.
18. Gupta RS, Carrion-Carire V, Weiss KB. The widening black/white gap in asthma hospitalizations and mortality. *J Allergy Clin Immunol*. 2006;117:351–358.
19. Smith LA, Hatcher-Ross JL, Wertheimer R, Kahn RS. Rethinking race/ethnicity, income, and childhood asthma: racial/ethnic disparities concentrated among the very poor. *Public Health Rep*. 2005;120:109–116.
20. Frank JD. American psychotherapy in perspective. In: *Persuasion and Healing: A Comparative Study of Psychotherapy*. Baltimore, MD: The Johns Hopkins University Press; 1974:21–51.
21. Clarke DM, Kissane DW. Demoralization: its phenomenology and importance. *Aust N Z J Psychiatry*. 2002;36:733–742.
22. Vernon SW, Roberts RE. Measuring nonspecific psychological distress and other dimensions of psychopathology: further observations on the problem. *Arch Gen Psychiatry*. 1981;38:1239–1247.
23. Roberts RE, Vernon SW. *Minority Status and Psychological Distress Reexamined: The Case of Mexican Americans in Research in Community and Mental Health*. Greenwich, CT: JAI Press Inc; 1984:4:131–164.
24. Whyatt RM, Barr DB, Camann DE, et al. Contemporary-use pesticides in personal air samples during pregnancy and blood samples at delivery among urban minority mothers and newborns. *Environ Health Perspect*. 2003;111:749–756.
25. Rauh VA, Whyatt RM, Garfinkel R, et al. Developmental effects of exposure to environmental tobacco smoke and material hardship among inner-city children. *Neurotoxicol Teratol*. 2004;26:373–385.
26. Perera FP, Rauh V, Whyatt RM, et al. A summary of recent findings on birth outcomes and developmental effects of prenatal ETS, PAH, and pesticide exposures. *Neurotoxicology*. 2005;26:573–587.
27. Dohrenwend BP, ShROUT PE, Egri G, Mendelsohn FS. Nonspecific psychological distress and other dimensions of psychopathology: measures for use in the general population. *Arch Gen Psychiatry*. 1980;37:1229–1236.
28. Donohue KM, Al-alem U, Perzanowski MS, et al. Anti-cockroach and anti-mouse IgE are associated with early wheeze and atopy in an inner-city birth cohort. *J Allergy Clin Immunol*. 2008;122:914–920.
29. Goldstein IF, Perzanowski MS, Lendor C, et al. Prevalence of allergy symptoms and total IgE in a New York City cohort and their association with birth order. *Int Arch Allergy Immunol*. 2005;137:249–257.
30. Patel MM, Chillrud SN, Correa JC, et al. Spatial and temporal variations in traffic-related particulate matter at New York City high schools. *Atmos Environ*. 2009;43:4975–4981.
31. ShROUT PE, Dohrenwend BP, Levav I. A discriminant rule for screening cases of diverse diagnostic types: preliminary results. *J Consult Clin Psychol*. 1986;54:314–319.
32. Lendor C, Johnson A, Perzanowski M, et al. Effects of winter birth season and prenatal cockroach and mouse allergen exposure on indoor allergen-specific cord blood mononuclear cell proliferation and cytokine production. *Ann Allergy Asthma Immunol*. 2008;101:193–199.
33. Liu CA, Wang CL, Chuang H, Ou CY, Hsu TY, Yang KD. Prenatal prediction of infant atopy by maternal but not paternal total IgE levels. *J Allergy Clin Immunol*. 2003;112:899–904.
34. Kurukulaaratchy RJ, Matthews S, Holgate ST, Arshad SH. Predicting persistent disease among children who wheeze during early life. *Eur Respir J*. 2003;22:767–771.

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35. Morgan WJ, Stern DA, Sherrill DL, et al. Outcome of asthma and wheezing in the first 6 years of life: follow-up through adolescence. *Am J Respir Crit Care Med.* 2005;172:1253–1258.
  36. Elenkov IJ, Chrousos GP. Stress, cytokine patterns and susceptibility to disease. *Baillieres Best Pract Res Clin Endocrinol Metab.* 1999;13:583–595.
  37. Wright RJ, Finn P, Contreras JP, et al. Chronic caregiver stress and IgE expression, allergen-induced proliferation, and cytokine profiles in a birth cohort predisposed to atopy. *J Allergy Clin Immunol.* 2004;113:1051–1057.
  38. Mirowsky J II, Ross CE. Minority status, ethnic culture, and distress: a comparison of Blacks, Whites, Mexicans, and Mexican Americans. *AJS.* 1980;86:479–495.
  39. Sherriff A, Peters TJ, Henderson J, Strachan D. Risk factor associations with wheezing patterns in children followed longitudinally from birth to 3(1/2) years. *Int J Epidemiol.* 2001;30:1473–1484.
  40. Gergen PJ, Fowler JA, Maurer KR, Davis WW, Overpeck MD. The burden of environmental tobacco smoke exposure on the respiratory health of children 2 months through 5 years of age in the United States: Third National Health and Nutrition Examination Survey, 1988 to 1994. *Pediatrics.* 1998;101:E8.
  41. Bartlett SJ, Kolodner K, Butz AM, Eggleston P, Malveaux FJ, Rand CS. Maternal depressive symptoms and emergency department use among inner-city children with asthma. *Arch Pediatr Adolesc Med.* 2001;155:347–353.
  42. Martinez FD. Respiratory syncytial virus bronchiolitis and the pathogenesis of childhood asthma. *Pediatr Infect Dis J.* 2003;22:S76–S82.
  43. Perzanowski MS, Miller RL, Thorne PS, et al. Endotoxin in inner-city homes: associations with wheeze and eczema in early childhood. *J Allergy Clin Immunol.* 2006;117:1082–1089.
  44. Kattan M, Mitchell H, Eggleston P, et al. Characteristics of inner-city children with asthma: the National Cooperative Inner-City Asthma Study. *Pediatr Pulmonol.* 1997;24:253–262.
  45. Rand CS. Adherence to asthma therapy in the preschool child. *Allergy.* 2002;57(suppl 74):48–57.
  46. Klinnert MD, Nelson HS, Price MR, Adinoff AD, Leung DY, Mrazek DA. Onset and persistence of childhood asthma: predictors from infancy. *Pediatrics.* 2001;108:E69.
  47. Horowitz K, McKay M, Marshall R. Community violence and urban families: experiences, effects, and directions for intervention. *Am J Orthopsychiatry.* 2005;75:356–368.

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eTable 1. Spearman  $\rho$  Correlations of Prenatal With Postnatal Demoralization Scores for Participants Included in the Wheeze Analysis

<b>Demoralization time point</b>	<b>Spearman <math>\rho</math> correlation with prenatal demoralization score</b>	<b><i>P</i> value</b>
1 Year after delivery	0.60	<.01
2 Years after delivery	0.59	<.01
3 Years after delivery	0.56	<.01
5 Years after delivery	0.55	<.01