# Parental psychosocial stress and asthma morbidity in Puerto Rican twins

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**Background: Little is known about paternal psychosocial factors and childhood asthma.**
**Objective: We sought to examine the link between maternal and paternal psychosocial stress and asthma outcomes in young children.**
**Methods: Parents of 339 pairs of Puerto Rican twins were interviewed individually about their own psychosocial stress and about asthma in their children at age 1 year and again about their child's asthma at age 3 years. Fathers were asked about symptoms of posttraumatic stress disorder (PTSD), depression, and antisocial behavior. Mothers were asked about depressive symptoms. Outcomes assessed in children included recent asthma symptoms, oral steroid use and hospitalizations for asthma in the prior year, and asthma diagnosis. Generalized estimated equation models were used for the multivariate analysis of parental psychosocial stress and asthma morbidity in childhood.**
**Results: After multivariable adjustment, paternal PTSD symptoms, depression, and antisocial behavior were each associated with increased asthma symptoms at age 1 year (eg, odds ratio, 1.08 for each 1-point increase in PTSD score; 95% CI, 1.03-1.14). Maternal depressive symptoms were associated with an increased risk of asthma hospitalizations at age 1 year. At age 3 years, maternal depressive symptoms were associated with asthma diagnosis and hospitalizations for asthma (odds ratio for each 1-point increase in symptoms, 1.16; 95% CI, 1.00-1.36). In an analysis combining 1- and 3-year outcomes, paternal depression was associated with oral steroid use, maternal depressive symptoms were associated with asthma hospitalizations and asthma diagnosis, and parental depression was associated with hospitalizations for asthma.**
**Conclusions: Both paternal and maternal psychosocial factors can influence asthma morbidity in young Puerto Rican children. (J Allergy Clin Immunol 2011;127:734-40.)**

***Key words:*** *Psychosocial stress, childhood wheeze, Puerto Rico, parental stress, asthma, paternal stress*

Asthma is a global public health problem that affects more than 6.8 million children and adolescents in the United States.[1,2] In this country the urban poor[3,4] are disproportionately affected, and Puerto Ricans have the highest lifetime prevalence of asthma.[5] Although death from asthma is rare, asthma mortality rates are highest among Puerto Ricans in the United States.[6]

There is increasing evidence of a link between stress and both asthma development and control. Psychological stress can be understood as a "social pollutant" that can affect biology when "breathed in,"[7] and it has been associated with difficulties in asthma management,[8,9] impaired functional status,[10] and increased asthma mortality.[11-13] Stress might not only cause asthma morbidity in adults but it can also affect their children.

In healthy children parental stress has been associated with an increased frequency of childhood illnesses and altered immune function.[14] In children with asthma, increased parental stress has been shown to be associated with altered functional status, hospitalizations for asthma,[15] and poor asthma control.[16] Parental stress is associated with an increased risk of asthma or wheeze in childhood.[17,18] Negative life stressors and maternal depression have been shown to be strong predictors of asthma morbidity.[19] The majority of previous studies have focused on maternal or "caregiver" stress more generally, without specifying whether this is the mother, father, or another person.

In addition to high rates of asthma, island Puerto Ricans have a high prevalence of psychosocial stress in both adults and children, mostly related to high levels of exposure to violence[20] and high levels of poverty, with 45% of the population living below the poverty level.[21] The prevalence rates of psychiatric disorders in island Puerto Ricans are high but comparable with those reported for the overall population of the mainland United States (approximately 25% in adults[22,23] and approximately 17% in children and adolescents[24]).

To examine the issue of parental stress and childhood asthma more closely, we analyzed the relation between indicators of parental psychosocial stress individually in mothers and fathers and asthma morbidity in a cohort of young Puerto Rican twins. We hypothesized that maternal and paternal psychosocial stress would be independently associated with increased asthma morbidity in children.

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*Abbreviations used*
CIDI 3.0: Composite International Diagnostic Interview version 3.0
DSM-IV: *Diagnostic and Statistical Manual of Mental Disorders, Fourth Edition*
ETS: Environmental tobacco smoke
PTSD: Posttraumatic stress disorder

# METHODS

## Population

All families with a multiple-gestation pregnancy in Puerto Rico in 2006 were considered for inclusion. Contact information was obtained from the Puerto Rico Neo-natal Twin Registry established with the assistance of the Puerto Rican Department of Health. Of the 481 families with multiple births in 2006, 82 were ineligible because the neonates were triplets or at least 1 twin was deceased. Of the 399 eligible families, 60 chose not to participate, leaving 339 (85%) families each with a set of twins (see Fig E1 in this article's Online Repository at www.jacionline.org). Although the original goal of this study (the Puerto Rican Infant Twin Study) was to examine the origins of child temperament, families were not selected for any illness. Mothers and fathers were interviewed separately and asked questions about demographic information (eg, household income and education level), child behavior and medical history, and their own psychological stress and medical history (including smoking and substance abuse) within the first year of life of the children. They were again interviewed about their children's medical history when the children were 3 years of age. Written informed consent was obtained from all study participants. The study was approved by the Institutional Review Board of the University of Puerto Rico.

## Measures

**Psychosocial stress.** Mothers and fathers were each questioned about psychosocial stress within the first year of life of their children. Maternal questionnaires included questions on depressive symptoms. Paternal questionnaires included questions on posttraumatic stress disorder (PTSD), antisocial behavior, and depression.

We used the Mood and Feelings Questionnaire[25,26] to ask mothers about depressive symptoms. The Mood and Feelings Questionnaire, an instrument designed for the evaluation of core depressive symptomatology and use in epidemiologic studies, has high internal reliability (Cronbach $\alpha = 0.9$). Although developed primarily for use in children and adolescents, it has been used previously in studies of adults.[27] The questions asked of mothers are listed in Table E1 in this article's Online Repository at www.jacionline.org.

Fathers were asked questions from the World Health Organization Composite International Diagnostic Interview version 3.0 (CIDI 3.0).[28] The CIDI 3.0 is a standardized diagnostic interview designed to assess current and lifetime mental disorders according to the definitions and criteria of the American Psychiatric Association's *Diagnostic and Statistical Manual of Mental Disorders, Fourth Edition* (DSM-IV). The instrument was translated and adapted for use among Spanish-speaking populations by using a comprehensive process guided by a conceptual model that focused on cross-cultural equivalence in 5 dimensions following a cultural adaptation model described in detail elsewhere.[29] For most DSM-IV diagnoses in both English and Spanish, the instrument has demonstrated adequate concordance based on the World Mental Health–CIDI assessments and the Structured Clinical Interview for Axis 1 Disorders.[30,31] A full list of questions can be found at http://www.hcp.med.harvard.edu/wmhcidi. DSM-IV disorders assessed in fathers included major depressive episode, social phobia, and drug and alcohol use and abuse. For the purposes of this analysis, we used major depressive episode from this questionnaire because of the low prevalence of other diagnoses (eg, substance abuse). Questions on PTSD symptoms were from the CIDI 3.0. All symptom questions from the CIDI 3.0 PTSD instrument were included; however, questions on traumatic events were altered. Questions on antisocial behavior were based on the standard DSM-IV criteria and developed by Lish et al.[32] This instrument has been used in prior studies with island and mainland Puerto Ricans.[33] Specific questions on PTSD and antisocial behavior are listed in Tables E2 to E3 of this article's Online Repository at www.jacionline.org.

A diagnosis of a major depressive episode was based on algorithms developed by the originators of the CIDI based on the DSM-IV.[34] Paternal PTSD and antisocial behavior and maternal depressive symptoms were assessed on a continuous scale with the answer of "yes" to any one question equaling 1 point in the score and a higher score representing more symptoms of each disorder. The total possible scores for PTSD, antisocial behavior, and depression were 17, 13, and 11, respectively. For the analysis considering depression in both parents, maternal depression was treated as a dichotomous variable, with a score for depressive symptoms of 2 or higher considered positive for depression.

**Other measures.** Other measures considered for inclusion in the multivariate analysis were child's sex, zygosity of the twins (monozygotic vs dizygotic), exposure to environmental tobacco smoke (ETS; including both *in utero* exposure and exposure from any active smoker in the household), paternal history of asthma, maternal history of asthma, parental (either parent with) history of asthma, gestational age, parental togetherness (defined as maternal report that the parents were living together), and indicators of socioeconomic status (household income, parental education [defined as the highest level attained by either parent], and receipt of public assistance).

**Outcomes.** Outcomes assessed at 1 year of age included parental report of asthma symptoms in the previous 4 weeks (nighttime symptoms, daytime symptoms, or use of albuterol), use of oral steroids in the previous year for asthma, asthma hospitalizations in the previous year, and physician-diagnosed asthma (see Table E4 in this article's Online Repository at www.jacionline.org). At age 3 years, parents for 312 (92%) of the 339 original families completed follow-up interviews. Outcomes assessed at age 3 years included parental report of an unplanned clinic or emergency department visit for asthma in the previous year, use of oral steroids in the previous year for asthma, asthma hospitalizations in the previous year, and asthma diagnosis (defined as physician-diagnosed asthma with wheezing in the previous year; see Table E5 in this article's Online Repository at www.jacionline.org). All outcomes combined the responses from mother and father such that an answer of "yes" by either the father or the mother was considered positive.

## Statistical analysis

To control for the correlation between twins in a household, we used generalized estimated equation analysis as implemented in PROC GENMOD in SAS version 9.1 (SAS Institute, Inc, Cary, NC). Stepwise regression was used to build multivariate models. Variables associated at a $P$ value of less than .20 and potential confounders were included in initial models for each outcome. The final models included all variables that were associated with the outcome at a $P$ value of less than .05, those that caused a change of greater than 10% in the effect estimate for the psychosocial exposure of interest, or both. All final models for outcome at age 1 year included ETS, household income, gestational age, and parental history of asthma. Models examining paternal psychosocial stress controlled for maternal depressive symptoms, and models examining maternal depressive symptoms controlled for paternal depression. Final models for outcomes at age 3 years included household income and parental history of asthma because no other variables (eg, ETS) were significant confounders. At both time points, we also examined parental depression as a linear variable, with values of 0, 1, or 2 representing the number of parents with depression.

In addition, for the outcomes that were in common at the 2 time points (steroid use, asthma hospitalizations, and asthma diagnosis), we performed a combined analysis of a binary outcome that represented an answer of "yes" at both time points or "no" at both time points. For this analysis, those with an answer of "yes" at one time point and "no" at the other were excluded to have a clear separation of the 2 groups.

# RESULTS

Baseline characteristics of the participating children (twins) and their parents are shown in Table I. Of the 339 fathers, 226

**TABLE I.** Baseline characteristics of parents and children from the Puerto Rican Infant Twin Study

| | No. (children) | No. (%) | Median (IQR) |
|---|---|---|---|
| Age | 678 | | 6 mo (4.3-9.5 mo) |
| Sex (% female) | 678 | 352 (52) | |
| Monozygotic | 678 | 240 (35) | |
| ETS | 678 | 111 (16) | |
| Maternal asthma | 672 | 162 (24) | |
| Paternal asthma | 584 | 110 (19) | |
| Parental asthma (either parent) | 678 | 246 (36) | |
| Household income (% above median) | 658 | 246 (37) | |
| Public assistance (% receiving) | 678 | 346 (51) | |
| Parental education (% ≥high school) | 678 | 600 (89) | |
| Gestational age | 662 | | 35 wk (34-37 wk) |
| Psychosocial measures | No. (parents) | | |
| Paternal PTSD | 339 | | 1 (0-5) |
| Paternal major depressive episode | 292 | 12 (4) | |
| Paternal antisocial behavior | 339 | | 13 (11-13) |
| Maternal depressive symptoms | 310 | | 2.0 (1-5) |
| Parental depression | 586 | | |
| Neither parent | | 292 (50) | |
| 1 Parent | | 274 (47) | |
| Both parents | | 20 (3) | |
| Outcomes (1 y of age) | No. (children) | | |
| Asthma symptoms (last 4 wk) | 678 | 411 (61) | |
| Oral steroid use (last 12 mo) | 678 | 121 (18) | |
| Hospitalizations for asthma (last 12 mo) | 678 | 61 (9) | |
| Asthma diagnosis | 671 | 127 (19) | |
| Outcomes (3 y of age) | | | |
| Urgent MD or ED visits (12 mo) | 624 | 95 (15) | |
| Oral steroid use (last 12 mo) | 624 | 147 (24) | |
| Hospitalizations for asthma (last 12 mo) | 624 | 53 (8) | |
| Asthma diagnosis | 624 | 152 (24) | |

*ED*, Emergency department; *MD*, physician's office.

(77%) had at least a high school education, and 207 (71%) were working full time; their mean age was 29.8 years (SD, 7 years). Of the 339 mothers, 277 (82%) had at least a high school education, and 118 (35%) were working either full or part time; their mean age was 26.8 years (SD, 6 years). Most (84%) of the 339 parental couples lived together.

Parental asthma, receipt of public assistance, and a household income lower than the median for Puerto Rico were all common among participants. Both a major depressive episode and PTSD were less common in participating fathers than previously reported in Puerto Ricans.[22] Depression in at least 1 parent was common. Consistent with prior data, asthma diagnosis was frequent among participating children at both time points.

## Outcomes at age 1 year

The results of the bivariate analyses of the relation between asthma outcomes and either psychosocial measures or other covariates (adjusted only for the correlation between twins) are shown in Table II. Paternal PTSD symptoms were significantly associated with recent asthma symptoms, use of oral steroids, and asthma diagnosis in their children. A paternal major depressive episode was strongly associated with use of oral steroids, asthma hospitalizations in the prior year, and asthma diagnosis in their children. Maternal depressive symptoms were associated with asthma hospitalizations in their children. The following variables were not significantly associated with any outcome: parental education, household income, twin zygosity, parental togetherness, and gestational age.

The results of the multivariate analyses of psychosocial measures and asthma outcomes at age 1 year are shown in Table III. In these analyses paternal PTSD, a major depressive episode, antisocial behavior, and maternal depressive symptoms were each significantly associated with recent asthma symptoms in children. Maternal depressive symptoms showed a trend toward association with asthma hospitalizations in children. Parental depression also showed a strongly significant association with recent asthma symptoms, such that each additional parent with depression was associated with a 1.70 increase in the odds of recent asthma symptoms. Associations with other outcomes were no longer significant after adjustment for confounders.

## Outcomes at age 3 years

In the bivariate analyses of psychosocial measures and outcomes at age 3 years, there were several significant associations (see Table IV), particularly with parental depression. In the multivariate analysis adjusting for paternal depression and other covariates (Table V), maternal depressive symptoms were significantly associated with asthma hospitalizations and asthma diagnosis. Paternal depression showed a non–statistically significant trend for an association with oral steroid use in children. When parental depression was examined as a linear variable (0, 1, or 2 parents with depression), there was a borderline significant association with higher rates of oral steroid use and asthma hospitalizations in the previous year. No significant associations were found with outcomes at age 3 years for paternal PTSD or antisocial behavior.

## Combined analysis

The results from the combined analysis of the 2 time points are shown in Table VI. Paternal depression was associated with recurrent oral steroid use for asthma. Maternal depressive symptoms were associated with recurrent hospitalizations for asthma and were borderline significantly associated with asthma diagnosis ($P = .053$). Parental depression was associated with recurrent hospitalizations for asthma.

# DISCUSSION

After adjustment for depression in the other parent and other covariates, we found that indicators of paternal psychosocial stress (PTSD symptoms) and psychiatric disorders (major depressive episode and antisocial behavior) were significantly

**TABLE II.** Bivariate analyses of the relation among psychosocial measures, covariates, and asthma outcomes at 1 year of age*

| | Asthma symptoms | | Oral steroids | | Hospitalizations for asthma | | Asthma diagnosis | |
|---|---|---|---|---|---|---|---|---|
| **Variable** | **OR (95% CI)** | ***P* value** | **OR (95% CI)** | ***P* value** | **OR (95% CI)** | ***P* value** | **OR (95% CI)** | ***P* value** |
| Psychosocial measures | | | | | | | | |
| Paternal PTSD | **1.10 (1.05-1.16)** | **<.001** | **1.06 (1.01-1.12)** | **.03** | 1.06 (0.99-1.12) | .1 | **1.06 (1.00-1.12)** | **.03** |
| Paternal major depressive episode | 4.10 (0.87-19.42) | .08 | **3.29 (1.11-9.70)** | **.03** | **5.10 (1.84-14.11)** | **.002** | **3.21 (1.08-9.46)** | **.03** |
| Paternal antisocial behavior | **1.08 (1.04-1.14)** | **<.001** | 1.05 (0.98-1.12) | .18 | 1.07 (0.98-1.16) | .13 | 1.02 (0.96-1.08) | .52 |
| Maternal depressive symptoms | 1.07 (0.98-1.17) | .13 | 1.04 (0.93-1.16) | .51 | **1.21 (1.06-1.38)** | **.004** | 1.02 (0.91-1.14) | .68 |
| Maternal depression (≥ median) | 1.25 (0.845-1.86) | .26 | 0.88 (0.52-1.47) | .61 | 1.39 (0.72-2.70) | .33 | 0.88 (0.53-1.46) | .62 |
| Parental depression | **1.59 (1.08-2.33)** | **.02** | 1.16 (0.70-1.92) | .56 | 1.79 (0.96-3.33) | .07 | 1.24 (0.76-2.03) | .4 |
| Covariates | | | | | | | | |
| ETS | 1.28 (0.77-2.12) | .34 | 1.55 (0.86-2.80) | .14 | **2.42 (1.19-4.92)** | **.01** | 1.45 (0.80-2.6) | .21 |
| Parental history of asthma | 1.42 (0.94-2.14) | .09 | **2.97 (1.76-5.03)** | **<.001** | **1.93 (0.99-3.75)** | **.050** | **2.62 (1.60-4.36)** | **<.001** |
| Female (vs male) sex | 1.02 (0.76-1.35) | .92 | 0.84 (0.58-1.21) | .34 | **0.48 (0.29-0.81)** | **.006** | 0.83 (0.58-1.18) | .31 |
| Median income† | 0.70 (0.46-1.08) | .11 | 1.05 (0.61-1.81) | .86 | 1.36 (0.66-2.77) | .4 | 1.06 (0.62-1.8) | .83 |
| Public assistance‡ | 0.71 (0.48-1.06) | .09 | **1.80 (1.06-3.05)** | **.03** | **2.48 (1.21-5.05)** | **.01** | **1.90 (1.10-3.2)** | **.02** |
| Parental education§ | 1.02 (0.55-1.88) | .96 | 0.69 (0.34-1.41) | .31 | 0.63 (0.26-1.55) | .32 | 0.58 (0.3-1.14) | .12 |
| Gestational age | 1.01 (0.95-1.08) | .69 | 1.05 (0.97-1.13) | .26 | 0.97 (0.87-1.08) | .63 | 1.05 (0.97-1.14) | .22 |

*OR*, Odds ratio.
*All analyses are adjusted for the correlation between twins.
†Reference group: household income greater than $18,000.
‡Reference group: families not receiving public assistance.
§Reference group: high school education or greater.

**TABLE III.** Multivariate analysis of parental psychosocial measures and asthma outcomes at 1 year of age*

| | Asthma symptoms | | Hospitalizations for asthma | |
|---|---|---|---|---|
| **Measures** | **OR (95% CI)** | ***P* value** | **OR (95% CI)** | ***P* value** |
| Paternal PTSD† | **1.08 (1.03-1.14)** | **.003** | 1.02 (0.94-1.10) | .69 |
| Paternal major depressive episode† | **9.95 (1.38-71.59)** | **.02** | 1.43 (0.25-8.31) | .69 |
| Paternal antisocial behavior† | **1.09 (1.04-1.15)** | **<.001** | 1.08 (0.97-1.20) | .17 |
| Maternal depressive symptoms‡ | **1.13 (1.02-1.25)** | **.02** | 1.14 (0.98-1.33) | .09 |
| Parental depression | **1.70 (1.14-2.53)** | **.01** | 1.21 (0.62-2.35) | .58 |

*OR*, Odds ratio.
*All models are adjusted for parental history of asthma, ETS, household income, gestational age, and the correlation between twins.
†Paternal models are also adjusted for maternal depressive symptoms.
‡The maternal model is also adjusted for paternal depression.

**TABLE IV.** Bivariate analyses between psychosocial measures and outcomes at 3 years of age*

| | ED/MD visits | | Oral steroids | | Hospitalizations for asthma | | Asthma diagnosis | |
|---|---|---|---|---|---|---|---|---|
| | **OR (95% CI)** | ***P* value** | **OR (95% CI)** | ***P* value** | **OR (95% CI)** | ***P* value** | **OR (95% CI)** | ***P* value** |
| Paternal PTSD | 1.05 (0.99-1.12) | .12 | 1.02 (0.96-1.08) | .53 | 1.02 (0.94-1.11) | .63 | 1.04 (0.99-1.09) | .14 |
| Paternal major depressive episode | **3.66 (1.17-11.44)** | **.03** | **3.66 (1.17-11.44)** | **.03** | 2.12 (0.43-10.53) | .36 | 2.24 (0.71-7.10) | .17 |
| Paternal antisocial behavior | 0.95 (0.90-1.01) | .12 | 0.96 (0.92-1.02) | .19 | 0.99 (0.91-1.07) | .76 | 0.98 (0.93-1.04) | .52 |
| Maternal depressive symptoms | 1.11 (0.99-1.23) | .06 | 1.06 (0.96-1.18) | .24 | 1.13 (0.99-1.29) | .06 | **1.13 (1.02-1.24)** | **.02** |
| Parental depression | 1.45 (0.86-2.44) | .16 | **1.60 (0.99-2.56)** | **.054** | **1.88 (1.00-3.53)** | **.050** | 1.51 (0.98-2.31) | .06 |

*ED*, Emergency department; *MD*, physician's office; *OR*, odds ratio.
*All analyses are adjusted for the correlation between twins.

associated with recent asthma symptoms in children at age 1 year but not with any asthma outcome in children at age 3 years. Maternal depressive symptoms were significantly associated with asthma hospitalizations at age 1 year and both asthma hospitalizations and asthma diagnosis at age 3 years. Examining the combined outcomes at ages 1 and 3 years, paternal depression was associated with recurrent oral steroid use, maternal depressive symptoms with hospitalizations for asthma and asthma diagnosis, and parental depression with hospitalizations for asthma.

To our knowledge, this is the first report of an association between maternal depression and asthma outcomes in childhood after accounting for paternal depressive disorder, as well as the first to report an independent association between indicators of paternal psychosocial stress and asthma outcomes in early childhood. Our findings add to a growing body of literature examining the link between psychosocial stress and asthma morbidity generally and specifically psychosocial stress in parents and asthma outcomes in their children.

**TABLE V.** Multivariate analysis of parental psychosocial measures and asthma outcomes at 3 years of age*

| | ED/MD visits | | Oral steroids | | Hospitalizations for asthma | | Asthma diagnosis | |
|---|---|---|---|---|---|---|---|---|
| | OR (95% CI) | *P* value | OR (95% CI) | *P* value | OR (95% CI) | *P* value | OR (95% CI) | *P* value |
| Paternal major depressive episode† | 1.24 (0.25-6.08) | .80 | 3.03 (0.84-10.97) | .09 | 1.42 (0.18-11.15) | .74 | 1.30 (0.32-5.16) | .71 |
| Maternal depressive symptoms‡ | 1.11 (0.98-1.27) | .10 | 1.08 (0.96-1.23) | .20 | **1.16 (1.00-1.36)** | **.050** | **1.13 (1.01-1.27)** | **.03** |
| Parental depression (linear) | 1.36 (0.76-2.41) | .30 | 1.61 (0.97-2.66) | .067 | **1.86 (0.98-3.56)** | **.060** | 1.42 (0.91-2.21) | .12 |

*ED*, Emergency department; *MD*, physician's office; *OR*, Odds ratio.
*Adjusted for household income, parental asthma, and correlation between twins (ETS and gestational age are not significant confounders).
†Paternal model is also adjusted for maternal depressive symptoms.
‡Maternal model is also adjusted for paternal depression.

**TABLE VI.** Analysis of combined outcomes at 1 and 3 years of age*

| | Oral steroids | | Hospitalizations for asthma | | Asthma diagnosis† | |
|---|---|---|---|---|---|---|
| | OR (95% CI) | *P* value | OR (95% CI) | *P* value | OR (95% CI) | *P* value |
| Paternal major depressive episode‡ | **5.66 (1.06-30.19)** | **.04** | 6.36 (0.33-123.35) | .22 | 1.79 (0.31-10.48) | .52 |
| Maternal depressive symptoms§ | 1.05 (0.88-1.26) | .56 | **1.26 (1.01-1.58)** | **.04** | **1.15 (1.00-1.33)** | **.053** |
| Parental depression (linear) | 1.51 (0.70-3.28) | .29 | **4.08 (1.14-14.66)** | **.03** | 1.36 (0.74-2.48) | .32 |

*OR*, Odds ratio.
*Outcomes are binary and considered positive if the child experienced the outcome at both time points and negative if the child did not experience the outcome at both time points. Children with the outcome at one time point but not at the other were excluded from analysis. All analyses were adjusted for household income, parental asthma, and correlation between twins (ETS and gestational age are not significant confounders).
†The combined outcome of asthma diagnosis was defined as physician-diagnosed asthma at age 1 year and physician-diagnosed asthma at age 3 years plus wheezing in the last year.
‡The paternal model is also adjusted for maternal depressive symptoms.
§The maternal model is also adjusted for paternal depression.

Consistent with prior studies examining maternal (but not paternal) depression,[17-19] we found that maternal depression was associated with asthma symptoms, hospitalizations for asthma, and asthma diagnosis in childhood after accounting for paternal depression. Previous studies of maternal depression and asthma have assessed children at various age groups and used various indicators of life or psychological stress. Some studies did not control for smoking,[15,19] which might partly explain the effects of stress or psychiatric disorders on asthma.[35] Together with prior findings, our results emphasize the importance of symptoms of psychosocial stress and not just psychiatric diagnoses in the relationship between stress and asthma.

No prior studies have examined the independent effects of paternal stress on asthma outcomes. Although associations between paternal depression and outcomes at age 3 years were not statistically significant, there was a trend toward association with increased use of oral steroids, which might have been significant with a larger sample size. Examining the combined 1- and 3-year outcomes, paternal depression was strongly associated with recurrent oral steroid use for asthma. Furthermore, no studies have looked at the combined effect of parental depression. We found a significant effect of each additional parent with depression on increased risk of recent asthma symptoms at age 1 year and found a trend toward association with steroid use, asthma hospitalizations, and asthma diagnosis at age 3 years. In the combined analysis we found a significant effect of parental depression on recurrent hospitalizations for asthma.

Comorbid asthma and psychosocial stress, specifically depression, have been well documented in both children and adults.[36,37] A broad range of biological mechanisms have been implicated in this association.[7,38-42] Parental stress has been associated with altered immune responses relevant to atopic disorders in childhood. Caregiver stress has been associated with increased total and allergen-specific IgE levels,[43] and parental stress has been linked to increased IL-4 and eosinophilic cationic protein release[44] in children. Compared with children with acute but no chronic family stress, those with acute and chronic family stress have increased levels of IL-4, IL-5, and IFN-γ.[45] Prior studies have shown decreased expression of glucocorticoid and $\beta_2$-adrenergic receptors,[46] which might lead to a decreased response to asthma medications.[8] Although studies on maternal stress focus on alterations in *in utero* exposure to certain hormones as a result of stress, postnatal events, such as early-life stress resulting from either parent's behavior, can plausibly affect child responses.[18] One potentially important mechanism by which this has been shown to occur in animal models is through DNA methylation.[47]

Behavioral effects might also contribute to the association between parental stress and childhood asthma. Psychological stress, especially depression, can affect parenting skills,[48] and affected parents might be less able to supervise their children's treatment. Alternatively, parental stress might influence the perception or reporting of asthma symptoms in their children.

Our findings have important implications. Discovering modifiable risk factors that can affect immune system development in early life[39] is essential in stemming the increasing prevalence of asthma and in intervening in particularly vulnerable groups, such as Puerto Ricans.[5,49] Island Puerto Ricans might be both more frequently exposed and more susceptible to psychosocial stressors[50,51] than other ethnic groups, with important health consequences in children.[52] Psychosocial stress, specifically depression, is treatable, and successful therapy of these disorders might affect the lives of parents and children alike.

The strengths of our study include a random sample of children (albeit of twins only) in a group with high asthma prevalence

(Puerto Ricans) but no specific bias as to socioeconomic or other factors. In addition, mothers and fathers were questioned independently rather than having one parent answer for both.

Our study has several limitations. First, the young age of the children precludes an accurate diagnosis of asthma, and questionnaires did not differentiate whether wheezing was due to a concurrent respiratory tract infection, a frequent cause of wheezing in young children. However, early childhood wheezing is a risk factor for subsequent asthma,[53-56] and childhood wheezing and hospitalizations, regardless of whether the children go on to have asthma, are an important cause of morbidity in young children.[57] Having outcomes at both 1 and 3 years of age and combining these outcomes strengthens the analysis because recurrent need for steroids or hospitalizations for asthma makes the diagnosis of asthma more likely.

Second, we did not have information on the presence of older siblings, which can affect both parental stress and asthma.

Third, some of the measures of psychosocial stress, specifically PTSD and antisocial behavior in fathers and depressive symptoms in mothers, were based on standardized questions but were not part of a diagnostic algorithm. However, our findings suggest that parental symptoms suggestive of these disorders, even without a definitive diagnosis, might be associated with asthma morbidity in childhood.

Fourth, associations do not prove causality. Although prior research has shown a bidirectional association between psychosocial factors and asthma,[58] we cannot establish whether parental psychosocial stress leads to increased asthma morbidity in young children or *vice versa*, particularly at age 1 year.

Finally, some data suggest that having twins might increase psychosocial stress for parents.[59,60] If this is the case, our cohort would be enriched to study parental stress and asthma. However, we cannot state this definitively without a control population.

In summary, our study showed a significant association between both maternal and paternal psychosocial stress and asthma morbidity in early childhood. More specifically, both maternal and paternal depression were associated with increased asthma morbidity at 1 and 3 years of age. Although further studies are warranted, our work suggests that parental psychosocial stress, especially parental depression, might be an important modifiable risk factor for asthma morbidity in childhood, especially in high-risk populations.

We thank all of the participants and staff involved in the Puerto Rican Infant Twin Study.

**Clinical implications: Both maternal and paternal psychosocial stress are associated with asthma morbidity in children. Further studies are needed to elucidate possible mechanisms and investigate interventions, especially for high-risk groups.**

## REFERENCES

1. American Lung Association. Trends in asthma morbidity and mortality. New York: American Lung Association; 2009.
2. American Lung Association. Asthma & children fact sheet. New York: American Lung Association; 2010.
3. Akinbami L. The state of childhood asthma, United States, 1980-2005. Adv Data 2006;(381):1-24.
4. Crocker D, Brown C, Moolenaar R, Moorman J, Bailey C, Mannino D, et al. Racial and ethnic disparities in asthma medication usage and health-care utilization: data from the National Asthma Survey. Chest 2009;136:1063-71.
5. Lara M, Akinbami L, Flores G, Morgenstern H. Heterogeneity of childhood asthma among Hispanic children: Puerto Rican children bear a disproportionate burden. Pediatrics 2006;117:43-53.
6. Homa DM, Mannino DM, Lara M. Asthma mortality in U.S. Hispanics of Mexican, Puerto Rican, and Cuban heritage, 1990-1995. Am J Respir Crit Care Med 2000;161:504-9.
7. Wright RJ, Cohen RT, Cohen S. The impact of stress on the development and expression of atopy. Curr Opin Allergy Clin Immunol 2005;5:23-9.
8. Haczku A, Panettieri RA Jr. Social stress and asthma: the role of corticosteroid insensitivity. J Allergy Clin Immunol 2010;125:550-8.
9. Wisnivesky JP, Lorenzo J, Feldman JM, Leventhal H, Halm EA. The relationship between perceived stress and morbidity among adult inner-city asthmatics. J Asthma 2010;47:100-4.
10. Moonie S, Sterling DA, Figgs LW, Castro M. The relationship between school absence, academic performance, and asthma status. J Sch Health 2008;78:140-8.
11. Strunk RC, Mrazek DA, Fuhrmann GS, LaBrecque JF. Physiologic and psychological characteristics associated with deaths due to asthma in childhood. A case-controlled study. JAMA 1985;254:1193-8.
12. Tough SC, Hessel PA, Ruff M, Green FH, Mitchell I, Butt JC. Features that distinguish those who die from asthma from community controls with asthma. J Asthma 1998;35:657-65.
13. Mitchell I, Tough SC, Semple LK, Green FH, Hessel PA. Near-fatal asthma: a population-based study of risk factors. Chest 2002;121:1407-13.
14. Caserta MT, O'Connor TG, Wyman PA, Wang H, Moynihan J, Cross W, et al. The associations between psychosocial stress and the frequency of illness, and innate and adaptive immune function in children. Brain Behav Immun 2008;22:933-40.
15. Weil CM, Wade SL, Bauman LJ, Lynn H, Mitchell H, Lavigne J. The relationship between psychosocial factors and asthma morbidity in inner-city children with asthma. Pediatrics 1999;104:1274-80.
16. Sharp LK, Curtis LM, Mosnaim G, Shalowitz MU, Catrambone C, Sadowski LS. The influence of caregiver's psychosocial status on childhood asthma and obesity. Ann Allergy Asthma Immunol 2009;103:386-94.
17. 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;165:358-65.
18. Kozyrskyj AL, Mai XM, McGrath P, Hayglass KT, Becker AB, Macneil B. Continued exposure to maternal distress in early life is associated with an increased risk of childhood asthma. Am J Respir Crit Care Med 2008;177:142-7.
19. Shalowitz MU, Berry CA, Quinn KA, Wolf RL. The relationship of life stressors and maternal depression to pediatric asthma morbidity in a subspecialty practice. Ambul Pediatr 2001;1:185-93.
20. Martinez-Taboas A, Canino G, Wang MQ, Garcia P, Bravo M. Prevalence and victimization correlates of pathological dissociation in a community sample of youths. J Trauma Stress 2006;19:439-48.
21. U.S. Census Bureau 2006-2008 American community survey 3-year estimates. Suitland (Md): U.S. Census Bureau; 2008.
22. Canino GJ, Bird HR, Shrout PE, Rubio-Stipec M, Bravo M, Martinez R, et al. The prevalence of specific psychiatric disorders in Puerto Rico. Arch Gen Psychiatry 1987;44:727-35.
23. Shrout PE, Canino GJ, Bird HR, Rubio-Stipec M, Bravo M, Burnam MA. Mental health status among Puerto Ricans, Mexican Americans, and non-Hispanic whites. Am J Community Psychol 1992;20:729-52.
24. Canino G, Shrout PE, Rubio-Stipec M, Bird HR, Bravo M, Ramirez R, et al. The DSM-IV rates of child and adolescent disorders in Puerto Rico: prevalence, correlates, service use, and the effects of impairment. Arch Gen Psychiatry 2004;61:85-93.
25. Mood and Feelings Questionnaire (MFQ) and references. Available at: http://devepi.duhs.duke.edu/mfq.html. Accessed August 9, 2010.
26. Angold A, Costello EJ, Messer S. Development of a short questionnaire for use in epidemiological studies of depression in children and adolescents. Int J Methods Psychiatr Res 1995;5:237-49.
27. Silberg JL, Maes H, Eaves LJ. Genetic and environmental influences on the transmission of parental depression to children's depression and conduct disturbance: an extended Children of Twins study. J Child Psychol Psychiatry 2010;51:734-44.
28. Kessler RC, Ustun TB. The World Mental Health (WMH) Survey Initiative Version of the World Health Organization (WHO) Composite International Diagnostic Interview (CIDI). Int J Methods Psychiatr Res 2004;13:93-121.
29. Alegria M, Vila D, Woo M, Canino G, Takeuchi D, Vera M, et al. Cultural relevance and equivalence in the NLAAS instrument: integrating etic and emic in the development of cross-cultural measures for a psychiatric epidemiology and services study of Latinos. Int J Methods Psychiatr Res 2004;13:270-88.
30. Haro JM, Arbabzadeh-Bouchez S, Brugha TS, de Girolamo G, Guyer ME, Jin R, et al. Concordance of the Composite International Diagnostic Interview Version 3.0 (CIDI 3.0) with standardized clinical assessments in the WHO World Mental Health surveys. Int J Methods Psychiatr Res 2006;15:167-80.

31. Alegria M, Shrout PE, Torres M, Lewis-Fernandez R, Abelson JM, Powell M, et al. Lessons learned from the clinical reappraisal study of the Composite International Diagnostic Interview with Latinos. Int J Methods Psychiatr Res 2009;18:84-95.
32. Lish JD, Weissman MM, Adams PB, Hoven CW, Bird H. Family psychiatric screening instruments for epidemiologic studies: pilot testing and validation. Psychiatry Res 1995;57:169-80.
33. Bird HR, Davies M, Duarte CS, Shen S, Loeber R, Canino GJ. A study of disruptive behavior disorders in Puerto Rican youth: II. Baseline prevalence, comorbidity, and correlates in two sites. J Am Acad Child Adolesc Psychiatry 2006;45:1042-53.
34. American Psychiatric Association. Diagnostic and statistical manual of mental disorders, Fourth Edition. Washington (DC): American Psychiatric Association; 1994.
35. Goodwin RD, Canino G, Ortega AN, Bird HR. Maternal mental health and childhood asthma among Puerto Rican youth: the role of prenatal smoking. J Asthma 2009;46:726-30.
36. Oraka E, King ME, Callahan DB. Asthma and serious psychological distress: prevalence and risk factors among US adults, 2001-2007. Chest 2010;137:609-16.
37. Prosser R, Carleton B, Smith A. The comorbidity burden of the treated asthma patient population in British Columbia. Chronic Dis Can 2010;30:46-55.
38. Chida Y, Sudo N, Sonoda J, Hiramoto T, Kubo C. Early-life psychological stress exacerbates adult mouse asthma via the hypothalamus-pituitary-adrenal axis. Am J Respir Crit Care Med 2007;175:316-22.
39. Chrousos GP. Stress, chronic inflammation, and emotional and physical well-being: concurrent effects and chronic sequelae. J Allergy Clin Immunol 2000;106(suppl): S275-91.
40. Dreger LC, Kozyrskyj AL, HayGlass KT, Becker AB, MacNeil BJ. Lower cortisol levels in children with asthma exposed to recurrent maternal distress from birth. J Allergy Clin Immunol 2010;125:116-22.
41. Undem BJ, Kajekar R, Hunter DD, Myers AC. Neural integration and allergic disease. J Allergy Clin Immunol 2000;106(suppl):S213-20.
42. Wright RJ, Rodriguez M, Cohen S. Review of psychosocial stress and asthma: an integrated biopsychosocial approach. Thorax 1998;53:1066-74.
43. Wright RJ, Finn P, Contreras JP, Cohen S, Wright RO, Staudenmayer J, 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;113:1051-7.
44. Wolf JM, Miller GE, Chen E. Parent psychological states predict changes in inflammatory markers in children with asthma and healthy children. Brain Behav Immun 2008;22:433-41.
45. Marin TJ, Chen E, Munch JA, Miller GE. Double-exposure to acute stress and chronic family stress is associated with immune changes in children with asthma. Psychosom Med 2009;71:378-84.
46. Miller GE, Chen E. Life stress and diminished expression of genes encoding glucocorticoid receptor and beta2-adrenergic receptor in children with asthma. Proc Natl Acad Sci U S A 2006;103:5496-501.
47. Murgatroyd C, Patchev AV, Wu Y, Micale V, Bockmuhl Y, Fischer D, et al. Dynamic DNA methylation programs persistent adverse effects of early-life stress. Nat Neurosci 2009;12:1559-66.
48. Mrazek DA, Klinnert MD, Mrazek P, Macey T. Early asthma onset: consideration of parenting issues. J Am Acad Child Adolesc Psychiatry 1991;30:277-82.
49. Cohen RT, Canino GJ, Bird HR, Shen S, Rosner BA, Celedon JC. Area of residence, birthplace, and asthma in Puerto Rican children. Chest 2007;131: 1331-8.
50. Galea S, Vlahov D, Tracy M, Hoover DR, Resnick H, Kilpatrick D. Hispanic ethnicity and post-traumatic stress disorder after a disaster: evidence from a general population survey after September 11, 2001. Ann Epidemiol 2004;14:520-31.
51. Ortega AN, Rosenheck R. Posttraumatic stress disorder among Hispanic Vietnam veterans. Am J Psychiatry 2000;157:615-9.
52. Graham-Bermann SA, Seng J. Violence exposure and traumatic stress symptoms as additional predictors of health problems in high-risk children. J Pediatr 2005;146: 349-54.
53. Ly NP, Gold DR, Weiss ST, Celedon JC. Recurrent wheeze in early childhood and asthma among children at risk for atopy. Pediatrics 2006;117:e1132-8.
54. Martinez FD, Wright AL, Taussig LM, Holberg CJ, Halonen M, Morgan WJ. Asthma and wheezing in the first six years of life. The Group Health Medical Associates. N Engl J Med 1995;332:133-8.
55. Jackson DJ, Gangnon RE, Evans MD, Roberg KA, Anderson EL, Pappas TE, et al. Wheezing rhinovirus illnesses in early life predict asthma development in high-risk children. Am J Respir Crit Care Med 2008;178:667-72.
56. Kusel MM, de Klerk NH, Kebadze T, Vohma V, Holt PG, Johnston SL, et al. Early-life respiratory viral infections, atopic sensitization, and risk of subsequent development of persistent asthma. J Allergy Clin Immunol 2007;119:1105-10.
57. Wright AL. Epidemiology of asthma and recurrent wheeze in childhood. Clin Rev Allergy Immunol 2002;22:33-44.
58. Chida Y, Hamer M, Steptoe A. A bidirectional relationship between psychosocial factors and atopic disorders: a systematic review and meta-analysis. Psychosom Med 2008;70:102-16.
59. Reinheckel A, Koppe I, Hinze L, Weise W. [Life situation of parents of twins and triplets: a qualitative study]. Z Geburtshilfe Neonatol 2000;204:55-9.
60. Sugimoto M, Yokoyama Y, Wada S, Matsubara M, Saito M, Sono J. [Anxiety and associated factors in mothers of twins or triplets as compared with mothers of singleton children]. Nippon Koshu Eisei Zasshi 2008;55:213-20.

## REFERENCES

E1. Angold A, Costello EJ, Messer S. Development of a short questionnaire for use in epidemiological studies of depression in children and adolescents. Int J Methods Psychiatr Res 1995;5:237-49.

E2. Mood and Feelings Questionnaire (MFQ) and references. Available at: http://devepi.duhs.duke.edu/mfq.html. Accessed August 9, 2010.

E3. Kessler RC, Ustun TB. The World Mental Health (WMH) survey initiative version of the World Health Organization (WHO) composite international diagnostic interview (CIDI). Int J Methods Psychiatr Res 2004;13:93-121.

E4. Lish JD, Weissman MM, Adams PB, Hoven CW, Bird H. Family psychiatric screening instruments for epidemiologic studies: pilot testing and validation. Psychiatry Res 1995;57:169-80.

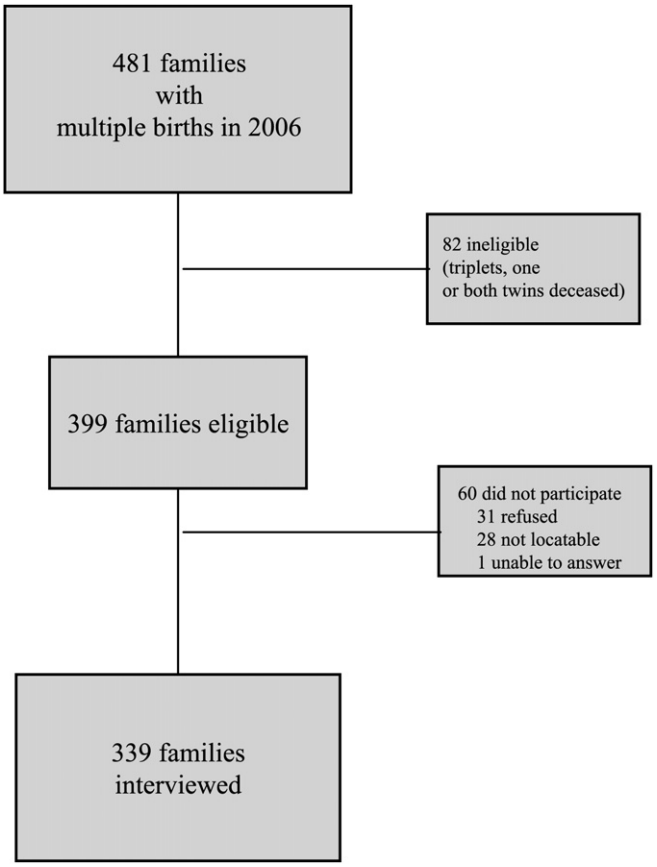



**FIG E1.** Flow chart of subject recruitment and participation.

**TABLE E1.** Questions on maternal depressive symptoms*

| In the last 3 months: |
|---|
| 1. have you felt miserable or unhappy? |
| 2. have you felt you were no good anymore? |
| 3. have you found it hard to think properly or concentrate? |
| 4. have you hated yourself? |
| 5. have you felt lonely? |
| 6. have you felt that you have done everything wrong? |
| 7. has there been a moment that you have felt depressed for at least 2 consecutive weeks? |
| 8. has there been a moment that for 2 weeks or more you have felt a loss of interest for the things or unable to enjoy the things you used to enjoy? |
| 9. have you ever received outpatient treatment for emotional problems? |
| 10. have you ever been hospitalized for emotional problems? |
| 11. have you felt that your (depression, drinking, emotional problems) has interfered with your ability to care for the twins the way you wanted to? |

*From the Mood and Feelings Questionnaire.[E1,E2]

**TABLE E2.** Questions on paternal PTSD*

| In the past year, have you been bothered by … |
|---|
| 1. repeated disturbing memories, thoughts, or images of a stressful experience? |
| 2. repeated disturbing dreams of a stressful experience? |
| 3. suddenly acting or feeling as if a stressful experience were happening again (as if you were reliving it)? |
| 4. feeling very upset when something reminded you of a stressful experience? |
| 5. having physical reactions (eg, heart pounding, trouble breathing, and sweating) when something reminded you of a stressful experience? |
| 6. avoiding thinking about or talking about a stressful experience or avoiding having feelings related to it? |
| 7. avoiding activities or situations because they reminded you of a stressful experience? |
| 8. trouble remembering important parts of a stressful experience? |
| 9. loss of interest in activities that you used to enjoy? |
| 10. feeling distant or isolated from other people? |
| 11. feeling emotionally numb or being unable to have loving feelings for those close to you? |
| 12. feeling as if your future will somehow be cut short? |
| 13. trouble falling or staying asleep? |
| 14. feeling irritable or having angry outbursts? |
| 15. having difficulty concentrating? |
| 16. being "super-alert," watchful, or on guard? |
| 17. feeling jumpy or easily startled? |

*From the World Health Organization CIDI 3.0.[E3]

**TABLE E3.** Questions on paternal antisocial behavior*

| |
|---|
| 1. Have you ever been arrested, in jail, or convicted of a crime other than drunk driving? |
| 2. Since the age of 15 years, have you ever mugged someone to steal money or anything else; broken into a car, a house, or a building; stolen anything from a store or a construction site; or stolen anything in any other way? |
| 3. Since you were 15 years old, have you ever done anything else for which you were arrested or would have been arrested if you had been caught? |
| 4. Have you ever pretended to be sick or physically harmed to collect insurance or any unemployment or disability compensation? |
| 5. Have you ever done anything to deceive others in a serious way, like using a fake name, using a false check, or falsifying a document to obtain some benefit? |
| 6. Are you someone who acts impulsively, without planning ahead, or who changes your plans all of the time? |
| 7. Have you moved repeatedly, leaving an apartment or a house shortly after you moved there, or have you abandoned a spouse or mate after a short time simply because you changed your mind? |
| 8. Have you ever used or threatened to use a stick, a knife, a firearm, a bottle, or a bar to wound or hurt someone else? |
| 9. Are you an irritable and aggressive person or one who frequently gets into physical fights? |
| 10. Do you frequently risk yourself by driving any type of motor vehicle recklessly at high speed in city streets or by driving drunk or high? |
| 11. Are you the type of person who would risk your life or someone else's without taking into consideration your own safety and the safety of others? |
| 12. Have you ever gotten into debts that you could not pay and therefore caused you problems, such as not being able to pay the rent or money you owed or having things repossessed or taken away because you could not keep up with the payments? |
| 13. Are you the type of person who does not meet responsibilities and obligations or does not keep their promises to others? |

*Questions on antisocial behavior were based on the standard DSM-IV criteria and developed by Lish et al.[E4]

**TABLE E4.** Questions for both parents on asthma in their children at 1 year of age

| |
|---|
| Asthma symptoms |
| 1. In the last 4 weeks, how often did (name of child) have trouble with coughing, wheezing, or shortness of breath first thing in the morning or during the day? |
| 2. In the last 4 weeks, how often did (name of child) wake up at night with a cough, wheezing, or shortness of breath? |
| 3. In the last 4 weeks, how often has (name of child) used his or her rescue inhaler or nebulizer medication (such as albuterol)? |
| Oral steroids for asthma |
| In the last 12 months, has (name of child) had any oral steroids (eg, prednisone burst, Prelone)? |
| Hospitalizations for asthma |
| In the last 12 months, has (name of child) been hospitalized for asthma? |
| Asthma diagnosis |
| Has (name of child) ever been given a diagnosis by a doctor as having asthma? |

**TABLE E5.** Questions for both parents on asthma in their children at 3 years of age

| |
|---|
| ED/MD visits for asthma |
| During the last 12 months, have you ever had to take (name of child) to the doctor, clinic, or emergency department so he or she can receive treatment for an asthma attack? |
| Oral steroids for asthma |
| During the last 12 months, has (name of child) had any oral steroids (eg, prednisone burst, Prelone)? |
| Hospitalizations for asthma |
| During the last 12 months, has (name of child) been hospitalized for asthma? |
| Asthma diagnosis* |
| 1. Has (name of child) ever been given a diagnosis by a doctor as having asthma? |
| 2. Has (name of child)'s chest sounded wheezy or whistling during the past 12 months? |

*Considered as "yes" for asthma diagnosis if the answers to both of the above questions were "yes."
*ED*, Emergency department; *MD*, physician's office.