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Parental psychosocial stress and asthma morbidity in Puerto Rican twins

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Abstract

Background—Little is known about paternal psychosocial factors and childhood asthma.

Objective—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 and again about their child's asthma at age 3. Fathers were asked about symptoms of post-traumatic stress disorder (PTSD), depression, and anti-social behavior. Mothers were asked about depressive symptoms. Outcomes assessed in children included recent asthma symptoms, oral steroid use and hospitalizations for

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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.

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 anti-social behavior were each associated with increased asthma symptoms at age 1 (e.g., OR =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 (OR 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 may influence asthma morbidity in young Puerto Rican children.

Keywords

psychosocial stress; childhood wheeze; Puerto Rico; parental stress; asthma; paternal stress

Introduction

Asthma is a global public health problem that affects over 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 T hough death from asthma is rare, asthma mortality rates are highest among Puerto Ricans in the U.S.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 status¹⁰ and increased asthma mortality.^{11–13} Stress may not only cause asthma morbidity in adults but also affect their children.

In healthy children, parental stress has been associated with an increased frequency of childhood illnesses and with 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 violence²⁰ 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 to those reported for the overall population of the mainland U.S. (~25% in adults22, 23 and ~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.

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 Rico Department of Health. Of the 481 families with multiple births in 2006, 82 were ineligible because the neonates were triplets or at least one twin was deceased. Of the 399 eligible families, 60 chose not to participate, leaving 339 (85%) families each with a set of twins. (See Figure E1 in the online repository for more details). Although the original goal of this study (the Puerto Rican Infant Twin Study or PRINTS) was to examine the origins of child temperament, families were not selected for any illness. Mothers and fathers were interviewed separately and asked questions on demographic information (e.g., household income, 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 age 3 years. 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 post-traumatic stress disorder (PTSD) anti-social behavior, and depression.

We used the Mood and Feelings Questionnaire (MFQ)25, 26 to ask mothers about depressive symptoms. The MFQ, an instrument designed for the evaluation of core depressive symptomatology and use in epidemiologic studies, has high internal reliability (Cronbach's 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 the online repository.

Fathers were asked questions from the World Health Organization (WHO) 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 Diagnostic and Statistical Manual of Mental Disorders, 4th edition (DSM-IV). The instrument was translated and adapted for use among Spanish-speaking populations using a comprehensive process guided by a conceptual model that focused on cross-cultural equivalence in five 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, drug and alcohol use and abuse. For the purposes of this analysis, we used major depressive episode from this questionnaire because of low prevalence of other diagnoses (e.g., 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 anti-social 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 Lange et al.

questions on PTSD and anti-social behavior are listed in Table E2–Table E3 of the online repository.

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 anti-social behavior and maternal depressive symptoms were assessed on a continuous scale with the answer of "yes" to any one question equaling one point in the score and a higher score representing more symptoms of each disorder. The total possible scores for PTSD, for anti-social 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 gender, 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 socio-economic status (household income, parental education [defined as the highest level attained by either parent], and receipt of public assistance).

Outcomes

Outcomes assessed at one year of age included parental report of asthma symptoms in the previous four weeks (night 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. (Table E4, online repository) 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). (Table E5, online repository). 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 utilized generalized estimation equation analysis, as implemented in PROC GENMOD in SAS version 9.1 (SAS Institute, Cary, NC, USA). Stepwise regression was used to build multivariate models. Variables associated at p<0.20 and potential confounders were included in initial models for each outcome. The final models included all variables that were associated with the outcome at p<0.05 and/or those that caused a change of greater than 10% in the effect estimate for the psychosocial exposure of interest. All final models for outcomes 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 for outcomes at age 3 years included household income and parental history of asthma, as no other variables (e.g., ETS) were significant confounders. At both time points, we also examined parental depression as a linear variable with values of zero, one or two representing the number of parents with depression.

In addition, for the outcomes that were in common at the two 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 two groups,.

Results

Baseline characteristics of the participating children (twins) and their parents are shown in Table I. Of the 339 fathers, 226 (77%) had at least a high school education and 207 (71%) were working full time; their mean age was 29.8 (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 (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 major depressive episode and PTSD were less common in participating fathers than previously reported in Puerto Ricans^{.22} Depression in at least one 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 the 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. 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, major depressive episode, anti-social behavior and maternal depressive symptoms were each significantly associated with recent asthma symptoms in children. Maternal depressive symptoms showed a trend towards association with asthma hospitalizations in children. Parental depression also showed a strongly significant associated with recent asthma symptoms, such that each additional parent with depression was associated with a 1.70 increase in 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 (zero, one or two 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 anti-social behavior.

Combined Analysis

The results from the combined analysis of the two 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 anti-social behavior) were significantly 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, and both asthma hospitalizations and asthma diagnosis at age 3. Examining the combined outcomes at age 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.

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 smoking15^{, 19} which may 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. Though associations between paternal depression and outcomes at age 3 were not statistically significant, there was a trend towards association with increased use of oral steroids, which may have been significant with a larger sample size. Examining the combined 1 year 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, and found a trend towards association with steroid use, asthma hospitalizations, and asthma diagnosis at age 3. In the combined analysis, we found a significant effect of parental depression on recurrent hospitalizations for asthma.

Co-morbid asthma and psychosocial stress, and specifically depression, has been welldocumented 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 elevated total and allergen-specific IgE levels,⁴³ and parental stress has been linked to increased IL-4 and eosinophilic cationic protein release⁴⁴ in children. Compared to 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 receptors⁴⁶ which may lead to decreased response to asthma medications.⁸ While studies on maternal stress focus on alterations in *in utero* exposure to certain hormones as a result of stress, post-natal 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 may also contribute to the association between parental stress and childhood asthma. Psychological stress, especially depression, may affect parenting skills,⁴⁸ and affected parents may be less able to supervise their child's treatment. Alternatively, parental stress may 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 life³⁹ is essential in stemming the rising prevalence of asthma and in intervening in particularly vulnerable groups such as Puerto Ricans.^{5, 49} Island Puerto Ricans may 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 may impact the lives of parents and children alike.

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 concurrent respiratory infection, a frequent cause of wheezing in young children. However, early childhood wheezing is a risk factor for subsequent development of asthma, 53-56 and childhood wheezing and hospitalizations, regardless of whether the children go on to develop asthma, are an important cause of morbidity in young children.⁵⁷ Having outcomes at both 1 year and 3 years of age, and combining these outcomes, strengthens the analysis as 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 may affect both parental stress and asthma. Third, some of the measures of psychosocial stress, specifically PTSD and anti-social 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, may 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. Lastly, some data suggests that having twins may increase psychosocial stress for parents.^{59, 60} If this is the case, our cohort would be enriched cohort 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 year and 3 years of age. Although further studies are warranted, our work suggests that parental psychosocial stress, especially parental depression, may be an important modifiable risk factor for asthma morbidity in childhood, especially in high risk populations.

Supplementary Material

Refer to Web version on PubMed Central for supplementary material.

Abbreviations

PTSD	post-traumatic stress disorder
PRINTS	Puerto Rican Infant Twin Study
MFQ	Mood and Feelings Questionnaire
WHO	World Health Organization
CIDI 3.0	Composite International Diagnostic Interview version 3.0
DSM-IV	Diagnostic and Statistical Manual of the American Psychiatric Association 4^{th} edition
ETS	environmental tobacco smoke

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Table I

Baseline Characteristics of Parents and Children from the PRINTS study

	N (children)	N (%)	Median (IQR)
Age	678		6m (4.3–9.5)
Sex (% female)	678	352 (52%)	
Monozygotic	678	240 (35%)	
Environmental tobacco exposure (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 ($\% \ge$ high school)	678	600 (89%)	
Gestational Age	662		35 wks (34–37
Psychosocial measures			
	N (parents)		
Paternal PTSD [#]	339		1 (0–5)
Paternal major depressive episode	292	12 (4%)	
Paternal anti-social behavior	339		13 (11–13)
Maternal depressive symptoms	310		2.0 (1-5)
Parental Depression	586		
neither parent		292 (50%)	
one parent		274 (47%)	
both parents		20 (3%)	
Outcomes (1yr of age)			
	N (children)		
Asthma symptoms (last 4 wks)	678	411 (61%)	
Oral Steroid use (last 12mos)	678	121 (18%)	
Hospitalizations for asthma (last 12mos)	678	61 (9%)	
Asthma diagnosis	671	127 (19%)	
Outcomes (3yrs of age)			
Urgent MD or ED visits (12mos)	624	95 (15%)	
Oral Steroid use (last 12mos)	624	147 (24%)	
Hospitalizations for asthma (last 12mos)	624	53 (8%)	
	624	152 (24%)	

[#]PTSD: post-traumatic stress disorder

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Variable	Asthma symptoms	smo	Oral Steroids	ls	Hospitalizations for asthma	asthma	Asthma Diagnosis	osis
	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]	0.03	1.06 [0.99, 1.12]	0.1	1.06 [1.00, 1.12]	0.03
Paternal major depressive episode	4.10 [0.87, 19.42]	0.08	3.29 [1.11, 9.70]	0.03	5.10 [1.84, 14.11]	0.002	3.21 [1.08, 9.46]	0.03
Paternal anti-social behavior	$1.08\ [1.04, 1.14]$	<.001	1.05 [.98, 1.12]	0.18	1.07 [0.98, 1.16]	0.13	1.02 [0.96, 1.08]	0.52
Maternal depressive symptoms	1.07 [0.98, 1.17]	0.13	$1.04\ [0.93, 1.16]$	0.51	1.21 [1.06, 1.38]	0.004	1.02[0.91, 1.14]	0.68
Maternal depression (≥median)	1.25 (0.845, 1.86]	0.26	0.88 [0.52, 1.47]	0.61	1.39 [0.72, 2.70]	0.33	$0.88 \ [0.53, 1.46]$	0.62
Parental depression	1.59 [1.08, 2.33]	0.02	1.16[0.70, 1.92]	0.56	1.79 [0.96, 3.33]	0.07	1.24 [0.76, 2.03]	0.4
				;		50 0		
Environmental tobacco smoke	1.28 [.77, 2.12]	0.34	1.55 $[.86, 2.80]$	0.14	2.42 [1.19, 4.92]	0.01	1.45 [.80, 2.6]	0.21
Parental history of asthma	1.42 [.94, 2.14]	0.09	2.97 [1.76, 5.03]	<.001	1.93 [.99, 3.75]	0.050	2.62 [1.60, 4.36]	<.001
Female (vs. male)	1.02 [.76, 1.35]	0.92	0.84 [.58, 1.21]	0.34	0.48 [.29, .81]	0.006	0.83 [.58, 1.18]	0.31
Median income †	0.70 [.46, 1.08]	0.11	1.05 [.61, 1.81]	0.86	1.36 [.66, 2.77]	0.4	1.06 [.62, 1.8]	0.83
Public assistance $\overset{\star}{\star}$	0.71 [.48, 1.06]	0.09	$1.80 \ [1.06, 3.05]$	0.03	2.48 [1.21, 5.05]	0.01	1.90 [1.10, 3.2]	0.02
Parental Education [§]	1.02 [.55, 1.88]	0.96	0.69 [.34, 1.41]	0.31	0.63 [0.26, 1.55]	0.32	0.58 [.3, 1.14]	0.12
Gestational Age	$1.01 \ [0.95, 1.08]$	0.69	1.05 [0.97, 1.13]	0.26	$0.97 \; [0.87, 1.08]$	0.63	1.05 [0.97, 1.14]	0.22
all analyses adjusted for the correlation between twins	on between twins							
$\# {\sc Prime} {\sc Prim} {\sc Prime} {\sc Prime} {\sc Prim} {\sc Prime} {\sc Prime} {\sc$								
τ	¢18 000							
	\$10,000							

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 ${\not t}$ reference group: families not receiving public assistance

 \S reference group: \geq high school education

Table III

Multivariate Analysis of Parental Psychosocial Measures and Asthma Outcomes at 1 year of age*

Measures	Asthma sympto	oms	Hospitalizatio asthma	ns for
Nicasul es	OR [95%CI]	p value	OR [95%CI]	p value
Paternal PTSD ^{#†}	1.08 [1.03, 1.14]	0.003	1.02 [0.94, 1.10]	0.69
Paternal major depressive episode †	9.95 [1.38, 71.59]	0.02	1.43 [0.25, 8.31]	0.69
Paternal anti-social behavior †	1.09 [1.04, 1.15]	<.001	1.08 [0.97, 1.20]	0.17
Maternal depressive symptoms [‡]	1.13 [1.02, 1.25]	0.02	1.14 [0.98, 1.33]	0.09
Parental depression	1.70 [1.14, 2.53]	0.01	1.21 [0.62, 2.35]	0.58

*All models adjusted for parental history of asthma, environmental tobacco smoke, household income, gestational age, and the correlation between twins.

 $^{\dagger} \mathrm{Paternal}$ models also adjusted for maternal depressive symptoms.

 ${}^{\not \! t}$ Maternal model also adjusted for paternal depression.

[#]PTSD: post-traumatic stress disorder

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Table IV

Bivariate Analyses between Psychosocial Measures and Outcomes at 3 years of age^*

	ED/MD visits	~	Oral steroids	S	Hospitalizations for asthma	sfor	Asthma Diagnosis	osis
	OR [95%CI]	p val	OR [95%CI]	p val	OR [95%CI] val OR [95%CI] p val OR [95%CI] p val OR [95%CI] p val	p val	OR [95%CI]	p val
Paternal PTSD	1.05 [0.99, 1.12]	0.12	1.02 [0.96, 1.08]	0.53	1.05 [0.99, 1.12] 0.12 1.02 [0.96, 1.08] 0.53 1.02 [0.94, 1.11] 0.63 1.04 [0.99, 1.09] 0.14	0.63	1.04 [0.99, 1.09]	0.14
Paternal major depressive episode	3.66 [1.17, 11.44]	0.03	3.66 [1.17, 11.44] 0.03 3.66 [1.17, 11.44]	0.03	2.12 [0.43, 10.53] 0.36	0.36	2.24 [0.71, 7.10]	0.17
Paternal antisocial behavior	$0.95\ [0.90, 1.01]$	0.12	0.95 [0.90, 1.01] 0.12 0.96 [0.92, 1.02]	0.19	0.99 [0.91, 1.07] 0.76	0.76	0.98 $[0.93, 1.04]$	0.52
Maternal depressive symptoms		0.06	$1.06\ [0.96, 1.18]$	0.24	1.11 [0.99, 1.23] 0.06 1.06 [0.96, 1.18] 0.24 1.13 [0.99, 1.29] 0.06 1.13 [1.02, 1.24] 0.02	0.06	1.13 [1.02, 1.24]	0.02
Parental depression	1.45[0.86, 2.44]	0.16	1.60 [0.99, 2.56]	0.054	1.45 [0.86, 2.44] 0.16 1.60 [0.99, 2.56] 0.054 1.88 [1.00, 3.53] 0.050 1.51 [0.98, 2.31] 0.06	0.050	1.51 [0.98, 2.31]	0.06

all analyses adjusted for the correlation between twins

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Table V

Multivariate Analysis of Parental Psychosocial Measures and Asthma Outcomes at 3 years of age^*

	ED/MD visits	s	Ural steroids	20	Hospitalizations for asthma	tor	Asthma Diagnosis	iosis
	OR [95%CI]	p val	OR [95%CI]	p val	OR [95%CI] p val OR [95%CI] p val OR [95%CI] p val	p val	OR [95%CI]	p val
Paternal major depressive episode ⁷ 1.24 [0.25, 6.08] 0.80 3.03 [0.84, 10.97] 0.09 1.42 [0.18, 11.15] 0.74 1.30 [0.32, 5.16] 0.71	1.24 [0.25, 6.08]	0.80	3.03 [0.84, 10.97]	0.09	1.42 [0.18, 11.15]	0.74	1.30 [0.32, 5.16]	0.71
Maternal depressive symptoms ${}^{\pm}$	1.11 [0.98, 1.27]	0.10	1.11 [0.98, 1.27] 0.10 1.08 [0.96, 1.23] 0.20 1.16 1.00, 1.36 0.050 1.13 1.01, 1.27 0.03	0.20	1.16 [1.00, 1.36]	0.050	1.13 [1.01, 1.27]	0.03
Parental depression (linear)	1.36 [0.76, 2.41]	0.30	1.36 [0.76, 2.41] 0.30 1.61 [0.97, 2.66] 0.067 1.86 [0.98, 3.56] 0.060 1.42 [0.91, 2.21] 0.12	0.067	1.86 [0.98, 3.56]	0.060	1.42[0.91, 2.21]	0.12

Paternal model also adjusted for maternal depressive symptoms.

 \dot{f}^{\dagger} Maternal model also adjusted for paternal depression.

Table VI

Analysis of combined outcomes at 1 and 3 years of age*

	Oral Steroids	s	Hospitalizations for asthma	asthma	Asthma Diagnosis $^{\$}$	sis [§]
	OR [95%CI]	p val	OR [95%CI] p val OR [95%CI]	p val	p val OR [95%CI] p val	p val
Paternal major depressive episode [†] 5.66 [1.06, 30.19] 0.04 6.36 [0.33, 123.35] 0.22 1,79 [0.31, 10.48] 0.52	5.66 [1.06, 30.19]	0.04	6.36 [0.33, 123.35]	0.22	1,79 [0.31, 10.48]	0.52
Maternal depressive symptoms [‡]	1.05 [0.88, 1.26]	0.56	1.05 [0.88, 1.26] 0.56 1.26 [1.01, 1.58]	0.04	0.04 1.15 [1.00, 1.33] 0.053	0.053
Parental depression (linear)	1.51 [0.70, 3.28]	0.29	51 [0.70, 3.28] 0.29 4.08 [1.14, 14.66] 0.03 1.36 [0.74, 2.48] 0.32	0.03	1.36 [0.74, 2.48]	0.32

* Outcomes binary and considered to be positive if child experienced the outcome at *both* time points, negative if child did not experience the outcome at *both* time points. Children with outcome at one time point but not at the other were excluded from analysis. All analyses were adjusted for household income, parental asthma, correlation between twins (ETS and gestational age 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.

 $\dot{\tau}$ Paternal model also adjusted for maternal depressive symptoms.

 $\overset{\sharp}{\mathcal{T}}_{M}$ Maternal model also adjusted for paternal depression.