

Original Article

Maternal Depressive Symptoms, Lung Function, and Severe Asthma Exacerbations in Puerto Rican Children

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What is already known about this topic? Little is known about the relationship between persistent or increasing maternal depressive symptoms over several years and lung function measures or severe asthma exacerbations in children and adolescents.

What does this article add to our knowledge? In this prospective study, increasing or persistent maternal depressive symptoms were associated with worse lung function measures (forced expiratory volume in 1 second [FEV₁] and FEV₁/forced vital capacity) and severe asthma exacerbations in Puerto Rican youth, a high-risk population.

How does this study impact current management guidelines? Physicians caring for children with asthma should be aware of potential maternal depression, which, if suspected, should be appropriately addressed.

BACKGROUND: Maternal depression has been linked to health care use for asthma in cross-sectional or short-term follow-up studies of school-aged children.

OBJECTIVE: To examine whether increased or persistent maternal depressive symptoms over approximately 5 years are associated with severe asthma exacerbations or worse lung function in youth.

METHODS: A prospective study of 386 youth living in Puerto Rico, aged 6 to 14 years at a baseline visit and 9 to 20 years at a second visit, was performed. Our exposure of interest was change in persistence of maternal depressive symptoms, assessed at both

visits using the Center for Epidemiologic Studies Depression Scale (CESD). Our outcomes of interest were change in percent predicted forced expiratory volume in 1 second (FEV₁) and FEV₁/forced vital capacity (FVC) between the first and second visits in all subjects, and ≥ 1 severe asthma exacerbation in the year before the second visit in subjects with asthma.

RESULTS: In a multivariable analysis, each 1-point increment in the CESD score was associated with decrements of 0.15% in percent predicted FEV₁ (95% confidence interval [CI] = -0.28% to -0.01%; $P = .03$) and 0.10% in percent predicted FEV₁/FVC (95% CI = -0.20% to 0.001%; $P = .05$) between visits, as well as with 1.03 times increased odds of ≥ 1 severe asthma exacerbation at the second visit (95% CI for odds ratio = 0.99 to 1.06, $P = .09$). In a multivariable analysis, the presence of maternal depressive symptoms (a CESD score ≥ 21 points) at the second visit or at both visits was significantly associated with 3.17 to 3.52 times increased odds of ≥ 1 severe asthma exacerbation in the year before the second visit.

CONCLUSIONS: Increasing or persistent maternal depressive symptoms over approximately 5 years are associated with worse lung function measures and severe asthma exacerbations among Puerto Rican youth, a high-risk population. © 2020 American Academy of Allergy, Asthma & Immunology (J Allergy Clin Immunol Pract 2020;■:■-■)

Key words: Maternal depression; Lung function; Asthma attacks; Puerto Rican; Children

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This work was supported by grants HL079966, HL117191, and MD011764 from the U.S. National Institutes of Health (NIH). E. L. Stevens was supported by grant T32 HL129949 from the U.S. NIH. The sponsor had no role in the design or implementation of the study, or the drafting and submission of the manuscript.

Conflicts of interest: J. C. Celedón has received research materials from GSK and Merck (inhaled steroids) and Pharmavite (vitamin D and placebo capsules), to provide medications free of cost to participants in NIH-funded studies, unrelated to this work. He is the President of the American Thoracic Society. The rest of the authors declare that they have no relevant conflicts of interest.

Received for publication July 17, 2020; revised October 5, 2020; accepted for publication October 6, 2020.

Available online ■■

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<https://doi.org/10.1016/j.jaip.2020.10.023>

Asthma affects nearly 6 million children in the United States.¹ Compared with non-Hispanic whites, Puerto Ricans share a disproportionate burden of asthma, both in the continental United States and in Puerto Rico.² Indeed, the estimated

*Abbreviations used**BMI- Body mass index**CESD- The Center for Epidemiologic Studies Depression Scale**CI- Confidence interval**EVA-PR- Epigenetic Variation and Childhood Asthma in Puerto Ricans study**FEV₁- Forced expiratory volume in 1 second**FVC- Forced vital capacity**ICS- Inhaled corticosteroids**OR- Odds ratio**PR-GOAL- Puerto Rico Genetics of Asthma and Lifestyle Study**SES- Socioeconomic status**SHS- Second-hand smoke*

prevalence of childhood asthma is twice as high in Puerto Ricans (13.6%) as in non-Hispanic whites (6.8%).¹

In the continental United States, Puerto Rican adults are more likely to report depressive symptoms than adults in other racial or ethnic groups (eg, Mexican Americans), particularly in females.^{3,4} Among Puerto Ricans, women are most often the primary caregiver of children, commonly to the point of self-sacrifice.⁵ Puerto Ricans are commonly exposed to risk factors for both depression and morbidity from asthma, including poverty, low educational attainment, and violence.^{6,7}

Previous studies have shown that pre- or postnatal maternal depression has been associated with childhood asthma,⁸⁻¹⁰ and a prior report showed that maternal depression during a child's school years was linked to emergency department visits for asthma over a 6-month period of follow-up.¹¹ To date, however, little is known about the relationship between persistent or increasing maternal depressive symptoms over several years on lung function measures or severe asthma exacerbations (encompassing emergency department visits and hospitalizations for asthma requiring treatment with systemic corticosteroids) in children and adolescents.

On the basis of prior findings, we hypothesized that increased or persistent maternal depressive symptoms over a period of approximately 5 years would be associated with worse lung function and severe asthma exacerbations among Puerto Rican youth. We examined this hypothesis in a prospective study of Puerto Ricans followed from ages 6 to 14 years to ages 9 to 20 years.

METHODS

Study population

PR-GOAL. Subject recruitment and study procedures for the Puerto Rico Genetics of Asthma and Lifestyle Study (PR-GOAL) have been previously described.¹² Participants were recruited from March 2009 through June 2010 from randomly selected households in the metropolitan area of San Juan and Caguas (Puerto Rico) using a multistage probabilistic sampling design. Based on this sampling design, 7073 households were selected and 6401 (91%) were contacted. Of these 6401 households, 1111 had ≥ 1 child who met inclusion criteria (age 6-14 years, 4 Puerto Rican grandparents, and residence in the same household for ≥ 1 year). Of these 1111 households, 438 (39.4%) had ≥ 1 child with asthma (a case). From these 438 households, 1 child with asthma was selected (at random if there was more than 1 such child). Similarly, only 1 child without asthma (a control subject) was randomly selected from the remaining

673 households. To reach a target sample size of 700 children, we attempted to enroll 783 of the 1111 eligible children. Parents of 105 of these 783 (13.4%) households refused to participate or could not be reached, leaving 678 study participants (351 cases and 327 controls). There were no significant differences in age, sex, or area of residence between eligible children who did ($n = 678$) and did not ($n = 105$) participate in PR-GOAL.

EVA-PR. Subject recruitment and study procedures for the Epigenetic Variation and Childhood Asthma in Puerto Ricans study (EVA-PR) were similar to those in PR-GOAL and have been previously described.¹³ In brief, subjects were recruited from the metropolitan area of San Juan and Caguas (Puerto Rico) from February 2014 through May 2017. Of the 1111 households that were randomly selected for PR-GOAL (see above), 1045 still had current and correct contact information and were thus screened for EVA-PR. Of these 1045 households, 180 were unreachable despite several efforts. Of the 865 households that were contacted, 720 had at least 1 child who met the following inclusion criteria: age 9 to 20 years, 4 Puerto Rican grandparents, and living in the same residence for at least 1 year. To reach a sample size of approximately 550 subjects, we attempted to enroll 638 of the 720 eligible children. Of the 638 children and adolescents whom we attempted to enroll, 543 (85.1%) agreed to participate. There were no significant differences in age, sex, or area of residence between subjects who did ($n = 543$) and did not ($n = 95$) agree to participate in EVA-PR.

Participants included in the current analysis. Of the 543 participants in EVA-PR, 406 had previously participated in PR-GOAL (see Figure 1). Of these 406 subjects, 386 (95.1%) had complete data on maternal depressive symptoms and other covariates of interest for both EVA-PR and PR-GOAL, and were thus included in the current analysis.

Study procedures

All 386 participants included in this analysis completed a protocol including administration of questionnaires and spirometry at both study visits (ie, for both the PR-GOAL and EVA-PR studies). One parent of each participant (more often [$>93\%$] the mother) completed a questionnaire adapted from that used in the Collaborative Study of the Genetics of Asthma.¹⁴ Data obtained from this questionnaire included information regarding the child's overall and respiratory health status, family history, demographics, and socioeconomic status (SES). The Center for Epidemiologic Studies Depression Scale (CESD), a 20-item widely employed and validated questionnaire, was used to assess maternal depressive symptoms.^{15,16} The total CESD score was calculated by summation of the scores for each item, leading to a total score ranging from 0 to 60 points.

Spirometry was conducted with an EasyOne spirometer (NDD Medical Technologies, Andover, Mass) according to the American Thoracic Society and European Respiratory Society recommendations.¹⁷ The best results for forced expiratory volume in 1 second (FEV₁) and forced vital capacity (FVC) were selected for data analysis.

Our outcomes of interest were change in percent predicted FEV₁ and change in percent predicted FEV₁/FVC between the first and second visits (with percent predicted values at each visit calculated using the Global Lung Function Initiative equations, which account for age, sex, race/ethnicity, and height),¹⁸ and severe asthma exacerbations at the second visit (defined as at least 1 hospitalization for asthma or at least 1 visit to the emergency department or urgent care for asthma, requiring treatment with systemic corticosteroids in the

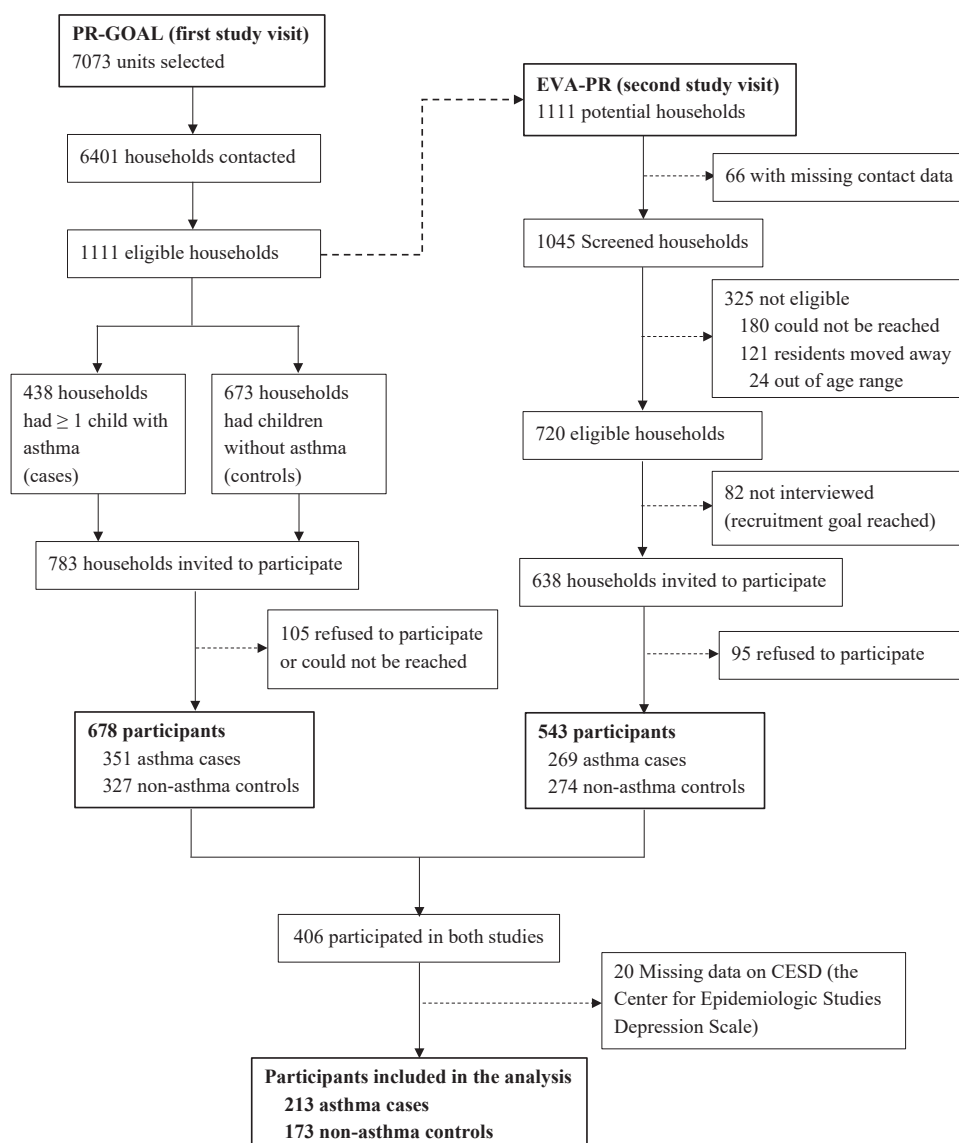


FIGURE 1. Study diagram for selection of the participants included in the current analysis. *EVA-PR*, Epigenetic Variation and Childhood Asthma in Puerto Ricans study; *PR-GOAL*, Puerto Rico Genetics of Asthma and Lifestyle Study.

previous year; or 1 or more courses of systemic steroids for asthma¹⁹ in the previous year).

Our exposure of interest was maternal depressive symptoms, which we analyzed as both a continuous variable (defined as the change in the CESD score between the first and the second visits) and a categorical variable (presence of maternal depressive symptoms at neither visit, at the first visit, at the second visit, or at both visits). Maternal depressive symptoms were defined as a CESD score ≥ 21 points, which has been deemed an adequate threshold for significant depressive symptoms in Puerto Rican adults, as well as an indicator of severe depressive symptoms in a general population of adults.^{15,16}

Written parental consent was obtained for participating children, from whom written assent was also obtained. *PR-GOAL* was approved by the institutional review boards of the University of Puerto Rico (San Juan, Puerto Rico), Brigham and Women's Hospital (Boston, Mass), and the University of Pittsburgh (Pittsburgh, Pa). *EVA-PR* was approved by the institutional review boards of the

University of Puerto Rico (San Juan) and the University of Pittsburgh (Pittsburgh, Pa).

Statistical analysis

Bivariate analyses were conducted using 2-tailed t tests or analysis of variance for categorical and continuous variables, χ^2 tests for categorical variables, and Spearman correlation coefficients for pairs of continuous variables. The multivariable analysis of severe asthma exacerbations in cases was always adjusted for age and sex (this was not necessary for the analysis of percent predicted lung function measures, which already accounted for age and sex) and use of inhaled corticosteroids (ICS) in the 6 months before the second study visit. The multivariable analysis of lung function was always adjusted for case-control (asthma) status. The time interval between the study visits and the following covariates (assessed at the second study visit) were considered for inclusion in the multivariable models, as either potential confounders or mediators of the relation

TABLE I. Participant characteristics by changes in CESD score or the presence of maternal depressive symptoms at second study visits

		Maternal depressive symptoms‡			
	Change in CESD score†	At neither study visit (n = 251)	At the first study visit only (n = 41)	At the second study visit only (n = 41)	At both the first and second study visits (n = 53)
All participants (n = 386)					
Asthma status					
Control	0 (−5, 3)	119 (68.8)	13 (7.5)	15 (8.7)	26 (15.3)
Case	0 (−7, 5)	132 (62.0)	28 (13.2)	26 (12.2)	27 (12.7)
Sex					
Male	0 (−6, 4)	136 (67.0)	25 (12.3)	17 (8.4)	25 (12.3)
Female	0 (−7, 5)	115 (62.8)	16 (8.7)	24 (13.1)	28 (15.3)
Type of health insurance					
Private insurance	0 (−5, 4)	103 (77.4)	13 (9.8)	9 (6.0)	8 (6.0)*
Others	−1 (−7, 5)	148 (58.5)	28 (11.1)	32 (12.7)	45 (17.8)
Annual household income					
<\$15,000	−1 (−6.5, 5)	136 (54.2)	29 (72.5)	30 (73.2)	37 (71.2)*
≥\$15,000	0 (−5, 4)	115 (45.8)	11 (27.5)	11 (26.8)	15 (28.9)
Maternal education					
Less than high school	0 (−6, 6)	45 (17.9)	7 (17.1)	12 (29.3)	11 (29.3)*
High school graduate	−1 (−8, 7)	66 (26.3)	13 (31.7)	16 (39.0)	22 (41.5)
College and above	0 (−5, 4)	140 (55.8)	21 (51.2)	13 (31.7)	20 (37.7)
Maternal asthma					
Yes	0 (−8, 7)	80 (58.0)	17 (12.3)	19 (13.8)	22 (15.9)
No	0 (−6, 4)	169 (69.0)	24 (9.8)	22 (9.0)	30 (12.2)
BMI z-score§	0.038	0.63 ± 1.08	0.64 ± 1.18	0.84 ± 0.94	0.87 ± 1.03
Current second-hand smoke exposure					
Yes	0 (−7, 6)	84 (62.2)	14 (10.4)	12 (8.9)	25 (18.5)
No	0 (−6, 4)	166 (66.4)	27 (10.8)	29 (11.6)	28 (11.2)
Use of inhaled corticosteroids in the previous 6 months					
Yes	0 (−8, 6)	34 (58.6)	9 (15.5)	9 (15.5)	6 (10.3)
No	0 (−6, 4)	214 (66.3)	31 (9.6)	31 (9.6)	47 (14.6)
Children with asthma (cases, n = 213)					
Severe asthma exacerbations in the previous year					
Yes	3 (−4.5, 9.5)	15 (41.7)	6 (16.7)	8 (22.2)	7 (19.4)*
No	−1 (−8, 4.5)	108 (65.9)	22 (13.4)	16 (9.8)	18 (11.0)

BMI, Body mass index.

**P* < .05.[†]Median (interquartile range) and mean ± standard deviation for BMI z-score.[‡]Center for Epidemiologic Studies Depression (CESD) score ≥ 21 points.[§]Analyzed by Spearman correlation for change in CESD score and analysis of variance for maternal depressive symptom.

between change in or persistence of maternal depressive symptoms and lung function measures or severe asthma exacerbations: type of health insurance (private vs others), annual household income (<vs ≥\$15,000/year, based on census data), maternal education (less than high school, completed high school, and college and above), maternal asthma, current exposure to second-hand smoke (SHS, defined as smoking by anybody in the child's household), and body mass index (BMI) z-score. Of these covariates, the only ones to be significantly associated or correlated with either the change in CESD score between study visits or maternal depressive symptoms at study visits were 3 indicators of SES and/or health care access: type of health insurance, household income, and maternal education status (Table I and Figure E1, available in this article's Online Repository at www.jaci-inpractice.org). However, only type of health insurance was also significantly associated with the change in lung function measures or severe asthma exacerbations (see Table I and Tables E2 and E3 in this article's Online Repository at www.jaci-inpractice.org). Thus, all models for lung function or severe asthma

exacerbations were additionally adjusted for type of health insurance. In addition, we conducted a mediation analysis based on a counterfactual framework to estimate the total, direct, and indirect effects of any covariate to be a potential mediator of the relation between maternal depressive symptoms and lung function of severe asthma exacerbation.^{20,21} In this analysis, no covariate was shown to be a significant mediator. All analyses were performed using SAS version 9.4 (SAS Institute, Cary, NC).

RESULTS

Table E1 (available in this article's Online Repository at www.jaci-inpractice.org) shows a comparison of the main baseline characteristics of the 386 subjects who participated in PR-GOAL (the first time point or study visit for our analysis) and were included in the current analysis against the 292 subjects who participated in PR-GOAL but were not included in this study because they did not participate in EVA-PR (n = 272) or had

TABLE II. Participant characteristics at the baseline (first) study visit

All participants (n = 386)	Subjects without asthma (controls, n = 173)	Subjects with asthma (cases, n = 213)
Age (y)	10 (8, 13)	10 (8, 12)
Male sex	84 (49)	119 (56)
Private health insurance	64 (37)	74 (35)
Annual household income $\geq$ \$15,000	60 (36)	77 (37)
Maternal education		
Less than high school	57 (33)	64 (30)
High school graduate	72 (42)	91 (43)
College and above	43 (25)	57 (27)
Maternal asthma	32 (19.1)	98 (46.2)**
BMI z-score	0.61 $\pm$ 1.12	0.90 $\pm$ 1.12*
Current second-hand smoke exposure	61 (35.3)	83 (39.2)
Use of inhaled corticosteroids in the previous 6 mo	—	70 (33)
Maternal depression		
CESD score†	10 (5, 19)	12 (6, 21)
Depressive symptoms‡	39 (23)	55 (26)
Lung function measures		
FEV ₁ percent predicted	97.3 $\pm$ 15.6	91.7 $\pm$ 14.9**
FEV ₁ /FVC percent predicted	94.2 (87.3, 99.5)	91.8 (85.6, 97.4)*
Severe asthma exacerbations in the previous year	—	109 (51%)

Values are presented as n (%) for binary variables, mean $\pm$ standard deviation for normally distributed continuous variables, or median (interquartile range) for non-normally distributed variables.

BMI, Body mass index; FEV₁, forced expiratory volume in 1 second; FVC, forced vital capacity.

* $P < .05$; ** $P < .01$ for comparison between non-asthma controls and asthma cases.

†Center for Epidemiologic Studies Depression score (CESD).

‡Depressive symptoms: CESD score $\geq$ 21 points.

missing data (n = 20), separately for asthma cases and non-asthma control subjects. Compared with non-asthma controls included in the current analysis (n = 173), those excluded (n = 154) were slightly older. There were no significant differences in maternal CESD score, maternal depressive symptoms, lung function measures, or any other characteristic at the first study visit between non-asthma controls who were and were not included in the current analysis. Compared with asthma cases included in the current analysis (n = 213), those excluded (n = 138) had a lower BMI z-score and were more likely to be slightly older and exposed to SHS. There were no significant differences in maternal CESD score, maternal depressive symptoms, lung function measures, or having had ≥ 1 severe asthma exacerbation in the year before the first or baseline visit between asthma cases who were and were not included in this analysis.

A comparison of the baseline characteristics of the asthma cases and non-asthma control subjects included in the current analysis is shown in Table II. Children with asthma (cases) had a higher BMI z-score and lower FEV₁ percent predicted and FEV₁/FVC percent predicted than controls. There were no significant differences in age, sex, type of health insurance, CESD score, or the presence of maternal depressive symptoms (a CESD score ≥ 21 points) between asthma cases and non-asthma controls at the baseline (first) study visit. Moreover, the time interval between the 2 visits was similar between asthma cases (4.85 (1.04) years) and non-asthma controls (4.91 (0.90) years). Of the 213 asthma cases, 70 (33%) had used ICS in the previous 6 months and 109 (51%) had at least 1 severe asthma exacerbation in the previous year.

Figure 2 and Table E2 (available in this article's Online Repository at www.jaci-inpractice.org) show the results of the

unadjusted and adjusted analyses of the change in CESD score between the 2 study visits and the change in percent predicted lung function measures between the 2 study visits. In a multivariable analysis adjusting for asthma status and type of health insurance, each 1-point increment in the CESD score was associated with a 0.15% decrement in percent predicted FEV₁ (95% confidence interval [CI] = -0.28% to -0.01% , $P = .03$) and a 0.10% decrement in percent predicted FEV₁/FVC (95% CI = -0.20 to 0.001 , $P = .05$). We found no significant association between the presence of maternal depressive symptoms at either visit or at both visits and the change in percent predicted FEV₁ or FEV₁/FVC (see Table E3 in this article's Online Repository at www.jaci-inpractice.org).

In the multivariable analysis of severe asthma exacerbations in the 213 asthma cases, each 1-point increment in CESD score between the 2 study visits was associated with 1.03 times increased odds of ≥ 1 severe asthma exacerbation in the year before the second visit (95% CI for odds ratio [OR] = 0.99 to 1.06, $P = .09$; see Table E4 in this article's Online Repository at www.jaci-inpractice.org). Table III shows the results of the unadjusted and adjusted analyses of maternal depressive symptoms at the first visit, at the second visit, or at both visits and ≥ 1 severe asthma exacerbation in the year before the second visit. In a multivariable model adjusting for age, sex, type of health insurance, and use of ICS in the previous 6 months, the presence of maternal depressive symptoms at the second visit and at both visits was significantly associated with 3.17 times and 3.52 times increased odds of ≥ 1 severe asthma exacerbation in the year before the second visit, respectively.

Because maternal asthma has been previously shown to interact with maternal depression on childhood asthma, we

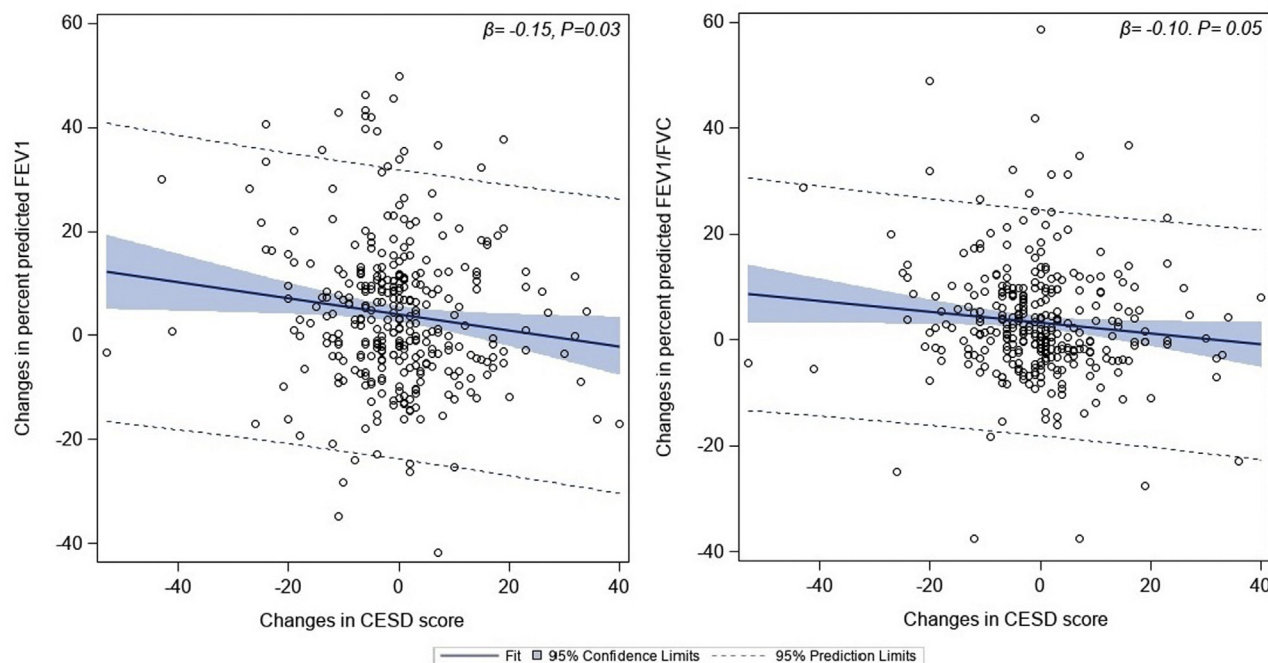


FIGURE 2. Results of the regression fit plots for changes in CESD score (total CESD score at the second study visit – total CESD score at the first study visit) and change in percent predicted FEV₁ (left panel) and change in percent predicted FEV₁/FVC (right panel). The multivariable models were adjusted for case-control (asthma) status and type of health insurance (private vs others). CESD, Center for Epidemiologic Studies Depression Scale; FEV₁, forced expiratory volume in 1 second; FVC, forced vital capacity.

TABLE III. Multivariable analysis of the relation between the presence of maternal depressive symptoms at study visits and severe asthma exacerbations in the year before the second study visit, among 213 asthma cases

Variable	Unadjusted		Adjusted*	
	OR (95% CI)	P value	OR (95% CI)	P value
Private health insurance†	0.40 (0.17, 0.97)	.04	0.46 (0.18, 1.17)	.10
Use of inhaled corticosteroids in the previous 6 mo†	4.31 (2.03, 9.18)	<.01	4.33 (1.88, 9.95)	<.01
Maternal depressive symptoms‡				
At neither study visit	1.0		1.0	
At the first study visit only	2.05 (0.72, 5.85)	.18	1.64 (0.51, 5.27)	.41
At the second study visit only	3.50 (1.30, 9.42)	.01	3.17 (1.03, 9.72)	.04
At both the first and second study visits	2.75 (0.99, 7.60)	.05	3.52 (1.10, 11.32)	.03

CESD, Center for Epidemiologic Studies Depression Scale; CI, confidence interval; OR, odds ratio.

*Model adjusted for all variables listed in the column.

†At the second study visit.

‡Total CESD score ≥ 21 points.

tested for such interaction in the final multivariable models. There was no significant interaction on any of the outcomes of interest ($P \geq .20$ in all instances).

Of the 386 study participants, 28 (7.2%) had a change in asthma status between the 2 study visits (15 control subjects were classified as having asthma at the second study visit and 13 cases could be classified as being control subjects at the second study visit). We thus conducted a sensitivity analysis after excluding these 28 subjects, obtaining similar results.

DISCUSSION

To our knowledge, this is the first study of change in or persistence of maternal depressive symptoms over time and lung

function or severe asthma exacerbations in children and adolescents. In a study of Puerto Rican youth followed from ages 6-14 years to ages 9-20 years, increased maternal depressive symptoms between the first and second study visits were associated with decrements in FEV₁ percent predicted and FEV₁/FVC percent predicted over time. Although increased maternal symptoms were also associated with severe asthma exacerbations at the second study visit, such association was not significant at $P < .05$. In this study, the presence of maternal depressive symptoms at the second study visit or at both study visits was significantly associated with more than 3-fold increased odds of severe asthma exacerbations at the second study visit. Our overall findings suggest that increased or persistent maternal depressive

symptoms over time are associated with poorer asthma control or worse asthma severity in Puerto Rican children and adolescents.

Two previous studies in Latin American children showed no association between depressive symptoms in a child's mother or caretaker and asthma hospitalizations²² or asthma control,²³ but those null findings could be explained by limited statistical power due to small sample size. In contrast, a study of 339 pairs of Puerto Rican twins followed up to age 3 years showed that maternal depressive symptoms in the child's first year of life were associated with asthma hospitalizations between ages 1 and 3 years (adjusted OR = 1.26, 95% CI = 1.01 to 1.58).²⁴ Consistent with our findings, a study of 158 inner-city school-aged children with asthma reported that a high level of maternal depressive symptoms was associated with 1.3 times increased odds of emergency department visits for asthma after 6 months of follow up (95% CI = 1.1 to 5.0).¹¹ Our results for increased maternal depressive symptoms and negative changes in lung function over time are partly consistent with those of a prior study in children with asthma, which demonstrated a lower FEV₁ among children of caregivers with depression or anxiety, albeit in unadjusted analyses.¹⁷ Compared with those prior reports, the current study has a larger sample size, longer duration of follow up, and an analytical approach that accounted for potential confounders such as type of health insurance and use of ICS.

Maternal depression may be linked to worse asthma or lung function in youth through various pathways.²⁵ First, depression may negatively impact a mother's memory, executive function, and motivation, affecting knowledge and management of her child's asthma, including adherence to prescribed treatments. Second, maternal depression may lead to negative parenting and thus increased stress or depression in the child, ultimately leading to autonomic and immune dysregulation and worse asthma.²⁴ Third, psychosocial stressors correlated with maternal depression (eg, violence, racism) may also worsen a child's asthma. Fourth, although our analysis was adjusted for ICS use and type of health insurance, greater asthma morbidity or severity in the child may have led to or worsened maternal depressive symptoms.²⁵ Indeed, a growing body of evidence suggests that the relationship between maternal depression and asthma control or asthma severity in youth is likely to be bidirectional and multifactorial.

Both maternal depression and childhood asthma are common and often co-occur in Puerto Ricans, emphasizing the public health importance of our findings. "Machismo" is observed in Puerto Rico families, in which a "macho" is a male who is characteristically willful, dominant over wife and family, authoritarian, not visibly affected by tender emotions, nor given to contribute to child-rearing or household chores. Thus, in traditional Puerto Rican culture, mothers frequently place the needs of the family above their own and typically serve as the primary caregiver to children, often to their own detriment.⁵ Further, as Puerto Ricans are disproportionately represented among the poor, they may have limited access to mental health services.²⁵ Moreover, Puerto Rican women may present with somatic complaints rather than classical symptoms of depression,²⁵ leading to potential underestimation of an already high prevalence of depression among Puerto Rican women.

Our study has additional limitations. First, our sample size—albeit larger than that of prior studies—may have limited our statistical power to detect modest associations between the

persistence of maternal depressive symptoms and lung function. Second, we lack data on maternal depressive symptoms or asthma in pre- or early post-natal life, when a child's immune system is more susceptible to external stimuli. Third, selection bias is possible in any observational study. However, such bias is an unlikely explanation for our results because there were no significant differences in the exposure (maternal depressive symptoms) or outcomes of interest between children who were and were not included in the current analysis. Fourth, we cannot exclude residual confounding by unmeasured variables such as paternal depression, maternal diet, or adherence to ICS.

Our findings support screening mothers of Puerto Rican children with asthma for depression. Further longitudinal studies are needed to better understand potential mediators and mechanisms of the link between maternal depression and morbidity from asthma.

Acknowledgments

E. L. Stevens and Y.-Y. Han participated in study conceptualization, led the data analysis, and wrote the first draft of the manuscript. F. Rosser participated in data analysis. E. Forno, E. Acosta-Pérez, and G. Canino participated in project administration. G. E. Miller participated in study conceptualization. J. C. Celedón obtained funding for the study, led project administration, and reviewed and edited the first draft of the manuscript. All authors reviewed the manuscript for intellectual content and approved submission of the manuscript. Y.-Y. Han and J. C. Celedón had full access to all the data in the study and take responsibility for the integrity of the data and the accuracy of the data analysis.

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TABLE E1. Baseline characteristics of participants who were (n = 386) and were not (n = 292) included in the current analysis

Variable	No asthma (controls), included (n = 173)	No asthma (controls), not included (n = 154)	Asthma cases, included (n = 213)	Asthma cases, not included (n = 138)
Age (y)	10 (8, 13)	11 (9, 13)*	10 (8, 12)	10 (8, 13)*
Male sex	84 (49)	75 (49)	119 (56)	82 (59)
Private health insurance	64 (37)	58 (38)	74 (35)	38 (28)
Annual household income $\geq$ \$15,000	60 (36)	56 (38)	77 (37)	42 (31)
Maternal education				
Less than high school	57 (33)	45 (29)	64 (30)	46 (34)
High school graduate	72 (42)	81 (53)	91 (43)	65 (47)
College and above	43 (25)	28 (18)	57 (27)	26 (19)
Maternal asthma	32 (19)	35 (23)	98 (46.2)	74 (54)
BMI z-score	0.61 $\pm$ 1.12	0.49 $\pm$ 1.10	0.90 $\pm$ 1.12	0.56 $\pm$ 1.23*
Current second-hand smoke exposure	61 (35)	52 (34)	83 (39)	72 (53)*
Use of inhaled corticosteroids in the previous 6 mo	—	—	70 (33)	44 (32)
Maternal depression				
CESD score†	10 (5, 19)	9 (4, 18)	12 (6, 21)	13 (6, 28)
Depressive symptoms‡	39 (23)	28 (19)	55 (26)	42 (32)
Lung function				
FEV ₁ percent predicted	97.27 (15.58)	98.52 (14.20)	91.74 (14.94)	94.90 (15.70)
FEV ₁ /FVC percent predicted	94.18 (87.31, 99.52)	96.60 (89.49, 100.51)	91.79 (85.58, 97.36)	93.33 (86.32, 97.87)
Children with asthma (cases)				
$\geq$ 1 severe asthma exacerbation in the previous year	—	—	109 (51)	65 (51)

Values are presented as n (%) for binary variables, mean (standard deviation) for normally distributed continuous variables, or median (interquartile range) for non-normally distributed variables.

BMI, Body mass index; FEV₁, forced expiratory volume in 1 second; FVC, forced vital capacity.

* $P < .05$.

†Center for Epidemiologic Studies Depression score (CESD).

‡Depressive symptoms: CESD score $\geq$ 21 points.

TABLE E2. Analysis of the relation between change in CESD score and percent predicted lung function measures

	Unadjusted		Adjusted*	
	β (95% CI)	P value	β (95% CI)	P value
Percent predicted FEV ₁				
Each 1-point change in CESD Score†	−0.15 (−0.29, −0.02)	.02	−0.15 (−0.28, −0.01)	.03
Asthma status	0.13 (−2.98, 3.25)	.93	0.06 (−3.03, 3.14)	.97
Private health insurance	−2.96 (−6.24, 0.31)	.07	−2.75 (−6.02, 0.52)	.10
Percent predicted FEV ₁ /FVC				
Each 1-point change in CESD Score†	−0.10 (−0.21, −0.001)	.048	−0.10 (−0.20, 0.001)	.05
Asthma status	−1.16 (−3.55, 1.22)	.34	−1.21 (−3.59, 1.16)	.32
Private health insurance	−0.88 (−3.39, 1.63)	.49	−0.73 (−3.24, 1.78)	.57

CESD, Center for Epidemiologic Studies Depression Scale; CI, confidence interval; FEV₁, forced expiratory volume in 1 second; FVC, forced vital capacity.

*Adjusted for asthma status and private health insurance at the second visit.

†Total CESD score at the second study visit minus total CESD score at the first study visit. As an example, a change of 20 points in the CESD score is associated with a negative change of 3% in percent predicted FEV₁, adjusting for asthma status and type of health insurance.

TABLE E3. Multivariable analysis of the presence of maternal depressive symptoms at the study visits and change in percent predicted lung function measures

	Unadjusted		Adjusted*	
	β (95% CI)	P value	β (95% CI)	P value
Percent predicted FEV ₁				
Asthma status†	0.13 (−2.98, 3.25)	.93	0.27 (−2.86, 3.41)	.86
Private health insurance‡	−2.96 (−6.24, 0.31)	.08	−3.76 (−7.13, −0.39)	.03
Maternal depressive symptoms‡				
At neither study visit	1.0		1.0	
At the first visit only	−0.16 (−5.21, 4.88)	.95	−0.62 (−5.69, 4.46)	.81
At the second visit only	−3.30 (−8.41, 1.81)	.20	−4.14 (−9.30, 1.02)	.11
At both the first and second visits	−2.67 (−7.31, 1.97)	.26	−3.78 (−8.51, 0.95)	.12
Percent predicted FEV ₁ /FVC				
Asthma status†	−1.16 (−3.55, 1.22)	.33	−1.37 (−3.77, 1.04)	.26
Private health insurance‡	−0.88 (−3.39, 1.64)	.49	−1.21 (−3.79, 1.37)	.36
Maternal depressive symptoms‡				
At neither study visit	1.0		1.0	
At the first visit only	3.06 (−0.79, 6.91)	.12	3.20 (−0.69, 7.01)	.11
At the second visit only	−1.62 (−5.52, 2.28)	.41	−1.66 (−5.61, 2.30)	.41
At both the first and second visits	−1.60 (−5.14, 1.94)	.37	−1.99 (−5.61, 1.63)	.28

CESD, Center for Epidemiologic Studies Depression Scale; CI, confidence interval; FEV₁, forced expiratory volume in 1 second; FVC, forced vital capacity.

*Models adjusted for all variables listed in the column.

†At the second study visit.

‡Total CESD score ≥ 21 points.

TABLE E4. Multivariable analysis of change in CESD score and severe asthma exacerbations in the year before the second study visit, among asthma cases (n = 213)

Variable	Unadjusted		Adjusted*	
	OR (95% CI)	P value	OR (95% CI)	P value
Change in CESD Score†	1.02 (0.99, 1.05)	.15	1.03 (0.99, 1.06)	.09
Private health insurance‡	0.40 (0.17, 0.97)	.04	0.34 (0.13, 0.89)	.03
Use of inhaled corticosteroids in the previous 6 mo‡	4.43 (2.21, 9.18)	<.01	4.17 (1.84, 9.44)	<.01

CESD, Center for Epidemiologic Studies Depression Scale; CI, confidence interval; OR, odds ratio.

*Models adjusted for age and sex, in addition to private health insurance.

†Total CESD score at the second study visit minus total CESD score at the first study visit.

‡At the second study visit.

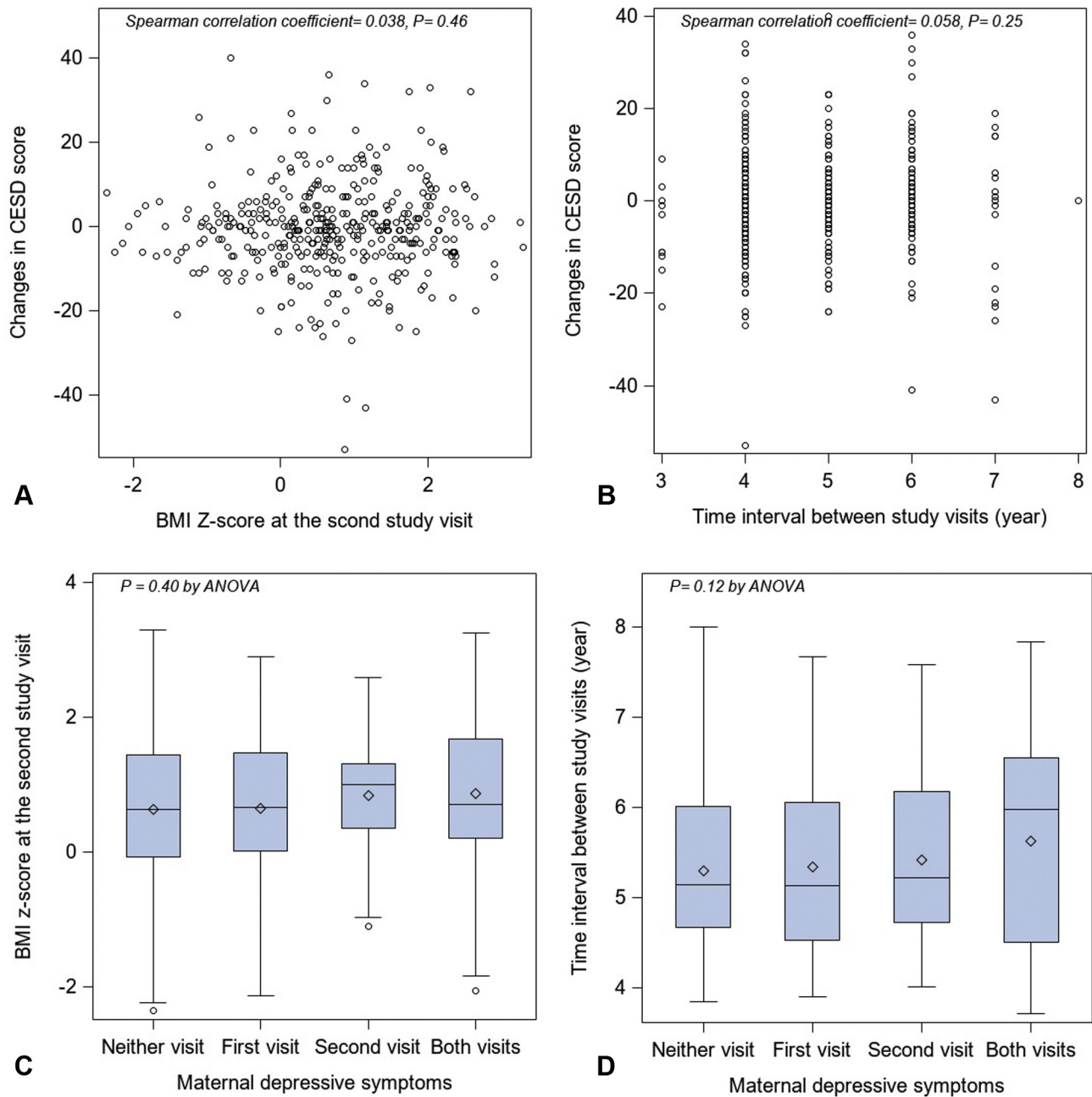


FIGURE E1. Correlation between changes in CESD score and BMI z-score at the second visit (**A**), changes in CESD score and time interval between study visits (**B**), maternal depressive symptoms at study visits and BMI z-score (**C**), and maternal depressive symptoms and time interval between visits (**D**). *BMI*, Body mass index; *CESD*, Center for Epidemiologic Studies Depression Scale.