Socioeconomic status, diet, and recurrent severe asthma exacerbations in Puerto Rican youth

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Background: Why Puerto Rican youths have higher rates of severe asthma exacerbations (SAEs) than their non-Hispanic White peers is unclear.
Objective: We aimed to identify risk factors associated with recurrent SAEs in Puerto Rican youths with asthma.
Methods: We performed cross-sectional and longitudinal analyses of recurrent SAEs in 209 Puerto Rican youths with asthma who participated in 2 cross-sectional studies approximately 5.2 years apart: the Puerto Rico Genetics of Asthma and Lifestyle study (visit 1, participants aged 6-14 years) and the Epigenetic Variation and Childhood Asthma in Puerto Ricans study (visit 2, participants aged 9-20 years). Recurrent SAEs were defined as at least 2 SAEs in the previous year.
Results: Of the youths in our study, there were 80 (38.3%) and 47 (22.4%) with recurrent SAEs at visit 1 and visit 2, respectively, and 31 participants (14.8%) had persistent recurrent SAEs (ie, recurrent SAEs at both visits). In multivariable analyses, low household income was significantly associated with 2.4 to 12.3 times increased odds of recurrent SAEs in all analyses, with stronger longitudinal associations. Low parental education level, nonprivate or employer-based health insurance, overweight or obesity, residential proximity to a major road, and low or moderate level of outdoor activity were each significantly associated with recurrent SAEs in at least 1 analysis. Further, persistence of low parental numeracy level, low household income, and an unhealthy diet were each associated with persistent recurrent SAEs.
Conclusion: In this study of Puerto Rican youths with asthma, persistence of low parental numeracy level, a low household income, and an unhealthy diet were associated with persistent recurrent SAEs. Our findings support policies promoting equity and healthy lifestyles for Puerto Rican children and their families. (J Allergy Clin Immunol Global 2024;3:100220.)

Key words: *Asthma, Puerto Rican, recurrent exacerbations, exacerbation-prone asthma, determinants of health*

In the United States, approximately 4.2 million children are affected by asthma,[1] with variable disease prevalence according to race and ethnicity. In this country, Puerto Ricans are disproportionately burdened with childhood asthma.[1] Compared with non-Hispanic White children, Puerto Rican children have higher rates of severe asthma exacerbations (SAEs),[2,3] a major cause of health care costs and school absences.

Childhood asthma is a heterogenous condition that can be divided into various phenotypes. Identifying such phenotypes is relevant to personalized medicine, as they are correlated with disease severity and treatment responses.[4-6] A distinct asthma phenotype is exacerbation-prone asthma (EPA), which has been variably defined as at least 1[7] to at least 3[8] asthma exacerbations per year.[9] To date, the causes of recurrent SAEs or the EPA phenotype have not been well studied in the general population or in Puerto Rican youths specifically.[3,10-13]

On the basis of our prior work and that of others, we hypothesized that risk factors that are both common and associated with asthma or worse asthma outcomes in Puerto Rican children and adolescents, including poverty and inadequate health insurance, lower parental education and numeracy levels, secondhand smoke (SHS) exposure, overweight or obesity, an unhealthy diet, and traffic-related air pollution, would be associated with recurrent SAEs in Puerto Rican youths. We examined this hypothesis in a longitudinal study of Puerto Rican youths with asthma.

METHODS

Study populations

The Puerto Rico Genetics of Asthma and Lifestyle study (PR-GOAL) has been described in detail elsewhere.[14] PR-GOAL included 678 Puerto Ricans aged 6 to 14 years with and without asthma who were recruited from March 2009 through June 2010 from randomly selected households in San Juan and Caguas (Puerto Rico) by using a multistage probabilistic design. In brief, the primary sampling units were randomly selected neighborhood clusters based on the 2000 US Census, and the secondary sampling units were randomly selected households within each primary sampling unit. A household was eligible if at least 1 resident was aged 6 to 14 years. A total of 6401 households selected for inclusion were contacted. Of these, 1,111 households had at least 1 child who met the inclusion criteria other than age (4 Puerto Rican grandparents and residence in the same household for at least 1 year). Of these 1,111 households, 438 (39.4%) had at least 1 eligible child with asthma (defined as physician-diagnosed asthma and wheeze in the prior year).

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Abbreviations used
EPA: Exacerbation-prone asthma
EVA-PR: Epigenetic Variation and Childhood Asthma in Puerto Ricans
ICS: Inhaled corticosteroid
PR-GOAL: Puerto Rico Genetics of Asthma and Lifestyle
PROPRA: Prospective Study of Puerto Ricans and Childhood Asthma
SAE: Severe asthma exacerbation
SDOH: Social determinant of health
SHS: Secondhand smoke

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 having neither physician-diagnosed asthma nor wheeze in the prior year) was randomly selected from the remaining 673 households. To reach our target sample size (~700 children), we randomly selected and attempted to enroll 783 of the 1,111 eligible children. The parents of 105 of these 783 children (13.4%) refused to participate or could not be reached, leaving 678 study participants (351 children with asthma and 327 controls).

From February 2014 to May 2017, we conducted a second study, the Epigenetic Variation and Childhood Asthma in Puerto Ricans (EVA-PR) study, which included 543 Puerto Rican youths aged 9 to 20 years with asthma (n = 269) and without asthma (n = 274) who were selected from the 1,111 household eligible for PR-GOAL.[15] Of the 543 participants in EVA-PR, 406 had participated in PR-GOAL and were thus included in the Prospective Study of Puerto Ricans and Childhood Asthma (PROPRA).[16] Only participants with asthma at both study visits in PROPRA (n = 209) are included in the current analysis (Fig 1, *A*), which focuses on SAEs.

All studies were approved by the institutional review boards of the University of Puerto Rico and the University of Pittsburgh. In all studies, written parental consent and child assent were obtained for participants younger than 18 years, and written consent was obtained from participants aged 18 years or older.

Study procedures

At both study visits, all participants completed a protocol that included administration of questionnaires, spirometry, and collection of blood samples. One of the child's caretakers (the mother in >93% of subjects) or the participants (if aged ≥18 years) completed a questionnaire on demographics, general and respiratory health, and family history,[17] as well as a 75-question semiquantitative food frequency questionnaire developed for Hispanic populations[17,18] and a slightly modified version of the validated Asthma Numeracy Questionnaire[19] (score range 0-3 points).[20] We derived a dietary score using data from the food frequency questionnaire, ranging from minus 2 (the least-healthy diet) to plus 2 (the healthiest diet).

Height and weight were measured to the nearest centimeter and kilogram, respectively, and body mass index *z* scores were calculated on the basis of 2,000 growth charts from the Centers for Disease Control.[21] Spirometry was conducted with an EasyOne spirometer (NDD Medical Technologies, Andover, Mass) according to American Thoracic Society and European Respiratory Society recommendations.[22] Percent predicted values for lung function measures at each visit were calculated by using the Global Lung Function Initiative equations, which account for age, sex, and height.[23] Serum IgE levels to each of 5 common allergens (house dust mite [*Dermatophagoides pteronyssinus* 1], cockroach [*Blattella germanica* 2], cat dander [*Felinus domesticus* 1], dog dander [*Canus familiaris* 1], and mouse urinary protein [*Mus musculus* 1]) were measured by using the UniCAP 100 system (Pharmacia & Upjohn, Kalamazoo, Mich). For each allergen, an IgE level of at least 0.35 IU/mL was considered positive. Peripheral blood eosinophil count (heretofore referred to as eosinophil count) was measured by using Coulter-Counter techniques.

As in previous work, home addresses were linked to the corresponding 15-digit 2000 US Census Federal Information Processing Standard code at the University of Puerto Rico. In ArcMAP10.1 (Arc-GIS 10.1, Esri, Redlands, Calif), centroids were created for each participant block. Distance to the nearest major roadway (defined by US Census classification system A1-A3)[24] was calculated for each participant centroid (ArcGIS, ESRI 2013 Street Maps). Close proximity to a major road was defined as living no more than 500 meters from a major roadway and previously shown to increase the risk of SAEs in Puerto Rican children.[25]

SAE was defined as a visit to the emergency department (ED) or urgent care for asthma or a hospitalization for asthma. In cross-sectional analyses, our outcome of interest was recurrent SAEs, defined as at least 2 SAEs in the previous year (Fig 1, *B*). In longitudinal analyses, our outcomes of interest were (1) recurrent SAEs in the year before the second visit or (2) persistent recurrent SAEs, defined as at least 2 SAEs in the year before the first visit and in the year before the second visit (Fig 1, *C*).

Our exposures of interest included social, physical, and individual determinants of health, namely, age, sex, low annual household income (<$15,000 per year, which was the median household income in Puerto Rico in 2008), type of health insurance (private or employer-based vs others), low parental education level (defined as neither parent having completed high school), low parental numeracy level (as in prior work, defined as an Asthma Numeracy Questionnaire score of 1 or lower),[26] parental history of asthma, prematurity, current SHS exposure, SHS in early life (*in utero* or in the first 2 years of life), having a pet in the home, sighting of pests or mold in the home, overweight or obesity (body mass index *z* score ≥ 85th percentile), an unhealthy diet (as in prior work, defined as a nonpositive score (0, –1, or –2),[27,28] residential proximity to a major road, inhaled corticosteroid (ICS) use within the prior 6 months, and low or moderate level of physical outdoor activity. In the longitudinal analyses, we examined persistent exposure to determinants of health that could change between visits. We examined the relationship between exposure at the first visit and recurrent SAEs at the second visit (Fig 1, *C*, Part 1), persistent exposure (ie, having that characteristic at both visit 1 and at visit 2 versus those without the exposure of interest at both study visits [ie, having that characteristic at visit 1 but not at visit 2, having that characteristic at visit 2 but not at visit 1, or not having that characteristic at either visit]) and recurrent SAEs at the second visit (Fig 1, *C*, Part 2), and persistent exposure and persistent recurrent SAEs (Fig 1 *C*, Part 3).

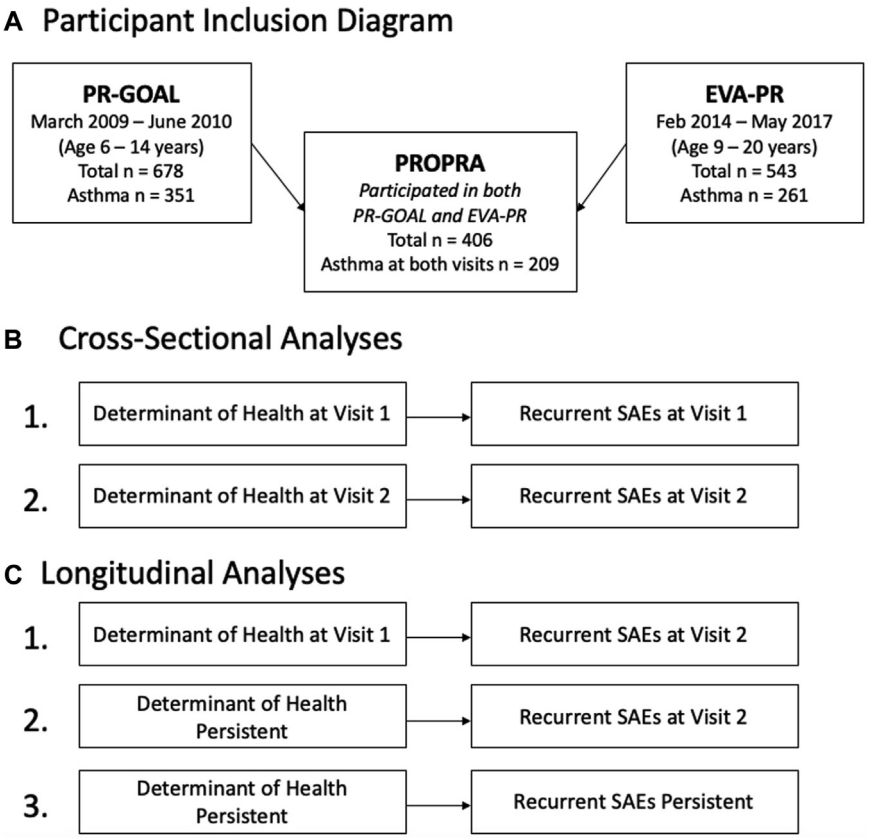

FIG 1. Flowchart for selection of participants and overview of analyses conducted in Puerto Rican youths. Recurrent SAE was defined as at least 2 SAEs in the year before the study visit. "Determinant of health, persistent" refers to having the determinant of health present at both study visits. "Recurrent SAEs, persistent" refers to having at least 2 SAEs in the year before both study visits.

Statistical analysis

Logistic regression was used for the multivariable analysis of recurrent SAEs (in cross-sectional and longitudinal analyses) and persistent recurrent SAEs (in longitudinal analyses only), with multivariable models developed by using bivariate analyses, our prior work, and published literature. Because household income and type of health insurance were correlated, we did not include them in the same models but instead replaced household income with type of health insurance in a sensitivity analysis.

To explore whether the estimated effects of selected covariates (household income, overweight or obesity, an unhealthy diet, and residential proximity to a major road) were modified by biomarkers of atopy or eosinophilia, we tested separately for an interaction between each of these covariates and (1) an eosinophil count of at least 150 cells/μL, (2) an eosinophil count of at least 300 cells/μL, and (3) at least 1 positive allergen-specific serum IgE result in the final multivariable models.

All analyses were conducted using SAS version 9.4 (SAS Institute, Cary, NC) or RStudio 2022.07.1 build 554.

RESULTS

As shown in Fig 1, there were 209 participants with asthma who participated in both study visits and were thus included in the current analysis. Recurrent exacerbations occurred in 80 participants (38.3%) at visit 1 and 47 (22.4%) at visit 2. Table I shows determinants of health for participants at each study visit, according to the presence of recurrent SAEs. At both visits, participants with recurrent SAEs were significantly more likely than those without recurrent SAEs to have a low household income, have low parental numeracy level, and have used an ICS in the prior 6 months. At the first visit, participants with recurrent SAEs were also significantly more likely than those without recurrent SAEs to live within 500 meters of a major road. At the second visit, participants with recurrent SAEs were also significantly more likely to lack private or employer-based health insurance, be overweight or obese and report a low or moderate level of outdoor activity, and have a lower level of parental education than participants without recurrent SAEs. Table II shows a comparison of lung function measures and markers of atopy for children at both study visits according to the presence of recurrent SAEs. There were no significant differences in lung function measures or atopy markers between participants with and without recurrent SAEs at either visit.

Table III shows the results of the cross-sectional multivariable analysis at visit 1 and at visit 2, which were adjusted for age, sex, parental education level, household income, overweight or obesity, an unhealthy diet, residential proximity to a major road, ICS use in the past 6 months, level of outdoor activity, and parental numeracy level. At visit 1, low household income, residential proximity to a major road, and ICS use in the previous 6 months were significantly associated with 2.4 to 3.8 times

TABLE I. Determinants of health at each study visit by presence or absence of recurrent SAEs

	Cross-sectional				Longitudinal	
	Visit 1		Visit 2		Persistence of the determinant*	
	≥2 SAEs in the year before visit 1		≥2 SAEs in the year before visit 2		≥2 SAEs in the year before both visits	
Determinant of health	**Yes (n = 80)**	**No (n = 129)**	**Yes (n = 47)**	**No (n = 162)**	**Yes (n = 31)**	**No (n = 178)**
Nonvariable determinants of health, no. (%)						
Female sex	35 (43.8)	54 (41.9)	**26 (55.3)**	**63 (38.9)**†	18 (58.1)	71 (39.9)
Parental history of asthma	53 (66.3)	83 (64.3)	34 (72.3)	109 (68.1)	18 (58.1)	105 (59.7)
Prematurity	5 (6.3)	8 (6.2)	3 (6.4)	9 (5.6)	3 (9.7)	6 (3.4)
SHS in early life (*in utero* or in the first 2 years of life)	40 (50.6)	63 (51.2)	26 (55.3)	74 (45.7)	12 (38.7)	66 (38.6)
Variable determinants of health						
Age (y), mean ± SD	9.4 ± 2.5	10.1 ± 2.4	14.9 ± 3.0	15.2 ± 2.8		
Annual household income < $15,000, no. (%)	**57 (72.2)**	**70 (55.6)**†	**39 (83.0)**	**87 (53.7)**‡	**27 (87.1)**	**86 (49.3)**‡
Lacks private or employer-based health insurance, no. (%)	54 (67.5)	81 (62.8)	**39 (83.0)**	**63 (38.9)**‡	23 (74.2)	99 (55.6)
Neither parent completed high school, no. (%)	13 (16.3)	19 (14.7)	**10 (21.3)**	**14 (8.6)**†	**6 (19.4)**	**14 (7.9)**†
Low parental numeracy, no. (%)§	**59 (73.8)**	**75 (58.1)**†	**22 (46.8)**	**48 (29.6)**†	**14 (45.2)**	**44 (24.7)**†
Current SHS exposure, no. (%)	31 (38.8)	49 (38.3)	14 (29.8)	62 (38.3)	5 (16.1)	52 (29.4)
Cat in the home, no. (%)‖	8 (10.0)	18 (14.1)	6 (12.8)	29 (17.9)	0 (0)	12 (6.8)
Dog in the home, no. (%)‖	58 (72.5)	79 (61.3)	32 (68.1)	121 (74.7)	16 (51.6)	98 (55.1)
Cat or dog in the home, no. (%)‖	59 (73.8)	83 (64.8)	33 (70.2)	128 (79.0)	16 (51.6)	107 (60.5)
Cockroaches observed in the home, no. (%¶)	60 (75.0)	103 (79.8)	28 (59.6)	113 (69.8)	99 (55.6)	15 (48.4)
Mouse or rat observed in the home, no. (%)¶	24 (30.0)	44 (34.1)	9 (19.2)	31 (19.1)	4 (12.9)	18 (10.1)
Mold or mildew observed in the home, no. (%)¶	31 (38.8)	63 (48.8)	17 (36.2)	81 (50.0)	5 (16.1)	51 (28.7)
Overweight or obesity, no. (%)	38 (50.0)	57 (50.4)	**28 (59.6)**	**62 (38.3)**‡	15 (50.0)	54 (34.0)
Unhealthy diet, no. (%)#	42 (52.5)	54 (41.9)	24 (53.2)	63 (38.9)	**12 (38.7)**	**33 (18.5)**†
Residence within 500 meters of a major road, no. (%)	**66 (82.5)**	**83 (63.8)**‡	37 (78.7)	116 (72.1)	25 (80.7)	115 (65.3)
ICS use, no. (%)¶	**36 (45.0)**	**38 (29.5)**†	**22 (46.8)**	**32 (20.1)**‡	**9 (29.0)**	**22 (12.6)**†
Low or moderate level of outdoor activity, no. (%)**	45 (56.3)	66 (51.2)	**39 (83.0)**	**89 (55.3)**‡	**17 (54.8)**	**61 (34.5)**†

Boldface indicates statistical significance.
*Persistence of the determinant defined as determinant being present at both study visits.
†$P < .05$.
‡$P < .01$.
§Low parental numeracy level defined as modified Asthma Numeracy Score of 1 or lower.
‖In the previous 6 months.
¶In the previous 12 months.
#Unhealthy diet defined as a dietary score less than 1.
**Self-report of spending a "short" or "moderate" amount of time outdoors versus spending "a lot of time" or "all the time" outdoors.

increased odds of recurrent SAEs. At visit 2, low household income, low parental education level, overweight or obesity, ICS use in the previous 6 months, and low to moderate level of outdoor activity were significantly associated with 3.3 to 4.6 times increased odds of recurrent SAEs.

Table E1 (see the Online Repository at www.jaci-global.org) compares the baseline characteristics of the 209 subjects who participated in both PR-GOAL (visit 1) and EVA-PR (visit 2), had asthma at both visits, and were thus included in PROPRA and in our present analyses versus the 128 subjects with asthma who participated in PR-GOAL but not in EVA-PR (and were thus not included in our current analyses). Compared with subjects included in PROPRA, those not included were slightly older and more likely to be exposed to SHS but less likely to be overweight or obese. There were no significant differences in recurrent SAEs, lung function measures, or any other characteristics between subjects who were and were not included in PROPRA.

The median time between the baseline and follow-up study visits was 5.2 years (range 3.7-8.0 years), and 31 of the 209 participants (14.8%) had persistent recurrent SAEs. Compared with the participants without persistent recurrent SAEs, those with persistent recurrent SAEs were significantly more likely to have a persistently lower annual household income, a lower parental education level, and a lower parental numeracy level; to consume an unhealthy diet and have a low or moderate level of outdoor activity at both visits; and to have used an ICS in the 6 months before both visits (ie, in PR-GOAL and in EVA-PR) (Table I). In a multivariable analysis adjusted for the same covariates as in the cross-sectional analyses plus the time interval between study visits, persistence of a low household income, low parental numeracy level, residential proximity to a major road, an unhealthy diet, and ICS use were significantly associated with 3.1 to 15.1 times increased odds of persistent recurrent SAEs, and persistence of low household income, low parental numeracy

TABLE II. Lung function measures and atopy markers at each visit, by at least 2 SAEs

	Visit 1		Visit 2	
	≥2 SAEs in the year before visit 1		≥2 SAEs in the year before visit 2	
Variable	Yes (n = 80)	No (n = 129)	Yes (n = 47)	No (n = 162)
FEV_1 (% predicted), mean ± SD	89.5 ± 14.5	93.2 ± 14.9	95.2 ± 13.3	96.3 ± 15.3
FVC (% predicted), mean ± SD	99.0 ± 15.6	101.5 ± 16.6	102.0 ± 12.2	101.5 ± 15.0
FEV_1/FVC, mean ± SD	0.81 ± 0.09	0.82 ± 0.08	0.82 ± 0.08	0.83 ± 0.08
Peripheral blood eosinophils (cells/μL), median [Q1-Q3]	375 [194-599]	416 [267-629]	259 [104-431]	245 [132-398]
Total IgE level (IU/mL), median [Q1-Q3]	361 [123-773]	323 [116-830]	270 [119-543]	299 [119-736]
≥1 positive allergen-specific IgE result, no. (%)	50 (68.5)	74 (67.3)	33 (71.7)	115 (74.7)

FVC, Forced vital capacity.

TABLE III. Cross-sectional analysis of determinants of health and recurrent SAEs

Variable	Determinant of health at visit 1 and odds of ≥2 SAEs* at visit 1, OR (95% CI)	Determinant of health at visit 2 and odds of ≥2 SAEs* at visit 2, OR (95% CI)
Unadjusted		
Neither parent completed high school	1.23 (0.52-2.42)	**2.86 (1.18-6.94)**
Low parental numeracy level†	**2.02 (1.10-3.72)**	**2.09 (1.08-4.06)**
Overweight or obesity	0.98 (0.55-1.78)	**2.38 (1.23-4.61)**
Unhealthy diet‡	1.54 (0.88-2.69)	1.79 (0.93-3.44)
Residence within 500 m of a major road	**2.56 (1.29-5.05)**	1.44 (0.66-3.13)
ICS use§	**1.95 (1.10-3.50)**	**3.49 (1.75-6.98)**
Low or moderate level of outdoor activity‖	1.23 (0.70-2.15)	**3.94 (1.73-8.97)**
Annual household income < $15,000	**2.07 (1.13-3.79)**	**4.20 (1.84-9.55)**
Lacks private or employer-based health insurance	1.23 (0.68-2.22)	**3.10 (1.36-7.07)**
Adjusted: Main model		
Neither parent completed high school	0.80 (0.33-1.97)	**4.42 (1.41-13.88)**
Low parental numeracy level†	1.99 (0.97-4.10)	1.61 (0.70-3.72)
Overweight or obesity	0.87 (0.45-1.68)	**3.28 (1.44-7.43)**
Unhealthy diet‡	1.19 (0.61-2.30)	1.32 (0.60-2.92)
Residence within 500 m of a major road	**3.77 (1.71-8.33)**	1.62 (0.65-4.08)
ICS use§	**3.62 (1.72-7.62)**	**4.57 (1.93-10.83)**
Low or moderate level of outdoor activity‖	1.01 (0.52-1.96)	**3.95 (1.53-10.20)**
Annual household income < $15,000	**2.36 (1.09-5.12)**	**4.29 (1.63-11.34)**
Adjusted: Secondary model		
Neither parent completed high school	0.85 (0.35-2.03)	**5.17 (1.66-16.13)**
Low parental numeracy level†	**2.16 (1.06-4.37)**	1.73 (0.76-3.95)
Overweight or obesity	0.84 (0.44-1.59)	**3.02 (1.36-6.73)**
Unhealthy diet‡	1.30 (0.67-2.51)	1.40 (0.64-3.06)
Residence within 500 m of a major road	**3.42 (1.56-7.46)**	1.51 (0.61-3.75)
ICS use§	**3.02 (1.45-6.30)**	**4.74 (2.03-11.13)**
Low or moderate level of outdoor activity‖	1.08 (0.56-2.06)	**3.61 (1.43-9.10)**
Lacks private or employer-based health insurance	1.12 (0.52-2.41)	**2.93 (1.11-7.74)**

All adjusted models were adjusted for the variables shown, as well as for age and sex. Boldface indicates statistical significance.
OR, Odds ratio.
*In the previous 12 months.
†Low parental numeracy level defined as a modifed Asthma Numeracy Score of 1 or lower.
‡Unhealthy diet defined as a dietary score lower than 1.
§In the previous 6 months.
‖Self-report of spedning a "short" or "moderate" amount of time outdoors verus spending "a lot of time" or "all the time" outdoors.

level, and ICS use were significantly associated with 2.6 to 6.8 times increased odds of recurrent SAEs at the second visit. In the adjusted analysis of exposures at visit 1 and recurrent SAEs at the second visit, household income at visit 1 (odds ratio = 5.7) and residential distance to a major roadway at visit 1 (odds ratio = 2.6) were associated with recurrent SAEs at visit 2 (Table IV).

Because of high correlation between household income and type of health insurance, we did not include them simultaneously in the same multivariable models. We instead repeated the multivariable analyses in all 3 studies after replacing household income with type of health insurance, obtaining similar results (Tables III and IV). In these secondary multivariable models, type of health insurance at visit 2 was associated with recurrent SAEs at visit 2 (Table III) but was not significant in the cross-sectional analysis at visit 1 or in any of the longitudinal analyses (Table IV).

We next tested for interaction between biomarkers of atopy or eosinophil count and select covariates on recurrent SAEs in the main multivariable cross-sectional and longitudinal models. After correction for the number of tests conducted, there were no significant interactions.

TABLE IV. Longitudinal analysis of determinants of health and recurrent severe asthma exacerbations

Variable	Determinant of health at visit 1 and odds of at least 2 SAEs at visit 2, OR (95% CI)	Persistence of determinant of health and odds of at least 2 SAEs at visit 2, OR (95% CI)*	Persistence of determinant of health and odds of persistence of recurrent SAEs, OR (95% CI)*
Unadjusted			
Neither parent completed high school	**2.43 (1.09-5.45)**	2.56 (0.98-6.71)	2.82 (0.99-7.99)
Low parental numeracy level†	1.42 (0.71-2.87)	**2.42 (1.22-4.79)**	**2.51 (1.14-5.50)**
Overweight or obesity	1.33 (0.67-2.64)	1.95 (0.98-3.89)	1.94 (0.89-4.27)
Unhealthy diet‡	1.05 (0.55-2.01)	1.79 (0.86-3.75)	**2.78 (1.23-6.28)**
Residence within 500 m of a major road	1.90 (0.86-4.23)	1.53 (0.73-3.18)	2.21 (0.86-5.68)
ICS use§	1.04 (0.53-2.05)	**2.53 (1.12-5.69)**	**2.84 (1.16-6.96)**
Low or moderate level of outdoor activity‖	1.57 (0.81-3.05)	**2.32 (1.20-4.48)**	**2.30 (1.07-5.00)**
Annual household income < $15,000	**4.66 (1.97-11.04)**	**4.67 (2.12-10.30)**	**6.91 (2.32-20.57)**
Lacks private or employer-based health insurance	**2.42 (1.23-5.20)**	**2.51 (1.22-5.19)**	2.30 (0.97-5.41)
Adjusted: Main model			
Neither parent completed high school	1.74 (0.86-4.44)	2.48 (0.74-8.31)	2.73 (0.69-10.87)
Low parental numeracy level†	1.18 (0.51-2.77)	**2.59 (1.08-6.23)**	**3.09 (1.07-8.91)**
Overweight or obesity	1.63 (0.76-3.49)	2.27 (0.99-5.21)	2.24 (0.83-6.02)
Unhealthy diet‡	0.82 (0.38-1.76)	2.10 (0.84-5.22)	**3.86 (1.32-11.27)**
Residence within 500 m of a major road	**2.58 (1.00-6.66)**	2.48 (0.99-6.20)	**3.33 (1.06-10.52)**
ICS use§	1.13 (0.48-2.65)	**5.28 (1.55-17.94)**	**15.14 (3.27-70.20)**
Low or moderate level of outdoor activity‖	1.20 (0.55-2.62)	2.14 (0.89-5.16)	2.46 (0.84-7.18)
Annual household income < $15,000	**5.73 (1.93-16.96)**	**6.78 (2.24-20.48)**	**12.25 (2.59-57.97)**
Adjusted: Secondary model			
Neither parent completed high school	1.74 (0.69-4.38)	2.83 (0.86-9.28)	3.25 (0.84-12.56)
Low parental numeracy level†	1.27 (0.56-2.88)	**2.72 (1.17-6.33)**	**3.43 (1.25, 9.43)**
Overweight or obesity	1.51 (0.71-3.18)	**2.31 (1.04-5.14)**	2.25 (0.88-5.76)
Unhealthy diet‡	0.79 (0.37-1.69)	1.85 (0.77-4.41)	**3.18 (1.19-8.50)**
Residence within 500 m of a major road	2.44 (0.96-6.22)	2.13 (0.88-5.13)	2.67 (0.90-7.93)
ICS use§	1.06 (0.46-2.46)	**3.37 (1.10-10.35)**	**5.91 (1.62-21.57)**
Low or moderate level of outdoor activity‖	1.20 (0.57-2.57)	1.88 (0.81-4.32)	2.23 (0.82-6.02)
Lacks private or employer-based health insurance	2.57 (0.97-6.80)	2.47 (0.96-6.33)	1.62 (0.53-5.00)

All models were adjusted for the variables shown, as well as for age at visit 2, sex, and interval between study visits. Boldface indicates statistical significance.

*In the previous 12 months.

†Low parental numeracy level defined as a modified Asthma Numeracy Score of 1 or lower.

‡Unhealthy diet defined as dietary score less than 1.

§In the previous 6 months.

‖Self-report of spending a "short" or "moderate" amount of time outdoors versus spending "a lot of time" or "all the time" outdoors.

DISCUSSION

Identifying predictors of an "exacerbation-prone asthma phenotype" could improve the management of difficult-to-control or severe asthma, yet relatively few studies have focused on identifying risk factors for *recurrent* SAEs among youths in general and in historically marginalized populations in particular.[3,10-13] Among Puerto Rican children and adolescents who participated in a longitudinal study over a median of 5.2 years, low household income in the prior 6 months was consistently associated with recurrent SAEs in both cross-sectional and longitudinal analyses. Of interest, a persistently (at both study visits) unhealthy diet and persistently low parental numeracy level were also significantly associated with persistently recurrent SAEs.

Building on prior work showing an association between social determinants of health and asthma incidence and health care utilization,[29,30] we found that low household income was significantly associated with recurrent SAEs in all cross-sectional and longitudinal analyses, including the longitudinal analysis looking at exposures at visit 1 and recurrent SAEs at visit 2. Other indicators of SES were significantly associated with recurrent SAEs at the second study visit (low parental education level and lack of private or employer-based health insurance) and in longitudinal analyses (low parental numeracy level). Our findings are consistent with and expand those for any (≥1) SAE[26,31,32] and are likely explained by factors including limited access to adequate health care (eg, specialist care[33]), access to and adherence with controller medications, and unmeasured exposures correlated with low SES.

The observed associations between ICS use in the previous 6 months and recurrent SAEs is likely due to "reverse causation," as youths with exacerbation-prone disease may be more likely to be prescribed an ICS,[34] particularly in Puerto Rico (because of noncoverage by nonprivate health insurance). ICS use at visit 1 was not associated with recurrent SAEs at visit 2, suggesting limited longitudinal association with recurrent SAEs in the absence of persistent ICS use. Similarly, reverse causation likely explains the observed link between low to moderate level of outdoor activity and recurrent SAEs at the second study visit.

Unhealthy dietary patterns have been associated with (any) SAE in some but not all studies.[35-37] Our findings of an association between persistently unhealthy diet and persistently recurrent SAEs are consistent with and expand those of our prior study showing that an unhealthy diet is associated with at least 1 SAE in Puerto Rican youths.[27] Interestingly, an unhealthy diet was not associated with recurrent SAEs in either cross-sectional study,

suggesting stronger negative effects of a chronically unhealthy diet on recurrent SAEs. A diet high in saturated fats and refined sugar but low in fruits and vegetables may lead to activation of T_H2-high immune responses and oxidative stress, in turn leading to SAEs.[27]

Recurrent SAEs were more common in participants at visit 1 (36.2%) than in those at visit 2 (22.6%), likely because of age differences (mean age = 10 years at visit 1 vs 15 years at visit 2).[3,38] This may be due in part to shorter duration of asthma at visit 1 than at visit 2, as shorter asthma duration has been linked to recurrent asthma exacerbations.[39] Although puberty and changes in sex hormones likely influence age- and sex-specific differences in asthma prevalence (more common in boys than in girls but more common in women than in men),[40,41] little is known about the relationship between puberty or sex hormones and recurrent SAEs. Interestingly, overweight or obesity was associated with recurrent SAEs at visit 2 but not visit at 1, which could again be explained by age-related differences in puberty status and sex hormone levels between the 2 study visits.[42-44]

Our study addresses the call for biopsychosocial models in pediatric asthma research.[45] Prior studies have found that associations between race or ethnicity and health care utilization for asthma are attenuated after controlling for structural and social determinants of health (SDOHs).[46,47] Because Puerto Rican youths are disparately affected by asthma,[1] we aimed to better understand the impact of SDOHs on the EPA phenotype in this high-risk population, identifying persistence of a low household income, low parental numeracy level, and an unhealthy diet as potentially modifiable risk factors for persistent recurrent SAEs. To our knowledge, this is the first study of SDOHs and recurrent SAEs in Puerto Rican youths and one of the first studies to measure the longitudinal effects of these exposures on an EPA phenotype.

We acknowledge additional study limitations. First, SAE was defined as an ED or urgent care visit or a hospitalization for asthma, and thus use of this term may have missed prescription of oral corticosteroids during scheduled visits to physicians' offices. However, most youths requiring an ED or urgent care visit or a hospitalization for asthma in Puerto Rico are treated with systemic steroids, and prescriptions from a primary care provider are infrequent in our study participants, who often use an acute health care setting when having an asthma exacerbation. Second, there is no consensus definition of recurrent SAEs, which we defined as at least 2 SAEs in the previous year. Third, selection bias is always possible in observational studies, although there were no significant differences in recurrent SAEs or most potential risk factors between subjects who participated in PR-GOAL and were included in PROPRA and those who were excluded. Fourth, we had limited statistical power to detect modest effects and weak to moderate interactions. Fifth, we lacked data on ICS adherence. However, only a relatively small proportion of participants in our studies were prescribed an ICS, and thus, access is a bigger concern than adherence. Finally, our findings may not be generalizable to youths in affluent communities, other racial or ethnic groups, or Puerto Rican children living outside Puerto Rico.

In summary, low household income was consistently associated with recurrent SAEs in cross-sectional and longitudinal analyses in a study of Puerto Rican youths with asthma, and a persistently unhealthy diet and persistently low parental numeracy level were significantly associated with persistence of recurrent SAEs over approximately 5.2 years. Our findings further emphasize the importance of policies promoting economic equity and a healthy lifestyle for Puerto Rican children while also increasing access to adequate medications and management of asthma in Puerto Rican youths.

DISCLOSURE STATEMENT

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Key messages

- **In cross-sectional and longitudinal analysis in this study of Puerto Rican youths, low household income was significantly associated with 2.4 to 12.3 times increased odds of recurrent SAEs, and a persistently unhealthy diet over time was associated with persistence of an exacerbation-prone phenotype.**
- **Low parental education level, nonprivate or non-employer-based health insurance, overweight or obesity, residential proximity to a major road, and low or moderate level of outdoor activity were associated with recurrent severe exacerbations in some but not all analyses.**

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