

African ancestry and lung function in Puerto Rican children

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Background: Puerto Rican and African American subjects share a significant proportion of African ancestry. Recent findings suggest that African ancestry influences lung function in African American adults.

Objective: We sought to examine whether a greater proportion of African ancestry is associated with lower FEV₁ and forced vital capacity (FVC) in Puerto Rican children independently of socioeconomic status, health care access, or key environmental/lifestyle factors.

Methods: We performed a cross-sectional case-control study of 943 Puerto Rican children aged 6 to 14 years with (n = 520) and without (n = 423) asthma (defined as physician-diagnosed asthma and wheeze in the prior year) living in Hartford, Connecticut (n = 383), and San Juan, Puerto Rico (n = 560). We estimated the percentage of African racial ancestry in study participants using genome-wide genotypic data. We tested whether African ancestry is associated with FEV₁ and FVC using linear regression. Multivariate models were adjusted for indicators of socioeconomic status and health care and selected environmental/lifestyle exposures.

Results: After adjustment for household income and other covariates, each 20% increment in African ancestry was significantly associated with lower prebronchodilator FEV₁ (−105 mL; 95% CI, −159 to −51 mL; *P* < .001) and FVC (−133 mL; 95% CI, −197 to −69 mL; *P* < .001) and postbronchodilator FEV₁ (−152 mL; 95% CI, −210 to −94 mL; *P* < .001) and FVC (−145 mL; 95% CI, −211 to −79 mL; *P* < .001) in children with asthma. Similar but weaker associations were found for prebronchodilator and postbronchodilator FEV₁ (change for each 20% increment in African ancestry, −78 mL; 95% CI, −131 to −25 mL; *P* = .004) and for postbronchodilator FVC among children without asthma.

Conclusions: Genetic factors, environmental/lifestyle factors, or both correlated with African ancestry might influence childhood lung function in Puerto Rican subjects. (J Allergy Clin Immunol 2012;■■■:■■■-■■■.)

Key words: Ancestry, FEV₁, forced vital capacity, Puerto Ricans, childhood

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Supported by National Institutes of Health (NIH) grant R01HL079966. J.M.B. receives support from NIH grant K12HD052892.

Disclosure of potential conflict of interest: A. A. Litonjua has received research support from the National Institutes of Health and has received author royalties from UpToDate, Inc. J. C. Celedón is on the advisory board for Genentech, has received research support from the National Institutes of Health, and has received author royalties from UpToDate. The rest of the authors declare that they have no relevant conflicts of interest.

Received for publication February 7, 2012; revised March 15, 2012; accepted for publication March 27, 2012.

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0091-6749/\$36.00

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doi:10.1016/j.jaci.2012.03.035

Childhood asthma is a major public health problem in the United States, particularly among certain ethnic minority groups and the economically disadvantaged.^{1,2} Members of 2 ethnic groups (Puerto Rican and African American subjects) have, on average, markedly higher asthma morbidity^{1,2} and African racial ancestry^{3,4} than Mexican American or white subjects.

The percentage of African ancestry was recently shown to be linearly and inversely associated with 2 measures of lung function (prebronchodilator FEV₁ and forced vital capacity [FVC]) in African American adults, whose mean African ancestry was 72.8% or greater.³ Because African ancestry is correlated with low socioeconomic status (SES), inadequate access to health care, and certain environmental exposures in African American subjects, this finding could be explained by any or all of these factors. Whether African ancestry is associated with lung function in children or in members of other ethnic groups with a lower average proportion of African ancestry (eg, Puerto Rican subjects) is also unknown.

We hypothesized that African ancestry is associated with lower FEV₁ and FVC in Puerto Rican children and that this association is independent of SES, health care access, or environmental/lifestyle factors potentially correlated with racial ancestry, lung function, or both. To test this hypothesis, we examined the relation between African ancestry (assessed by using genome-wide genotypic data) and lung function measures in a cohort of Puerto Rican children with and without asthma.

Abbreviations used

BMI: Body mass index
 ETS: Environmental tobacco smoke
 FVC: Forced vital capacity
 ICS: Inhaled corticosteroid
 LAMP: Local Ancestry in admixed Populations
 PSU: Primary sampling unit
 SES: Socioeconomic status
 SNP: Single nucleotide polymorphism

METHODS**Subject recruitment**

From September 2003 to July 2008, children were recruited from 15 public elementary/middle schools in Hartford that enrolled a significant proportion (42% to 94%) of Puerto Rican children. Informational flyers with a study description were distributed to all parents of children in grades K to 8 in participating schools by mail ($n = 10,881$) or in person during open houses and other school activities ($n = 885$). Parents of 640 children completed a screening questionnaire. Of these 640 children, 585 (91.4%) were eligible for inclusion; parents of 449 (76.7%) of these 585 children agreed to participate. There were no significant differences in age, sex, or area of residence between eligible children who did ($n = 449$) and did not ($n = 136$) agree to participate. Of the 425 children from whom blood samples were collected, 416 (98%) had sufficient DNA for genotyping and were included in the initial analysis.

From March 2009 to June 2010, children in San Juan were chosen from randomly selected households by using a scheme similar to that of a prior study.⁵ In brief, households in the Standard Metropolitan Area of San Juan were selected by using a multistage probability sample design.⁵ Primary sampling units (PSUs) were randomly selected neighborhood clusters based on the 2000 US Census, and secondary sampling units were randomly selected households within each PSU. A household was eligible if 1 or more residents were children 6 to 14 years old. In households with more than 1 eligible child, a maximum of 5 children were randomly selected. Within each housing unit selected, children were enumerated, and 1 child per eligible household was selected for screening. In households with multiple eligible children, 1 child was randomly selected by using Kish tables. On the basis of the sampling design, 7073 households were selected, and 6401 (90.5%) were contacted. Of these 6401 households, 1111 had 1 or more children within the age range of the study who met other inclusion criteria (see below). In an effort to reach our target sample size (approximately 700 children), we attempted to enroll a random sample ($n = 783$) of these 1111 children. Parents of 106 of these 783 eligible households refused to participate or could not be reached. There were no significant differences in age, sex, or area of residence between eligible children who did ($n = 677$ [86.5%]) and did not ($n = 106$ [13.5%]) agree to participate. Blood samples were collected in 592 (87.3%) of these 677 children; 583 (98.5%) of these 592 children had sufficient DNA for genotyping and were included in the initial analyses.

At both study sites, the main recruitment tool was a screening questionnaire given to parents of children aged 6 to 14 years to obtain information about the child's respiratory health and Puerto Rican ancestry. We selected as cases children who had physician-diagnosed asthma, wheeze in the prior year, and 4 Puerto Rican grandparents. We selected as control subjects children who had no physician-diagnosed asthma, no wheeze in the prior year, and 4 Puerto Rican grandparents.

Study procedures

Study participants completed a protocol (see the **Methods** section in this article's Online Repository at www.jacionline.org) that included completion of questionnaires, spirometry, and collection of blood (for DNA extraction), as well as measurements of total and allergen-specific IgE levels in serum and 25-hydroxy-vitamin D levels (hereafter referred to as vitamin D) in plasma and measurement of dust mite and cockroach allergen levels in dust samples. Written parental consent was obtained for participating children, from whom

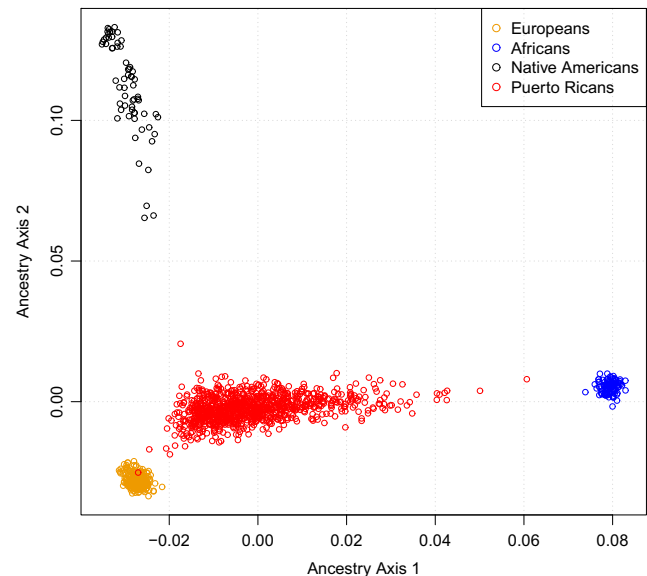


FIG 1. Principal component plot of study subjects (Puerto Rican subjects) compared with HapMap populations representing European and African ancestry and Human Genome Diversity Project populations representing Native American ancestry.

written assent was also obtained. The study was approved by the Institutional Review Boards of Connecticut Children's Medical Center (Hartford, Conn), the University of Puerto Rico (San Juan, Puerto Rico), Brigham and Women's Hospital (Boston, Mass), and the University of Pittsburgh (Pittsburgh, Pa).

Spirometry was conducted with an EasyOne (NDD Medical Technologies, Andover, Mass) spirometer according to American Thoracic Society recommendations.⁶ The best results on measurement of FEV₁ and FVC were selected for data analysis. After completing baseline spirometry, subjects were given 200 µg (2 puffs) of albuterol administered through a metered-dose inhaler with a spacer, and spirometry was repeated after 15 minutes.

Genotyping and estimation of racial ancestry. Genotyping of approximately 2.5 million markers was conducted in DNA from study subjects by using the HumanOmni2.5 BeadChip (Illumina, Inc, San Diego, Calif). We removed single nucleotide polymorphisms (SNPs) that were not in Hardy-Weinberg equilibrium ($P < 10^{-6}$) in control subjects and had minor allele frequencies of less than 1% or failure rates of greater than 2%. Ancestry was estimated by using the Local Ancestry in admixed Populations (LAMP) method and software.^{7,8} The analysis was restricted to SNPs that were present in all 3 ancestral populations and that were not in tight linkage disequilibrium (by using the software default of $r^2 \geq 0.1$), leaving a final sample of 85,059 SNPs. The algorithm uses ancestral proportions from prior studies (in this case Tang et al⁹) and data from reference panels to estimate ancestral proportions for racially admixed populations. Puerto Rican subjects are an admixture of European, African, and Native American populations. To approximate this admixture, we used reference panels from HapMap¹⁰ for European (CEU [Utah residents from Western and Central Europe] and TSI [Tuscans]) and African (YRI [Yorubans from West Africa]) subjects and from the Human Genome Diversity Project for Native American subjects.¹¹ For visualization of ancestry in Fig 1, principal components were calculated for the study subjects and the 3 ancestral proportions by using EIGENSTRAT¹² on the common SNPs in the study population and the 3 ancestral populations. Additional information on the study methods is available in the **Methods** section in this article's Online Repository at www.jacionline.org.

Statistical analysis. Our primary outcomes were FEV₁ and FVC measured before (prebronchodilator) and after (postbronchodilator) administration of inhaled albuterol. Secondary outcomes included other measures of lung function and allergy and asthma severity or control as follows: FEV₁/FVC, bronchodilator responsiveness ((Postbronchodilator FEV₁ – Baseline

TABLE I. Baseline characteristics of participating children*

Covariate	San Juan		Hartford		Combined cohort	
	Cases (n = 287)	Control subjects† (n = 273)	Cases (n = 233)	Control subjects† (n = 150)	Cases (n = 520)	Control subjects† (n = 423)
Age (y)	10.1 (2.6)	10.5 (2.7)	9.8 (2.8)	9.5 (2.6)	10 (2.7)	10.1 (2.7)
Female sex	116 (40%)	142 (52%)#	119 (51%)	73 (49%)	235 (45%)	215 (51%)
BMI (z score)	0.7 (1.2)	0.5 (1.1)¶	1 (1.3)	0.7 (1.3)¶	0.8 (1.3)	0.6 (1.2)#
≥1 Parent graduated from high school	235 (82%)	215 (79%)	154 (66%)	115 (77%)¶	389 (75%)	330 (78%)
Household income <\$15,000/y	193 (69%)	173 (66%)	132 (63%)	87 (63%)	325 (66%)	260 (65%)
Private or employer-based health insurance	87 (30%)	95 (35%)	50 (23%)	34 (24%)	137 (27%)	129 (31%)
Parental history of asthma	193 (67%)	86 (32%)**	153 (66%)	62 (41%)**	346 (67%)	148 (35%)**
Current exposure to ETS	131 (46%)	99 (36%)¶	109 (47%)	60 (40%)	240 (46%)	159 (38%)#
Exposure to <i>in utero</i> smoking	33 (12%)	26 (10%)	45 (19%)	26 (17%)	78 (16%)	52 (13%)
Premature birth	27 (9%)	15 (6%)	12 (5%)	7 (5%)	39 (8%)	22 (5%)
Use of ICSs in the prior 6 mo	90 (31%)		81 (35%)		171 (33%)	
Plasma vitamin D level (ng/mL)	32.5 (8.2)	31 (7.6)¶	24.4 (7.1)	25.4 (7.3)	28.9 (8.7)	29 (7.9)
<i>Dermatophagoides pteronyssinus</i> in house dust (μg/g)‡	0.7 (0.5)	0.7 (0.5)	−0.5 (0.5)	−0.5 (0.6)	0.2 (0.8)	0.3 (0.8)¶
<i>Blattella germanica</i> in house dust (μg/g)‡	0.3 (0.7)	0.3 (0.7)	0.2 (0.7)	0.2 (0.7)	0.3 (0.7)	0.2 (0.7)
Prebronchodilator FEV ₁ (mL)§	1896 (670)	2043 (749)¶	1913 (685)	1956 (687)	1904 (676)	2012 (728)¶
Postbronchodilator FEV ₁ (mL)§	2031 (723)	2125 (760)	2027 (730)	2051 (703)	2029 (725)	2100 (741)
Prebronchodilator FVC (mL)§	2346 (799)	2458 (890)	2331 (837)	2338 (839)	2339 (816)	2415 (873)
Postbronchodilator FVC (mL)§	2423 (838)	2479 (884)	2389 (835)	2374 (811)	2408 (836)	2444 (860)
Prebronchodilator FEV ₁ /FVC ratio	0.81 (0.09)	0.84 (0.09)#	0.82 (0.08)	0.84 (0.09)¶	0.82 (0.09)	0.84 (0.09)**
Postbronchodilator FEV ₁ /FVC ratio	0.84 (0.09)	0.86 (0.08)#	0.85 (0.09)	0.87 (0.06)	0.84 (0.09)	0.86 (0.07)#
Bronchodilator response to albuterol as percentage of FEV ₁	4.9 (11.2)	4 (7.9)	4.7 (9.7)	2.3 (8.4)¶	4.8 (10.6)	3.4 (8.1)¶
Total IgE (IU/mL)‡	2.5 (0.7)	2.2 (0.7)**	2 (0.7)	1.8 (0.6)#	2.3 (0.7)	2.1 (0.7)**
IgE to cockroach (<i>Blattella germanica</i>) ≥0.35 IU/mL	114 (40%)	74 (27%)#	69 (32%)	28 (20%)#	183 (37%)	102 (25%)**
IgE to dust mite (<i>Dermatophagoides pteronyssinus</i>) ≥0.35 IU/mL	183 (64%)	121 (45%)**	81 (42%)	45 (33%)	264 (55%)	166 (41%)**
≥1 Severe asthma exacerbation in the prior year	201 (70%)		114 (49%)		315 (61%)	
Percentage of African ancestry	25.2 (11.7)	24.7 (12.5)	21.9 (7.7)	21.6 (9.9)	23.7 (10.3)	23.6 (11.7)

*Values are numbers (percentages) for binary variables or means (SDs) for continuous variables.

†Comparison between cases and control subjects at each study site and the combined cohort: ¶*P* < .05, #*P* < .01, and ***P* < .001.‡Allergen and total IgE levels were transformed to a logarithmic (log₁₀) scale.§FEV₁ and FVC are presented as absolute values because of the lack of predicted values for Puerto Rican subjects.

||One or more visits to the emergency department or urgent care requiring steroids, hospitalization, or intravenous or oral steroids for asthma in the prior year.

FEV₁/[Baseline FEV₁] × 100), total IgE level, positive IgE level to dust mite, positive IgE level to cockroach, and 1 or more severe asthma exacerbations (≥1 visit to the emergency department or urgent care requiring steroids, hospitalization, or intravenous or oral steroids for asthma) in the prior year.

All analyses were conducted separately in children with and without asthma, first for each study site and then for the combined cohort. Because of their potential correlation with African ancestry, lung function, or both, the following covariates were examined in bivariate analyses: parental history of asthma, household income (<\$15,000 vs ≥\$15,000 [near the median income for households in Puerto Rico in 2008–2009]¹³), private or employer-based health insurance versus other insurance, use of inhaled corticosteroids [ICSs] in the previous 6 months, prematurity,^{14,15} current exposure to environmental tobacco smoke (ETS),¹⁶ *in utero* ETS exposure, body mass index (BMI)¹⁷ as a z score (based on 2000 Centers for Disease Control and Prevention growth charts¹⁸), indoor exposure to dust mite (Der p 1)¹⁹ and cockroach (Bla g 2) allergens,²⁰ plasma vitamin D levels,²¹ and (for the analyses of the combined cohort) study site (Hartford vs San Juan). Given prior results for African ancestry and lung function in African American adults,³ we examined linear trends for the relation between quintiles of African ancestry and the covariates/outcomes of interest by using linear regression in bivariate analyses. Linear regression was then used for the multivariate analysis. A stepwise approach was used to build all multivariate models. All of the final models included African ancestry, age, sex, height, height squared, BMI, household income, ICS use, and (for the combined cohort) study site. Other variables remained in the final models if they were significant at a *P* value of less than .05 or if they satisfied a change in estimate criterion (≥10%) in the parameter estimate (β coefficient). LAMP version 2.3 (<http://lamp.icsi.berkeley.edu/lamp/>)

was used for ancestry estimation and SAS version 9.2 (SAS Institute, Inc, Cary, NC) was used for all other analyses.

RESULTS

Subjects' characteristics and estimation of racial ancestry

After excluding subjects with a low marker call rate, 383 (92%) of the 416 participants from Hartford and 560 (96.1%) of the 583 participants from San Juan remained in this analysis, for a total of 943 children with (cases, *n* = 520) and without (control subjects, *n* = 423) asthma. A comparison of children who were and were not included in this analysis (based on having blood samples and genotypic data) is shown in Table E1 in this article's Online Repository at www.jacionline.org. San Juan cases or control subjects included in the current analysis were significantly more likely to have a lower household income than those not included; there was no significant difference in lung function measures or in our secondary outcomes between the 2 groups. Hartford cases included in this analysis had a lower household income and were less likely to have used ICSs in the prior year or to have been born premature than those not included. There was no significant difference in lung function measures or in our secondary outcomes between the 2 groups. Compared with control subjects not included in our analysis in Hartford, those included were more likely to be

TABLE II. African ancestry, selected covariates, and lung function measures in Puerto Rican children with asthma*

Covariates	Quantiles of African Ancestry					P value for trend
	Quintile 1 (0% to 14.9%)	Quintile 2 (15.0% to 19.3%)	Quintile 3 (19.4% to 24.2%)	Quintile 4 (24.3% to 31.9%)	Quintile 5 (32% to 80.8%)	
Age (y)	10 (3)	10 (3)	9.8 (2.6)	9.7 (2.6)	10 (3)	.4
Female sex	44 (47%)	44 (41%)	51 (47%)	47 (44%)	49 (46%)	.9
BMI (z score)	0.8 (1.16)	0.94 (1.12)	0.92 (1.34)	0.91 (1.31)	0.65 (1.43)	.4
≥1 Parent graduated from high school	69 (74%)	86 (80%)	79 (73%)	76 (72%)	79 (75%)	.5
Household income <\$15,000/y	51 (58%)	57 (58%)	69 (70%)	67 (66%)	81 (79%)	.001
Private or employer-based health insurance	35 (39%)	34 (32%)	25 (24%)	24 (23%)	19 (18%)	.0003
Parental history of asthma	60 (65%)	74 (70%)	71 (66%)	75 (71%)	66 (62%)	.8
Current exposure to ETS	40 (43%)	42 (40%)	52 (48%)	58 (55%)	48 (45%)	.2
Exposure to <i>in utero</i> smoking	10 (12%)	15 (15%)	19 (18%)	20 (19%)	14 (14%)	.5
Premature birth	6 (7%)	9 (9%)	10 (9%)	7 (7%)	7 (7%)	.8
Use of ICSs in the prior 6 mo	36 (39%)	35 (33%)	37 (34%)	35 (33%)	28 (26%)	.1
Plasma vitamin D level (ng/mL)	29 (9)	29 (8)	28 (9)	29 (9)	30 (8)	.4
<i>Dermatophagoides pteronyssinus</i> in house dust (μg/g)†	0.14 (0.78)	−0.01 (0.73)	0.2 (0.82)	0.09 (0.79)	0.4 (0.69)	.009
<i>Blattella germanica</i> in house dust (μg/g)†	0.26 (0.77)	0.22 (0.73)	0.21 (0.71)	0.35 (0.83)	0.23 (0.65)	.8
Prebronchodilator FEV ₁ (mL)‡	1989 (694)	1965 (769)	1918 (665)	1838 (679)	1819 (555)	.03
Postbronchodilator FEV ₁ (mL)‡	2162 (760)	2136 (815)	2033 (694)	1935 (706)	1895 (613)	.002
Prebronchodilator FVC (mL)‡	2404 (879)	2438 (917)	2356 (827)	2287 (787)	2216 (643)	.04
Postbronchodilator FVC (mL)‡	2518 (869)	2526 (958)	2405 (797)	2320 (774)	2281 (754)	.01
Prebronchodilator FEV ₁ /FVC ratio	0.83 (0.07)	0.81 (0.09)	0.82 (0.08)	0.8 (0.09)	0.82 (0.09)	.4
Postbronchodilator FEV ₁ /FVC ratio	0.86 (0.08)	0.85 (0.08)	0.85 (0.08)	0.83 (0.1)	0.84 (0.1)	.04
Bronchodilator response as percentage of baseline FEV ₁	5.4 (10.6)	5.7 (9.8)	4.7 (9)	4.7 (13.1)	3.7 (9.8)	.2
Total IgE (IU/mL)†	2.2 (0.7)	2.3 (0.7)	2.3 (0.7)	2.3 (0.7)	2.4 (0.7)	.03
IgE to cockroach (<i>Blattella germanica</i>) ≥0.35 IU/mL	26 (30%)	35 (35%)	38 (37%)	36 (35%)	48 (46%)	.04
IgE to dust mite (<i>Dermatophagoides pteronyssinus</i>) ≥0.35 IU/mL	42 (52%)	55 (57%)	50 (50%)	56 (57%)	61 (60%)	.35
≥1 Severe asthma exacerbation in the prior year§	44 (47%)	51 (48%)	48 (44%)	42 (40%)	63 (59%)	.28

*Values are numbers (percentages) for binary variables or means (SDs) for continuous variables.

†Allergen and total IgE levels were transformed to a logarithmic (log₁₀) scale.

‡FEV₁ and FVC are presented as absolute values because of lack of predicted values for Puerto Rican subjects.

§One or more visits to the emergency department or urgent care requiring steroids, hospitalization, or intravenous or oral steroids for asthma in the prior year.

boys; there was no significant difference in lung function measures between the 2 groups.

We performed a principal-components analysis, which clusters participants based on similar racial ancestry (Fig 1).¹² The Puerto Rican children in our study primarily fall along an axis between the European and African cohorts in HapMap, suggesting that they have mainly admixed European and African ancestry, with a smaller component of Native American ancestry. The mean estimated ancestral proportions for study participants are shown in Table E2 in this article's Online Repository at www.jacionline.org.

The main characteristics of study participants are summarized in Table I. Compared with control subjects (at each study site and in the combined cohort), cases were significantly more likely to have parental history of asthma and higher BMI and total IgE levels and to have a positive IgE level to cockroach and a lower prebronchodilator FEV₁/FVC ratio. Compared with control subjects in San Juan and in the combined cohort, cases were significantly more likely to have lower postbronchodilator FEV₁/FVC ratio and to be currently exposed to ETS. Consistent with previous findings in Puerto Rican children and adults,⁴ there was no significant difference in African ancestry between cases and control subjects.

Bivariate analysis

We then tested whether African ancestry is associated with the covariates or outcomes of interest in children with asthma (cases)

at each study site (see Table E3 in this article's Online Repository at www.jacionline.org) and the combined cohort (Table II). In the bivariate analyses of all cases, percentage of African ancestry was significantly associated with lower household income, not having private or employer-based health insurance, lower (prebronchodilator or postbronchodilator) FEV₁ and FVC, a higher level of *Dermatophagoides pteronyssinus* (dust mite) allergen in house dust, higher total IgE levels, and a positive IgE level to cockroach (Table II). There was no significant association between African ancestry and prebronchodilator FEV₁/FVC ratio, bronchodilator response, or having 1 or more severe asthma exacerbations in the previous year.

Multivariate analysis

Table III shows the results of the multivariate analysis of African ancestry and FEV₁ and FVC in cases at each study site and for the combined cohort. There was a significant inverse association between the percentage of African ancestry and prebronchodilator and postbronchodilator FEV₁ and FVC in San Juan and in the combined cohort. In Hartford African ancestry was inversely associated with FEV₁ and FVC, but this association was only statistically significant for postbronchodilator FEV₁. We found no significant modification of the effect of African ancestry on any lung function measure by any covariate.

Because of high collinearity between household income and type of health insurance, we did not include both variables in the

TABLE III. Multivariate analysis of percentage of African ancestry and measures of lung function in cases*

Predictors	Prebronchodilator FEV ₁ (mL)	Prebronchodilator FVC (mL)	Postbronchodilator FEV ₁ (mL)	Postbronchodilator FVC (mL)
San Juan, Puerto Rico				
Unadjusted				
Each 20% increment in African ancestry	−97 (−234 to 39); .2	−129 (−291 to 34); .1	−163 (−312 to −14); .03	−154 (−328 to 20); .08
Multivariate model				
Each 20% increment in African ancestry	−117 (−179 to −54); <.001	−145 (−217 to −73); <.001	−165 (−233 to −97); <.001	−155 (−233 to −77); <.001
Household income <\$15,000/y	−46 (−128 to 37); .3	−69 (−164 to 26); .2	−86 (−174 to 3); .06	−55 (−157 to 47); .3
Use of ICSs in the prior year	−59 (−142 to 24); .2	−25 (−121 to 71); .6	−95 (−184 to −5); .04	−95 (−198 to 8); .07
BMI (z score)	72 (39 to 104); <.001	100 (63 to 138); <.001	90 (54 to 125); <.001	115 (74 to 156); <.001
Hartford, Connecticut				
Unadjusted				
Each 20% increment in African ancestry	−114 (−346 to 117); .3	−152 (−434 to 130); .3	−200 (−457 to 57); .1	−238 (−532 to 57); .1
Multivariate model				
Each 20% increment in African ancestry	−92 (−210 to 26); .1	−94 (−225 to 37); .2	−136 (−257 to −14); .03	−119 (−249 to 11); .07
Household income <\$15,000/y	−85 (−174 to 5); .07	−122 (−230 to −15); .03	−73 (−168 to 23); .1	−79 (−189 to 31); .2
Use of ICSs in the prior year	−44 (−143 to 55); .4	−28 (−141 to 86); .6	−60 (−162 to 41); .2	−73 (−185 to 39); .2
BMI (z score)	48 (11 to 84); .01	103 (60 to 146); <.001	69 (30 to 108); <.001	110 (66 to 154); <.001
<i>Dermatophagoides pteronyssinus</i> in house dust (μg/g)‡	−79 (−170 to 13); .09		−86 (−178 to 6); .07	
Combined cohort				
Unadjusted				
Each 20% increment in African ancestry	−102 (−218 to 15); .09	−129 (−269 to 12); .07	−169 (−297 to −40); .01	−167 (−315 to −19); .03
Multivariate model				
Each 20% increment in African ancestry§	−105 (−159 to −51); <.001	−133 (−197 to −69); <.001	−152 (−210 to −94); <.001	−145 (−211 to −79); <.001
Household income <\$15,000/y	−55 (−114 to 4); .07	−91 (−161 to −21); .01	−73 (−137 to −10); .02	−66 (−138 to 7); .08
Use of ICSs in the prior year	−56 (−117 to 5); .07	−32 (−104 to 40); .4	−87 (−152 to −22); .009	−89 (−163 to −15); .02
BMI (z score)	62 (38 to 86); <.001	101 (73 to 130); <.001	82 (56 to 108); <.001	113 (83 to 142); <.001

† All multivariate models were additionally adjusted for age, sex, height, and height squared; the model for the combined cohort additionally was adjusted for study site.

*β Coefficient (95% CI); P value.

‡*Dermatophagoides pteronyssinus* allergen levels were log₁₀ transformed.§As an example, the prebronchodilator FEV₁ of a child with 60% African ancestry would be, on average, 105 mL lower than that of a child with 40% African ancestry and 210 mL lower than that of a child with 20% African ancestry.

same models. Replacing household income with insurance type or changing the threshold for household income from \$15,000 or greater to \$30,000 or greater yielded similar findings (see Table E4 in this article's Online Repository at www.jacionline.org). There was no significant association between African ancestry and total/cockroach-specific IgE level or FEV₁/FVC ratio after adjustment for household income and other covariates.

We then assessed whether African ancestry is associated with FEV₁, FVC, or both in control subjects (Table IV). In the multivariate analysis for San Juan and the combined cohort, percentage of African ancestry was inversely associated with lung function measures; for the combined cohort, this association was significant for all outcomes except prebronchodilator FVC. In this analysis the results in Hartford were nonstatistically significant but in the same direction as in San Juan.

DISCUSSION

We found that African ancestry is significantly associated with lower (prebronchodilator and postbronchodilator) FEV₁ and FVC

in Puerto Rican children with asthma and with (prebronchodilator and postbronchodilator) FEV₁ and postbronchodilator FVC in Puerto Rican children without asthma. Our assessment of African ancestry is robust and likely very precise because we obtained estimates of African ancestry that are nearly identical to those from our primary method (LAMP) when we used a Bayesian method (STRUCTURE²²) that does not take *a priori* ancestral proportions into account (*r* for results from LAMP and STRUCTURE = 0.99, *P* < .0001).

Kumar et al³ reported a linear inverse association between African ancestry and prebronchodilator FEV₁ and FVC in a cohort of 777 African American adults without asthma, which was then replicated in 2 cohorts including 1392 African American adults without asthma. Our results extend those findings to children (with and without asthma) who have markedly lower average proportions of African ancestry (Puerto Rican subjects) than African American subjects.³ Although we do not have an adequate comparison group for our results in children with asthma (cases), our estimate of the effect of African ancestry on prebronchodilator FEV₁ or prebronchodilator FVC in children without asthma

TABLE IV. Multivariate analysis of African ancestry and measures of lung function in control subjects*

Predictors	Prebronchodilator FEV ₁ (mL)	Prebronchodilator FVC (mL)	Postbronchodilator FEV ₁ (mL)	Postbronchodilator FVC (mL)
San Juan, Puerto Rico				
Unadjusted				
Each 20% increment in African ancestry	−87 (−232 to 59); .2	−9 (−182 to 164); .9	−86 (−239 to 67); .3	−58 (−236 to 120); .5
Multivariate models				
Each 20% increment in African ancestry	−92 (−155 to −29); .004	−70 (−146 to 5); .07	−86 (−150 to −22); .008	−80 (−157 to −2); .04
Household income <\$15,000/y	−100 (−182 to −17); .02	−88 (−186 to 11); .08	−113 (−195 to −32); .007	−73 (−172 to 26); .1
BMI (z score)	5 (−32 to 43); .8	20 (−25 to 64); .4	23 (−13 to 60); .2	58 (14 to 103); .01
Hartford, Connecticut				
Unadjusted				
Each 20% increment in African ancestry	−131 (−358 to 95); .3	−141 (−417 to 136); .3	−129 (−378 to 120); .3	−151 (−438 to 137); .3
Multivariate models				
Each 20% increment in African ancestry	−43 (−132 to 47); .4	−43 (−169 to 82); .5	−61 (−153 to 30); .2	−75 (−176 to 26); .1
Household income <\$15,000/y	23 (−72 to 117); .6	−109 (−241 to 23); .1	80 (−15 to 176); .1	38 (−68 to 143); .5
BMI (z score)	41 (4 to 78); .03	138 (86 to 189); <.001	63 (25 to 100); .001	106 (65 to 148); <.001
Combined cohort				
Unadjusted				
Each 20% increment in African ancestry	−87 (−208 to 33); .2	−30 (−175 to 116); .7	−87 (−216 to 42); .2	−68 (−218 to 82); .4
Multivariate models				
Each 20% increment in African ancestry†	−78 (−130 to −27); .003	−55 (−121 to 10); .1	−78 (−131 to −25); .004	−75 (−138 to −12); .02
Household income <\$15,000/y	−61 (−123 to 1); .05	−95 (−173 to −16); .02	−55 (−118 to 8); .08	−50 (−124 to 24); .2
BMI (z score)	25 (−2 to 51); .07	72 (38 to 106); <.001	44 (17 to 71); .002	82 (50 to 114); <.001

†All multivariate models were additionally adjusted for age, sex, height, and height squared; the model for the combined cohort additionally was adjusted for study site.

*β Coefficient (95% CI); P value.

‡As an example, the prebronchodilator FEV₁ of a child with 60% African ancestry would be, on average, 78 mL lower than that of a child with 40% African ancestry and 156 mL lower than that of a child with 20% African ancestry.

(control subjects) is similar to that reported for the 2 replication cohorts of African American subjects included in a previous study. Unlike the prior analysis in African American subjects,³ ours accounted for factors potentially correlated with African ancestry and lung function or asthma morbidity in subjects of African descent in the United States, including indicators of SES and health care, ETS exposure, prematurity, allergen exposure, and plasma vitamin D level.

The estimated effect of African ancestry on FEV₁ or FVC was larger in cases than in control subjects in our study, and this difference was not explained by variables commonly associated with increased morbidity among children with asthma (see above).

Although this might represent true modification of the effect of ancestry by asthma, we cannot exclude the possibility that African ancestry is associated with nonadherence with prescribed medications among Puerto Rican children independently of indicators of SES or type of health insurance. Of note, however, we obtained similar results when the analysis was restricted to cases using ICSs (data not shown).

Differential entry of subjects because of reasons related to both the exposure and outcome of interest (selection bias) and chance are unlikely explanations for our findings. First, if children with asthma were more likely to enter the study because of both a high proportion of African ancestry and increased disease severity, African ancestry would have been associated with at least 1 of our secondary outcomes (eg, severe asthma exacerbations or total/allergen-specific IgE levels), which was not the case.

Second, although only a small proportion of parents invited to participate in Hartford completed a screening questionnaire, the participation rates among eligible children in Hartford and San Juan were 76.5% and 86.5%, respectively, which are high for a study of an ethnic minority group. Even though our results were more significant in San Juan than in Hartford, they were of similar magnitude and in the same direction across study sites, despite differences in sample size, average percentage of African ancestry, and recruitment approach.

Third (and most importantly), our results are consistent with those of a prior study of 2,962 African American adults.³ Because our study was hypothesis driven and our primary outcomes were not truly independent (eg, prebronchodilator and postbronchodilator FEV₁ are correlated), we did not adjust for multiple testing. However, our significant results in cases ($10^{-7} < P < 10^{-4}$ for all lung function measures) or control subjects ($P \leq .02$ for all lung function measures except prebronchodilator FVC) would remain so after applying a Bonferroni correction (eg, $P < .025$ [0.05/2 primary outcomes] in all instances). Among cases, our results for lung function would remain significant even after a conservative adjustment for testing all primary and secondary outcomes ($P < .006$ [0.05/8] in all instances).

We recognize additional limitations to our findings, including potential misclassification of certain covariates (eg, prematurity and early-life ETS exposure) in our cross-sectional study (eg, the observed association between reported ICS use and increased risk of disease exacerbations is likely because of prescription patterns

for children with greater asthma severity). In addition, we are unable to distinguish separate effects of European or Native American ancestry because of the modest proportion of Native American ancestry (12.4%) in study participants.

Our results for lung function in cases differ from those of Salari et al,²³ who reported no association between African ancestry and prebronchodilator FEV₁ in 181 Puerto Rican subjects (8–40 years old) with asthma. Differences between that study and ours include sample size, richness of genome-wide genotyping, and age range of participants. Our negative findings for African ancestry and asthma *per se* are consistent with those of a prior case-control study of 291 Puerto Rican subjects aged 8 to 40 years.⁴ In that study there was a significant interaction between African ancestry and SES on asthma, which was not replicated in the current analysis (data not shown). In contrast to our results, a case-control study of 733 Afro-Caribbeans from Cartagena, Colombia, found an association between African ancestry and asthma and a higher total IgE level. However, that study only accounted for area of residence as a surrogate marker of SES and environmental/lifestyle factors.²⁴

In summary, our findings suggest that African ancestry is associated with lower FEV₁ and FVC in Puerto Rican children independently of SES and health care access, ETS and allergen exposure, and vitamin D level. Genetic variants predominantly found in West African subjects, early-life environmental/lifestyle factors that might be correlated with African ancestry but were unmeasured in this study (eg, maternal nutrition), or both might influence lung development and growth during childhood in Puerto Rican subjects. Future analyses combining local admixture mapping with genome-wide association studies should help identify polymorphisms or haplotypes associated with lung function in Puerto Rican subjects and other populations of African descent.

We thank all participating children and their families for their invaluable participation in the study.

Key messages

- African ancestry is associated with reduced FEV₁ and FVC in Puerto Rican children independently of indicators of SES, health care access, and key environmental/lifestyle exposures.
- Genetic variants, early-life environmental/lifestyle factors, or both correlated with African ancestry might influence lung development and growth during childhood in Puerto Rican subjects.

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METHODS

Subject recruitment

From September 2003 to July 2008, children were recruited from 15 public elementary/middle schools in Hartford that enrolled a significant proportion (42% to 94%) of Puerto Rican children. Informational flyers with a study description were distributed to all parents of children in grades K to 8 in participating schools by mail ($n = 10,881$) or in person during open house and other school activities ($n = 885$). Parents of 640 children completed a screening questionnaire. Of these 640 children, 585 (91.4%) were eligible for inclusion; parents of 449 (76.7%) of these 585 children agreed to participate. There were no significant differences in age, sex, or area of residence between eligible children who did ($n = 449$) and did not ($n = 136$) agree to participate. Of these 449 children, 95 (21.2%) were recruited between September 2003 and October 2005, and 354 (78.8%) were recruited between September 2006 (after funding from the National Institutes of Health) and July 2008. Of the 425 children from whom blood samples were collected, 416 (98%) had sufficient DNA for genotyping and were included in this analysis.

From March 2009 to June 2010, children in San Juan were chosen from randomly selected households by using a scheme similar to that of a prior study.^{E1} In brief, households in the Standard Metropolitan Area of San Juan were selected by using a multistage probability sample design.^{E1} PSUs were randomly selected neighborhood clusters based on the 2000 US Census, and secondary sampling units were randomly selected households within each PSU. A household was eligible if 1 or more residents were children 6 to 14 years old. In households with more than 1 eligible child, a maximum of 5 children were randomly selected. Within each housing unit selected, children were enumerated, and 1 child per eligible household was selected for screening. In households with multiple eligible children, 1 child was randomly selected by using Kish tables. On the basis of the sampling design, a total of 7073 households were selected for inclusion; 6401 (90.5%) were contacted. Of these 6401 households, 1111 had 1 or more children within the age range of the study who met other inclusion criteria (see below). In an effort to reach our target sample size (approximately 700 children), we attempted to enroll a random sample ($n = 783$) of these 1111 children. Parents of 106 (13.5%) of these 783 eligible households refused to participate or could not be reached, leaving 677 participants. There were no significant differences in age, sex, or area of residence between eligible children who did and did not agree to participate.

In both study sites the main recruitment tool was a screening questionnaire given to parents of children aged 6 to 14 years to obtain information about the child's respiratory health and Puerto Rican ancestry. All participants (cases and control subjects) had to have 4 Puerto Rican grandparents and be living in the same household for 1 or more years. We selected as cases children with physician-diagnosed asthma and wheeze in the prior year and as control subjects children with no physician-diagnosed asthma and no wheeze in the prior year.

Study procedures

Questionnaires. The parents of each participant completed a questionnaire used in the Genetics of Asthma in Costa Rica Study, which was slightly modified from one used in the Collaborative Study of the Genetics of Asthma.^{E2}

Spirometry. All spirometry was conducted with an EasyOne (NDD Medical Technologies) spirometer. All subjects had to be free of respiratory illnesses for at least 4 weeks before spirometry, and they were also instructed (when possible) to avoid use of inhaled short- and long-acting bronchodilators for at least 4 and 12 hours before testing, respectively. Forced expiratory maneuvers were judged to be acceptable if they met or exceeded American Thoracic Society criteria modified for children.^{E3} As many as 8 forced expiratory flow volume maneuvers from total lung capacity were performed to obtain 3 acceptable measures. After performing baseline spirometry, subjects were given 2 puffs (180 μ g) of albuterol through a metered-dose inhaler with a spacer. After waiting 15 minutes, each subject repeated the spirometric maneuvers to assess bronchodilator responsiveness.

Dust sample collection. Dust samples were obtained from 3 areas in the home: the one in which the child sleeps (usually a bedroom), the living room/television room, and the kitchen. The dust was sifted through a 50-mesh metal sieve, and the fine dust was reweighed, extracted, and placed in aliquots for analysis of allergens from dust mite (Der p 1) and cockroach (Bla g 2) by using the 2-site mAb Multiplex array assay^{E4} with the same reagents used in the established ELISA assays.

Measurements of serum total and allergen-specific IgE and plasma vitamin D levels. Serum levels of total IgE, IgE to dust mite (Der p 1), and IgE to cockroach (*Blattella germanica*) were determined by using the UniCAP 100 system (Pharmacia & Upjohn, Kalamazoo, Mich). For each allergen, an IgE level of greater than or equal to 0.35 IU/mL was considered positive. Levels of plasma 25-hydroxy-vitamin D (hereafter referred to as vitamin D) were measured by using the Waters HPLC system with tandem mass spectrophotometry (Waters Corp, Milford, Mass).

Genotyping and data cleaning. Genotyping of approximately 2.5 million SNPs was conducted in DNA from study subjects by using the HumanOmni2.5 BeadChip (Illumina, Inc). Each batch included at least 1 replicate sample. Two channel intensities were brought into the Beadstudio workspace, and reclustering was performed with project samples. Subjects with a call rate of less than 95% and SNPs with a call frequency of less than 95% were *a priori* removed. The remaining markers were then cleaned according to Illumina guidelines (http://www.illumina.com/documents/products/technotes/technote_infinium_genotyping_data_analysis.pdf). BeadStudio workspaces were exported to ped file format, and further subject and marker cleaning was performed with R (www.r-project.org) scripts in conjunction with PLINK 1.07.^{E5} Subject relatedness was estimated by using IBD in PLINK. Sex assignment was based on the X-homozygosity estimate. Samples showing sex discordances when compared with phenotype files were removed. We removed SNPs that were not in Hardy-Weinberg equilibrium ($P < 10^{-6}$) in control subjects and had minor allele frequencies of less than 1% or failure rates of greater than 2%.

Estimation of racial ancestry. After restricting to markers present in all 3 ancestral populations and the study population, there were 277,527 SNPs available for analysis input into the LAMP program.^{E6,E7} We used the software-recommended default r^2 value of greater than 0.1 to remove SNPs in linkage disequilibrium with each other, leaving a total of 85,059 SNPs for estimation of ancestry. The LAMP algorithm uses ancestral proportions from previous studies (in this case from Tang et al^{E8}) and data from reference panels to estimate ancestral proportions in racially admixed populations. Because Puerto Rican subjects are an admixture of European, African, and Native American populations, we used the CEU (Utah residents with Northern and Western European descent) and Yoruban (West African) reference panels from HapMap^{E9} and Native American reference panels (Mayan, Pima, Surui, Karitiana, and Colombian) from the Human Genome Diversity Project.^{E10} For visualization of ancestry, principal components were calculated for the study subjects and the 3 ancestral proportions by using EIGENSTRAT^{E11} on the common SNPs in the study population and the 3 ancestral populations.

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TABLE E1. Comparison of cases and control subjects who were and were not included in the current analysis*

Covariates	Cases		Control subjects	
	Included in analysis		Included in analysis	
San Juan, Puerto Rico	Yes (n = 287)	No (n = 64)	Yes (n = 273)	No (n = 53)
Age (y)	10 (3)	9.8 (2.7)	10 (3)	10 (3)
Female sex	40%	53%	52%	47%
BMI (z score)	0.71 (1.25)	0.6 (1.49)	0.5 (1.14)	0.62 (1.1)
≥1 Parent graduated from high school	82%	83%	79%	89%
Household income <\$15,000/y	69%	51%	66%	46%
Private or employer-based health insurance	30%	39%	35%	51%
Parental history of asthma	67%	59%	32%	33%
Current exposure to ETS	46%	38%	36%	26%
Exposure to <i>in utero</i> smoking	12%	10%	10%	8%
Premature birth	9%	6%	6%	0%
Use of ICSs in the prior 6 mo	31%	38%		
Serum vitamin D level (ng/mL)	32 (8)	33 (10)	31 (8)	30 (6)
<i>Dermatophagoides pteronyssinus</i> in house dust (μg/g)†	0.66 (0.51)	0.58 (0.49)	0.65 (0.5)	0.57 (0.63)
<i>Blattella germanica</i> in house dust (μg/g)†	0.34 (0.73)	0.07 (0.65)	0.29 (0.68)	−0.07 (0.61)
Prebronchodilator FEV ₁ (mL)‡	1896 (670)	1747 (733)	2043 (748)	2138 (659)
Postbronchodilator FEV ₁ (mL)‡	2031 (723)	1884 (763)	2124 (759)	2188 (780)
Prebronchodilator FVC (mL)‡	2346 (799)	2197 (1008)	2459 (889)	2572 (800)
Postbronchodilator FVC (mL)‡	2423 (838)	2255 (990)	2478 (882)	2495 (882)
Prebronchodilator FEV ₁ /FVC ratio	0.81 (0.09)	0.81 (0.09)	0.84 (0.09)	0.84 (0.11)
Postbronchodilator FEV ₁ /FVC ratio	0.84 (0.09)	0.84 (0.12)	0.86 (0.08)	0.88 (0.1)
Bronchodilator response to albuterol as percentage of FEV ₁	4.9 (11.2)	5.3 (11.7)	3.9 (7.9)	2.5 (11.4)
Total IgE (IU/mL)‡	2.5 (0.7)	2.6 (0.6)	2.2 (0.7)	2.1 (0.6)
IgE to cockroach (<i>Blattella germanica</i>) ≥0.35 IU/mL	40%	48%	27%	19%
IgE to dust mite (<i>Dermatophagoides pteronyssinus</i>) ≥0.35 IU/mL	64%	67%	45%	31%
≥1 Severe asthma exacerbation in the prior year§	53%	47%		
Hartford, Connecticut	Yes (n = 233)	No (n = 34)	Yes (n = 150)	No (n = 32)
Age (y)	9.8 (2.8)	10 (3)	9.5 (2.6)	10 (4)
Female sex	51%	44%	49%	72%
BMI (z score)	1 (1.3)	1.1 (1.1)	0.72 (1.29)	0.96 (1.24)
≥1 Parent graduated from high school	66%	68%	77%	62%
Household income <\$15,000/y	52%	15%	60%	56%
Private or employer-based health insurance	26%	14%	26%	25%
Parental history of asthma	66%	48%	41%	33%
Current exposure to ETS	47%	50%	40%	59%
Exposure to <i>in utero</i> smoking	19%	23%	17%	10%
Premature birth	5%	16%	5%	0%
Use of ICSs in the prior year	35%	58%		
Serum vitamin D level (ng/mL)	24 (7)	28 (9)	25 (7)	25 (10)
<i>Dermatophagoides pteronyssinus</i> in house dust (μg/g)†	−0.51 (0.5)	−0.44 (0.9)	−0.49 (0.57)	−0.63 (0.39)
<i>Blattella germanica</i> in house dust (μg/g)†	0.15 (0.74)	0.15 (0.74)	0.17 (0.69)	0.31 (0.79)
Prebronchodilator FEV ₁ (mL)‡	1913 (685)	1972 (886)	1956 (687)	2199 (805)
Postbronchodilator FEV ₁ (mL)‡	2027 (730)	2071 (935)	2051 (703)	2180 (849)
Prebronchodilator FVC (mL)‡	2331 (837)	2486 (1109)	2338 (839)	2545 (904)
Postbronchodilator FVC (mL)‡	2389 (835)	2451 (1057)	2374 (811)	2520 (989)
Prebronchodilator FEV ₁ /FVC ratio	0.82 (0.08)	0.8 (0.11)	0.84 (0.09)	0.86 (0.09)
Postbronchodilator FEV ₁ /FVC ratio	0.85 (0.09)	0.84 (0.08)	0.87 (0.06)	0.87 (0.06)
Bronchodilator response to albuterol as percentage of FEV ₁	4.7 (9.7)	5.4 (13.1)	2.3 (8.4)	2.8 (8.4)
Total IgE (IU/mL)†	2 (0.7)	2.2 (0.7)	1.8 (0.6)	1.7 (0.7)
Positive IgE to cockroach (<i>Blattella germanica</i>) ≥0.35 IU/mL	32%	42%	20%	13%
Positive IgE to dust mite (<i>Dermatophagoides pteronyssinus</i>) ≥0.35 IU/mL	42%	38%	33%	0%
≥1 Severe asthma exacerbation in the prior year§	29%	41%		

*Means (SDs) for continuous variables and percentages for binary variables. A comparison of cases and control subjects included in the current analysis is shown in Table I.

†Allergen and total IgE levels were transformed to a logarithmic (log₁₀) scale.

‡FEV₁ and FVC are presented as absolute values because of the lack of predicted values for Puerto Rican subjects.

§One or more visits to the emergency department or urgent care requiring steroids, hospitalization, or intravenous or oral steroids for asthma in the prior year.

||P < .05 for comparison within each outcome for cases or control subjects who were and were not included in this analysis.

TABLE E2. Prior ancestral proportions used for LAMP analysis and resulting average ancestral proportion

Cohort	European	African	Native American
Prior*	67.0%	18.0%	15.0%
Hartford, Connecticut	64.9%	21.9%	13.3%
San Juan, Puerto Rico	63.2%	25.0%	11.8%
Combined cohort	63.9%	23.7%	12.4%

*Prior proportions are used in the LAMP algorithm to optimize estimation of ancestral proportions. Values are from Tang et al.^{E7}

TABLE E3. African ancestry, selected covariates, and lung function measures in Puerto Rican children with asthma*

Covariates	Quintiles of African ancestry					P value for trend
	Quintile 1 (0% to 14.9%)	Quintile 2 (15.0% to 19.3%)	Quintile 3 (19.4% to 24.2%)	Quintile 4 (24.3% to 31.9%)	Quintile5 (32% to 80.8%)	
San Juan, Puerto Rico						
Age (y)	10 (3)	10 (3)	9.6 (2.7)	9.9 (2.5)	10 (2)	.4
Female sex	24 (46%)	21 (40%)	22 (39%)	13 (28%)	36 (46%)	.8
BMI (z score)	0.6 (1.15)	0.83 (1.22)	0.74 (1.1)	0.76 (1.28)	0.66 (1.41)	1
≥1 Parent graduated from high school	47 (90%)	44 (83%)	44 (79%)	40 (85%)	60 (76%)	.07
Household income <\$15,000/y	26 (50%)	35 (67%)	41 (76%)	28 (61%)	63 (82%)	.001
Private or employer-based health insurance	23 (44%)	20 (38%)	17 (30%)	14 (30%)	13 (16%)	.0004
Parental history of asthma	36 (69%)	36 (69%)	39 (70%)	32 (68%)	50 (63%)	.4
Current exposure to ETS	19 (37%)	23 (43%)	24 (43%)	27 (57%)	38 (48%)	.1
Exposure to <i>in utero</i> smoking	4 (9%)	6 (13%)	7 (13%)	7 (16%)	9 (12%)	.6
Premature birth	3 (6%)	7 (13%)	5 (9%)	5 (11%)	7 (9%)	.9
Use of ICSs in the prior 6 mo	19 (37%)	17 (32%)	18 (32%)	18 (38%)	18 (23%)	.2
Plasma vitamin D level (ng/mL)	33 (9)	33 (8)	31 (8)	33 (8)	32 (8)	.8
<i>Dermatophagoides pteronyssinus</i> in house dust (μg/g)†	0.59 (0.55)	0.51 (0.53)	0.83 (0.49)	0.68 (0.51)	0.68 (0.45)	.1
<i>Blattella germanica</i> in house dust (μg/g)†	0.38 (0.8)	0.35 (0.74)	0.28 (0.7)	0.4 (0.82)	0.31 (0.63)	.7
Prebronchodilator FEV ₁ (mL)‡	2038 (680)	1991 (799)	1812 (650)	1819 (675)	1842 (568)	.06
Postbronchodilator FEV ₁ (mL)‡	2186 (728)	2220 (861)	1931 (657)	1899 (704)	1937 (632)	.01
Prebronchodilator FVC (mL)‡	2477 (853)	2514 (933)	2235 (812)	2272 (760)	2264 (660)	.06
Postbronchodilator FVC (mL)‡	2533 (839)	2643 (1002)	2291 (771)	2298 (752)	2357 (784)	.07
Prebronchodilator FEV ₁ /FVC ratio	0.83 (0.07)	0.79 (0.1)	0.81 (0.08)	0.79 (0.1)	0.81 (0.09)	.7
Postbronchodilator FEV ₁ /FVC ratio	0.86 (0.07)	0.84 (0.08)	0.84 (0.08)	0.82 (0.1)	0.83 (0.11)	.03
Bronchodilator response as percentage of baseline FEV ₁	4.8 (9.3)	6.5 (11.2)	6.2 (9.8)	3.8 (16.2)	3.9 (9.5)	.3
Total IgE (IU/mL)†	2.3 (0.7)	2.5 (0.7)	2.4 (0.7)	2.5 (0.6)	2.5 (0.7)	.05
IgE to cockroach (<i>Blattella germanica</i>) ≥0.35 IU/mL	16 (31%)	25 (47%)	19 (35%)	16 (34%)	38 (49%)	.2
IgE to dust mite (<i>Dermatophagoides pteronyssinus</i>) ≥0.35 IU/mL	31 (61%)	37 (70%)	31 (56%)	32 (68%)	52 (67%)	.6
≥1 Severe asthma exacerbation in the prior year§	35 (67%)	39 (74%)	38 (68%)	30 (64%)	59 (75%)	.6
Hartford, Connecticut						
Age (y)	9.9 (2.8)	9.8 (3.1)	10 (3)	9.5 (2.7)	9.8 (2.7)	.6
Female sex	20 (49%)	23 (43%)	29 (56%)	34 (58%)	13 (48%)	.4
BMI (z score)	1 (1.1)	1.1 (1)	1.1 (1.5)	1 (1.3)	0.63 (1.5)	.4
≥1 Parent graduated from high school	22 (54%)	42 (78%)	35 (67%)	36 (61%)	19 (70%)	.7
Household income <\$15,000/y	25 (69%)	21 (47%)	27 (61%)	39 (71%)	17 (68%)	.3
Private or employer-based health insurance	12 (33%)	14 (28%)	8 (18%)	10 (18%)	6 (24%)	.1
Parental history of asthma	24 (59%)	38 (70%)	32 (62%)	43 (74%)	16 (59%)	.6
Current exposure to ETS	21 (51%)	19 (36%)	28 (54%)	31 (53%)	10 (37%)	.9
Exposure to <i>in utero</i> smoking	6 (15%)	9 (17%)	12 (23%)	13 (22%)	5 (19%)	.4
Premature birth	3 (7%)	2 (4%)	5 (10%)	2 (3%)	0 (0%)	.3
Use of ICSs in the prior 6 mo	17 (41%)	18 (34%)	19 (37%)	17 (29%)	10 (37%)	.5
Plasma vitamin D level (ng/mL)	24 (6)	25 (7)	24 (9)	25 (7)	24 (7)	.9
<i>Dermatophagoides pteronyssinus</i> in house dust (μg/g)†	−0.55 (0.53)	−0.53 (0.49)	−0.53 (0.41)	−0.41 (0.62)	−0.6 (0.35)	.6
<i>Blattella germanica</i> in house dust (μg/g)†	0.11 (0.7)	0.1 (0.7)	0.14 (0.72)	0.31 (0.85)	0.01 (0.65)	.6
Prebronchodilator FEV ₁ (mL)‡	1928 (714)	1942 (748)	2020 (669)	1853 (688)	1754 (522)	.3
Postbronchodilator FEV ₁ (mL)‡	2126 (814)	2055 (768)	2133 (722)	1963 (713)	1787 (557)	.08
Prebronchodilator FVC (mL)‡	2314 (913)	2369 (906)	2471 (833)	2298 (813)	2081 (582)	.3
Postbronchodilator FVC (mL)‡	2496 (922)	2412 (908)	2517 (816)	2337 (797)	2085 (644)	.08
Prebronchodilator FEV ₁ /FVC ratio	0.84 (0.07)	0.82 (0.08)	0.82 (0.08)	0.81 (0.09)	0.84 (0.08)	.5
Postbronchodilator FEV ₁ /FVC ratio	0.85 (0.09)	0.86 (0.08)	0.85 (0.09)	0.84 (0.1)	0.86 (0.08)	.8
Bronchodilator response as percentage of baseline FEV ₁	6.5 (12.7)	4.8 (8.2)	3.3 (8)	5.4 (10.1)	3.4 (10.9)	.5
Total IgE (IU/mL)†	2 (0.7)	2 (0.7)	2.1 (0.7)	2 (0.6)	2 (0.7)	.9
IgE to cockroach (<i>Blattella germanica</i>) ≥0.35 IU/mL	10 (28%)	10 (21%)	19 (39%)	20 (35%)	10 (38%)	.1
IgE to dust mite (<i>Dermatophagoides pteronyssinus</i>) ≥0.35 IU/mL	11 (37%)	18 (42%)	19 (42%)	24 (46%)	9 (38%)	.7
≥1 Severe asthma exacerbation in the prior year§	23 (56%)	27 (50%)	29 (56%)	22 (37%)	13 (48%)	.2

*Values are numbers (percentages) for binary variables or means (SDs) for continuous variables.

†Allergen and total IgE levels were transformed to a logarithmic (log₁₀) scale.‡FEV₁ and FVC were presented as absolute values because of lack of predicted values for Puerto Rican subjects.

§One or more visits to the emergency department or urgent care requiring steroids, hospitalization, or intravenous or oral steroids for asthma in the prior year.

TABLE E4. Multivariate analysis of African ancestry and measures of lung function in all cases by using alternate measures of SES or health care access*

Predictors	Prebronchodilator FEV ₁ (mL)	Prebronchodilator FVC (mL)	Postbronchodilator FEV ₁ (mL)	Postbronchodilator FVC (mL)
Household income <\$30,000/y				
Unadjusted				
20% increase in African ancestry	−102 (−218 to 15); .09	−129 (−269 to 12); .07	−169 (−297 to −40); .01	−167 (−315 to −19); .03
Multivariate model†				
20% increase in African ancestry	−117 (−174 to −61); <.001	−146 (−213 to −79); <.001	−163 (−223 to −104); <.001	−154 (−222 to −86); <.001
Household income <\$30,000/y	−93 (−168 to −18); .02	−99 (−187 to −10); .03	−103 (−182 to −24); .01	−103 (−194 to −13); .03
Use of ICSs in the prior year	−52 (−116 to 12); .1	−18 (−94 to 57); .6	−68 (−135 to −1); .05	−55 (−131 to 22); .2
BMI (z score)	64 (39 to 89); <.001	102 (72 to 132); <.001	79 (52 to 106); <.001	107 (76 to 138); <.001
Insurance status				
Unadjusted				
20% increase in African ancestry	−102 (−218 to 15); .09	−129 (−269 to 12); .07	−169 (−297 to −40); .01	−167 (−315 to −19); .03
Multivariate model†				
20% increase in African ancestry	−114 (−167 to −61); <.001	−146 (−209 to −83); <.001	−156 (−213 to −99); <.001	−157 (−223 to −92); <.001
No private or employer-based health insurance	11 (−50 to 73); .7	25 (−49 to 98); .5	−7 (−74 to 61); .8	21 (−56 to 99); .6
Use of ICSs in the prior year	−36 (−94 to 23); .2	−14 (−84 to 55); .7	−75 (−138 to −12); .02	−74 (−146 to −1); .05
BMI (z score)	61 (38 to 84); <.001	97 (69 to 124); <.001	83 (57 to 108); <.001	109 (80 to 138); <.001

*β Coefficient (95% CI); P value.

†All multivariate models were additionally adjusted for age, sex, height, and height squared.