

Differences in allergic sensitization by self-reported race and genetic ancestry

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Background: Many allergic conditions occur more frequently in African American patients when compared with white patients; however, it is not known whether this represents genetic predisposition or disparate environmental exposures.

Objective: We sought to assess the relationship of self-reported race and genetic ancestry to allergic sensitization.

Methods: We included 601 women enrolled in a population-based cohort study whose self-reported race was African American or white. Genetic ancestry was estimated by using markers that differentiate West African and European ancestry. We assessed the relationship between allergic sensitization (defined as ≥ 1 allergen-specific IgE results) and both self-reported race and genetic ancestry. Regression models adjusted for sociodemographic variables, environmental exposures, and location of residence.

Results: The average proportion of West African ancestry in African American participants was 0.69, whereas the mean proportion of European ancestry in white participants was 0.79. Self-reported African American race was associated with allergic sensitization when compared with those who reported being white (adjusted odds ratio, 2.19; 95% CI, 1.22–3.93), even after adjusting for other variables. Genetic ancestry was not significantly associated with allergic sensitization after accounting for location of residence (adjusted odds ratio, 2.09 for urban vs suburban residence; 95% CI, 1.32–3.31). **Conclusion:** Self-reported race and location of residence appeared to be more important predictors of allergic sensitization when compared with genetic ancestry, suggesting that the disparity in allergic sensitization by race might be primarily a result of environmental factors rather than genetic differences. (*J Allergy Clin Immunol* 2008;122:820-7.)

Key words: Self-reported race, race-ethnicity, continental population group, IgE, allergic sensitization

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It is generally acknowledged that race is a complex construct used to broadly categorize individuals into population groups.^{1,2} Self-reported race can reflect biogeographic ancestry (eg, West African, European, East Asian, or Native American)^{3,4}; however, racial categories are also correlated with socioeconomic status,⁵ environmental exposures,⁶ and location of residence.⁷ Although racial categories might correlate with ancestry and its attendant genetic variation, there can be considerable admixture within these groups. For example, African American subjects demonstrate a wide range of predominantly West African and European admixture and, on average, comprise 80% West African ancestry.⁸

Differences in the prevalence of allergic conditions by race-ethnicity have now been well described.⁹⁻¹¹ Total and allergen-specific levels of IgE, which are considered to be markers of allergic inflammation and sensitization, have been shown to be consistently higher among black or African American individuals when compared with white individuals.^{12,13} However, it is not known whether these differences in allergic status can be ascribed predominantly to genetic variation or extrinsic exposures.

Were differences in allergic sensitization by race caused by genetic variation, we would expect allergic status to be more strongly correlated with genetic ancestry, as opposed to self-reported race. Conversely, were environmental or social

Abbreviations used

AIM: Ancestral informative marker
gSD: Geometric SD
OR: Odds ratio
VIF: Variance inflation factor

exposures of primary importance for sensitization, we would expect self-reported race to be more strongly associated.

To examine either possibility, we studied a well-characterized cohort of women enrolled in the Wayne County Health Environment Allergy and Asthma Longitudinal Study. Race was assessed by means of patient self-report, and biogeographic ancestry was estimated by using genetic ancestral informative markers (AIMs). We studied the relationship between both self-reported race and geographic ancestry and allergic sensitization before and after adjusting for other potential explanatory variables, such as age, income, education, smoking status, pet and endotoxin exposure, and location of residence.

METHODS

Study population

This study was approved by the Institutional Review Board at Henry Ford Health System and was compliant with its Health Insurance Portability and Accountability Act policy. Recruitment for this study has been described previously.¹⁴ Briefly, expectant mothers receiving care from a large, integrated health care delivery system in metropolitan Detroit, Michigan, were invited to participate. To be eligible, pregnant women in their second and third trimesters had to be at least 21 years of age, live in a geographically defined area of metropolitan Detroit, and attend one of 5 clinics in the area for their prenatal care. Mothers' signed consent was required for participation. The intent of this study was to follow both the newborn and parents longitudinally to identify environmental and genetic factors associated with the development of atopy and associated conditions.

Data collection

The mothers and children participating in this study had multiple encounters after delivery (ie, 1, 6, 12, and 24 months postpartum); however, for the purposes of this analysis, we focus on data collected at the 1-month home visit. At this visit, field staff administered a survey that included sociodemographic questions, an assessment of smoking status, and items concerning environmental exposures, such as pets in the home. Mothers' blood was collected for DNA, total serum IgE levels, and allergen-specific IgE levels. House dust samples were collected and analyzed for endotoxin levels.

Analysis of total serum IgE levels and allergic sensitization

From the collected venous blood, plasma was separated, frozen, and shipped in batches for analysis of total and allergen-specific IgE in the laboratory of one of the coinvestigators (DRO). Total IgE was measured by using the total IgE protocol of Pharmacia CAP (Pharmacia Diagnostics AB, Portage, Mich), according to established protocols. Assays for allergen-specific IgE were performed with the same commercial assay procedure. The samples were analyzed for IgE specific to the following 7 common aeroallergens: dog (*Canis domesticus*), cat (*Felis domesticus*), cockroach (*Blattella germanica*), ragweed (short, *Ambrosia artemisiifolia*), grass (timothy, *Phleum pratense*), *Alternaria alternata*, and dust mite (*Dermatophagoides farinae*). Individual allergen-specific IgE results of 0.35 IU/mL or greater were considered to be positive. Allergic sensitization was defined as having 1 or more positive allergen-specific IgE results to one of the 7 aeroallergens tested.

Collection of dust and measurement of endotoxin

Dust was collected from 5 locations in the house. However, for the purposes of this analysis, we used dust collected from mothers' bedroom floors as a proxy of endotoxin exposure. Our procedure for dust collection and endotoxin measurement has been described in detail previously.¹⁴ In brief, a standardized sampling procedure was used to collect dust, whereby a measured string loop was laid out in the shape of a square covering an area of 1 m², and the area was vacuumed for 2 minutes. Dust samples were sieved through a 292- μ m mesh filter (Spectra Mesh Polyethylene; Spectrum, Laguna Hills, Calif) on an orbital shaker for 2 hours. An aliquot of the dust passing through the sieve was extracted in PBS containing 0.05% Tween 20 at room temperature at a ratio of 50 μ g of dust to 1 mL of PBS. Dust particles were removed from the extracting fluid by using a serum filter system (Fisher Scientific, Pittsburgh, Pa), followed by centrifugation at 25,000g for 20 minutes.

Endotoxin activity in dust was measured with the fluorescent microplate assay based on recombinant Limulus factor C (PyroGene Recombinant Factor C; Cambrex Bio Science, Walkersville, Md) and an endotoxin standard (Cambrex Bio Science). Endotoxin-free microtiter plates and pipettes were used for all assays. Results were reported as endotoxin units per milligram of dust. Test results falling below the lower limit of the assay were assigned a value of 50% of the assay's lower limit if there was satisfactory recovery of the internal control in the sample.

Genotyping

Participating mothers' genomic DNA was isolated from whole blood with the FlexiGene DNA Kit (Qiagen, Valencia, Calif). Genotyping was performed on DNA isolated from 722 study participants by the genomics core at the University of California, San Francisco. Both the Mapping 500K Array and the Genome-Wide Human SNP Array 5.0 (Affymetrix, Inc, Santa Clara, Calif) were used for genotyping. The Mapping 500K Array uses 2 chips containing single nucleotide polymorphisms found within 200 to 1100 bp of *NspI* and *SlyI* restriction fragments. The Genome-Wide Human SNP Array 5.0 differs from the Mapping 500K Array in that *NspI* and *SlyI* fractions are assayed on a single chip. For each individual, 500 ng of genomic DNA was digested with *NspI* and *SlyI* restriction enzymes. DNA was then ligated to adaptors that recognize the overhangs created by the restriction enzyme digest. These adaptors are recognized by using PCR primers specific for these added sequences. Adaptor-ligated DNA fragments were amplified under conditions optimized to amplify fragments in the 200- to 1100-bp size range. Amplified DNA was purified with polystyrene beads, fragmented, labeled, and hybridized to the GeneChip array. The Affymetrix Power Tools software package was used to make genotype calls and assess the quality control call rates for both GeneChip arrays. We removed 42 individuals from the analysis because of missing data for 1 chip (ie, among those genotyped with 2 chip arrays) or call rates that did not meet our quality control standards. Average call rates exceeded 95% on the remaining individuals.

Admixture analysis

Genotype data from 3 ancestral populations (ie, 42 Europeans, 37 West Africans, and 30 Native Americans from Mexico) was provided by 2 of the coinvestigators (EGB and SC). The 37 West African samples were from individuals living in London, United Kingdom, and South Carolina who were either nonadmixed or had very low levels of admixture. The 42 European samples were from Coriell's North American Caucasian panel (Coriell Institute for Medical Research, Camden, NJ). The Native American samples (Mayan, n = 15; Nahua, n = 15) were recruited from villages in Tlapa in the state of Guerrero, Mexico, by one of the coinvestigators (MDS). DNA from these individuals had been genotyped with the GeneChip Mapping 100K Set (Affymetrix, Inc, Santa Clara, Calif). Delta (δ) values were calculated for the individual alleles, where δ is the absolute difference in allele frequency between 2 ancestral populations. A δ value of 1 implies that the allele is completely informative for ancestry, whereas a δ value of 0 implies that the marker is not informative for ancestry. Because a large majority of our study population self-reported either white or African

American race, we selected 493 single nucleotide polymorphisms that were informative (ie, $\delta > 0.65$) for estimating African and European ancestry. Each of these AIMs was also required to have less than 5% missing values in our study population and be in Hardy-Weinberg equilibrium within both ancestral groups.

We used the software package PSMIX¹⁵ to estimate individual admixture among our study population. This software uses maximum likelihood estimation to estimate individual admixture, as described by Tang and colleagues.¹⁶ The threshold for stopping was either a less than 10^{-6} change in the parameter estimate between consecutive iterations or a total of 10,000 iterations. To confirm our admixture estimates, we repeated our estimates using another program, STRUCTURE,¹⁷ which uses a Bayesian algorithm to compute individual admixture proportions. In addition, we separately restricted our analysis to AIMs greater than 2 cM and 5 cM apart to reduce the influence of linkage disequilibrium. Correlation between ancestry estimates generated with STRUCTURE and PSMIX was greater than 0.99, even after stratifying by self-reported race.

Statistical analysis

For the purposes of this study, we restricted our analysis to the 601 (88.4%) of 680 study participants who reported being either white or African American and who had genotype data. The primary outcome of this analysis was allergic sensitization. Analyses were also repeated assessing total serum IgE level as the outcome.

Student *t* tests and χ^2 tests were used to compare differences between study participants who reported being of either white or African American race. Regression models assessed the relationship of both total serum IgE (linear models) and seroatopy (logistic models) on the independent variables self-reported race-ethnicity (dichotomous) and ancestral admixture (continuous). Total serum IgE was log transformed to normalize the distribution and reduce the effect of extreme outliers. We separately adjusted regression models for other potential mediators, including sociodemographic variables (ie, age, self-reported income, and level of education), environmental exposures (ie, individual smoking status, endotoxin levels in the home, and pet ownership), and location of residence (ie, urban vs suburban). Those living within the cities of Detroit, Hamtramck, or Highland Park (ie, within the outer city limit of Detroit) were considered urban residents. Persons living outside the outer Detroit city limits were considered suburban residents. Pet ownership was the number of dogs, cats, or both in the household and was categorized at 0, 1, and 2 or more pets, as we have done previously.¹⁸ We performed separate analyses of the relationship of self-reported race, genetic ancestry, and location of residence to outcomes after stratifying by the other of these 3 variables.

As *post hoc* analyses, we also examined factors associated with sensitization to individual aeroallergens. Also, as a check, we repeated our analyses incorporating Native American admixture in our regression models. The inclusion or exclusion of this variable had no substantive effect on our findings. We assessed collinearity between self-reported race, genetic ancestry, and location of residence by assessing the variance inflation factor (VIF) of each regression coefficient when regressing log-transformed total serum IgE on these variables simultaneously. In this analysis the VIF values for these variables were 2.31, 1.56, and 1.81, respectively. A high VIF suggests collinearity with at least 1 other variable in the regression model, and our VIF values were much less than the cutoff value of 10 described elsewhere.¹⁹ This supported our inclusion of these variables in the regression models simultaneously. All analyses were performed with SAS version 9.1 (SAS Institute, Inc, Cary, NC).²⁰ A *P* value of less than .05 was considered statistically significant.

RESULTS

Of the 601 women included in this analysis, 385 (64.1%) reported being African American, and 216 (35.9%) reported being white. The comparison of characteristics among those reporting African American and white race is shown in Table I.

Participants reporting being African American were younger, had lower household incomes, differed in their degree of education, were more likely to reside in an urban location, and were less likely to have a dog or cat living in the home when compared with participants who reported being white. However, white participants were more likely to report Latino (6.0% vs 0.8%, $P < .0001$) or Arabic (8.3% vs 0.0%, $P < .0001$) ethnicity when compared with African American participants. African American participants were more likely to demonstrate allergic sensitization and had higher total serum IgE levels when compared with the white participants. There were also consistent differences in the individual allergen-specific IgE results between groups, and these reached statistical significance for cockroach, ragweed, timothy grass, and *Alternaria* species.

Fig 1 shows the distribution of admixture among individuals who reported being African American and white, respectively. As can be seen, there was considerable variation in West African and European ancestry in both groups. The average proportion of West African ancestry in self-reported African American participants was $0.69 (\pm 0.26 \text{ SD})$, whereas the mean proportion of European ancestry in white participants was $0.79 (\pm 0.31 \text{ SD})$. As a check of our self-reported race data, we compared self-reported race with participants' report of how they believed they were perceived by others. There were a total of 7 (1.2%) instances in which these were discordant, and in 5 of these cases, participants believed others would categorize them as a race other than African American or white. Including or excluding these 7 individuals did not substantively alter our findings; therefore they were included in all analyses.

Table II shows the unadjusted and adjusted relationship between self-reported race and allergic sensitization. Individuals who reported being African American were significantly more likely to demonstrate allergic sensitization when compared with individuals who reported being white. This relationship persisted even after adjusting for age, income, educational level, smoking status, dog and cat ownership, house dust endotoxin levels, and location of residence.

West African ancestry was also predictive of allergic sensitization (Table III). However, the relationship between West African ancestry and allergic sensitization was no longer statistically significant after adjusting for location of residence (Table III, model 4). In this model urban residence was a significant predictor of allergic sensitization (odds ratio [OR], 2.09; 95% CI, 1.32–3.31).

The same pattern was seen for total IgE levels in that self-reported African American race was a consistently positive predictor of IgE levels even after adjusting for age, income, educational level, smoking status, dog and cat ownership, house dust endotoxin levels, and location of residence (see Table E1 in this article's Online Repository at www.jacionline.org). In contrast, West African ancestry was not associated with IgE levels after accounting for location of residence (see Table E2, model 4, in this article's Online Repository at www.jacionline.org). In this model urban residence and not genetic ancestry was a significant positive predictor of total serum IgE levels. The consistent relationship between location of residence and both allergic sensitization and total serum IgE levels after stratification by ancestral proportion is also shown in Tables E3 and E4 (available in this article's Online Repository at www.jacionline.org).

Including both self-reported race and admixture simultaneously in regression models showed that only the former

TABLE I. Characteristics of women participants in the Wayne Health, Environment, Atopy and asthma Longitudinal Study stratified by self-reported race

	All women (n = 601)	Self-reported race		P value*
		African American (n = 385)	White (n = 216)	
Age (y), mean $\pm$ SD†	29.8 $\pm$ 5.1	29.2 $\pm$ 5.2	31.0 $\pm$ 4.7	<.0001
Self-reported Latino ethnicity, no. (%)	16/601 (2.7)	3/385 (0.8)	13/216 (6.0)	<.0001
Self-reported Arabic ethnicity, no. (%)	18/601 (3.0)	0/385 (0.0)	18/216 (8.3)	<.0001
Household income, mean $\pm$ SD‡	\$59,231 $\pm$ \$41,695	\$50,782 $\pm$ \$35,415	\$74,455 $\pm$ \$47,533	<.0001
Education, no. (%)				<.0001
<High school	29/600 (4.8)	19/385 (4.9)	10/215 (4.7)	
High school graduate or equivalent	104/600 (17.3)	77/385 (20.0)	27/215 (12.6)	
Some college	289/600 (48.1)	211/385 (54.8)	78/215 (36.3)	
College graduate or greater	178/600 (29.7)	78/385 (20.2)	100/215 (46.5)	
Urban location of residence, no. (%)	330/601 (54.9)	304/385 (79.0)	26/216 (12.0)	<.0001
Current smoker, no. (%)	58/514 (11.3)	37/319 (11.6)	21/195 (10.8)	.773
Dog living in home, no. (%)	135/503 (26.8)	61/312 (19.6)	74/191 (38.7)	<.0001
Cat living in home, no. (%)	89/503 (17.7)	22/312 (7.1)	67/191 (35.1)	<.0001
Home dust endotoxin level (EU/mg), mean $\pm$ SD§	36.8 $\pm$ 79.6	40.7 $\pm$ 91.6	30.9 $\pm$ 55.9	.199
Allergic sensitization, no. (%)	278/506 (54.9)	203/320 (63.4)	75/186 (40.3)	<.0001
Allergen-specific IgE results by allergen, no. (%)				
Dog	97/506 (19.2)	69/320 (21.6)	28/186 (15.1)	.073
Cat	101/504 (20.0)	67/319 (21.0)	34/185 (18.4)	.478
Cockroach	65/505 (12.9)	60/319 (18.8)	5/186 (2.7)	<.0001
Ragweed	147/506 (29.1)	113/320 (35.3)	34/186 (18.3)	<.0001
Timothy grass	127/506 (25.1)	100/320 (31.3)	27/186 (14.5)	<.0001
<i>Alternaria</i> species	101/503 (20.1)	86/318 (27.0)	15/185 (8.1)	<.0001
Dust mite	112/506 (22.1)	79/320 (24.7)	33/186 (17.7)	.070
Total serum IgE level (IU/mL), geometric mean $\pm$ gSD¶	37.8 $\pm$ 4.4	52.6 $\pm$ 4.0	21.4 $\pm$ 4.4	<.0001

*P value for the comparison of individuals reporting African American race with those reporting white race.

†Number with data = 600, 385, and 215, respectively.

‡Number with data = 566, 364, and 202, respectively.

§Number with data = 453, 275, and 178, respectively.

||Allergic sensitization was defined as having 1 or more positive allergen-specific IgE results to one of the 7 aeroallergens tested.

¶Number with data = 510, 323, and 187, respectively.

remained significantly associated with allergic sensitization and total serum IgE levels (data not shown). Similarly, West African ancestry was no longer significantly associated with allergic sensitization or total serum IgE levels after stratifying by self-reported race (Table IV and see Table E5 in this article's Online Repository at www.jacionline.org, respectively). However, after stratifying by ancestral proportion, there were still significant differences in the prevalence of allergic sensitization and total serum IgE levels by self-reported race (Table V and see Table E6 in this article's Online Repository at www.jacionline.org, respectively).

Likewise, there were still significant differences in the prevalence of allergic sensitization and total serum IgE levels by self-reported race after stratifying by location of residence. Among individuals with an urban location of residence, 60.5% of African American participants demonstrated allergic sensitization when compared with 30.0% of white participants ($P = .002$), and geometric mean total serum IgE levels were 52.8 ($\pm$ 4.01 geometric SD [gSD]) and 21.0 ($\pm$ 4.8 gSD) among African American and white participants, respectively ($P < .0001$). Among individuals living in suburban locations, 56.5% of African American participants demonstrated allergic sensitization when compared with 41.6% of white participants ($P = .045$), and geometric mean total serum IgE levels were 51.9 ($\pm$ 4.06 gSD) and 21.4 ($\pm$ 4.4 gSD) among African American and white participants, respectively ($P = .006$).

Post hoc regression analysis demonstrated that self-reported African American race was significantly associated with allergic sensitization to dog, cockroach, timothy grass, and *Alternaria* species (and was of borderline statistical significance with ragweed sensitization), even after adjusting for age, income, education, smoking status, pet ownership, home endotoxin levels, and location of residence (see Table E7 in this article's Online Repository at www.jacionline.org). Urban residence was also significantly associated with cockroach sensitization in these models (OR, 2.86; 95% CI, 1.05–7.82). On the other hand, West African ancestry was not significantly associated with sensitization to any specific allergen; however, urban residence was significantly associated with sensitization to cockroach (OR, 4.60; 95% CI, 1.83–11.54) and timothy grass (OR, 1.94; 95% CI, 1.13–3.31) in these models (see Table E8 in this article's Online Repository at www.jacionline.org).

Removing individuals who reported Latino or Arabic ethnicity (either each group alone or both groups together) from the analysis had no bearing on the results presented; the same relationships remained statistically significant (data not shown). The estimated average proportion of African ancestry among those reporting both Latino ethnicity and African American race ($n = 3$) was 0.66 ($\pm$ 0.07 SD), that for those reporting Latino ethnicity and white race ($n = 13$) was 0.06 ($\pm$ 0.04 SD), and that for those reporting Arabic ethnicity ($n = 18$) was 0.16 ($\pm$ 0.26 SD).

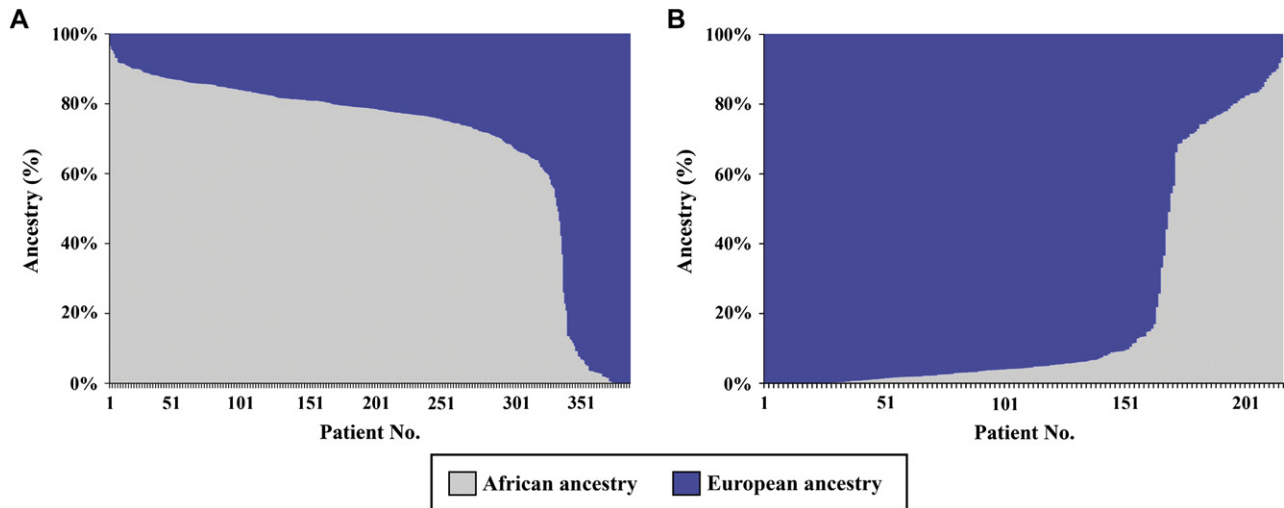


FIG 1. Individual admixture estimates for the 385 participants who reported being African American (**A**) and for the 216 participants who reported being white (**B**). Each patient number (*column*) comprises an individual and their admixture, where gray represents African ancestry and blue represents European ancestry.

TABLE II. Unadjusted and adjusted relationship between self-reported race and allergic sensitization*

Predictor variable(s)	Odds of allergic sensitization							
	Model 1†		Model 2‡		Model 3§		Model 4	
	OR (95% CI)	P value	aOR (95% CI)	P value	aOR (95% CI)	P value	aOR (95% CI)	P value
African American self-reported race	2.57 (1.77-3.72)	<.0001	2.88 (1.91-4.35)	<.0001	2.79 (1.74-4.49)	<.0001	2.19 (1.22-3.93)	.009
Age			0.85 (0.56-1.30)	.458	0.81 (0.51-1.29)	.364	0.81 (0.50-1.29)	.365
Income			1.01 (0.96-1.06)	.710	1.02 (0.96-1.07)	.592	1.02 (0.97-1.08)	.491
Education			1.08 (0.87-1.40)	.584	0.99 (0.73-1.35)	.964	1.00 (0.74-1.36)	.998
Smoking status					0.87 (0.44-1.72)	.682	0.86 (0.43-1.71)	.668
Pet ownership					1.12 (0.84-1.49)	.455	1.11 (0.83-1.48)	.483
Dust endotoxin level					0.95 (0.82-1.09)	.458	0.95 (0.82-1.09)	.448
Urban location of residence							1.47 (0.85-2.52)	.167

aOR, Adjusted odds ratio.

*Allergic sensitization is defined as having 1 or more positive allergen-specific IgE results to one of the 7 aeroallergens tested. Logistic regression is used to model the relationship of allergic sensitization on the variables listed. Models adjust for all variables with results shown in the column.

†Model 1 compares individuals who reported being of African American race with those who reported being white.

‡Model 2 includes model 1 plus sociodemographic variables for age (per 10-year increase), income (per \$10,000 increase), and education (categorized as less than high school, high school graduate, some college, and college graduate or greater).

§Model 3 includes model 2 plus environmental exposure variables for smoking (current smoker = 1 and all others = 0), pet ownership (number of dogs, cats, or both owned categorized as 0, 1, and ≥2), and dust endotoxin levels (log transformed).

||Model 4 includes model 3 plus location of residence (residing in the cities of Detroit, Hamtramck, or Highland Park = 1 and all others = 0).

DISCUSSION

Differences between continental groups (eg, West African, East Asia, and Europe) account for approximately 10% to 15% of total genetic variation.²¹ This genetic variation could contribute to differences in disease prevalence between populations as a result of differences in either the frequency or effect of alleles implicated in disease pathogenesis.^{22,23} Because between-group genetic variation tends to follow historic geographic boundaries,²⁴ we would expect that the difference in allergic sensitization among African American and white subjects in the United States would be closely associated with continental ancestry (ie, West African and European, respectively) if this disparity had a primarily genetic explanation. However, we found current location of residence (ie, urban versus suburban) to be more strongly

predictive of allergic sensitization when compared with geographic ancestry, suggesting the primacy of current environmental exposures for this outcome.

In contrast to ancestry, we also found that self-reported race was a robust predictor of allergic sensitization, even after adjusting for sociodemographic variables, environmental exposures, and location of residence. For example, even among persons living within the city of Detroit, 60.5% of African American participants demonstrated allergic sensitization when compared with 30.0% of white participants ($P = .002$). This suggests that additional unmeasured social or environmental factors might underlie the relationship between self-reported race and allergic sensitization, even among those residing in seemingly similar locations. Because Detroit is a highly segregated metropolitan

TABLE III. Unadjusted and adjusted relationship between genetic ancestry and allergic sensitization*

Predictor variable(s)	Odds of allergic sensitization							
	Model 1†		Model 2‡		Model 3§		Model 4	
	OR (95% CI)	P value	aOR (95% CI)	P value	aOR (95% CI)	P value	aOR (95% CI)	P value
African ancestry	1.75 (1.08-2.82)	.022	1.73 (1.04-2.86)	.034	1.84 (1.05-3.22)	.032	1.34 (0.73-2.43)	.343
Age			0.80 (0.53-1.20)	.285	0.76 (0.48-1.20)	.241	0.78 (0.49-1.24)	.289
Income			0.99 (0.94-1.04)	.630	1.00 (0.95-1.05)	.950	1.01 (0.96-1.07)	.612
Education			1.02 (0.79-1.32)	.875	0.94 (0.70-1.26)	.672	0.97 (0.72-1.32)	.866
Smoking status					0.87 (0.44-1.70)	.676	0.85 (0.43-1.69)	.644
Pet ownership					0.96 (0.73-1.25)	.747	1.01 (0.77-1.33)	.947
Dust endotoxin level					0.95 (0.82-1.09)	.452	0.94 (0.82-1.09)	.435
Urban location of residence							2.09 (1.32-3.31)	.002

aOR, Adjusted odds ratio.

*Allergic sensitization is defined as having 1 or more positive allergen-specific IgE results to one of the 7 aeroallergens tested. Logistic regression is used to model the relationship of allergic sensitization on the variables listed. Models adjust for all variables with results shown in the column. Proportion of African ancestry (ie, admixture) was assessed with 493 AIMs that differentiate African and European ancestry.

†Model 1 includes proportion of African ancestry (range, 0-1).

‡Model 2 includes model 1 plus sociodemographic variables for age (per 10-year increase), income (per \$10,000 increase), and education (categorized as less than high school, high school graduate, some college, and college graduate or greater).

§Model 3 includes model 2 plus environmental exposure variables for smoking (current smoker = 1 and all others = 0), pet ownership (number of dogs, cats, or both owned categorized as 0, 1, and ≥2), and dust endotoxin levels (log transformed).

||Model 4 includes model 3 plus location of residence (residing in the cities of Detroit, Hamtramck, or Highland Park = 1 and all others = 0).

TABLE IV. Adjusted relationship between genetic ancestry and allergic sensitization after stratifying by self-reported race*

Predictor variable(s)	Odds of allergic sensitization			
	Individuals reporting African American race		Individuals reporting white race	
	aOR (95% CI)	P value	aOR (95% CI)	P value
African ancestry	1.29 (0.50-3.32)	.593	0.51 (0.18-1.47)	.214
Age	0.96 (0.53-1.73)	.878	0.58 (0.25-1.31)	.187
Income	1.00 (0.92-1.10)	.938	1.02 (0.95-1.10)	.574
Education	0.86 (0.58-1.28)	.452	1.40 (0.81-2.43)	.229
Smoking status	1.09 (0.45-2.63)	.848	0.62 (0.17-2.29)	.473
Pet ownership	1.18 (0.76-1.83)	.465	1.02 (0.69-1.52)	.915
Dust endotoxin level	0.91 (0.76-1.09)	.315	1.02 (0.79-1.33)	.866
Urban location of residence	1.77 (0.92-3.37)	.085	0.82 (0.28-2.41)	.722

aOR, Adjusted odds ratio.

*Allergic sensitization is defined as having 1 or more positive allergen-specific IgE results to one of the 7 aeroallergens tested. Logistic regression is used to model the relationship of allergic sensitization on the variables listed. The proportion of African ancestry (ie, admixture) was assessed with 493 AIMs that differentiate African and European ancestry. Models adjust for all variables shown in the column, including age (per 10-year increase), income (per \$10,000 increase), education (categorized as less than high school, high school graduate, some college, and college graduate or greater), smoking status (current smoker = 1 and all others = 0), pet ownership (number of dogs, cats, or both owned categorized as 0, 1, and ≥2), dust endotoxin levels (log transformed), and location of residence (residing in the cities of Detroit, Hamtramck, or Highland Park = 1 and all others = 0).

area,^{25,26} it is quite plausible that African American and white participants had different exposures, regardless of urban or suburban location of residence. For example, African American individuals comprise 77% of the city's population but only 7% of the surrounding population,²⁷ and Fig 2 shows the relative geographic separation of African American and white study participants even within the city.

Sensitization to cockroach antigen appeared to be the one exception where another predictor, urban location of residence, was statistically significant when adjusting for self-reported race. Perhaps this is because cockroach exposure is highly skewed to urban settings. For example, in a study of the homes of children with asthma in the Baltimore area, 64% of homes in the city had evidence of cockroach infestation compared with 0% of suburban homes.²⁸ In addition, the housing characteristics associated with cockroach infestation, such as living in an apartment (compared

with a house)²⁹ and increasing physical deterioration of the dwelling,³⁰ can also be associated with urban living.

Increased likelihood of dog sensitization despite lower pet ownership suggests that factors other than higher allergen exposure can contribute to increased allergic sensitization in African American patients when compared with white patients. Historically, expressways were built through African American neighborhoods in the city of Detroit, and African Americans increasingly occupied the surrounding areas.²⁶ This can contribute to greater exposure to air pollution and particulate matter. Studies in both human subjects and animal models suggest that exposure to traffic particulate matter enhances allergic sensitization and IgE production to aeroallergens.³¹⁻³³ Perhaps this and other local environmental exposures might explain, in part, the general increased allergic sensitization seen in African American participants.

TABLE V. Difference in allergic sensitization among those who reported African American and white race stratified by the proportion of African ancestry*

African ancestry	Allergic sensitization, no. (%)		P value†
	Self-reported African American race	Self-reported white race	
0% to 33%	30/47 (63.8)	61/139 (43.9)	.019
34% to 66%	16/29 (55.2)	4/6 (66.7)	.680
67% to 100%	157/244 (64.3)	10/41 (24.4)	<.0001

*Allergic sensitization is defined as having 1 or more positive allergen-specific IgE results to one of the 7 aeroallergens tested. The proportion of African ancestry (ie, admixture) was assessed with 493 AIMs that differentiate African and European ancestry.
†P value is for testing the difference in the proportion with allergic sensitization between those who reported African American race and those who reported white race.

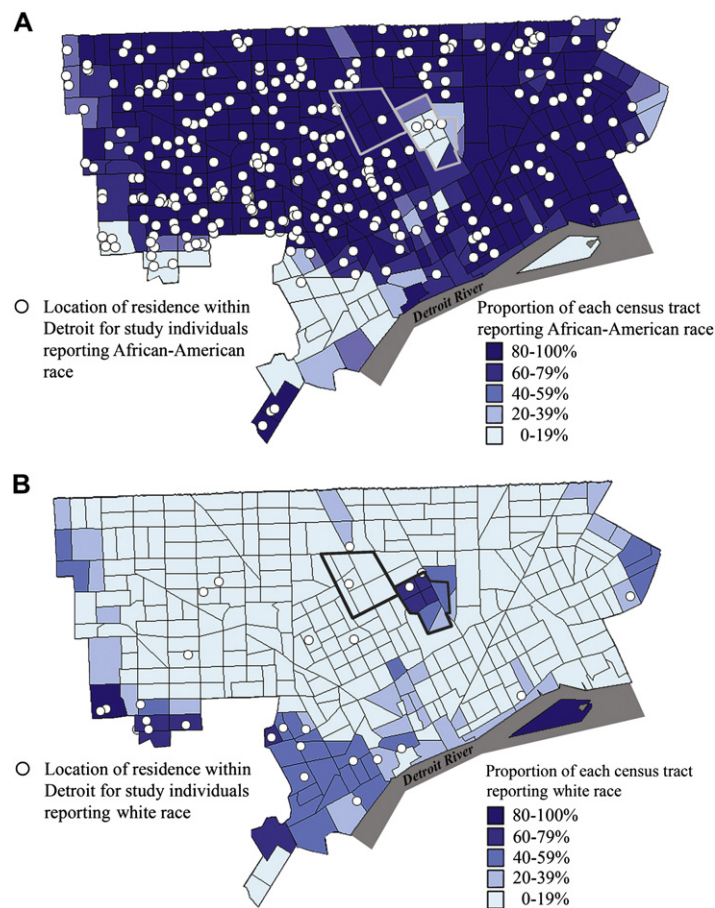


FIG 2. Distribution of study participants within the city limits of Detroit (also includes Hamtramck and Highland Park shown with *bolded outlines*). Participants who reported being African American are shown against the proportion of individuals within each census tract who reported being African American (**A**), and participants who reported being white are shown against the proportion of individuals within each census tract who reported being white (**B**). Census tract proportions are taken from year 2000 US Census data.

It is important to note that although biogeographic ancestry did not appear to explain differences in allergic sensitization, genetics might still play an important role in determining allergic sensitization. However, these genetic determinants can occur at a similar frequency and have a similar effect among persons with West African and European ancestry. There is also the possibility of gene-environment interactions that differ by race-ethnicity but were not explored.³⁴ In addition, because this

is a cross-sectional study in adults, we might have passed the window in which the exposures assessed, such as pet exposure and endotoxin, can influence IgE levels. However, this would not influence our conclusions regarding the effect of ancestry, which did not vary.

People who reported being African American or reported being white in our study also had, on average, less West African (ie, 69%) and European ancestry (ie, 79%), respectively, than has

been reported elsewhere.^{4,8} Perhaps this reflects instances in which racial identity was based in part on sociocultural factors related to one's surroundings rather than genetic ancestry. However, we did not observe differences in West African ancestry between African American participants with either an urban or suburban residence, and similarly, we did not observe differences in European ancestry among white participants residing in those broad categories (see Table E9 in this article's Online Repository at www.jacionline.org). It is also possible that these estimates are unique to Wayne County, Michigan, where 571 (95%) of the 601 participants resided at the time of the study. Native American ancestry was also present to a much lesser extent within our cohort. However, *post hoc* analysis did not find that including Native American ancestry would have affected our results. To ensure that the self-reported race categories and ancestry estimates were entered correctly, we compared self-reported race with the race that participants believed others saw them as, and we calculated ancestry using multiple methods. The consistency of these checks lends further support to our findings. Despite a relatively large study size, our numbers for analysis became much smaller after stratifying (eg, by self-reported race, genetic ancestry, or location of residence). Although we have no reason to believe that this negatively influenced our results, our findings should be replicated in other large and diverse, population-based cohorts.

In conclusion, we found that location of residence was a stronger predictor of allergic sensitization when compared with ancestry. These findings suggest that the disparity in atopy between African American and white patients might be primarily due to environmental rather than genetic factors. However, self-reported race continued to be a strong predictor of allergic sensitization, even after adjusting for sociodemographic variables, environmental exposures, and location of residence, suggesting that other important social and environmental confounders exist and have yet to be fully characterized. Until this time, self-reported race will likely continue to be an important predictor of allergic status and related conditions.³⁵

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Clinical implications: These data suggest that efforts to eliminate disparities in allergic sensitization should focus on contributing environmental factors.

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TABLE E1. Unadjusted and adjusted relationship between self-reported race and total serum IgE levels*

Predictor variable(s)	Outcome variable = total serum IgE level							
	Model 1†		Model 2‡		Model 3§		Model 4	
	Parameter estimate	P value	Parameter estimate	P value	Parameter estimate	P value	Parameter estimate	P value
African American self-reported race	0.901	<.0001	0.917	<.0001	0.837	<.0001	0.716	.001
Age			−0.094	.520	−0.139	.405	−0.140	.402
Income			−0.011	.536	−0.014	.484	−0.012	.558
Education			0.062	.506	0.070	.522	0.074	.499
Smoking status					0.132	.5948	0.128	.606
Pet ownership					0.023	.823	0.020	.848
Dust endotoxin level					−0.052	.315	−0.053	.309
Urban location of residence							0.186	.348

*The outcome variable, total serum IgE, is log transformed to normalize its distribution. Linear regression is used to model the relationship of total serum IgE on the variables listed. Models adjust for all variables with results shown in the column.

†Model 1 compares individuals who reported being of African American race with those who reported being white.

‡Model 2 includes model 1 plus sociodemographic variables for age (per 10-year increase), income (per \$10,000 increase), and education (categorized as less than high school, high school graduate, some college, and college graduate or greater).

§Model 3 includes model 2 plus environmental exposure variables for smoking (current smoker = 1 and all others = 0), pet ownership (number of dogs, cats, or both owned categorized as 0, 1, and ≥2), and dust endotoxin levels (log transformed).

||Model 4 includes model 3 plus location of residence (residing in the cities of Detroit, Hamtramck, or Highland Park = 1 and all others = 0).

TABLE E2. Unadjusted and adjusted relationship between genetic ancestry and total serum IgE levels*

Predictor variable(s)	Outcome variable = total serum IgE level							
	Model 1†		Model 2‡		Model 3§		Model 4	
	Parameter estimate	P value	Parameter estimate	P value	Parameter estimate	P value	Parameter estimate	P value
African ancestry	0.598	.001	0.578	.002	0.531	.012	0.303	.170
Age			−0.152	.313	−0.191	.263	−0.174	.302
Income			−0.029	.113	−0.027	.172	−0.016	.421
Education			0.023	.814	0.024	.827	0.053	.632
Smoking status					0.131	.605	0.120	.632
Pet ownership					−0.097	.339	−0.060	.555
Dust endotoxin level					−0.052	.323	−0.054	.302
Urban location of residence							0.510	.003

*The outcome variable, total serum IgE, is log transformed to normalize its distribution. Linear regression is used to model the relationship of total serum IgE on the variables listed. Models adjust for all variables with results shown in the column. The proportion of African ancestry (ie, admixture) was assessed with 493 AIMs that differentiate African and European ancestry.

†Model 1 includes proportion of African ancestry (range, 0-1).

‡Model 2 includes model 1 plus sociodemographic variables for age (per 10-year increase), income (per \$10,000 increase), and education (categorized as less than high school, high school graduate, some college, and college graduate or greater).

§Model 3 includes model 2 plus environmental exposure variables for smoking (current smoker = 1 and all others = 0), pet ownership (number of dogs, cats, or both owned categorized as 0, 1, and ≥2), and dust endotoxin levels (log transformed).

||Model 4 includes model 3 plus location of residence (residing in the cities of Detroit, Hamtramck, or Highland Park = 1 and all others = 0).

TABLE E3. Difference in allergic sensitization between those with an urban location of residence and those with a suburban location of residence stratified by ancestral proportion*

African ancestry	Allergic sensitization, no. (%)		P value†
	Urban location of residence	Suburban location of residence	
0% to 33%	27/50 (54.0)	64/136 (47.1)	.414
34% to 66%	14/23 (60.9)	6/12 (50.0)	.721
67% to 100%	132/203 (65.0)	35/82 (42.7)	<.0001

*Allergic sensitization was defined as having 1 or more positive allergen-specific IgE results to one of the 7 aeroallergens tested. The proportion of African ancestry (ie, admixture) was assessed with 493 AIMs that differentiate African and European ancestry. Those living within the cities of Detroit, Hamtramck, or Highland Park were considered urban residents. Persons living outside the outer Detroit city limit were considered suburban residents.

†P value is for testing the difference in the proportion with allergic sensitization between those with an urban location of residence and those with a suburban location of residence.

TABLE E4. Difference in total serum IgE levels between those with an urban location of residence and those with a suburban location of residence stratified by ancestral proportion*

African admixture	Geometric mean total serum IgE (IU/mL) $\pm$ gSD		P value†
	Urban location of residence	Suburban location of residence	
0% to 33%‡	40.00 $\pm$ 4.60	24.63 $\pm$ 4.22	.056
34% to 66%§	47.80 $\pm$ 3.76	44.86 $\pm$ 4.19	.570
67% to 100%	52.23 $\pm$ 4.07	30.50 $\pm$ 5.01	.011

*The proportion of African ancestry (ie, admixture) was assessed with 493 AIMs that differentiate African and European ancestry. Those living within the cities of Detroit, Hamtramck, or Highland Park were considered urban residents. Persons living outside the outer Detroit city limit were considered suburban residents.

†P value is for testing the difference in total serum IgE levels between those with an urban location of residence and those with a suburban location of residence.

‡Number with data available = 50 and 136, respectively.

§Number with data available = 23 and 12, respectively.

||Number with data available = 205 and 84, respectively.

TABLE E5. Adjusted relationship between genetic ancestry and total serum IgE levels after stratifying by self-reported race*

Predictor variable(s)	Outcome variable of total serum IgE level			
	Individuals reporting African American race		Individuals reporting white race	
	Parameter estimate	P value	Parameter estimate	P value
African ancestry	0.201	.545	−0.370	.325
Age	−0.234	.249	−0.080	.787
Income	0.032	.280	−0.040	.150
Education	0.069	.609	0.015	.941
Smoking status	0.467	.114	−0.528	.245
Pet ownership	−0.100	.502	0.129	.387
Dust endotoxin level	−0.088	.147	0.001	.990
Urban location of residence	0.286	.213	−0.085	.828

*The outcome variable, total serum IgE level, is log transformed to normalize its distribution. Linear regression is used to model the relationship of total serum IgE level on the variables listed. The proportion of African ancestry (ie, admixture) was assessed with 493 AIMs that differentiate African and European ancestry. Models adjust for all variables shown in the column, including age (per 10-year increase), income (per \$10,000 increase), education (categorized as less than high school, high school graduate, some college, and college graduate or greater), smoking status (current smoker = 1 and all others = 0), pet ownership (number of dogs, cats, or both owned categorized as 0, 1, and ≥2), dust endotoxin levels (log transformed), and location of residence (residing in cities of Detroit, Hamtramck, or Highland Park = 1 and all others = 0).

TABLE E6. Difference in total serum IgE levels among those who reported African American and white race stratified by the proportion of African admixture*

African admixture	Geometric mean total serum IgE (IU/mL) $\pm$ gSD		P value†
	Self-reported African American race	Self-reported white race	
0% to 33%‡	49.36 $\pm$ 3.85	23.18 $\pm$ 4.35	.001
34% to 66%§	50.95 $\pm$ 4.16	30.95 $\pm$ 2.18	.264
67% to 100%	53.48 $\pm$ 4.04	15.50 $\pm$ 4.77	<.0001

*The proportion of African ancestry (ie, admixture) was assessed with 493 AIMs that differentiate African and European ancestry.

†P value is for testing the difference in the total serum IgE levels between those who reported African American race and those who reported white race.

‡Number with data available = 47 and 139, respectively.

§Number with data available = 29 and 6, respectively.

||Number with data available = 247 and 42, respectively.

TABLE E7. Relationship between self-reported race and allergic sensitization to individual aeroallergens*

Predictor variable(s)	Odds of allergic sensitization to individual allergens													
	Dog		Cat		Cockroach		Ragweed		Timothy grass		Alternaria species		Dust mite	
	aOR (95% CI)†	P value	aOR (95% CI)†	P value	aOR (95% CI)†	P value	aOR (95% CI)†	P value	aOR (95% CI)†	P value	aOR (95% CI)†	P value	aOR (95% CI)†	P value
African American self-reported race	2.38 (1.08-5.21)	.030	1.79 (0.84-3.78)	.129	3.85 (1.05-14.08)	.042	1.79 (0.93-3.47)	.083	2.09 (1.04-4.20)	.039	2.59 (1.10-6.09)	.029	1.33 (0.64-2.76)	.439
Age	1.14 (0.63-2.06)	.668	1.03 (0.58-1.83)	.928	0.59 (0.28-1.23)	.160	0.88 (0.53-1.46)	.614	0.94 (0.56-1.59)	.827	0.74 (0.40-1.36)	.331	0.95 (0.54-1.65)	.851
Income	1.01 (0.94-1.08)	.796	1.01 (0.94-1.08)	.810	1.05 (0.97-1.14)	.251	0.94 (0.88-1.01)	.103	0.99 (0.92-1.06)	.725	0.94 (0.85-1.03)	.181	1.02 (0.96-1.09)	.518
Education	0.93 (0.63-1.37)	.717	1.00 (0.68-1.46)	.998	0.65 (0.42-1.01)	.057	1.24 (0.88-1.74)	.220	1.14 (0.80-1.61)	.471	0.72 (0.49-1.06)	.098	0.76 (0.53-1.08)	.123
Smoking status	1.04 (0.44-2.44)	.930	1.19 (0.52-2.71)	.674	1.35 (0.53-3.42)	.526	0.77 (0.35-1.70)	.516	0.78 (0.35-1.76)	.552	0.84 (0.36-1.97)	.680	0.54 (0.22-1.31)	.175
Pet ownership	1.31 (0.91-1.88)	.149	1.13 (0.79-1.61)	.512	1.08 (0.66-1.78)	.750	0.93 (0.67-1.29)	.659	0.97 (0.69-1.36)	.859	1.08 (0.72-1.61)	.713	1.24 (0.88-1.74)	.224
Dust endotoxin level	0.89 (0.75-1.07)	.214	0.98 (0.82-1.17)	.811	0.86 (0.70-1.05)	.141	0.83 (0.71-0.97)	.017	0.93 (0.79-1.09)	.350	0.94 (0.79-1.12)	.505	0.94 (0.79-1.10)	.436
Urban location of residence	0.74 (0.37-1.46)	.378	0.72 (0.37-1.41)	.339	2.86 (1.05-7.82)	.040	1.15 (0.64-2.07)	.650	1.35 (0.73-2.50)	.339	1.34 (0.66-2.72)	.418	1.40 (0.72-2.72)	.314

aOR, Adjusted odds ratio.

*Allergic sensitization is defined as having a positive allergen-specific IgE test result to the specific aeroallergens tested. Logistic regression is used to model the relationship of allergic sensitization on the variables listed.

†Models adjust for all variables with results shown in the column. Variables include self-reported race (African American race = 1 and white = 0), age (per 10-year increase), income (per \$10,000 increase), education (categorized as less than high school, high school graduate, some college, and college graduate or greater), smoking (current smoker = 1 and all others = 0), pet ownership (number of dogs, cats, or both owned categorized as 0, 1, and ≥2), dust endotoxin levels (log transformed), and location of residence (residing in the cities of Detroit, Hamtramck, or Highland Park = 1 and all others = 0).

TABLE E8. Relationship between genetic ancestry and allergic sensitization to individual aeroallergens*

Predictor variable(s)	Odds of allergic sensitization to individual allergens													
	Dog		Cat		Cockroach		Ragweed		Timothy grass		Alternaria species		Dust mite	
	aOR (95% CI)†	P value	aOR (95% CI)†	P value	aOR (95% CI)†	P value	aOR (95% CI)†	P value	aOR (95% CI)†	P value	aOR (95% CI)†	P value	aOR (95% CI)†	P value
African ancestry	2.19 (0.98-4.88)	.056	1.50 (0.70-3.22)	.299	2.04 (0.67-6.23)	.209	1.46 (0.75-2.87)	.268	1.15 (0.57-2.31)	.698	2.05 (0.87-4.83)	.099	1.36 (0.65-2.85)	.416
Age	1.12 (0.62-2.02)	.710	1.01 (0.57-1.80)	.968	0.57 (0.27-1.19)	.136	0.86 (0.52-1.42)	.554	0.90 (0.54-1.52)	.708	0.72 (0.39-1.31)	.281	0.94 (0.54-1.64)	.839
Income	1.00 (0.94-1.08)	.879	1.00 (0.94-1.08)	.883	1.04 (0.96-1.13)	.329	0.94 (0.87-1.01)	.083	0.98 (0.92-1.05)	.613	0.93 (0.85-1.02)	.137	1.02 (0.96-1.09)	.543
Education	0.92 (0.62-1.34)	.648	0.98 (0.68-1.43)	.929	0.65 (0.42-1.01)	.058	1.22 (0.87-1.71)	.249	1.11 (0.78-1.56)	.563	0.72 (0.49-1.06)	.093	0.76 (0.53-1.07)	.118
Smoking status	1.04 (0.44-2.45)	.925	1.19 (0.52-2.70)	.683	1.35 (0.53-3.42)	.529	0.77 (0.35-1.70)	.519	0.78 (0.34-1.76)	.546	0.82 (0.35-1.94)	.653	0.54 (0.22-1.32)	.177
Pet ownership	1.20 (0.85-1.70)	.303	1.06 (0.75-1.49)	.739	1.01 (0.62-1.65)	.971	0.88 (0.64-1.20)	.416	0.89 (0.64-1.23)	.486	1.00 (0.68-1.48)	.998	1.21 (0.87-1.68)	.260
Dust endotoxin level	0.90 (0.75-1.07)	.225	0.98 (0.82-1.17)	.815	0.85 (0.69-1.05)	.128	0.83 (0.71-0.97)	.016	0.92 (0.79-1.08)	.332	0.94 (0.79-1.12)	.482	0.94 (0.79-1.11)	.438
Urban location of residence	0.97 (0.54-1.75)	.916	0.89 (0.50-1.59)	.703	4.60 (1.83-11.54)	.001	1.43 (0.86-2.37)	.172	1.94 (1.13-3.31)	.016	1.78 (0.95-3.36)	.073	1.52 (0.87-2.67)	.143

aOR, Adjusted odds ratio.

*Allergic sensitization is defined as having a positive allergen-specific IgE test result to the specific aeroallergens tested. Logistic regression is used to model the relationship of allergic sensitization on the variables listed. The proportion of African ancestry (ie, admixture) was assessed with 493 AIMs that differentiate African and European ancestry.

†Models adjust for all variables with results shown in the column. Variables include proportion of African ancestry (range 0-1), age (per 10-year increase), income (per \$10,000 increase), education (categorized as less than high school, high school graduate, some college, and college graduate or greater), smoking (current smoker = 1 and all others = 0), pet ownership (number of dogs, cats, or both owned categorized as 0, 1, and ≥ 2), dust endotoxin levels (log transformed), and location of residence (residing in the cities of Detroit, Hamtramck, or Highland Park = 1 and all others = 0).

TABLE E9. Proportion of African and European ancestry among study participants stratified by location of residence*

	Urban location of residence	Suburban location of residence
Proportion of African ancestry among individuals reporting African American race, mean ± SD (no.)	0.70 ± 0.26 (304)	0.66 ± 0.29 (81)
Proportion of European ancestry among individuals reporting white race, mean ± SD (no.)	0.81 ± 0.31 (26)	0.79 ± 0.31 (190)

*Participants living within the cities of Detroit, Hamtramck, or Highland Park were considered urban residents, whereas persons living outside the outer Detroit city limits were considered suburban residents.