

Allergic diseases among Asian children in the United States



To the Editor:

Recent studies have uncovered remarkably elevated rates of allergic disease among Asian immigrants to Australia,¹ and previous studies in the United States suggest that children of Asian immigrants may have higher risks of eczema and food allergy but lower rates of asthma.^{2,3} However, because nationally representative surveys typically have small numbers of Asian participants, there is little population-level data on the prevalence of allergic diseases among Asian children in the United States. The National Health Interview Survey provides a unique data source to explore the effect of Asian race on allergy as Asians were oversampled beginning in 2006. Using National Health Interview Survey data from 2007 to 2016, we sought to determine the prevalence of allergic disease among Asian-American children and to examine the contribution of child and parental migration to estimates of disease burden.

Children 17 years and younger were included. Allergic conditions and race were defined on the basis of self-report. Children of Asian race were further questioned about Asian subcategory, and data on Asian-Indian, Chinese, and Filipino subcategories were made available. Other Asian subpopulations were grouped for purposes of analysis on the basis of small sample size. Survey weights, sampling units, and strata were used in all analyses to create a nationally representative sample and account for the complex survey design. We first examined the overall prevalence of allergic diseases by race. Next, to understand the effects of race independent of age, sex, family income relative to federal poverty level, and parental and child nativity, we used multivariable logistic regression models that included these factors. Interaction terms and stratification were used to evaluate for effect modification by race and age (see this article's [Methods](#) section in the Online Repository at www.jacionline.org), and analyses of Asian subpopulations were performed. All analyses used Stata/IC version 14.2 (Stata Corporation, College Station, Tex), and non-Hispanic white children were used as the reference population, except for subpopulation analyses, in which non-Asian children were used as the reference population because of constraints of sampling methodology (see this article's [Methods](#) section in the Online Repository).

Sample size and demographic information are presented in [Tables E1](#) and [E4](#) in this article's Online Repository at www.jacionline.org. In unadjusted analyses, Asian children had somewhat higher rates of food allergy (6.2% vs 5.5%) and eczema (11.8% vs 11.2%), and lower rates of asthma (5.7% vs 9.0%), than non-Hispanic white children (see [Tables E1](#) and [E5](#) in this article's Online Repository at www.jacionline.org). This was true even though Asian children had much higher rates of birth outside the United States (20.3% vs 1.5%) and foreign-born parents (76.9% vs 6.2%) than did white children, factors that were both found to be protective against all 3 allergic diseases. Thus, in analyses adjusted for the protective effects of nativity, Asians had even higher risk of food allergy and eczema, and also had a higher risk of asthma, compared with non-Hispanic white children, with odds ratios (ORs) of 1.22 (95% CI, 1.05-1.42), 1.47 (95% CI, 1.31-1.64), and 1.15 (95% CI, 1.00-1.32), respectively ([Table I](#)).

Thirty-nine percent of reporting parents were males and 61% were females, and there was no interaction between sex of reporting parent and parental nativity on the allergic outcomes (data not shown). There was no significant interaction between race and nativity (see [Table E3](#) in this article's Online Repository at www.jacionline.org) or race and age on the odds of food allergy or eczema. There was evidence that the relationship between race and asthma did differ by age category but not by nativity, with Asian race conferring higher odds of asthma in all but the 12- to 17-year-old group (see [Table E2](#) in this article's Online Repository at www.jacionline.org).

We then examined Asian subpopulations, finding markedly higher rates of all allergic diseases in Filipino children compared with non-Asian children in adjusted models: OR, 1.57 (95% CI, 1.25-1.98) for food allergy, 1.51 (95% CI, 1.25-1.82) for eczema, and 1.38 (95% CI 1.13-1.69) for asthma ([Fig 1](#)). There were trends toward increased odds in the remaining Asian subpopulations for food allergy (Asian Indian: OR, 1.16, 95% CI, 0.89-1.47; Chinese: OR, 1.23, 95% CI, 0.88-1.58; and Other Asian: OR, 1.30, 95% CI, 1.01-1.60), and eczema (Asian Indian: OR, 1.18, 95% CI, 0.91-1.45; Chinese: OR, 1.48, 95% CI, 1.16-1.81; and Other Asian: OR, 1.29, 95% CI, 1.06-1.52). Of the Asian subpopulations, only Filipinos demonstrated an elevated rate of asthma compared with non-Asian populations (Asian Indian: OR, 0.79, 95% CI, 0.57-1.08; Chinese: OR, 0.74, 95% CI, 0.51-1.07; and Other Asian: OR, 0.81, 95% CI, 0.64-1.03).

Taken together, these findings suggest an increased propensity for allergic diseases among Asian populations in the United States that fully emerges only after accounting for the protective effect of foreign child and parental birth. With subsequent generations, the increased risk of allergic disease in immigrant populations may become more pronounced as the protective effect of foreign birth wanes. This increased propensity for allergic disease may reflect gene by environment interaction or epigenetic modification. Environmental exposures in this population, as well as in-country rates of allergic diseases, should be further studied.

Asian populations are not homogeneous, and we found especially high rates of all 3 allergic diseases, including asthma, among Filipino-American children, which is notable given that asthma was less prevalent in Asian children overall. It remains unclear why certain Asian subpopulations are protected against asthma but have a much higher risk of eczema and food allergy, whereas others demonstrate increased risk of all 3. Further research into the genetic and environmental risk factors responsible for the different propensities to these diseases may provide broader insight into the mechanisms of these diseases.

The protective effect of birth outside the developed world has been previously demonstrated,⁴ but the effect of parental birth has been less consistent, with some studies demonstrating higher rates of allergic diseases in children of immigrants⁵⁻⁷ and others finding a protective effect of parental immigration on asthma and eczema.⁶ It is thought that microbial exposures may explain the protective effect of birth outside the United States on allergy, but how foreign parental birth may affect a child's risk of allergy is much less clear, and may reflect cultural practices, dietary habits, or awareness of allergic diseases. Further research into the specific mechanisms by which child and parental nativity may affect the development of allergic disease is needed.

TABLE I. Effect of race and nativity on odds of allergic diseases*

Variable	OR (95% CI)		
	Food allergy (6,209; 5.3%, 5.4%)	Eczema (13,700; 11.8%, 11.8%)	Asthma (10,725; 9.2%, 9.0%)
Race			
Non-Hispanic white (54,896; 48.7%, 66.0%)†	Reference	Reference	Reference
Non-Hispanic black (18,352; 16.3%, 12.8%)	1.11 (1.00-1.23)	1.65 (1.54-1.76)	1.97 (1.84-2.12)
Hispanic (31,829; 28.3%, 16.0%)	0.82 (0.73-0.92)	1.03 (0.96-1.11)	1.28 (1.18-1.39)
Asian (7,571; 6.7%, 5.2%)	1.22 (1.05-1.42)	1.47 (1.31-1.64)	1.15 (1.00-1.32)
Nativity category			
Child US-born	Reference	Reference	Reference
Parent US-born (83,520; 72.0%, 77.7%)			
Child US-born	0.93 (0.83-1.03)	0.67 (0.62-0.72)	0.59 (0.55-0.64)
Parent foreign-born (26,603; 22.9%, 18.2%)			
Child foreign-born	0.72 (0.58-0.89)	0.44 (0.37-0.52)	0.28 (0.22-0.34)
Parent foreign-born (4,941; 4.3%, 3.3%)			
Child foreign-born	1.12 (0.81-1.57)	0.77 (0.57-1.03)	0.70 (0.51-0.95)
Parent US-born‡ (928; 0.8%, 0.8%)			
Age (y)	0.99 (0.99-1.00)	0.97 (0.97-0.98)	1.06 (1.05-1.06)
Sex			
Female (56,628; 48.6%, 51.1%)	0.99 (0.93-1.06)	1.03 (0.98-1.08)	0.77 (0.73-0.82)
Income§	0.99 (0.95-1.04)	0.98 (0.95-1.02)	0.79 (0.77-0.82)

Odds ratios in boldface represent statistically significant comparisons.

*Adjusted for age, sex, and income.

†N, unweighted proportion, weighted proportion (accounting for complex survey structure).

‡Foreign-birth to US-born parents is a small group with likely varying backgrounds.

§Income-to-poverty ratio is an ordinal variable, with categories of ≤Federal Poverty Level, 1-2 times Federal Poverty Level, ≥2 times Federal Poverty Level.

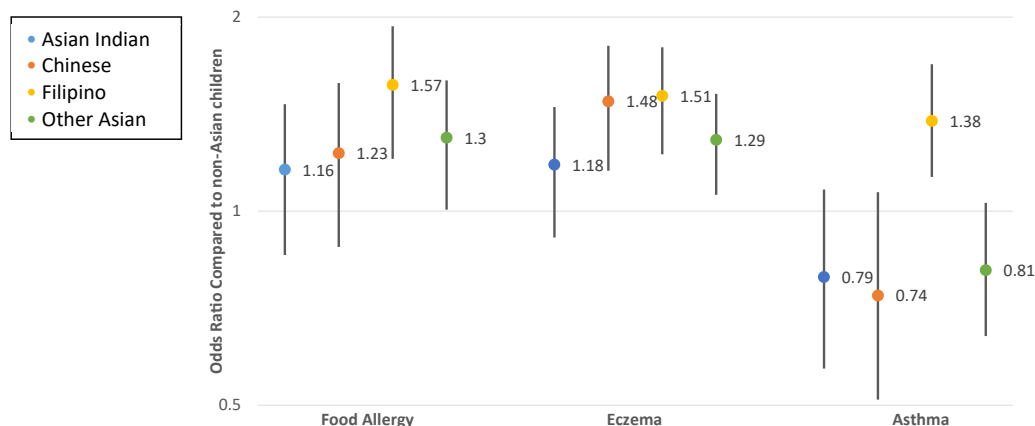


FIG 1. Odds of allergic diseases among Asian subpopulations compared with non-Asian children, adjusted for age, sex, and income. Other Asian includes Asian subpopulations without sufficient numbers for reporting, such as Korean, Japanese, and mixed Asian children.

Limitations of this study include self-report of allergic disease,⁸ which lacks specificity, and which may be highly influenced by medical care and parental knowledge. In addition, self-reported place of birth and inability to discern more than 1 generation of immigration or duration of residence in the United States limit the specificity of analyses. Furthermore, because of survey design, data on only 1 parent were available, although nativity status concordance is greater than 80% in married couples.⁹ Granular data regarding children's racial origin, particularly for those of mixed race, were not available nor were data on some smaller Asian subgroups. However, these limitations are balanced by the uncommon and distinctive nature of this nationally representative survey with detailed data about

Asian populations and subpopulations, a group identified in previous studies to potentially be at a higher risk for allergic disease, yet one that has remained relatively unstudied in the United States. Data regarding immigration, an important modifier of allergic disease, were also available for both parents and children, allowing adjustment for this important and dynamic measure.

In conclusion, our study demonstrates increased prevalence of food allergy, eczema, and asthma among Asian children once adjusted for child and parental nativity, along with a pronounced risk of these diseases in the Filipino population, an important population for future study with 57% higher odds of food allergy, 51% higher odds of eczema, and 38% higher odds of asthma.

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Prenatal exposure to traffic-related air pollution, the gestational epigenetic clock, and risk of early-life allergic sensitization



To the Editor:

The Developmental Origins of Health and Disease paradigm posits that an adverse early-life environment induces gradients at birth that can alter lifetime health trajectories, including the development of atopic diseases. An important adverse environmental factor that has received considerable scrutiny is air pollution. Meta-analyses of birth cohort studies suggest that early-life exposure to traffic-related air pollution (TRAP) is associated with an increased risk of asthma and allergic sensitization, with a caveat that there is substantial variability across studies.¹ In seeking to understand the underlying biology, the study of epigenetics offers a plausible mechanism by which such environmental exposures in early life can get “under the skin” to regulate the activity of genes relevant to allergy and asthma.²

We used a recently developed biomarker of fetal development—epigenetic gestational age (eGA)—to further characterize the relationship between *in utero* exposure to TRAP and allergic sensitization. As a biomarker, eGA holds great promise because it may identify infants who deviate from the typical developmental profile, allowing targeted early preventative

interventions. In adults, patterns of DNA methylation (DNAm) at specific CpG sites are used to estimate “epigenetic age” and this is highly correlated with chronological age.³ Moreover, deviations between epigenetic and chronological age have been associated with many age-related health outcomes.⁴ Using umbilical cord blood DNAm profiles, similar estimates of eGA have been created.^{5,6} Although deviations in epigenetic age as quantified by DNAm in adults are typically associated with morbidity, the direction of the change in newborns in relation to various health outcomes is only beginning to be defined. In this context, we developed our hypotheses that deviation in eGA from chronological age (a variable referred to as “delta gestational age” or dGA) is associated with both prenatal TRAP exposures and early-life allergic sensitization, and that the relationship between prenatal TRAP exposure and sensitization risk is mediated in part by dGA.

In an atopy-enriched subset of the Canadian Healthy Infant Longitudinal Development (CHILD) cohort ($n = 145$, 29% having a positive skin prick test result to at least 1 of 10 standardized allergens at age 1 year), the mean gestational age (GA) was 276 ± 7.9 days or 39.4 weeks (see this article's Methods section in the Online Repository at www.jacionline.org). The mean eGA was 243 ± 8.2 and 279 ± 5.8 days as calculated by the 2 available gestational epigenetic clock algorithms developed by Knight et al⁵ and Bohlin et al.⁶ Both algorithms resulted in eGAs that were statistically associated with chronological GA (Fig 1, A and B). Given the stronger positive correlation using the method of Bohlin et al ($r = 0.66$; $P < .001$) compared with that of Knight et al ($r = 0.44$; $P = .001$), all further analyses were conducted on the basis of Bohlin et al's eGA.

All subsequent analyses did not control for the following features because no statistical differences were observed: child's sex, maternal factors (age, health status, parity, gestational diabetes, ethnicity, and antibiotic use), and child's birth weight (GA- and sex-standardized z score). Mode of delivery, which was strongly associated with dGA (see Table E1 in this article's Online Repository at www.jacionline.org), was included in our analyses. Children born by elective cesarian section had a statistically larger deviation between their eGA and chronological GA (5.74 days; 95% CI, 0.35-8.23).

Children of mothers exposed to higher levels of TRAP during the first trimester of pregnancy were at increased risk of allergic sensitization at age 1 year ($P = .06$; see Table E1). These children also had a larger deviation, meaning their eGA was larger than their chronological age (2.1 days; 95% CI, 0.11-4.08, for each $10 \mu\text{g}/\text{m}^3$ increase in NO_2 exposure, which approximates an interquartile increase). Proximity to green space (as quantified from satellite imagery using the normalized difference vegetation index) was not associated with a change in dGA (see Table E1).

Building on this observation, we further established that infants with a 1-day deviation in dGA were 8% more likely to be sensitized to allergens at age 1 year (odds ratio, 1.07; 95% CI, 1.00-1.14; $P = .05$) (Fig 1, C). Finally, when estimating the direct effect of air pollution (ie, adjusting for dGA), an *in utero* exposure increase of $10 \mu\text{g}/\text{m}^3$ NO_2 was associated with a 34% increased risk of allergic sensitization (odds ratio, 1.34; 95% CI, 0.97-1.87), compared with the 42% increase (odds ratio, 1.42; 95% CI, 1.02-1.99) without dGA adjustment (see Table E2 in this article's Online Repository at www.jacionline.org).

METHODS

We used data from the National Health Interview Survey (NHIS) from the 10-year period spanning 2007 to 2016. The NHIS is a cross-sectional household survey consisting of personal interviews of the US civilian noninstitutionalized population using a multistage probability sample design,^{E1} designed by the National Center for Health Statistics (NCHS) and conducted by the US Census Bureau. The annual sample size of the NHIS is approximately 35,000 households, with a household response rate ranging from 68% to 87% between 2007 and 2016. Oversampling of black and Hispanic households began in 1985 and that of Asian households in 2006, with data collected regarding Asian subpopulations beginning in 1992.^{E1} From each sampled household, 1 family was selected, with 1 adult and 1 child selected randomly from within each family for additional data collection. As described elsewhere,^{E1} the NHIS follows multistage stratified sample design. The 2006 to 2015 survey is based on an area sampling frame for housing units in place at the time of US Census 2000. A subsample of the initial sample was selected for interviewing, with housing units in areas having higher concentrations of black, Hispanic, and Asian persons in US Census 2000 retained at higher rates. In addition, all households in the subsample with 1 or more black, Hispanic, or Asian members were retained in the survey. We included sampled children who were 17 years and younger for whom allergic disease data were available.

Variable ascertainment

Allergic conditions were defined on the basis of answers to the following questions^{E2}:

1. During the past 12 months has [your child] had ... Any kind of food or digestive allergy?
2. During the past 12 months, has [your child] had ... Eczema or any kind of skin allergy?
3. Has a doctor or other health professional EVER told you that [your child] had asthma?
4. [If yes] Does your child still have asthma?

Food allergy and eczema were defined as affirmative answers to questions 1 and 2, respectively. Asthma was defined as affirmative answers to both questions 3 and 4. Race was self-identified, and subjects were able to specify more than 1 race as well as Hispanic ethnicity. Respondents were asked about identified Asian subpopulation if Asian was selected. These subpopulations included Chinese, Japanese, Vietnamese, Filipino, Asian Indian, and Korean. To protect privacy, groups without sufficient sample size were lumped together for purposes of reporting (ie, Korean, Japanese, and those of more than 1 Asian subgroup were combined into an “other Asian” category in the data release). If a respondent chose more than 1 racial category, they were able to choose 1 primary race, and their data were aggregated and analyzed by the primary race selected.

Family income level was classified according to the ratio of family income to the federal poverty level on the basis of household size. Place of birth (ie, within or outside of the United States) of the adult respondent was included as the place of parental nativity if the sample adult reported that he or she was the parent of the sample child.

Statistical analysis

To adjust for complex survey design, we used the Final Annual weight, which is provided by the NCHS together with the publicly available NHIS data, and is based on design, ratio, nonresponse, and poststratification adjustments. The survey analysis commands using the survey weights, sampling units, and strata created by the NCHS were used in all analyses to allow for weight adjustment of all final results, creating a nationally representative sample and accounting for the complex survey design. We used Stata/IC version 14.2 (Stata Corporation, College Station, Tex) for all analyses.

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TABLE E1. Overall demographic characteristics of study population by race/ethnicity, using survey weighting

Characteristic	Overall	Non-Hispanic white	Non-Hispanic black	Hispanic	Asian
Total (percentage in weighted estimates)	116,428 (100%)	54,896 (59.1%)	18,352 (14.9%)	31,829 (20.8%)	7,571 (5.2%)
Age (y), mean (SE of estimate)	8.6 (0.02)	8.8 (0.03)	8.7 (0.05)	8.1 (0.03)	8.3 (0.08)
% female (SE of estimate)	49.0 (0.002)	48.7 (0.002)	49.5 (0.005)	48.6 (0.003)	49.8 (0.007)
Nativity					
Child born outside the United States, % (95% CI)	4.2 (4.0-4.3)	1.5 (1.4-1.6)	2.6 (2.3-3.0)	8.8 (8.3-9.2)	20.3 (19.1-21.7)
Parent born outside the United States, % (95% CI)	21.5 (20.9-22.1)	6.2 (5.9-6.6)	12.9 (11.9-14.0)	57.0 (55.9-58.1)	76.9 (75.3-78.3)
Allergic disease					
Food allergy, % (95% CI)	5.4 (5.2-5.5)	5.5 (5.3-5.7)	5.9 (5.4-6.4)	4.3 (4.0-4.6)	6.2 (5.5-6.9)
Eczema, % (95% CI)	11.8 (11.5-12.0)	11.2 (10.8-11.5)	16.8 (16.1-17.5)	9.7 (9.3-10.1)	11.8 (10.8-12.7)
Asthma, % (95% CI)	9.0 (8.8-9.3)	8.0 (7.6-8.3)	15.3 (14.7-15.9)	8.2 (7.8-8.6)	5.7 (5.1-6.3)

Means and percentages are reported with SEs and 95% CIs of the weighted estimates because analyses were based on complex survey data.

TABLE E2. Stratified analyses by age category*

Variable	OR (95% CI)		
	Food allergy	Eczema	Asthma
Stratified analysis by age, ≤5 y			
Race			
Non-Hispanic white	Reference	Reference	Reference
Non-Hispanic black	1.11 (0.94-1.31)	1.86 (1.67-2.07)	2.83 (2.40-3.34)
Hispanic	0.77 (0.63-0.94)	1.03 (0.91-1.15)	1.48 (1.25-1.75)
Asian	1.27 (1.00-1.61)	1.47 (1.23-1.77)	1.38 (1.03-1.84)
Nativity category			
Child US-born	Reference	Reference	Reference
Parent US-born			
Child US-born	0.82 (0.67-0.98)	0.64 (0.57-0.71)	0.51 (0.43-0.60)
Parent foreign-born			
Child foreign-born	0.58 (0.32-1.03)	0.39 (0.25-0.57)	0.39 (0.23-0.66)
Parent foreign-born			
Child foreign-born	1.03 (0.44-2.37)	0.69 (0.37-1.29)	0.71 (0.33-1.51)
Parent US-born†			
Stratified analysis by age, ages 5-12 y			
Race			
Non-Hispanic white	Reference	Reference	Reference
Non-Hispanic black	1.18 (0.99-1.39)	1.64 (1.48-1.82)	2.05 (1.84-2.28)
Hispanic	0.83 (0.70-0.99)	1.07 (0.96-1.20)	1.32 (1.17-1.48)
Asian	1.26 (0.97-1.62)	1.58 (1.30-1.91)	1.31 (1.07-1.60)
Nativity category			
Child US-born	Reference	Reference	Reference
Parent US-born			
Child US-born	1.06 (0.91-1.23)	0.68 (0.60-0.77)	0.61 (0.55-0.69)
Parent foreign-born			
Child foreign-born	0.72 (0.50-1.04)	0.43 (0.33-0.55)	0.26 (0.19-0.36)
Parent foreign-born			
Child foreign-born	1.18 (0.72-1.93)	0.68 (0.45-1.02)	0.46 (0.27-0.79)
Parent US-born†			
Stratified analysis by age, ages 12-17 y			
Race			
Non-Hispanic white	Reference	Reference	Reference
Non-Hispanic black	1.02 (0.86-1.21)	1.37 (1.21-1.56)	1.61 (1.32-1.61)
Hispanic	0.86 (0.70-1.05)	0.98 (0.85-1.12)	1.13 (0.99-1.30)
Asian	1.13 (0.82-1.55)	1.29 (1.03-1.62)	0.85 (0.66-1.08)
Nativity category			
Child US-born	Reference	Reference	Reference
Parent US-born			
Child US-born	0.93 (0.75-1.14)	0.70 (0.61-0.82)	0.61 (0.52-0.71)
Parent foreign-born			
Child foreign-born	0.76 (0.57-1.00)	0.47 (0.36-0.61)	0.29 (0.22-0.38)
Parent foreign-born			
Child foreign-born	1.11 (0.65-1.87)	0.89 (0.57-1.38)	0.90 (0.58-1.38)
Parent US-born†			

*Adjusted for age, sex, and income.

†Foreign-birth to US-born parents is a small group with likely varying backgrounds.

TABLE E3. Effect of nativity on odds of allergic diseases, stratified by race*

Nativity category	OR (95% CI)		
	Food allergy	Eczema	Asthma
Non-Asian			
Child US-born	Reference	Reference	Reference
Parent US-born			
Child US-born	0.80 (0.73-0.88)	0.64 (0.60-0.68)	0.61 (0.57-0.66)
Parent foreign-born			
Child foreign-born	0.70 (0.56-0.87)	0.46 (0.38-0.55)	0.29 (0.24-0.36)
Parent foreign-born			
Child foreign-born	1.24 (0.88-1.77)	0.76 (0.55-1.07)	0.70 (0.50-0.98)
Parent US-born†			
Asian			
Child US-born	Reference	Reference	Reference
Parent US-born			
Child US-born	1.18 (0.89-1.56)	0.79 (0.63-0.98)	0.70 (0.52-0.96)
Parent foreign-born			
Child foreign-born	0.61 (0.41-0.92)	0.41 (0.29-0.59)	0.30 (0.16-0.56)
Parent foreign-born			
Child foreign-born	1.01 (0.53-1.90)	0.81 (0.46-1.44)	0.73 (0.38-1.41)
Parent US-born†			

*Adjusted for age, sex, and income.

†Foreign-birth to US-born parents is a small group with likely varying backgrounds.

TABLE E4. Overall demographic characteristics of Asian study population

Characteristic	Asian	Asian Indian	Chinese	Filipino	Other Asian
Total (percentage in weighted estimates)	7571	1698 (24.4%)	1396 (18.8%)	1823 (22.2%)	2654 (34.6%)

TABLE E5. Effect of race on odds of allergic diseases,* not adjusted for nativity

Variable	OR (95% CI)		
	Food allergy	Eczema	Asthma
Race			
Non-Hispanic white	Reference	Reference	Reference
Non-Hispanic black	1.10 (1.00-1.22)	1.62 (1.51-1.73)	1.92 (1.79-2.06)
Hispanic	0.78 (0.71-0.85)	0.84 (0.79-0.90)	0.96 (0.89-1.03)
Asian	1.13 (0.98-1.29)	1.05 (0.95-1.17)	0.72 (0.63-0.81)
Age (y)	0.99 (0.99-1.00)	0.97 (0.97-0.98)	1.06 (1.05-1.06)
Sex: female	0.99 (0.93-1.06)	1.03 (0.99-1.09)	0.77 (0.73-0.82)
Income†	1.00 (0.96-1.05)	1.00 (0.97-1.03)	0.81 (0.78-0.84)

*Adjusted for age, sex, and income.

†Income-to-poverty ratio is an ordinal variable, with categories of ≤Federal Poverty Level, 1-2 times Federal Poverty Level, ≥2 times Federal Poverty Level.