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## Understanding racial disparities in childhood asthma using individual- and neighborhood-level risk factors

Esteban Correa, PhD<sup>a</sup>, Lili Ding, PhD<sup>b</sup>, Andrew F. Beck, MD MPH<sup>c,d</sup>, Cole Brokamp, PhD<sup>b</sup>, Mekibib Altaye<sup>b</sup>, Robert S. Kahn, MD MPH<sup>c</sup>, Tesfaye B. Mersha, PhD<sup>a</sup>

<sup>a</sup>Division of Asthma Research, Cincinnati Children's Hospital Medical Center, Department of Pediatrics, University of Cincinnati, College of Medicine, Cincinnati, OH

<sup>b</sup>Division of Biostatistics and Epidemiology, Cincinnati Children's Hospital Medical Center, Department of Pediatrics, University of Cincinnati, College of Medicine, Cincinnati, OH

<sup>c</sup>Division of General and Community Pediatrics, Cincinnati Children's Hospital Medical Center, Department of Pediatrics, University of Cincinnati, College of Medicine, Cincinnati, OH

<sup>d</sup>Division of Hospital Medicine, Cincinnati Children's Hospital Medical Center, Department of Pediatrics, University of Cincinnati, College of Medicine, Cincinnati, OH

### Abstract

**Background:** Racial disparities in childhood asthma outcomes result from a complex interplay of individual- and neighborhood-level factors.

**Objectives:** To examine racial disparities in asthma-related emergency department (ED) visits between African American (AA) and European American (EA) children.

**Methods:** This is a retrospective study of patients <18 years who visited the ED at Cincinnati Children's for asthma, 2009–2018. The outcome was number of ED visits during a year. We assessed 11 social, economic, and environmental variables. Mediation and mixed-effects analyses were used to assess relationships between race, mediators, and number of ED visits.

**Results:** A total of 31,114 children (46.1% AA, 53.9% EA) had 186,779 asthma-related ED visits. AA children had more visits per year than EA children (2.23 vs 2.15;  $p < 0.001$ ). Medicaid insurance was associated with a 7% increase in ED visits compared with commercial insurance (1.07; 95% Confidence interval [CI]=1.03–1.1). Neighborhood socioeconomic deprivation was associated with an increased rate of ED visits in AA, not EA children. Area-level PM<sub>2.5</sub>, pollen, and outdoor mold were associated with an increased rate of ED visits for both AA and EA children (all  $p < 0.001$ ). Associations between race and number of ED visits were mediated by insurance (standardized coefficient [ $s\beta$ ]=0.048;  $p < 0.001$ ) and area-level deprivation ( $s\beta$ =0.084;  $p < 0.001$ ), PM<sub>2.5</sub> ( $s\beta$ =0.002;  $p < 0.001$ ), and outdoor mold ( $s\beta$ =0.006;  $p < 0.001$ ), altogether

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Conflicts of interest:  
none

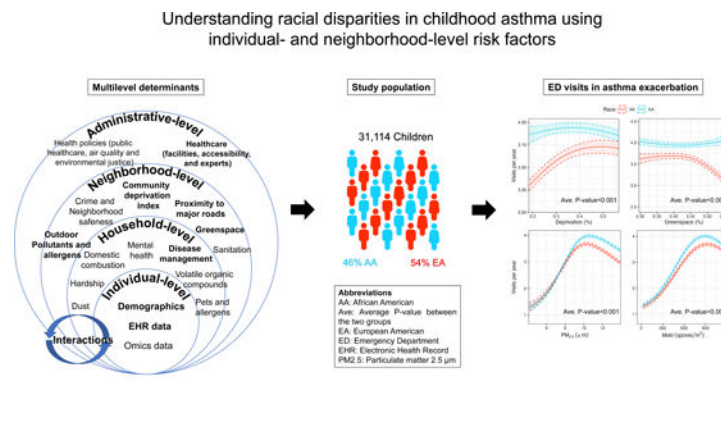
accounting for 55% of race's effect on ED visits. Race was not associated with number of ED visits ( $s\beta=0.006$ ;  $p=0.796$ ) after accounting for mediators.

**Conclusions:** Racial disparities in asthma-related ED visits are mediated by social, economic, and environmental factors which may be amenable to interventions aimed at improving outcomes and eliminating inequities.

## Capsule summary

We determine the effect of a range of individual- and neighborhood-level factors on racial disparities for asthma-related ED visits using mediation and mixed-effects analyses.

## Graphical Abstract



## Keywords

Asthma; racial disparities; mixed-effects analysis; mediation analysis; electronic health records; environmental exposure

## INTRODUCTION

Asthma is the most common non-communicable chronic disease of childhood.(1) It is the third ranking cause of hospitalization among children less than 18 years of age, and it is a leading cause of school absences.(2) The cost burden for the U.S. healthcare system alone surpassed \$82 billion in 2019.(3) However, despite clinical advances, asthma prevalence, morbidity, and mortality all continue to be higher for children who identify as Black or African American (AA) compared to those who identify as white or European American (EA).(4) Hospitalization or death due to asthma are four and seven times higher in AAs than EAs, respectively.(5)

Previous studies have evaluated links between racial disparities in asthma outcomes and a range of risk factors. Hill et al reviewed the contribution of biological and environmental triggers to racial disparities among asthmatic children, suggesting these disparities are the result of gene-environment interactions, hardships, and ethnicity.(6) At a neighborhood-level, DePriest et al found that less greenspace and more violence were associated with increased asthma risk in AA children.(7) Keet et al found that living in poor, urban areas

was a risk factor for child asthma morbidity.(8) More recently, Grunwell et al., found that neighborhood with high social vulnerability levels resulted in environmental triggers, affecting pediatric intensive care admissions in asthma.(9)

Despite this growing evidence, the study of multilevel asthma risk factors has been more limited, with scarce information available on the contributions and interplay between both individual and neighborhood-level exposures.(10) This limitation on understanding multilevel exposures may affect the unique position of physicians and policymakers to address modifiable individual- and neighborhood-level determinants of both asthma outcomes and disparities in those outcomes. Therefore, we sought to evaluate the role of asthma-associated risk factors, across multiple levels, in association with rate of asthma-related emergency department (ED) visits, using mediation and mixed effects negative binomial regression analyses. Specifically, we sought to examine differences in rate of ED visits among AA and EA children, considering a range of potentially underlying social, economic, and environmental exposures across individual and neighborhood levels.

## **METHODS**

### **Study population**

We conducted a retrospective population-based cohort study using data from and linked to Cincinnati Children's Hospital Medical Center's (CCHMC) electronic health record (EHR). CCHMC is an urban academic medical center in Southwestern Ohio serving residents of the Greater Cincinnati metropolitan area that includes counties in Indiana, Kentucky, and Ohio. EHR data for 31,114 patients that visited the ED for asthma between 2009 and 2018 were extracted based on ICD asthma codes (ICD-9: 493, ICD-10: J45). The exclusion criteria for ED visits were (1) those visits from children who self- or parent identified as a race other than AA or EA, (2) age at visit equal to or greater than 18 years, and (3) visits with incomplete information on covariates. Workflow of the study and the analytic framework is shown in Figure 1. ED encounters included key data for linked individuals, including sociodemographic characteristics, lab tests, and insurance provider. We also extracted the patient's home address associated with the relevant encounter to enable geocoding and connection to potentially relevant neighborhood-level variables. Specifically, we geocoded the address to the census tract geography and linked the census tract to data from the 2015 American Community Survey 5-Year Estimates (ACS) for sociodemographic factors, satellite imagery for air pollutants, and ground-based stations for allergens.(11)

### **Primary outcome**

The outcome of interest was defined as the number of registered ED visits during a year. Repeated measures (patients with ED visits in more than one year) were included during the entire time course.

### **Individual-level factors**

The primary independent variable was patient race, defined according to self or caregiver report (AA and EA). Additional individual-level independent variables were selected according to those known to be associated with asthma exacerbations and/or shown to

affect the association between race and asthma-related healthcare reported on previous studies.(6, 10, 12–14) We obtained these variables from the EHR. Age at visit(s) within the same year and gender (male or female) were included due to their association with asthma exacerbations. Insurance type was categorized as commercial and Medicaid.

### Neighborhood-level factors

Neighborhood-level factors linked to geocoded patients' address at each visit included proximity, environmental and allergen measures. For proximity measures, we calculated distances to the CCHMC facility, to main roads (primary roadways, U.S. highway, state highway, or county highway system). Greenspace was calculated as the average normalized vegetation index (NDVI) at 0.5, 1.5, and 2.5 kms of patient's location. Neighborhood-level socioeconomic deprivation index is an estimation of material deprivation using six different census-tract-level socioeconomic variables from the American Community Survey. (11) The index ranges from 0 to 1 where 0 indicates lowest and 1 indicates highest deprivation. Finally, we included weekly averages of daily particulate matter less than 2.5  $\mu\text{m}$  [ $\text{PM}_{2.5}$ ], pollen, and outdoor mold. Risk factors were extracted longitudinally, then averaged for continuous variables and last registered for medical insurance over a study year of each patient's follow-up period. The detailed description of deprivation index and outdoor environmental exposures can be found in the Methods section in the Online Repository.

### Statistical analysis

Descriptive statistics were derived as means (with standard deviation [SD]) for continuous variables and frequencies (with percentages) for categorical variables. Associations between race and each individual- and neighborhood-level variable were tested using Chi-square ( $\chi^2$ ) or t-tests, as appropriate. A Variance Inflation Factor (VIF) was examined to assure no multicollinearity ( $\text{VIF} < 5$ ) in the list of risk factors.(15) Mediation analysis was used to test the direct and indirect effect of race on number of ED visits through individual- and neighborhood-level risk factors.(16) We implemented a longitudinal modelling strategy using mixed effects negative binomial regression models to assess the association of risk factors and their interactions with rate of ED visits during the entire time course. Finally, the study cohort was split into three subsets (only AAs, only EAs, and both AAs and EAs together) where predictive models for rate of ED visits were built in the training data (75%) and tested in the testing data (25%). The Methods section in this article's Online Repository at [www.jacionline.org](http://www.jacionline.org) provides additional details about VIF, unadjusted visits rates, and 95% confidence intervals, (Table E1).

**Mediation analysis**—Following Mersha *et. al.*, we determined the pathway between an independent variable X (race) and dependent variable Y (number of ED visits) using mediation analysis.(16) To implement the mediation analysis, number of ED visits were categorized into a binary outcome using the median of ED visits of all patients. In our mediation model (Figure 2),  $X \rightarrow Y$ , X is thought to cause M (mediator), and M causes Y ( $X \rightarrow M \rightarrow Y$  representing the indirect effect of X on Y). We formulated hypotheses of the direct and indirect effect on the basis of previous reports.(17) Direct effects of race on number of ED visits were built following the illustration at Figure 2. estimated after adjusting for age and gender covariates, using Probit analysis. The total effect ( $\phi$ ) from race

to number of ED visits was thought to be the sum of standardized direct effect ( $\Theta$ ) and all indirect effects ( $\delta_j$ ),  $j=1,2, \dots, J$ , where  $J$  is the total number of indirect paths from  $X$  to  $Y$ .

$$\varphi = \theta + \sum_{j=1}^J \delta_j$$

The  $j$ th indirect effect  $\delta_j$  is calculated as the product of all standardized coefficients ( $s\beta_{ij}$ ),  $i = 1, \dots, I_j$  within the path  $j$  (18)

$$\delta_j = \beta_{1j} \times \beta_{2j} \times \dots \times \beta_{I_j j}.$$

To assess the magnitude of each mediator, a percentage over the total effect of race on number of ED visits is calculated for each significant mediator.

**Mixed-effects analysis**—We implemented a mixed-effects negative binomial model with smooth splines. (19) The outcome variable  $Y_{ij}$  was the number of visits for patient  $i$  at year  $j$ . Independent individual-level variables were age, gender, race and insurance type. Independent neighborhood-level variables included proximity to CCHMC, proximity to a main road, greenspace, deprivation index, and outdoor exposures (PM<sub>2.5</sub>, pollen, and outdoor mold). Interactions between race and neighborhood-level variables were examined. The model also included the interaction effect between age and gender due to their association with asthma exacerbations:

$$g(E(Y_{ij})) = \beta_0 + b_{0i} + \text{race}_i + \text{gender}_i + \text{insurance}_{ij} + f_1(x_{\text{age}, ij}) * \text{gender}_i + (f_2(x_2, ij) + \dots + f_m(x_m, ij)) * \text{race}_i$$

In this equation,  $x_2, ij$  to  $x_m, ij$  refers to fixed effects including yearly average of proximity to CCHMC, proximity to main road, and greenspace, deprivation index, and outdoor exposures (PM<sub>2.5</sub>, pollen, and outdoor mold). The model also includes a subject-specific random intercept  $b_{0i}$  for repeated measures (patients who experience ED visits in more than one year). Here,  $g(\cdot)$  is the natural logarithm link function for negative binomial count data, and  $E(Y_{ij})$  is the expected value. For interpretation purposes, partial effects were plotted using the exponential function, including the intercept. Complementary to expected rate of visits and 95% confidence intervals (CI), visit rate ratios (VRR) were constructed with specific contrasts values at Q1 and Q3 quartiles, for 25<sup>th</sup> percentile and 75<sup>th</sup> percentile, respectively. (20)

**Prediction model development and validation**—We then evaluated whether our model using both individual- and neighborhood-level factors would be predictive of rate of ED visits in three subsets of the cohort (only AAs, only EAs, and both AAs and EAs together). Our models were developed using the training data and overall performance of these models was evaluated using the mean absolute error (MAE) in both, training, and testing data. MAE quantifies how close predicted rates of visits are to the observed outcome. The MAE score can range from 0, for a perfect model, to  $\infty$ , for a model with very

large errors. QQ plots are provided for all models. All analyses were conducted using the R environment, *ggplot* for graphics, *lme4* for multivariable models, *lavaan* package for mediation analysis.(19, 21–23)

## RESULTS

### Visits characteristics and racial disparities

Of the 43,487 individuals who experienced an asthma-related ED visit, 31,114 were <18 years of age at index visit, AA or EA and had complete information on covariates. These included individuals contributed 186,779 total asthma-related ED visits where patients were <18 years of age at the visits. The cohort was comprised of 14,330 AA children, contributing 103,488 asthma-related ED visits, and 16,784 EA children, contributing 83,291 visits. Table 1 and Figure E2 present descriptive statistics of the sample included in the study. Among registered ED visits, there were more visits for AA children per year (2.23 vs 2.15;  $p<0.001$ ), and there were more visits covered by Medicaid insurance for AA children (82.6% vs 43.3%;  $p<0.001$ ).

Compared to EA children, AA children were more likely to live in areas with higher deprivation (0.47 vs 0.30;  $p<0.001$ ) and were more likely to live closer to the CCHMC base facility (9.0 km vs 21.6 km;  $p<0.001$ ) and main roads (0.67 km vs 0.76 km;  $p<0.001$ ).

Conversely, the proportion of greenspace was on average 3 points higher in the areas in which EA children lived (0.45 vs 0.42;  $p<0.001$ ). However, EA children were exposed to higher  $PM_{2.5}$  (10.63 $\mu$ m vs 10.35 $\mu$ m;  $p<0.001$ ) compared to AA children. AA children had slightly higher exposure to pollen (110.27 gr/m<sup>3</sup> vs 106.39 gr/m<sup>3</sup>,  $p=0.001$ ) and outdoor mold (1,139.82 spores/m<sup>3</sup> vs 1,057.01 spores/m<sup>3</sup>;  $p<0.001$ ).

There was a spatial agreement between the number of visits registered and deprivation, greenspace, and proximity to CCHMC (figure 3). Visits from Hamilton County were more likely to be AA compared to other counties in Cincinnati metropolitan area where EA visits were more likely.

### Mediation analysis

In our mediation analysis, we assessed associations among race, individual and neighborhood level variables, and number of ED visits (Figure 3). The direct effect of race on number of ED visits was not significant, after adjusting for all other variables (Table 2). However, the effect of race on ED visits was significantly mediated by Medicaid insurance (standardized coefficients [ $s\beta$ ]=0.048;  $p<0.001$ ), neighborhood socioeconomic deprivation ( $s\beta=0.084$ ;  $p<0.001$ ), exposure to  $PM_{2.5}$  ( $s\beta=0.002$ ;  $p<0.001$ ), and exposure to outdoor mold ( $s\beta=0.006$ ;  $p<0.001$ ). This effect was not mediated by proximity to CCHMC, proximity to main roads, greenspace, and exposure to pollen. Medical insurance, neighborhood socioeconomic deprivation, exposure to  $PM_{2.5}$ , and exposure to outdoor mold accounted for 55% of race effect on number of ED visit



### Factors and interactions associated with rate of ED visits

Table 3 and Figure 4 summarize the results from the mixed-effects negative binomial models for the association between rate of ED visits and the assessed independent variables. For individual-level variables, we observed a non-linear interaction effect between age and gender. Age (Q3=12.2 years old vs Q1=4.4 years old) was associated with a 10% increase in rate of visits in both, females and males ( $p=0.001$ ). Medicaid insurance was associated with a 7% increased rate of visits ( $p<0.001$ ).

For neighborhood-level variables, visits from AA children living in most deprived (Q1=0.51) vs those living in least deprived areas (Q3=0.27) were associated to 10% higher rate of visits ( $p=0.033$ ). For outdoor environmental exposures, most polluted areas (Q3=12.08  $\mu\text{m}$ ) were associated with a 10% and 20% increased rate of visits in AA and EA children (both  $p<0.001$ ), respectively. Also, pollen (Q3=118.65  $\text{gr}/\text{m}^3$  vs Q1=6.5  $\text{gr}/\text{m}^3$ ) was associated with higher rate of visits in both AA and EA (all  $p<0.001$ ), 1.8 and 1.9 respectively. Similarly, an increase in outdoor mold exposure (Q3=1,675,65 spores/ $\text{m}^3$  vs Q1=312.49 spores/ $\text{m}^3$ ) was associated with 20% higher rate of visits in both AA and EA (all  $p<0.001$ ). However, there were no significant interactions between EA race and deprivation, proximity to CCHMC, and greenspace, and between AA race and proximity to major roads, with respect to the relationship with rate of ED visits.

### Prediction model and validation

Using MAE we evaluated errors of all models developed. The result showed that MAE metric for the testing data were similar to the training data estimates (Table 4). In all subsets in both datasets, training, and testing, mixed-effects negative binomials models had the lowest MAE scores, compared to classic negative binomial versions. QQ plots showed that mixed-effects models had the lowest difference between observed and predicted rate of ED visits (Figure E3).

## DISCUSSION

In this study, we used a large EHR dataset from 2009 to 2018 including more than 186,000 ED visits from about 31,000 children to systematically investigate racial disparities in asthma-related ED visits using association and mediation analyses. We were able to longitudinally adjust for individual factors and neighborhood-level information linked to the patient's home address at the time of each ED event. ED visits were also more likely to occur among children covered by Medicaid insurance, particularly for AA children. AA children were also more likely to live in more deprived areas, live close to CCHMC, live close to greenspace, be more exposed to outdoor pollutants, and use the ED more frequently than EA children. Our findings support the notion that racial disparities in asthma-related ED visits are mediated by social, economic, and environmental factors at both individual and neighborhood levels.

There were differences in the exposures of children identifying as AA compared to those identifying as EA. Those differences influenced asthma-related ED visit frequency. For example, AA children were significantly more likely to live in more socioeconomically

deprived neighborhoods. They were also more likely to be exposed to air pollutants and certain allergens. Our mixed-effects model showed that Medicaid-insured children (more common insurance type in AA children) were more likely to use ED frequently than commercially insured children. Several implications might be derived from these identified differences.(16, 24, 25) First, our exploratory data analysis revealed that visits from Hamilton County were more likely to be from AA children compared to other counties in Cincinnati metropolitan area where ED visits from EA children were more likely (Figure 3). As a consequence of living in urban areas such as Hamilton County, children might have complex family and social characteristics associated with their locations (hardship and accessibility) and be more exposed to environmental asthma “triggers” (e.g., closer to main roads, less greenspace availability, or higher PM<sub>2.5</sub> exposure due to car pollution).(13, 26) Second, Medicaid-insured patients may use the ED as a more regular source of health care compared to children enrolled in commercial plans given differential access to primary or preventive care.(27) Also, minoritized groups may have more difficulty managing chronic disease like asthma due to limited access to additional health care supports (e.g., pharmacy), limited health literacy, reduced trust in health care providers, and additional factors rooted in structural racism.(17, 28, 29)

Higher exposure to PM<sub>2.5</sub>, pollen, and outdoor mold exposures were consistently associated with higher rates of ED visits in both AA and EA children. Comparing children living in more polluted to less polluted quartiles, AA and EA children had visits rate ratios of 1.1 and 1.2, respectively (p<0.001). Previous studies have shown that a causal relationship probably exists between early-life exposure to air pollutants, like PM<sub>2.5</sub>, and asthma burden.(30–32) Similarly, higher visits rate ratios were reported for high levels of pollen and outdoor mold. Although evidence of racial disparities in aeroallergen sensitization has been documented elsewhere, specific racial differences in exposure to pollens and outdoor molds are still not well understood.(33) Similarly, using genetic data from a prospective cohort study of 695 self-identified black and white children with an asthma-related admission, Mersha et al showed that although an increase in African ancestry is associated with increased odds of asthma readmission, genetic variations played far less of a role in explaining asthma readmission rates than social and environmental factors.(16) Although our mediation analysis varies some from Mersha’s ancestry analysis study in terms of independent variables and outcomes, deprivation was also the highest contributor as their estimate for hardship (33% vs. 40%), indicating the role of social, economic, and environmental risk factors in likelihood of asthma ED visits.

The present study has notable strengths. We used longitudinally available individual-level information from an EHR which allowed more detailed specification of the outcome as well as adjustments for individual-level factors available across the entire time course. Presence of the patient’s home address tied to each included ED visit enabled addition of neighborhood-level information and exposures at the time of the visit. From the multivariable analysis, we accounted for non-linear interactions, retaining neighborhood-level exposures without arbitrary categorization and patients’ locations to avoid loss of information or bias. Third, our descriptive analysis showed differences, by race, in insurance type, deprivation, distance to CCHMC and main roads, greenspace availability, and outdoor exposures drive racial disparities in asthma outcomes. Similarly, our mixed effects model



with multilevel factors showed significant effects and interactions of race with risk factors (deprivation, proximity to healthcare provider, proximity to major roads, greenspace, PM<sub>2.5</sub> and allergens). Taking all these variables into a mediation analysis, we found no direct effect of race on number of ED visits. Instead, it was mediated through social, economic, and environmental variables.

Our study has several limitations worth noting. Although we found clear racial disparities in the rate of asthma-related ED visits, this study was conducted in a single geographic area and healthcare facility. However, as the only pediatric institution in the study area, we capture the majority of ED events.(34). In Cincinnati, and the areas in close proximity to the main CCHMC campus, there are higher concentrations of individuals who identify as Black or AA. Suburban communities that are further from the main CCHMC campus have higher concentrations of individuals who identify as white or EA. This is reflective of racial and economic segregation that persists in Cincinnati, like other parts of the country. It is possible that the further away a family lives from the ED, the more they are dissuaded from seeking care in that site. They may find alternative sites of care (e.g., adult facility, primary care office) or not seek care at all. That said, CCHMC dominates the regional market share for inpatient utilization and emergency pediatric care. Still, there may be ED visits missed, especially in those areas further from the main campus.

It is also possible that our findings will not generalize to other regions with differing demographic or health care access characteristics. Second, our race reporting systems in the EHR database make it difficult to assess those who see themselves as mixed race, multiracial, or of another race/ethnicity.(35) Third, the total effect obtained in the mediation analysis might include unmeasured mediators or confounders. Although both contextual (neighborhood) and individual level measures are critically important in defining disease risk, we had limited individual-level data available within the EHR. Future research might include additional potential individual-level variables (e.g., prescriptions, allergen sensitization, immunologic measures, and second-hand smoking), housing characteristics (e.g., in-home pests, indoor mold, and household income) that are not available in our study. Future studies may also wish to evaluate other biologically plausible interactions including race-sex and race-age interactions, each of which might influence the number of asthma-related ED visits.(36)

There are several implications of our findings. First, we could improve the deleterious environmental factors through healthy homes programs and clean air policies. This may reduce asthma exacerbations and the number of ED visits. Second, we can augment preventive care by enhancing access to primary care and pharmacies; this could include care extenders like community health workers (CHW) or care managers. CHW initiatives such as The Seattle-King County Healthy Homes Project have been particularly successful in support of behavior change in asthma modifiable risk-factors, reducing urgent health services and enhancing quality of life scores.(37) The fact that AA and EA children who have the same social, economic, and environmental circumstances visit the ED in a similar frequency suggests that we should recognize race for what it is, a sociopolitical construct emblematic of sociopolitical factors as opposed to genetic ones.

In conclusion, previous efforts to understand racial disparities in asthma-related ED visits have been limited by the variables used. Our analysis was designed to address multiple levels of exposures and mechanisms simultaneously. In addition, we implemented analyses that offer high-resolution insights into the underlying spatial risk factors in childhood asthma. The assessment of multi-level risk factors that drive racial disparities in asthma offers a good opportunity to inform the design of targeted intervention strategies to equitably reduce the asthma burden. Our approach is distinct from previous efforts in that we used individual and neighborhood-level exposures in mediation models to systematically assess racial disparities and identify areas at risk for childhood asthma which can be subsequently used to mitigate racial disparities in pediatric asthma. Our findings offer potential avenues for intervention for policymakers to address racial gaps in the experience of asthma and other complex diseases.

## Supplementary Material

Refer to Web version on PubMed Central for supplementary material.

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## Abbreviations

<b>AA</b>	African American
<b>ACS</b>	American Community Survey
<b>CCHMC</b>	Cincinnati Children's Hospital Medical Center
<b>CDC</b>	Centers for Disease Control and Prevention
<b>CI</b>	Confidence interval
<b>EA</b>	European American
<b>ED</b>	Emergency Department
<b>EHR</b>	Electronic health records
<b>ICD-9/10</b>	International Classification of Disease 9/10.
<b>MAE</b>	Mean absolute error
<b>NB</b>	Negative binomial
<b>PM<sub>2,5</sub></b>	Particulate matter 2.5 $\mu\text{m}$
<b>QQ</b>	quantile-quantile
<b>s<math>\beta</math></b>	Standardized coefficients
<b>SD</b>	Standard deviation

<b>VIF</b>	Variance Inflation Factor
<b>VRR</b>	Visits rate ratio
<b>US</b>	United States

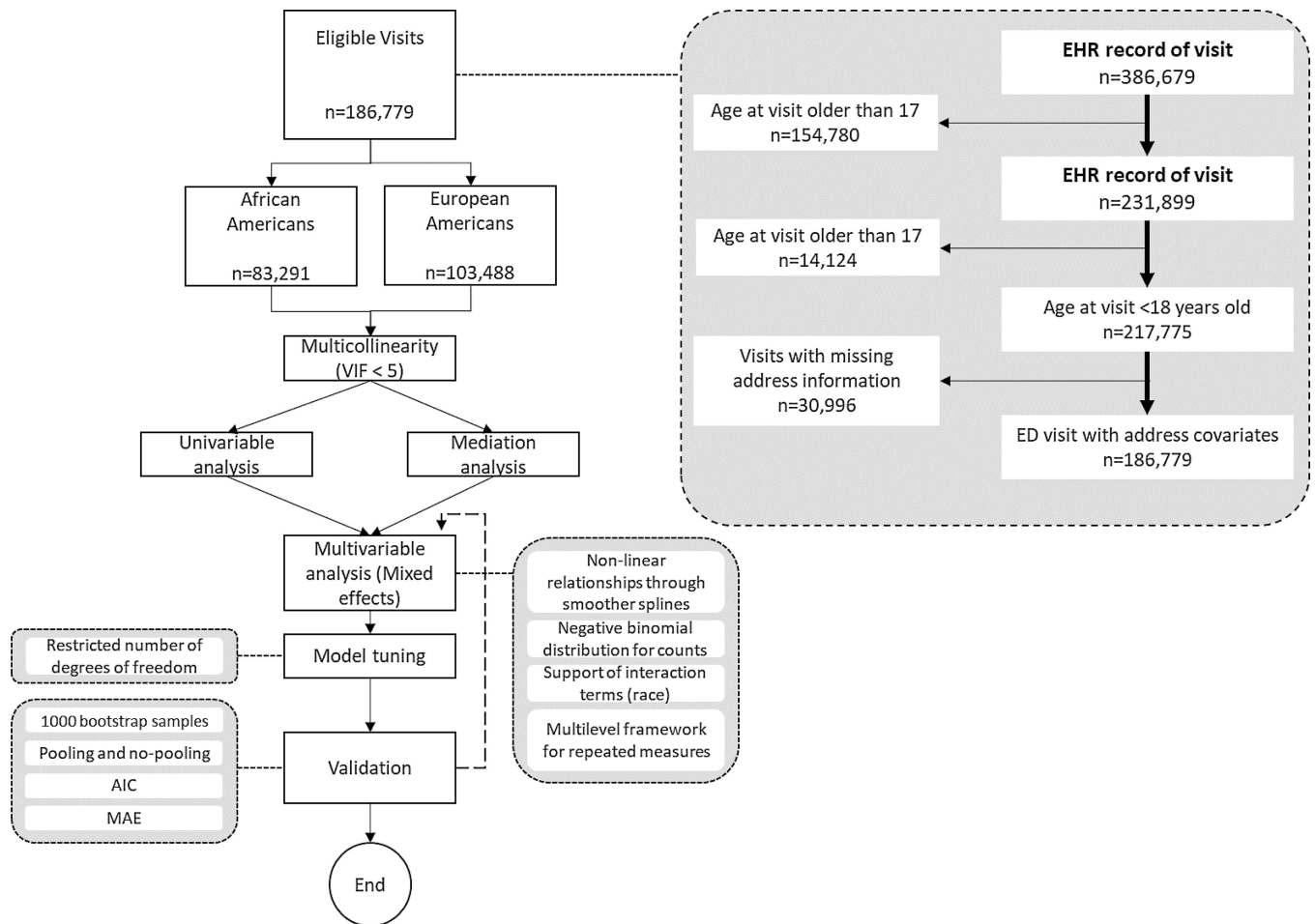
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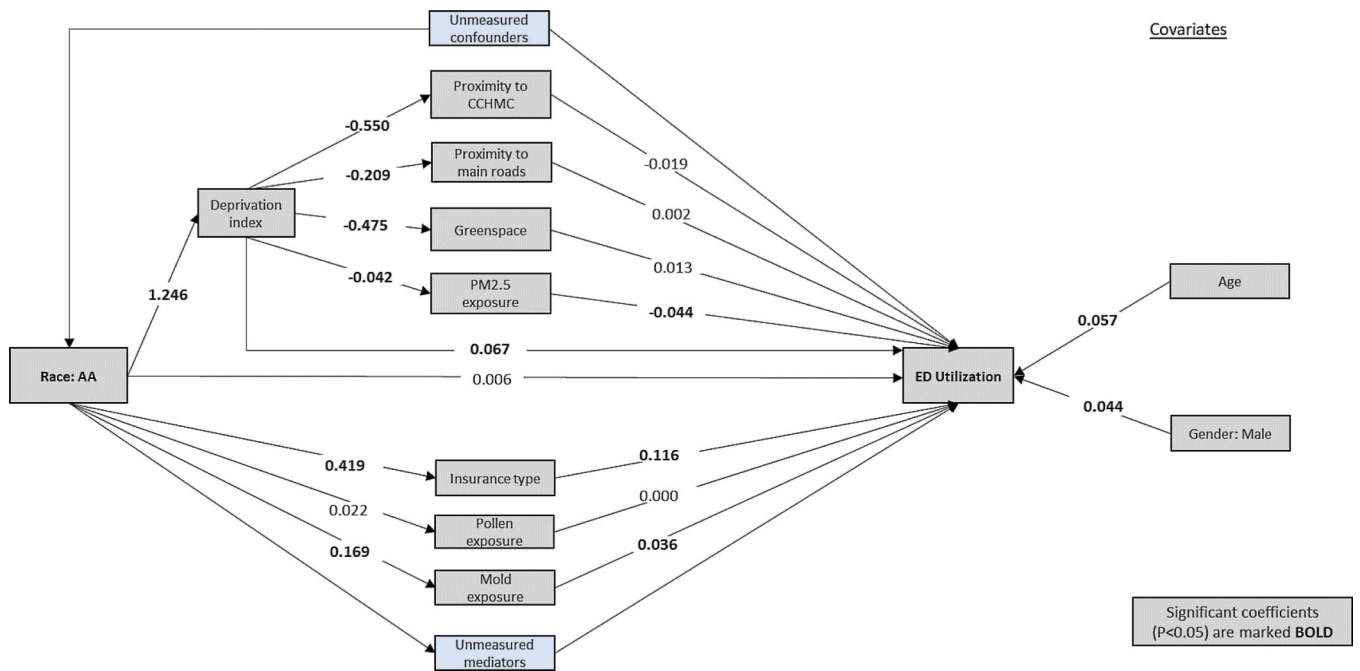
**Key messages**

- African American children were more likely to have Medicaid, live in socioeconomically deprived areas, be close to less green space availability, and visit the ED more frequently than European American children.
- Medical insurance, neighborhood socioeconomic deprivation, exposure to PM<sub>2.5</sub>, and exposure to outdoor mold accounted for 55% of race's effect on ED visit.
- Race was not directly associated with a child's number of ED visits. Racial disparities in number of ED visits were mediated by social, economic, and environmental factors at both individual and neighborhood levels.

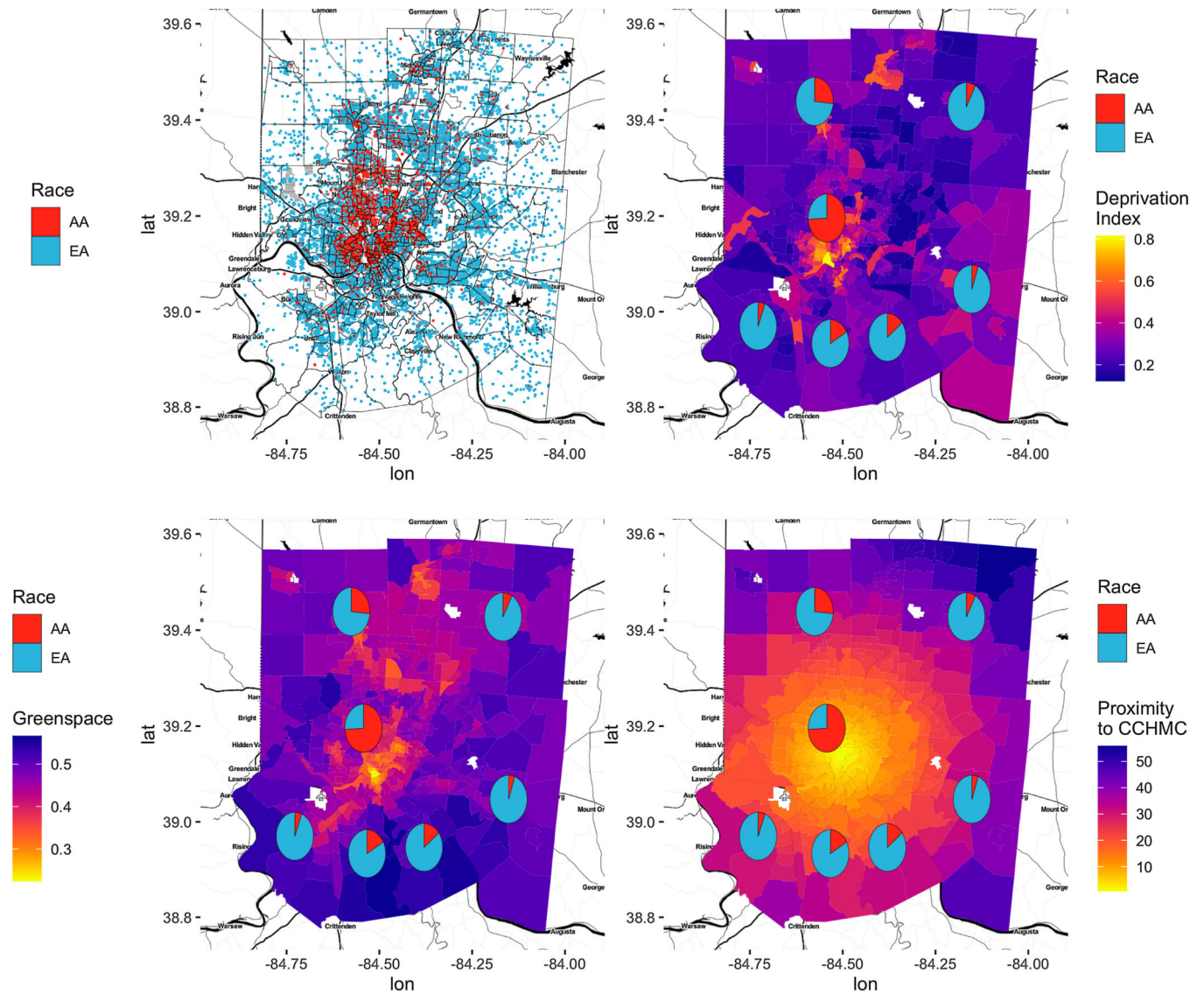


**Figure 1.** Schematic diagram and exclusion criteria of this study. The study includes a total of 31,114 children with valid covariates.

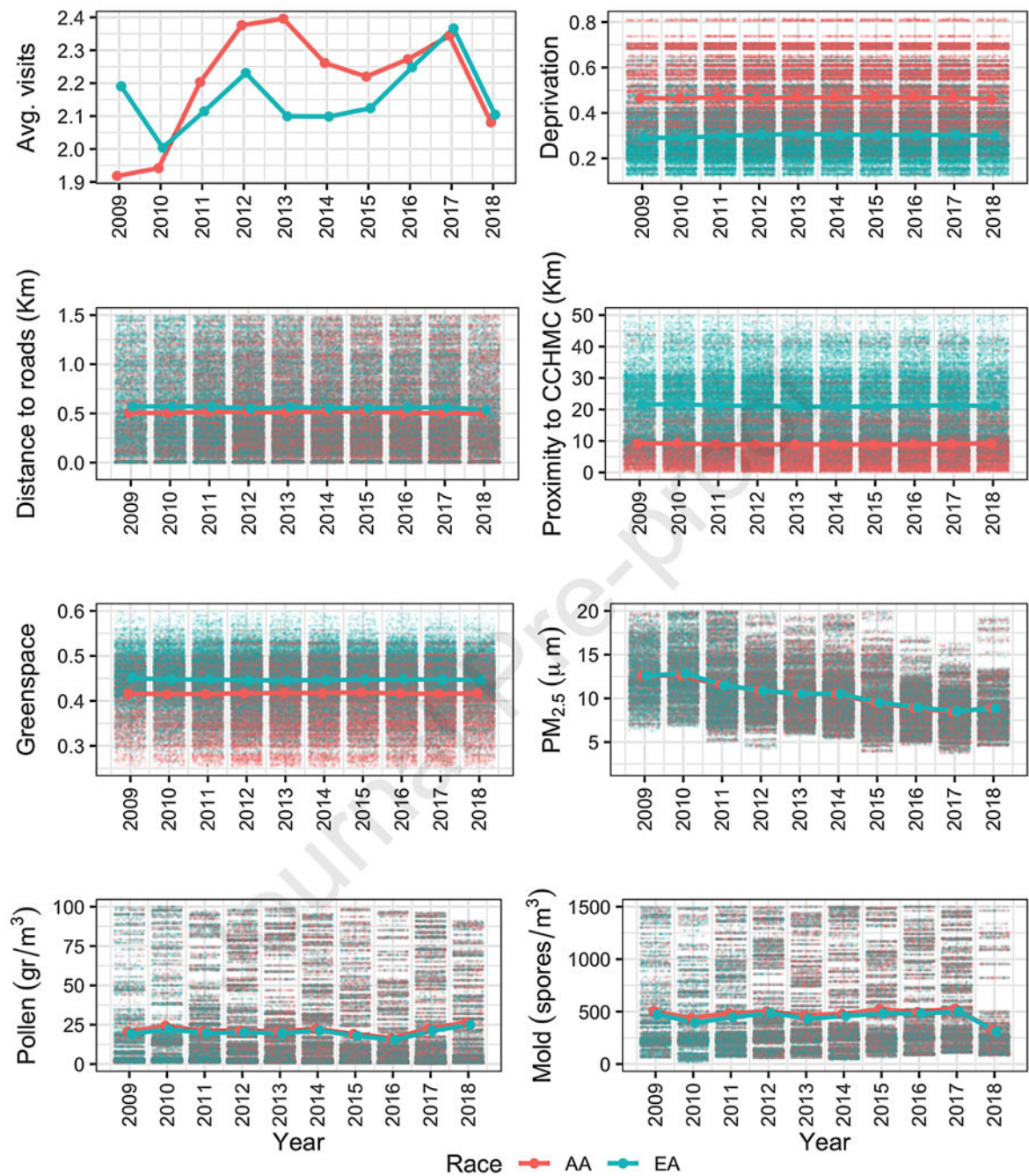




**Figure 2.** Mediation model for the independent variable - race, mediators, covariates and the dependent variable – number of ED visits. Measured and unmeasured pathways. Measured variables are indicated by gray boxes, unmeasured variables are indicated by blue boxes. The values shown are standardized coefficients (sβ), with statistical significance (p<0.05) marked in bold.



**Figure 3.** Exploratory data analysis of ED visits and covariates. Only those covariates with spatial agreement are shown: (A) number of ED Visits by race, (B) deprivation index vs. race, (C) greenspace vs. race, and (D) and proximity to CCHMC vs race.



**Figure 4.**

Non-linear interactions associated with rate of ED visits: (A) Age vs. gender, (B) deprivation index vs. race, (C) proximity to CCHMC vs. race, (D) proximity to major roads vs. race, (E) greenspace vs. race, (F) PM<sub>2.5</sub> vs. race, (G) pollen exposure vs. race, (H) and outdoor mold exposure vs. race.

**Table 1.**

ED visits characteristics by self-reported race including individual-and neighborhood-level risk factors.

Characteristic	Overall, No. (%) or Mean (SD)	AA, No. (%) or Mean (SD)	EA, No. (%) or Mean (SD)	P-value *
Patients' cohort	31114	14330 (46.1%)	16784 (53.9%)	
Total ED visits	186779	103488 (55.4)	83291 (44.6%)	
ED Visits per year	2.20 (2.47)	2.23 (2.54)	2.15 (2.39)	<0.001
<b>Individual-level</b>				
Age at visit (years)	8.59 (4.69)	8.78 (4.68)	8.34 (4.69)	0.015
<b>Gender</b>				
Female	75769 (40.6)	6723 (42.8)	6781 (40.4)	<0.001
Male	111010 (59.4)	8983 (57.2)	10006 (59.6)	
<b>Insurance type</b>				
Commercial	65231 (34.9)	17984 (17.4)	47247 (56.7)	<0.001
Medicaid	121548 (65.1)	85504 (82.6)	36044 (43.3)	
<b>Neighborhood-level</b>				
Deprivation index	0.39 (0.16)	0.47 (0.15)	0.30 (0.12)	<0.001
Proximity to CCHMC's facility (km)	14.63 (11.03)	9.02 (7.09)	21.59 (11.08)	<0.001
Proximity to major roads (km)	0.71 (0.62)	0.67 (0.59)	0.76 (0.65)	<0.001
Proportion of greenspace (%)	0.43 (0.06)	0.42 (0.06)	0.45 (0.06)	<0.001
PM2.5 ( $\mu\text{m}$ )	10.48 (3.34)	10.35 (3.28)	10.63 (3.41)	<0.001
Daily pollen exposure (gr/m <sup>3</sup> )	108.54 (227.12)	110.27 (227.18)	106.39(227.03)	<0.001
Daily outdoor mold exposure (spores/m <sup>3</sup> )	1,102.89 (923.05)	1,139.82(929.06)	1,057.01(913.46)	<0.001

P-values are from either a X2 or t-test comparing the differences when grouped by self-reported race;

\* P-value&lt;0.05.

**Table 2.**

Summary of direct and indirect effects on number of ED visits. ED visits were categorized using the median ED visits in all patients (1.33). The sum of the standardized coefficients along each path is estimated for each indirect effect.

Characteristic	Estimate	95% CI		P-value*	Proportion
Total effect	0.252	0.209	0.295	<0.001	
<b>Direct effects</b>					
Race-AA	0.006	-0.039	0.051	0.796	
<b>Indirect effects, mediated by:</b>					
Insurance-Medicaid	0.048	0.034	0.062	<0.001	19%
Deprivation index	0.084	0.047	0.121	<0.001	33%
Via Proximity to CCHMC	0.013	-0.003	0.029	0.078	
Via Proximity to major roads	-0.001	-0.005	0.003	0.765	
Via Greenspace	-0.008	-0.018	0.002	0.110	
Via PM <sub>2.5</sub>	0.002	0.002	0.002	<0.001	1%
Pollen exposure	0.000	0.000	0.000	0.941	
Outdoor mold exposure	0.006	0.004	0.008	<0.001	2%

\*. P-value<0.05; CI: Confidence interval; AA: African American.



**Table 3.**

Expected rate of visits and visit rate ratios showing associations between risk factors and ED visits for asthma. Individual-level variables and interactions between race and neighborhood-level variables were examined.

Factors	Expected visits (95% CI)	P-value *	Expected visits (95% CI)	P-value *
<b>Gender</b>		0.709		
Female	Ref			
Male	1.02 (0.93 to 1.11)			
<b>Race</b>		0.545		
AA	Ref			
EA	1.13 (0.76 to 1.69)			
<b>Insurance type</b>		<0.001		
Commercial	Ref			
Medicaid	1.07 (1.03 to 1.10)			
<b>Interactions</b>	<b>Group</b>	<b>P-value *</b>	<b>Group</b>	<b>P-value *</b>
<b>Deprivation (%)</b>	AA	0.033	EA	0.011
Quartile 1: 0.27	3.51 (3.46 to 3.57)		3.92 (3.86 to 3.97)	
Quartile 3: 0.51	3.73 (3.65 to 3.8)		3.9 (3.84 to 3.95)	
Visits Ratio	1.1		1.0	
<b>Proximity to CCHMC by Race</b>	AA	0.025	EA	0.346
Quartile 1: 6.6	3.69 (3.63 to 3.76)		3.87 (3.81 to 3.92)	
Quartile 3: 22.3	3.69 (3.64 to 3.75)		3.89 (3.82 to 3.96)	
Visits Ratio	1.0		1.0	
<b>Proximity to major roads (Km)</b>	AA	0.199	EA	0.009
Quartile 1: 0.25	3.58 (3.52 to 3.64)		3.84 (3.79 to 3.89)	
Quartile 3: 1.04	3.61 (3.55 to 3.67)		3.79 (3.74 to 3.85)	
Visits Ratio	1.0		1.0	
<b>Greenspace (%)</b>	AA	0.007	EA	0.551
Quartile 1: 0.40	3.69 (3.63 to 3.75)		3.94 (3.89 to 4)	
Quartile 3: 0.47	3.58 (3.52 to 3.65)		3.96 (3.9 to 4.01)	
Visits Ratio	1.0		1.0	
<b>PM<sub>2.5</sub> (µm)</b>	AA	<0.001	EA	<0.001
Quartile 1: 8.45	3.19 (3.13 to 3.25)		3.3 (3.24 to 3.35)	
Quartile 3: 12.08	3.41 (3.35 to 3.47)		3.81 (3.76 to 3.87)	
Visits Ratio	1.1		1.2	
<b>Pollen exposure (gr/m<sup>3</sup>)</b>	AA	<0.001	EA	<0.001
Quartile 1: 6.5	2.21 (2.15 to 2.27)		2.27 (2.22 to 2.33)	
Quartile 3: 118.65	3.93 (3.87 to 3.99)		4.23 (4.17 to 4.28)	
Visits Ratio	1.8		1.9	
<b>Outdoor mold exposure(Spores/m<sup>3</sup>)</b>	AA	<0.001	EA	<0.001



Factors	Expected visits (95% CI)	P-value*	Expected visits (95% CI)	P-value*
Quartile 1: 312.49	1.92 (1.86 to 1.98)		2.06 (2 to 2.12)	
Quartile 3: 1675.65	2.35 (2.29 to 2.41)		2.39 (2.34 to 2.44)	
Visits Ratio (VR)	1.2		1.2	
<b>Age at visit (years)</b>	Female	<0.001	Male	0.001
Quartile 1: 4.4	3.57 (3.51 to 3.63)		3.65 (3.6 to 3.71)	
Quartile 3: 12.2	3.81 (3.75 to 3.87)		3.84 (3.78 to 3.9)	
Visits Ratio	1.1		1.1	

\*. P-value<0.05; CI: Confidence interval; Ref: Reference group

VR: Ratio of the rates between the two quartiles.

**Table 4.**

Validation performance for ED visits models in three subsets of the cohort (only AAs, only EAs, and both AAs and EAs together) were examined. MAE including 95% CI were obtained for training and testing data, using 1000 bootstrap iterations and 3:1 random splits.

Model	Dataset	MAE 95% CI
Full NB	Train	1.403 (1.364 to 1.434)
	Test	1.396 (1.353 to 1.447)
Full Mixed-effects NB	Train	0.8 (0.778 to 0.805)
	Test	0.869 (0.864 to 0.934)
AAs NB	Train	1.428 (1.372 to 1.469)
	Test	1.444 (1.357 to 1.494)
AAs Mixed-effects NB	Train	0.797 (0.783 to 0.82)
	Test	0.957 (0.862 to 0.962)
EAs NB	Train	1.386 (1.323 to 1.419)
	Test	1.399 (1.312 to 1.436)
EAs Mixed-effects NB	Train	0.79 (0.761 to 0.803)
	Test	0.862 (0.838 to 0.932)

NB: Negative binomial; AA: African American; EA: European American; MAE: Mean absolute error; CI: Confidence interval.