Outdoor aeroallergen impacts on asthma exacerbation among sensitized and nonsensitized Philadelphia children

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Background: Outdoor aeroallergens, such as pollens and molds, are known triggers of asthma exacerbation; however, few studies have examined children's aeroallergen response based on sensitization.

Objective: Our aim was to compare the relative impact of aeroallergen levels on asthma exacerbation between pediatric patients with asthma who tested positive or negative for sensitization to particular allergens.

Methods: A case-crossover design study was conducted to examine associations between outdoor aeroallergen levels and asthma exacerbation events among children living in Philadelphia, Pennsylvania, who were treated within a large pediatric care network. Sensitization to common allergens was characterized in a subset of patients with asthma exacerbation who had undergone skin prick testing (5.5%). Odds ratios (ORs) and 95% CIs were estimated in all patients with asthma exacerbation and in those sensitized or not sensitized to aeroallergens.

Results: Children who were sensitized to a particular allergen had higher odds of asthma exacerbation with exposure to the allergen (ie, early-season tree pollen, oak tree pollen, early-season weed pollen, and late-season molds) than did all patients with asthma or nonsensitized patients. For example, the association between early-season tree pollen and asthma exacerbation among sensitized children (>90th percentile vs ≤25th, OR = 2.28 [95% CI = 1.23-4.22]) was considerably stronger than that estimated among all patients (OR = 1.34 [95% CI = 1.19-1.50]), and it was also substantially different from the lack of association seen among nonsensitized children (OR = 0.89 [95% CI = 0.51-1.55] [*P* value for heterogeneity = .03]).

Conclusion: More prevalent allergy testing may be useful for prevention of asthma exacerbation by informing interventions targeted to sensitized children and tailored for particular aeroallergens. (J Allergy Clin Immunol Global 2024;3:100248.)

Key words: *Pediatric asthma, allergy, aeroallergen, pollen, mold, seasonal*

Outdoor aeroallergens such as pollens and molds are known triggers of asthma exacerbation. In allergic asthma, allergen exposure in sensitized individuals causes increased specific IgE antibody production and eosinophilic airway inflammation.[1] The impact of aeroallergens on asthma morbidity can be particularly pronounced among children, given that more than half of pediatric patients with asthma are thought to have an allergic component.[2,3] Multiple studies have demonstrated exposure-response gradients between community pollen and mold levels and the number of children presenting to clinical care for asthma exacerbation[4-7]; however, there has been little research assessing risks among sensitized patients. Given that allergy is a strong determinant of asthma severity and clinical response overall,[8,9] it is important to gain a better understanding of response to aeroallergens among sensitized children specifically.

The objective of this study was to estimate the association between outdoor levels of pollens and molds and risk of asthma exacerbation among patients with and without allergen sensitization. To this end, a case-crossover design study was used to study children living in Philadelphia, Pennsylvania, who were treated for asthma exacerbation within a large pediatric care network, as well as among sensitization subgroups identified from results of skin prick testing for common allergens. The study hypothesis was that sensitized patients with asthma are more likely than nonsensitized patients to experience an asthma exacerbation following high–aeroallergen level days.

METHODS

Study design and population

A case-crossover design study was used to examine outdoor aeroallergen levels in relation to the odds of asthma exacerbation. The study population included children (aged <18 years) who were diagnosed with asthma within the Children's Hospital of Philadelphia (CHOP) from 2011 through 2016 and had a Philadelphia address at the time of the patient visit. A patient with asthma exacerbation was defined as a patient assigned a diagnosis code for asthma and a prescription of systemic steroid at the same visit.[10] Case events occurring fewer than 7 days apart in the same child were restricted to the first exacerbation. For each case event,

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Abbreviations used
CHOP: Children's Hospital of Philadelphia
OR: odds ratio

control dates were selected by using a time-stratified design, with time strata defined on the basis of calendar month and year. Control dates were matched with case events on the basis of day of the week within the same month.[11]

Patient data were extracted from electronic health records; these data included the child's sex and race/Hispanic ethnicity, as well as variables specific to each exacerbation event, including the following: child's age and payment source (Medicaid/State Children's Health Insurance Program [SCHIP] vs other); the treatment setting (primary care clinic, allergy specialty, other outpatient, emergency department, hospitalization); prescriptions for asthma medications in the past year (grouped as reliever medications, inhaled steroids, systemic steroids, and other asthma medications [such as biologics]); and the comorbidities allergic rhinitis, eczema, or food allergy listed as a previous or current diagnosis.

Allergy testing

Records for allergy skin prick tests performed within CHOP were linked to the study population of patients with asthma; these records were available for skin prick tests conducted from April 2012 through May 2018. Testing was conducted for any of 34 common plant or fungus allergens (see the Supplemental Material in the Online Repository at www.jaci-global.org), including specific allergens (eg, *Quercus* species [oak]) and mixtures (eg, tree mix). Positive test results were defined as a wheal 3 mm or larger or flare 5 mm or larger, and children were classified as sensitized during the asthma exacerbation study period (2011-2016) if they tested positive on any date during the recorded period (2012-2018). Likewise, children were classified as nonsensitized to a particular allergen if they were tested and the test yielded a negative result. Children's sensitization status was classified for the following outdoor aeroallergens: any mold/fungus (as a broad group); pollen from trees (broad group); pollen from grasses (broad group); pollen from weeds (broad group); and specific allergens (genus in italics, common name in parentheses), namely, *Acer* (maple), *Betula* (birch), *Quercus* (oak), and *Ambrosia* (ragweed). Common names have been used in the remainder of this article. These particular aeroallergens were selected for the study on the basis of number of children tested, to allow adequate estimation of aeroallergen response by sensitization status. Additionally, children's sensitization to common house dust was characterized on the basis of the results of skin prick tests to *Dermatophagoides pteronyssinus* and *Dermatophagoides farinae* to classify subgroups with polysensitization to dust and outdoor aeroallergens.

Pollen and mold data

Outdoor aeroallergen measurements were taken by The Asthma Center in Philadelphia on most weekdays during the pollen season (roughly from mid-March through October) of each year of the study period in accordance with the standards outlined by the American Academy of Allergy, Asthma & Immunology. Airborne pollen grains and mold spores were collected using a Burkard volumetric spore trap (Burkard Manufacturing Co Ltd, Rickmansworth, United Kingdom) located on the rooftop of a 6-story office building in downtown Philadelphia.[12] Each morning after a 24-hour sampling period, the sampling plate was collected from the trap and a trained counter conducted microscopic analysis, counting pollen grains and mold spores manually. The resulting counts were converted into air concentrations expressed as pollen grains or mold spores per cubic meter of air. Missing values for days without measurement (30.5% of all days in the study period, including most weekend days) were imputed by linear interpolation from the values on adjacent days.[4]

For each aeroallergen, its "season" was defined (Table I) as follows: (1) the daily aeroallergen concentration was summed across the days of each calendar year, and the dates of the 5th and 95th percentiles of the cumulative sum were identified for the year and (2) the aeroallergen's season was then defined across all years of the study (2011-2016) as the months encompassing all 5th and 95th percentiles of the aeroallergen distributions in all years. Additionally, "early" and "late" seasons were defined for the broad groups of molds and pollen from the total trees, grasses, and weeds—split at the midpoint month of each aeroallergen group's season—to analyze these aeroallergens during discrete time periods so as to avoid interseasonal confounding by factors such as children's return to school in the fall and seasonal respiratory viruses, as well as because the specific aeroallergens within these broad groups differ somewhat depending on the time of year.[4,13-15] An aeroallergen was included in the study if it was detected on at least 25% of all days during its defined season and also had a corresponding skin prick allergy test.

TABLE I. Aeroallergens and categorized levels (grains or spores/m^3) within defined seasons

Aeroallergen	Season	Lowest category (percentile)*	Highest category (>90th percentile)
Trees, early	March-June	≤39.7 (25th)	>850.1
Trees, late	July-October	≤2.13 (75th)	>3.6
Maple trees	March-May	≤12.7 (75th)	>30.6
Birch trees	March-June	≤4.1 (50th)	>46.6
Oak trees	April-June	≤1.5 (25th)	>442.1
Grasses, early	April-July	≤2.2 (25th)	>31.8
Grasses, late	August-October	≤2.2 (50th)	>6.6
Weeds, early	April-July	≤2.2 (25th)	>17.3
Weeds, late	August-October	≤10.8 (25th)	>64.2
Ragweed	July-October	≤3.5 (25th)	>31.7
Molds, early	March-July	≤1358.5 (25th)	>5371.1
Molds, late	August-October	≤2943.7 (25th)	>5777.8

*Percentile cutoff for lowest category varies based on the proportion of days with no detection of the aeroallergen.

Environmental covariates

Meteorologic data from the National Centers for Environmental Information Climate Data Online[16] included daily values for average dry bulb temperature (degrees Fahrenheit) and average relative humidity (%). These data were assigned to each case patient from the monitor closest to his or her address.

Statistical analysis

The analysis was limited to the dates with available aeroallergen measurement data across all years of the study, as March 18 through October 30 of each year from 2011 through 2016.

The characteristics of asthma exacerbation case events occurring during the study period were summarized, including the distribution of case patients by calendar month, children's demographics, and aspects of clinical care. The frequencies of these characteristics were compared between children with a positive result of testing to any of the outdoor aeroallergens (sensitized children) and those with only negative test results (nonsensitized children), using the chi-square statistic and its associated *P* value.

The relative odds of asthma exacerbation associated with daily aeroallergen levels were estimated using conditional logistic regression, according to which the aeroallergen levels on the case days (asthma exacerbation event days) were compared with aeroallergen levels on the matched control days. Each aeroallergen was categorized on the basis of percentiles of its distribution, typically as no more than the 25th percentile, in the range from higher than the 25th percentile to the 50th percentile, higher than the 50th percentile to the 75th percentile, higher than the 75th percentile to the 90th percentile, and higher than the 90th percentile. For some aeroallergens, however, because of a large of proportion days with nondetects, the lowest category was set as no more than the 50th percentile or no more than the 75th percentile (Table I). The odds ratio (OR) and 95% CI were estimated for each aeroallergen level category relative to the lowest category among 3 groups of patients: (1) all patients (those who experienced an asthma exacerbation regardless of whether they received a skin test); (2) sensitized patients (those with a positive test result for a particular aeroallergen); and (3) nonsensitized patients (those with negative test result(s) for only a particular aeroallergen). The specific aeroallergen/sensitization pairings evaluated were for the broad groups of molds/fungus, trees, grasses, and weeds, as well as more specifically for maple trees, birch trees, oak trees, and ragweed. Furthermore, associations between the broad aeroallergen groups and asthma exacerbation were estimated among children with and without polysensitization to house dust. The difference between the magnitude of the effect estimates in sensitized and nonsensitized children (ie, heterogeneity or interaction) was evaluated by using a *z* score–based test statistic calculated from the log of the ORs and the SEs.[17,18]

Each aeroallergen was analyzed for all days of its defined season, over all the years of the study period. Associations with aeroallergens were estimated for exposure lagged over 2 days (ie, average of the aeroallergen levels on the date of the exacerbation and on the 2 days prior); this lag period was selected *a priori* on the basis of previous research in the same study population in which the best-fitted models for various pollen types were most frequently estimated for cumulative pollen levels 2 days before the exacerbation event.[4] Potential confounders, selected *a priori*, were adjusted in every model; they included an indicator for holiday, average dry bulb temperature (lagged 5 days, natural cubic spline with 4 degrees of freedom), and average relative humidity (unlagged, natural cubic spline with 4 degrees of freedom). In addition, tree pollen variables were adjusted for molds, and grass pollen, weed pollen, and molds were adjusted for total tree pollen.

RESULTS

A total of 28,540 asthma exacerbation events occurred among 13,891 children during the study period. A small proportion of these children had a skin prick test result recorded in CHOP (5.5%); the tested children were similar to the nontested children with regard to sex, race, and health insurance (see Table E1 in the Online Repository at www.jaci-global.org). A majority of the tested children (73.2%) were tested for at least 1 outdoor aeroallergen (pollen or mold), and more than half of these children (60.0%) had a positive test result indicating sensitization to at least 1 outdoor aeroallergen.

Table II summarizes the characteristics of asthma exacerbation case events that occurred during the study period (note that in Table II, the frequencies are for case events, not children, and a single child could have experienced multiple case events during the study). A comparison of asthma exacerbation events between children who tested positive for at least 1 outdoor aeroallergen (n = 1263) with those who tested negative (n=769) revealed that the sensitized case events were more likely to occur among males, children who were Black non-Hispanic or of another/unknown race, older children (aged ≥5 years), and those with private insurance/a nonpublic payer, as well as among patients with asthma who also had allergic rhinitis or eczema. The sensitized and nonsensitized patients did not differ in terms of the month of occurrence, exacerbation treatment setting, or prescribed asthma medications, except for a higher frequency of "other" asthma medication prescriptions among sensitized patients.

Fig 1 shows the adjusted ORs for the association of each aeroallergen with the odds of asthma exacerbation among all patients, as well as for patients who were sensitized or not sensitized to the particular outdoor aeroallergen (Fig 1 shows adjusted ORs for the highest vs lowest category of each aeroallergen; risk estimates for all aeroallergen levels are provided in Table E2 [see the Online Repository at www.jaci-global.org]). Not every aeroallergen was associated with higher odds of asthma exacerbation. However, when associations were found, the relative odds of asthma exacerbation in association with exposure were generally higher among sensitized patients than among all patients or among nonsensitized patients despite wide CIs given the small number of children who received skin testing for any particular allergen.

Tree pollen was significantly associated with higher odds of asthma exacerbation among all patients and among sensitized children (Fig 1), with larger ORs found during the early season (March-June), when tree pollen levels were highest (Table I [90th percentile = 850 $\mu g/m^3$ and 3.6 $\mu g/m^3$ during the early and late seasons, respectively]). The OR for the association between early-season tree pollen and asthma exacerbation among sensitized children (>90 percentile vs ≤25th percentile, OR = 2.28 [95% CI = 1.23-4.22]) was considerably stronger than that estimated among all patients (OR = 1.34 [95% CI = 1.19-1.50]), and it was also substantially different from the lack of association in nonsensitized children (OR = 0.89 [95% CI = 0.51-1.55] [*P* value for heterogeneity = .03]). Furthermore, a positive exposure-response gradient was observed by increasing levels of early-season tree pollen among sensitized children, in contrast to no association at any exposure level among nonsensitized children (Fig 2, *A*). Elevated odds of asthma exacerbation were also estimated in association with exposure to the specific tree pollen types (maple, birch, and oak), and the ORs were

TABLE II. Asthma exacerbation case event characteristics, by sensitization to outdoor aeroallergen (N [%])

Case characteristic*	All cases (N = 28,540)	Nonsensitized cases (n = 769)	Sensitized cases (n = 1263)	*P* value†
Month				.61
March (March 18-30)	2,241 (7.8)	64 (8.3)	107 (8.5)	
April	4,731 (16.6)	131 (17.0)	199 (15.8)	
May	4,659 (16.3)	108 (14.0)	217 (17.2)	
June	2,884 (10.1)	80 (10.4)	112 (8.9)	
July	2,169 (7.6)	69 (9.0)	110 (8.7)	
August	2,584 (9.1)	69 (9.0)	108 (8.6)	
September	4,343 (15.2)	120 (15.6)	185 (14.7)	
October (October 1-30)	4,929 (17.3)	128 (16.6)	225 (17.8)	
Sex				<.0001
Female	11,222 (39.3)	335 (43.6)	418 (33.1)	
Male	17,318 (60.7)	434 (56.4)	845 (66.9)	
Race/ethnicity				<.0001
Hispanic/Latinx	1,646 (5.8)	50 (6.5)	61 (4.8)	
Black, non-Hispanic	23,231 (81.4)	628 (81.7)	1102 (87.3)	
White, non-Hispanic	2,162 (7.6)	73 (9.5)	58 (4.6)	
Other or unknown	1,501 (5.2)	18 (2.3)	42 (3.3)	
Age				<.0001
<2 y	3,571 (12.5)	105 (13.6)	88 (7.0)	
2 to <5 y	9,065 (31.8)	358 (46.6)	480 (38.0)	
5 to <12 y	11,744 (41.1)	299 (38.9)	666 (52.7)	
12-18 y	4160 (14.6)	7 (0.9)	29 (2.3)	
Public payer (Medicaid/SCHIP)	20,474 (71.7)	584 (75.9)	892 (70.6)	.009
Case treatment setting				.23
Outpatient visit	9,610 (33.7)	334 (43.4)	540 (42.7)	
Emergency department visit	10,476 (36.7)	243 (31.6)	367 (29.1)	
Hospitalization	8,454 (29.6)	192 (25.0)	356 (28.2)	
Primary care network site	8,215 (28.8)	300 (39.0)	466 (36.9)	.34
Allergy/immunology care site specialty	1,231 (4.3)	61 (7.9)	112 (8.9)	.46
Asthma medication prescribed in past year				
Reliever medication	23,045 (80.8)	710 (92.3)	1176 (93.1)	.51
Inhaled steroid	4,417 (15.5)	210 (27.3)	380 (30.1)	.18
Systemic steroid	20,627 (72.3)	671 (87.3)	1113 (88.1)	.56
Other	8,043 (28.2)	359 (46.7)	660 (52.3)	.01
Comorbidity				
Allergic rhinitis	8,266 (29.0)	277 (36.0)	567 (44.9)	<.0001
Eczema	9,418 (33.0)	360 (46.8)	914 (72.4)	<.0001
Food allergy	584 (2.0)	27 (3.5)	58 (4.6)	.24

SCHIP, State Children's Health Insurance Program.
"Cases" are asthma exacerbation events, which frequently occurred multiple times in a single child/patient during the study period; therefore, the numbers in this table are larger than the number of children in the study population.
*Characteristics of the case event on the day of the exacerbation (time-varying for month, age, insurance, medications, and comorbidities).
†*P* value for the chi-square test for difference in the characteristic (percentages) between asthma exacerbation case events occurring in nonsensitized versus sensitized patients.

highest among children who were sensitized to the specific tree allergens, although the CIs in these analyses were very wide (Fig 1).

Grass pollen was not associated with elevated odds of asthma exacerbation in any analysis, even among children who tested positive for sensitization to grasses.

Early-season weed pollen (April-July) was associated with higher odds of asthma exacerbation (Fig 1), with a weak association among all patients (>90th percentile vs ≤25th percentile, OR = 1.10 [95% CI = 1.00-1.21]) and a strong association among sensitized children (>90th percentile vs ≤25th percentile, OR = 2.64 [95% CI = 1.31-5.29]), but no association among nonsensitized children (*P* value for heterogeneity = .01). An exposure-response gradient was not clear, even among sensitized children, as elevated odds were predominantly seen at only the highest level of exposure (Fig 2, *B*). Ragweed pollen was inversely associated with odds of asthma exacerbation in the study population, even among sensitized children (OR = 0.71 [95% CI = 0.32-1.58]). Late-season weed pollen (August-October) was dominated by ragweed, and as such, it was not associated with elevated odds of asthma exacerbation in any analysis, despite generally higher overall levels of weed pollen during the late season than in the early season (Table I [90th percentile = 64.2 $\mu g/m^3$ and 17.3 $\mu g/m^3$ during late and early seasons, respectively]).

Late-season mold exposure (August-October) was strongly associated with higher odds of asthma exacerbation among children sensitized to molds (>90th percentile vs ≤25th percentile, OR = 2.71 [95% CI = 1.21-6.11]), whereas there was no association among all patients together (OR = 1.05 [95% CI = 0.94-1.18]) or nonsensitized patients (Fig 1). Although the CI was very wide for the sensitized subgroup, the risk estimate differed substantially from that in the nonsensitized subgroup (*P* value for heterogeneity = .01). This relationship with late-season mold exposure among sensitized patients also followed a clear exposure-response gradient by increasing mold level (Fig 2, *C*). There was no association between the highest levels of

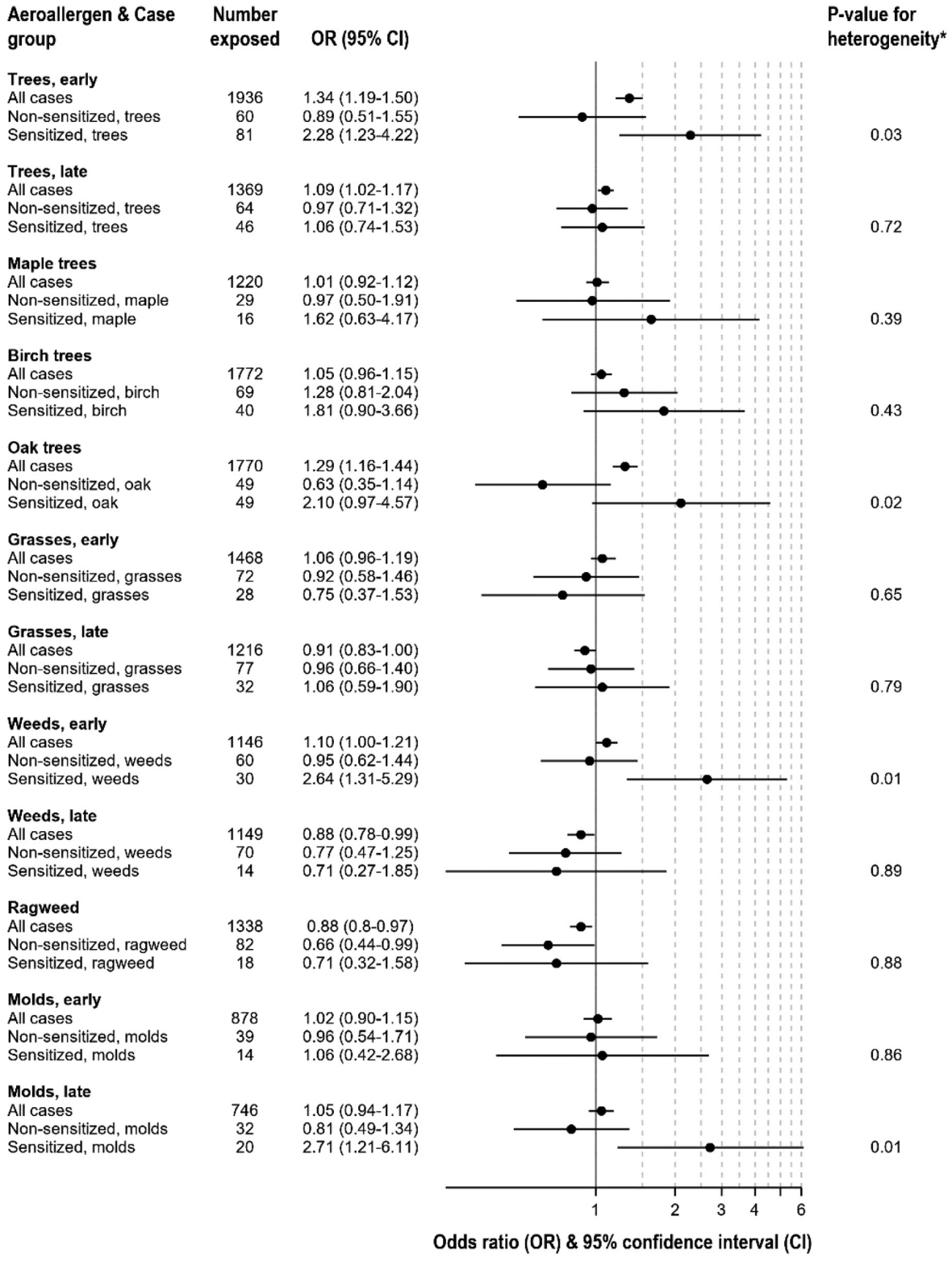

FIG 1. Aeroallergen associations with asthma exacerbation among all patients with asthma, nonsensitized patients, and sensitized patients. ORs and 95% CIs for aeroallergen concentrations higher than the 90th percentile versus for the lowest-level category.

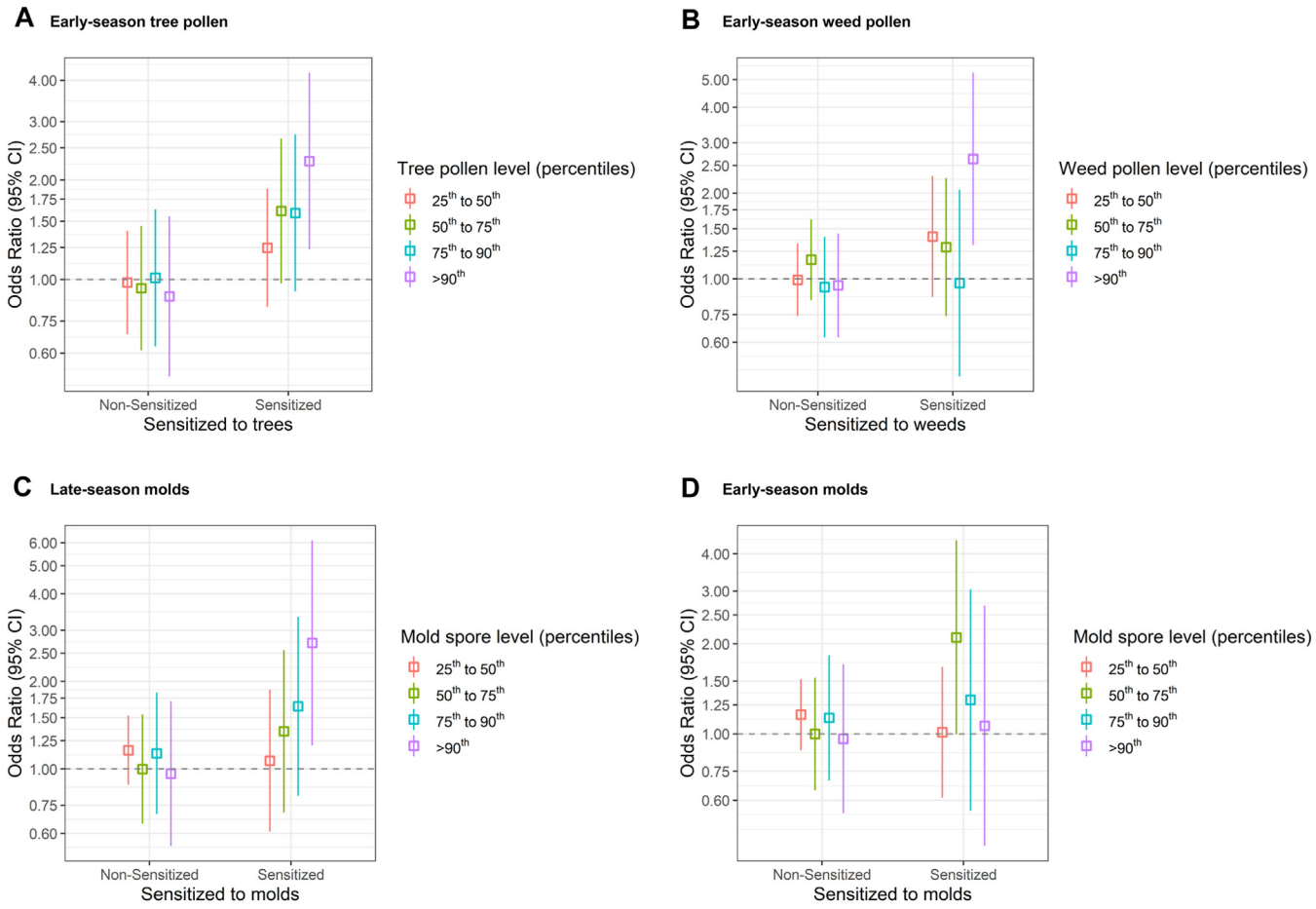

FIG 2. A-D, Aeroallergen associations with asthma exacerbation among sensitized and nonsensitized patients. ORs and 95% CIs for aeroallergen concentration categories split by percentiles (vs ≤ 25th percentile). **A,** Early-season tree pollen. **B,** Early-season weed pollen. **C,** Late-season molds. **D,** Early-season molds.

early-season mold exposure (March-July) and asthma exacerbation, even among sensitized children (Fig 1); however, a nonmonotonic exposure-response relationship was observed, with elevated odds estimated in association with early-season mold levels between the 50th and 75th percentiles (OR = 2.10 [95% CI = 1.00-4.43]) (Fig 2, *D*).

Associations between outdoor aeroallergens and asthma exacerbation among sensitized children were, for some allergens, somewhat stronger when the child was also sensitized to house dust (ie, polysensitization [see Table E3 in the Online Repository at www.jaci-global.org]), such as for early-season tree pollen (>90th percentile vs ≤25th percentile: polysensitized, OR = 3.40 [95% CI = 1.33 -8.71]; nonpolysensitized, OR = 1.98 [95% CI = 0.83-4.74] [*P* value for heterogeneity = .42). However, the small numbers within these subgroups hindered precise estimation and assessment of heterogeneity.

DISCUSSION

From our study of the impacts of outdoor aeroallergen on asthma exacerbation in Philadelphia children, we found that children who were sensitized to a particular allergen had higher odds of asthma exacerbation following exposure to that allergen than did all patients with asthma or nonsensitized patients, which is consistent with our hypothesis and coherent with knowledge about allergy. Furthermore, there were essentially no positive associations with aeroallergen exposures among the nonsensitized children in our study. Allergy testing was far from the norm in our study population, resulting in small subgroups for the comparisons of interest and limiting the potential for translation of our findings to management of patients with asthma in this population.

Ours is one of only a few studies to estimate the differential degree of reaction to aeroallergens based on allergen sensitization within a general population of patients. We found that the association between outdoor molds and asthma exacerbation was significantly stronger among children with molds/fungus sensitization than among nonsensitized patients. These findings are consistent with prior work that utilized a similar methodology to demonstrate that children with positive results of skin prick tests to outdoor fungal spores were more likely to be hospitalized for an asthma exacerbation following exposure to the fungal spores than were children without known mold sensitization.[19] Similarly, the rate of asthma exacerbation among 676 adults in a desert climate was higher among mold-sensitized patients than among nonsensitized patients during the fall season (Sept-Nov), which is when measured outdoor levels of *Alternaria* and *Cladosporium* mold species were at their highest.[20] In our study,

we also found differential asthma exacerbation by sensitization status in association with tree and weed pollens. Likewise, a study of adults in Italy (N = 1070) found that airway inflammation was related in an exposure-dependent, interactive manner to both sensitization and the number of tree, grass, and weed pollen species present in the ambient environment.[21]

Even among sensitized children, several aeroallergens that we studied, including grasses and ragweed, were not associated with asthma exacerbation. These pollens were detected at low counts in Philadelphia, and it is possible that the levels were too low to trigger a measurable response within the population. In our previous study in the same population,[4] grasses were associated with higher odds of asthma exacerbation only at pollen levels higher than 52 grains/m^3, which is an extreme that was too infrequent for examination within the small subgroup of sensitized children examined in this study. It is also possible that exposure misclassification obscured some of the aeroallergen relationships with asthma exacerbation. The aeroallergens for our study were sampled from 1 location in downtown Philadelphia, and previous studies have indicated high spatial variability of ragweed pollen that is strongly influenced by nearby vegetation and land use.[22,23]

As our results indicate, outdoor aeroallergens are a trigger of asthma exacerbation in sensitized children. The health burden from aeroallergens is expected to worsen with changing climate patterns—with lengthened pollen seasons and increased overall pollen levels in response to hotter temperatures.[24,25] It is thus increasingly important that clinicians be armed with data to inform strategies for management of aeroallergen-related risks in their patients.[26] Avoidance of the outdoors on high-pollen days is a typical clinical recommendation for control of asthma symptoms,[27] but our results suggest that patients may benefit from more specific recommendations based on their individual sensitization status with respect to particular allergens—interventions such as proactive taking of antihistamines during certain months, tailored immunotherapy, or sensitization-profile specific messaging. Such interventions may be promising, but they require assessment of their efficacy in preventing asthma exacerbation in sensitized patients.

A major strength of our study is the time-stratified case-crossover design, which compares environmental conditions on the day of a child's asthma exacerbation with environmental conditions on matched days within the same month. The within-child matched design avoids issues of confounding owing to differences between children in terms of characteristics that do not change in the short term (from day to day), such as socioeconomic status or underlying airway sensitivity. Our study did not adjust for other air pollutants such as ozone or particulate matter, although we previously reported that these pollutants did not confound associations between aeroallergens and asthma exacerbation in our study population.[4] We did not have information on children's diagnoses of respiratory viruses, which constitute a major cause of asthma exacerbation among both patients with allergy and patients without allergy and a possible confounder—especially during late summer when children return to school. Likewise, we did not have information on exposures to indoor allergens (eg, indoor molds) which, like outdoor aeroallergens, may vary seasonally within short time periods and possibly confound the associations of interest.

Our use of electronic health record data specific to each child at the time of each asthma exacerbation enabled linkage of allergy test results to clinical outcomes for individual patients. However, inference from our study is limited by the small number of children with skin test results, which severely limited statistical power. It is also possible that the small group of tested children differed from the majority of patients with asthma in terms of asthma management and health care–seeking behaviors, potentially skewing our study results. In addition, some children may have received allergy testing outside the CHOP system, precluding complete identification of tested patients. Nevertheless, the low frequency of allergy testing among patients with asthma in our study (5.5%) is within the range observed in previous studies of US children (2.8%)[28] and adults (7.2%),[29] providing assurance in our data. Another limitation of our study is that the time period of the recorded skin prick test results overlapped with, but was slightly later than, the asthma exacerbation study period. Therefore, we cannot know that children who tested positive were sensitized at the time when they experienced an asthma exacerbation. Such misclassification may have hindered detection of associations among sensitized subgroups of children.

Despite our study's limitations, our linked clinical data set, coupled with regional aeroallergen measurements, allowed a novel analysis comparing impacts of seasonal pollens and molds between sensitized and nonsensitized pediatric patients with asthma. Ultimately, we anticipate that this study may encourage more widespread allergy testing and a more nuanced approach to prevention of asthma exacerbation in children with asthma.

DISCLOSURE STATEMENT

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