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Permalink

<https://escholarship.org/uc/item/7t90s21j>

Journal

International archives of allergy and immunology, 187(2)

ISSN

1423-0097

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Publication Date

2026-05-28

Data Availability

The data associated with this publication are available upon request.

Peer reviewed

Inhalant Allergen Sensitization: Prevalence, Risk Factors, and Geographic Variation in the USA

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Keywords

Inhalant allergen · Seasonal allergen · Sensitization · USA · Risk factors · Geography

Abstract

Introduction: We aimed to assess the prevalence of IgE-mediated sensitization to two perennial (dust mite and animal) and four seasonal allergen sources (tree, grass, weed, and mold/fungi) using data from a national clinical reference laboratory (Quest Diagnostics). **Methods:** Patients tested in 2019 for ≥ 1 specific serum IgE toward 4 dust mites, 14 animals, 32 trees, 12 grasses, 21 weeds, or 19 mold/fungi allergens were included. Patients with ≥ 1 specific IgE ≥ 0.10 kU/L within a source were considered sensitized for the source. Chi-square tests and multivariate logistic regression were used to compare the estimated prevalence of allergic sensitization related to demographics, geography, and clinical diagnosis. **Results:** Sensitization for dust mite, animal, tree, grass, weed, and mold/fungi sources was 38.0% (21,161/55,735), 32.1% (21,888/68,035), 34.5% (22,975/66,567), 30.3% (21,664/71,575), 31.2% (22,960/73,605), and 19.7% (13,514/68,574), respectively. Across allergen sources, males had higher prevalence (from lowest to highest: 25.3% mold/fungi to 43.0% dust mite) compared to

females (from lowest to highest: 16.1% mold/fungi to 34.6% dust mite); prevalence peaked in 10–19 years (from lowest to highest: 29.7% mold/fungi to 54.2% dust mite) and then decreased with increasing age; large metropolitan areas (from lowest to highest: 39.6% dust mite to 20.7% mold/fungi) had higher prevalence compared to small-to-medium metro (from lowest to highest: 36.6% dust mite to 17.9% mold/fungi) or nonmetro areas (from lowest to highest: 32.4% dust mite to 19.5% mold/fungi); a higher prevalence was observed in patients with asthma, atopic dermatitis, or rhinitis than in those with none of these diagnoses reported. Sensitization to perennial and seasonal allergens showed regional variation. **Conclusions:** Prevalence of allergic sensitization to perennial and seasonal allergens is associated with patient age and sex, census regions, level of urbanization, and allergic disease states. These factors should be considered when designing and selecting allergen panels for diagnosing and treating symptomatic patients.

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Published by S. Karger AG, Basel

Edited by: O. Palomares, Madrid.

Introduction

Allergic disease prevalence, including asthma, allergic rhinitis, and atopic dermatitis remains high in the United States (US), causing a significant health burden among those afflicted [1, 2], including healthcare utilization, quality of life, and societal productivity [3]. Central to pathogenesis of these allergic diseases is allergic inflammation driven by specific IgE (sIgE) to inhalant allergens to which patients are sensitized [4]. Identifying sIgE antibodies against these allergens is pivotal to diagnose allergic diseases [5]. Accurate identification of culprit allergens is especially important to clinically manage allergic diseases, including therapy selection (e.g., allergen avoidance/mitigation, design of allergen immunotherapy, and choice of biologic agents) [6].

Several large-scale surveys on the prevalence of inhalant allergen sensitization in the US exist, including three National Health and Nutrition Examination Surveys (NHANES) where allergen-sIgE levels toward multiple environmental allergens were measured during various time periods from 1976 through 2006, but each has limitations. While these studies were geographically comprehensive, including a wide range of age-groups and a large random sample of the general US population, they surveyed a limited number of representative allergens [7, 8]. Only two species of fungi, trees, and weeds were included in the NHANES 2005–2006. Other large-scale studies that included more allergens had limited geographic coverage. For instance, an extensive survey of allergen sensitization to 36 species of trees, grasses, and weeds among children 2–8 years of age was limited to the Great Basin area of Nevada [9].

There is an unmet need to accurately characterize patterns of sensitization to a wide range of inhalant allergens in a geographically comprehensive fashion; such a study would help optimize diagnosis and treatment of allergic diseases. Using data from a large US national reference laboratory (Quest Diagnostics) with over 400,000 specimens tested in 2019, this study aimed to investigate the sensitization prevalence in allergen-sIgE tests to two perennial and four seasonal allergen sources, consisting of 102 inhalant allergens, across the US. Furthermore, the distinct patterns of allergic sensitization regarding age-group, gender, geography, and disease state were examined, thus identifying the potential risk factors for IgE-mediated sensitization to these six allergen sources. This knowledge can help guide patient evaluation and management through more informed allergen test selection.

Methods

In this cross-sectional, retrospective study, 107,877 patients were tested for at least one of 102 inhalant allergens for two perennial allergen sources (4 dust mites and 14 animals) and four seasonal allergen sources (32 trees, 12 grasses, 21 weeds, and 19 mold/fungi allergens) in 2019 using allergen-sIgE testing at Quest Diagnostics, a national reference laboratory serving patients in every US state (except Hawaii) and the District of Columbia. Quest Diagnostics annually serves one in three adult Americans and half the physicians and hospitals in the US, and it maintains one of the world's largest databases of identifiable clinical laboratory results [10]. All included allergens were ordered individually, as opposed to by regional respiratory allergy panels, for the patients across the US who received testing for any cause. The focus on individually ordered allergens aimed to mitigate the influence of arbitrary geographic regional variations introduced by panel testing, thereby ensuring a more clinically based, nationally representative dataset. Testing was performed using the ImmunoCAP™ (ThermoFisher Scientific, Waltham, MA, USA) sIgE blood test that uses a fluoroenzyme immunoassay (non-RAST) method. In this study, the threshold for a positive allergen-sIgE test, which was considered indicative of sensitization, was the level of detection (≥ 0.10 kU/L). This threshold was chosen instead of 0.35 kU/L for a positive test result based on recent recommendations suggesting that sIgE concentrations between 0.10 kU/L and 0.35 kU/L may be clinically relevant in some patients [11]. Within an allergen source, patients with at least one positive allergen sIgE were considered sensitized or atopic for the source.

Patient characteristics including age, sex, and state of residence for determining census regions and divisions were extracted and included in analysis; they were recorded in a manner to avoid identification or linkage to individual patients.

Disease states were categorized based on *International Classification of Diseases, Tenth Revision, Clinical Modification (ICD-10-CM)* diagnosis codes. In this study, specific ICD-10 codes were grouped into larger categories: asthma, atopic dermatitis, and rhinitis. Within a disease state, patients with no ICD-10 code or other ICD-10 codes were classified as “not indicated.” ICD-10 codes for sinusitis were excluded because sinusitis has multiple causes with similar symptoms in many other conditions beyond allergy.

Levels of urbanization categorized to describe the characteristics of sensitized patients were based on ERS' 2023 Rural-Urban Continuum Codes [12], a classification

scheme that distinguishes big metropolitan (metro) counties with a population of ≥ 1 million, small-to-medium metropolitan counties with a population < 1 million, and nonmetropolitan (nonmetro/rural) counties with a population of any size, adjacent or not adjacent to a metro area. Chi-square tests and multivariate logistic regression (modeling sensitized vs. not sensitized) were employed to compare the estimated prevalence of allergic sensitization related to demographics, census regions, level of urbanization, and clinical diagnosis. In logistic modeling, adjusted odds ratios with 95% confidence intervals were estimated and compared with reference to different levels of patient age and sex, census regions, level of urbanization, and disease state.

The need for informed consent was waived because this study was deemed exempt by the WCG Institutional Review Board, an independent ethical review board, based on federal regulation 45 CFR Parts 46 and 164. The study followed the Strengthening the Reporting of Observational Studies in Epidemiology (STROBE) reporting guideline for cross-sectional studies [13]. Data analyses were performed using SAS Studio 3.6 on SAS version 9.4 (Cary, NC, USA).

Results

This study analyzed 404,091 test results from 107,877 patients aged 37.1 ± 24.1 (mean $\pm$ SD) years, including 39.0% males and 61.0% females for whom perennial or seasonal allergen-sIgE testing was ordered. The demographics, census regional distribution, levels of urbanization, and disease diagnoses were reported for two perennial and four seasonal allergens sources (Table 1). Of patients tested, the mean ($\pm$ SD) ages in years ranged from 38.1 ± 24.3 for molds/fungi to 35.1 ± 24.3 for animals. Across all allergen sources, females comprised 60–61% of the study population; patients were mostly from the South (32.1% weed to 39.0% dust mite), followed by the Northeast (24.0% dust mite to 31.9% weed), the West (16.6% dust mite to 18.7% mold/fungi), and then the Midwest (6.8% dust mite/tree/weed to 7.4% mold/fungi); more patients lived in the big metro counties (57.9% dust mite to 61.3% weed), followed by small-to-medium metro counties (21.8% weed/mold/fungi to 23.4% tree) and then by nonmetro (rural) counties (5.8% animal to 6.3% grass). Across all allergen sources, about 8–9% of patients had a diagnosis of asthma (8.1% tree to 9.5% grass), 2–3% a diagnosis of atopic dermatitis (2.3% weed/mold/fungi to 3.0% dust mite/animal), and 43–47% a diagnosis of rhinitis (43.6% mold/fungi to 46.6% tree).

For two perennial sources, prevalence of allergen sensitization was 38.0% for dust mites and 32.2% for animals; for the four seasonal sources, prevalence of allergen sensitization was 34.5% for trees, 30.3% for grasses, 31.2% for weeds, and 19.7% for molds/fungi (Table 2). Within each source of allergens, there was a wide range of sensitization to individual antigens (online suppl. Fig. E1–E6; for all online suppl. material, see <https://doi.org/10.1159/000545508>). In two perennial sources, the lowest was to duck feathers (1.5%) and highest to *Dermatophagoides pteronyssinus* (36.6%); in four seasonal sources, the lowest was to *Chaetomium globosum* (3.5%) and highest to Western ragweed (43.3%) (Table 2).

Across allergen sources, prevalence of allergic sensitization to all inhalant allergens peaked in 10–19 years (29.7% mold/fungi to 54.2% dust mite), then declined into senescence, for males and females combined; males had higher prevalence (25.3% mold/fungi to 43.0% dust mite) compared to females (16.1% mold/fungi to 34.6% dust mite), for all age-groups combined (data not shown). Sensitization rates to all allergens sources, perennial and seasonal, appeared to plateau in the elderly and increase slightly among elderly males (70–79 to ≥ 80 years: 20.2%–23.2%) as did sensitization toward house dust mites (70–79 to ≥ 80 years: 29.3%–29.2%). The percentage of males sensitized to all sources of inhalant allergens was significantly higher across all age-groups compared to females (all $p < 0.01$); the largest difference in prevalence between males and females was in 20–29 years for weeds (16.2%) and grasses (15.7%) (Fig. 1).

Allergic sensitization toward inhalant allergens varied significantly by the US census region. Grass (40.3%), tree (39.4%), and weed (37.1%) allergens were most prevalent in the West, dust mite allergens were more prevalent in the Northeast (40.4%) and South (39.0%), and animal (35.2%) and mold/fungi (23.2%) allergens were most prevalent in the Midwest (all $p < 0.01$) (Fig. 2). Patients residing in large metropolitan areas had higher sensitization rates to all inhalant allergens (20.7% mold/fungi to 39.6% dust mite) compared to those living in small-to-medium metro (17.9% mold/fungi to 36.5% dust mite) and nonmetro regions (19.5% mold/fungi to 32.4% dust mite) (all $p < 0.01$) (Fig. 3).

Patients with a reported ICD-10 diagnosis of any atopic-related disease (asthma, atopic dermatitis, or rhinitis) had higher prevalence of sensitization to all inhalant allergens compared to those with no such diagnosis indicated. Across all allergen sources, prevalence of sensitization was higher for patients with asthma

Table 1. Characteristics of study populations

Characteristics	Dust mite (n = 55,735)	Animal (n = 68,035)	Tree (n = 66,567)	Grass (n = 71,575)	Weed (n = 73,605)	Mold/fungi (n = 68,574)
Age, years						
Mean±SD	35.6±24.6	35.1±24.3	36.3±24.1	37.3±24.0	37.4±23.8	38.1±24.3
Median	35.0	34.0	36.0	38.0	38.0	39.0
IQR (25th Pctl–75th Pctl)	46.0 (11.0, 57.0)	45.0 (11.0, 56.0)	44.0 (13.0, 57.0)	44.0 (14.0, 58.0)	44.0 (14.0, 58.0)	45.0 (14.0, 59.0)
Age-group, n (%)						
0–5 years	7,180 (12.9)	8,702 (12.8)	7,184 (10.8)	7,233 (10.1)	7,091 (9.6)	6,988 (10.2)
6–9 years	4,897 (8.8)	6,065 (8.9)	5,811 (8.7)	5,846 (8.2)	5,905 (8.0)	5,349 (7.8)
10–19 years	7,760 (13.9)	9,768 (14.4)	9,518 (14.3)	9,510 (13.3)	9,804 (13.3)	8,832 (12.9)
20–29 years	4,670 (8.4)	6,033 (8.9)	5,859 (8.8)	6,617 (9.2)	7,015 (9.5)	5,774 (8.4)
30–39 years	5,940 (10.7)	7,343 (10.8)	7,390 (11.1)	8,167 (11.4)	8,532 (11.6)	7,655 (11.2)
40–49 years	6,386 (11.5)	7,834 (11.5)	8,021 (12.1)	8,820 (12.3)	9,158 (12.4)	8,372 (12.2)
50–59 years	6,716 (12.1)	8,105 (11.9)	8,208 (12.3)	9,148 (12.8)	9,512 (12.9)	8,945 (13.0)
60–69 years	6,791 (12.2)	7,947 (11.7)	8,145 (12.2)	8,986 (12.6)	9,258 (12.6)	9,101 (13.3)
70–79 years	4,162 (7.5)	4,826 (7.1)	4,981 (7.5)	5,549 (7.8)	5,617 (7.6)	5,779 (8.4)
≥80 years	1,233 (2.2)	1,412 (2.1)	1,450 (2.2)	1,699 (2.4)	1,713 (2.3)	1,779 (2.6)
Gender, n (%)						
Female	33,561 (60.2)	41,211 (60.6)	40,163 (60.3)	43,754 (61.1)	45,153 (61.4)	41,669 (60.8)
Male	22,174 (39.8)	26,824 (39.4)	26,404 (39.7)	27,821 (38.9)	28,452 (38.7)	26,905 (39.2)
Census region, n (%)						
Northeast	13,353 (24.0)	18,352 (27.0)	16,884 (25.4)	20,687 (28.9)	23,511 (31.9)	18,031 (26.3)
Midwest	3,812 (6.8)	4,963 (7.3)	4,520 (6.8)	4,964 (6.9)	5,004 (6.8)	5,059 (7.4)
South	21,742 (39.0)	24,533 (36.1)	24,596 (37.0)	25,905 (36.2)	23,628 (32.1)	23,812 (34.7)
West	9,435 (16.9)	12,203 (17.9)	12,376 (18.6)	12,238 (17.1)	13,430 (18.3)	12,809 (18.7)
No data	7,393 (13.3)	7,984 (11.7)	8,191 (12.3)	7,781 (10.9)	8,032 (10.9)	8,863 (12.9)
Metro level ^a , n (%)						
Big metro (population ≥1 million)	32,262 (57.9)	40,991 (60.3)	38,684 (58.1)	42,935 (60.0)	45,089 (61.3)	40,484 (59.0)
Small-to-medium metro (population <1 million)	12,709 (22.8)	15,078 (22.2)	15,586 (23.4)	16,308 (22.8)	16,036 (21.8)	14,964 (21.8)
Nonmetro	3,322 (6.0)	3,924 (5.8)	4,048 (6.1)	4,491 (6.3)	4,385 (6.0)	4,205 (6.1)
No data	7,442 (13.4)	8,042 (11.8)	8,249 (12.4)	7,841 (11.0)	8,095 (11.0)	8,921 (13.0)
Asthma diagnosis, n (%)						
Indicated	4,758 (8.5)	5,591 (8.2)	5,367 (8.1)	6,823 (9.5)	6,641 (9.0)	6,216 (9.1)
Not indicated	50,977 (91.5)	62,444 (91.8)	61,200 (91.9)	64,752 (90.5)	66,964 (91.0)	62,358 (90.9)
Atopic dermatitis diagnosis, n (%)						
Indicated	1,687 (3.0)	2,034 (3.0)	1,610 (2.4)	1,722 (2.4)	1,716 (2.3)	1,585 (2.3)
Not indicated	54,048 (97.0)	66,001 (97.0)	64,957 (97.6)	69,853 (97.6)	71,889 (97.7)	66,989 (97.7)
Rhinitis diagnosis, n (%)						
Indicated	25,322 (45.4)	30,619 (45.0)	31,015 (46.6)	31,357 (43.8)	32,827 (44.6)	29,883 (43.6)
Not indicated	30,413 (54.6)	37,416 (55.0)	35,552 (53.4)	40,218 (56.2)	40,778 (55.4)	38,691 (56.4)

^aClassification derives from the Rural-Urban Continuum Codes (RUCC) published by the USDA Economic Research Service (2013).

(28.0% mold/fungi to 44.8% dust mite) compared to those with no asthma indicated (18.9% mold/fungi to 37.3% dust mite); similarly a higher prevalence among patients with atopic dermatitis (31.4% mold/fungi to 52.7% animal) than those with no atopic dermatitis reported

(19.4% mold/fungi to 37.8% dust mite); a higher prevalence for patients with rhinitis (21.1% mold/fungi to 40.1% dust mite) than those with no reported rhinitis (18.6% mold/fungi to 36.2% dust mite) (all $p < 0.01$) (Fig. 4). In multivariate logistic regression (modeling

Table 2. Prevalence of sensitization by allergen source

Allergen source	Species, within source, <i>n</i>	Prevalence of sensitization for source ^a	Lowest to highest prevalence of sensitization for individual species, within source ^b
Dust mite	4	38.0 (21,161/55,735)	23.9 (344/1,437 for storage mite) to 36.6 (17,904/48,865 for <i>Dermatophagoides pteronyssinus</i>)
Animal	14	32.2 (21,888/68,035)	1.5 (69/4,722 for duck feathers) to 30.4 (16,787/55,185 for dog dander)
Tree	32	34.5 (22,975/66,567)	6.4 (418/6,542 for queen palm) to 42.1 (430/1,021 for hazelnut tree)
Grass	12	30.3 (21,664/71,575)	22.5 (4,034/17,939 for Bahia grass) to 32.4 (1,144/3,527 for red top grass)
Weed	21	31.2 (22,960/73,605)	16.2 (571/3,526 for yellow dock weed) to 43.3 (2,736/6,313 for Western ragweed)
Mold/fungi	19	19.7 (13,514/68,574)	3.5 (48/1,384 for <i>Chaetomium globosum</i>) to 16.9 (1,468/8,674 for <i>Candida albicans</i>)

^aNumerator: number of patients with at least one positive test (sIgE ≥ 0.1 kU/L) for any species within the source; denominator: number of patients with at least one test for any species within the source. ^bNumerator: number of patients with a positive test result (sIgE ≥ 0.1 kU/L) for an individual species; denominator: number of patients tested for an individual species.

sensitized vs. not sensitized), adjusted odds ratios (with 95% confidence intervals) showed the same patterns demonstrated in the univariate analysis (Fig. 5).

Discussion

Using data from a national laboratory (Quest Diagnostics), this study is among the largest cross-sectional studies to examine perennial and seasonal inhalant allergen sensitization in the US. Over 400,000 test results were used, including patients from all age ranges (Table 1; Fig. 1–5; online suppl. Fig. E1–E6). Inhalant allergen sensitization trends and risk factors found in this study are similar to those reported by other investigators, although there are few similar studies of this size. Previously, the largest and most comprehensive population-based study on allergen sensitization was NHANES 2005–2006 that showed similar results. However, the NHANES study only included 10,348 participants, albeit randomly sampled, and measured sIgE antibodies toward only 15 inhalant allergens [8]. The largest US comprehensive allergen sensitization study involved 8 million patients tested by a national reference laboratory (LabCorp) and showed trends and risk factors for allergen sensitization similar to those reported in the NHANES 2005–2006 and our study; however, the LabCorp results only included fungal allergens [14]. Other similar studies are limited in scope (geographic sampling limitations,

number of allergens measured, included ages) [9, 15–17]. Adding our results to existing data provides a strong, updated evidence-based rationale for design of effective clinical allergy testing.

This study demonstrates that sociodemographic factors are associated with distinct sensitization patterns. Similar to NHANES 2005–2006 and multiple similar studies, this study shows that prevalence of both seasonal and perennial allergen sensitization peaks in late childhood and early adulthood then decreases with age (Fig. 1) [8, 14–17]. This may be due to interplay between developmentally regulated host immune response and allergen exposure. Young atopic children can mount robust IgE responses to food allergens as exemplified by high prevalence of food allergies in early childhood, but they may not be sensitized to inhalant allergens due to insufficient duration and quantity of allergen exposure [18]. Conversely, elderly adults may have age-related changes in immune function that lowers rates of sensitization despite many more years of allergen exposure [19].

More than 50% of patients older than age 5 and 30% of patients younger than age 5 were sensitized to at least one inhalant allergen. Dust mite sensitization had highest prevalence (38.0%) while fungi sensitization was lowest (19.7%) when patients of all age-groups were combined (Table 2). During early childhood, sensitization to animal allergens was highest, followed by dust mites and tree allergens. Prevalence of dust mite and tree sensitization

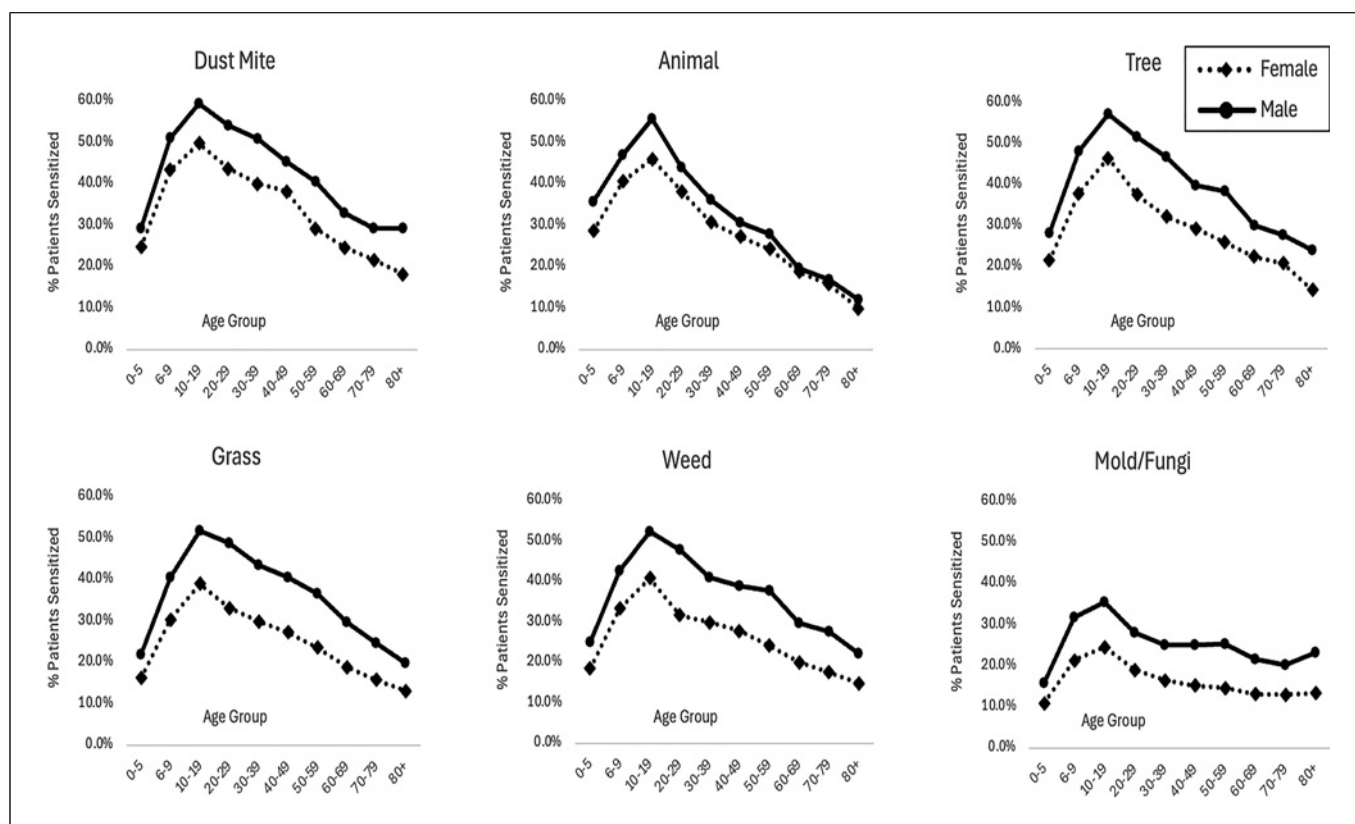


Fig. 1. Sensitization by gender and age, within a source. p value from chi-square test: all <0.0001 .

continued to be the highest during adulthood with animal allergen sensitization rates decreasing with age. Exposure to more ubiquitous allergens such as dust mites and animals during early childhood likely contributes to this pattern [20]. In contrast to our study, other surveys showed low prevalence of tree antigen sensitization in early life (NHANES 2005–2006) [8]. These older studies, however, included fewer seasonal allergens. For instance, only a few species of trees were included, while the current study used up to 32 tree species [8]. The pattern of fungal allergen sensitization was different from other pollen allergens in that after a decrease from early adulthood, fungal sensitization plateaued without further reduction into elderly age (Fig. 1). It is possible that certain patients are persistently exposed to fungal allergens such as dermatophytes, throughout life, resulting in continued new sensitizations [21, 22]. For instance, prevalence of sensitization to *Candida* species was persistently higher than other fungi in the LabCorp fungal allergen sensitization study [8].

In the current study, male sex was associated with allergic sensitization at all age ranges. We found

higher positive percentages of sIgE tests among males compared to females with seasonal and perennial allergens, suggesting that there are sex-associated differences in expression of IgE (Fig. 1). Our data are consistent with other similar studies, although NHANES 2005–2006 found higher male prevalence among participants 6 years and older but no differences in younger children [8]. Higher rates of allergen sensitization among males contrast with higher prevalence of allergic disease such as asthma among female patients, especially in older age-groups [23, 24]. This suggests that pathogenesis of some atopic diseases involves pathways in addition to IgE-mediated allergic sensitization.

The prevalence of sensitization to individual allergens was substantially different across different geographic regions (Fig. 2). These observations were consistent with other large epidemiological studies such as NHANES 3 and LabCorp's national study on fungal sensitization [7, 14]. Persistent exposure to allergens is usually required for allergic sensitization and atopic patients will be exposed to different fauna in different geographic locations



Fig. 2. Sensitization across 4 census regions within a source. *p* value from chi-square test: all <0.0001.

resulting in differential sensitization to seasonal pollen allergens across the country. Patterns of sensitization to animal allergens likely depend upon patterns in pet and domestic animal ownership unique to various regions. Dust mite allergens have been shown to be more prevalent in warmer more humid climates, which may explain the higher prevalence of sensitization to these antigens in the South [6].

Allergic sensitization to seasonal and perennial allergens was more prevalent in large metropolitan

versus smaller and nonmetropolitan areas (Fig. 3). These data are similar to multiple studies and support the “hygiene hypothesis” of increasing worldwide atopy; urbanization, removed from farming environmental exposures, facilitates development of a T2 lymphocyte-predominant immune axis and development of IgE-mediated sensitization and inflammation [25, 26].

Speculation exists that longer plant growing seasons due to climate change results in increasing rates of

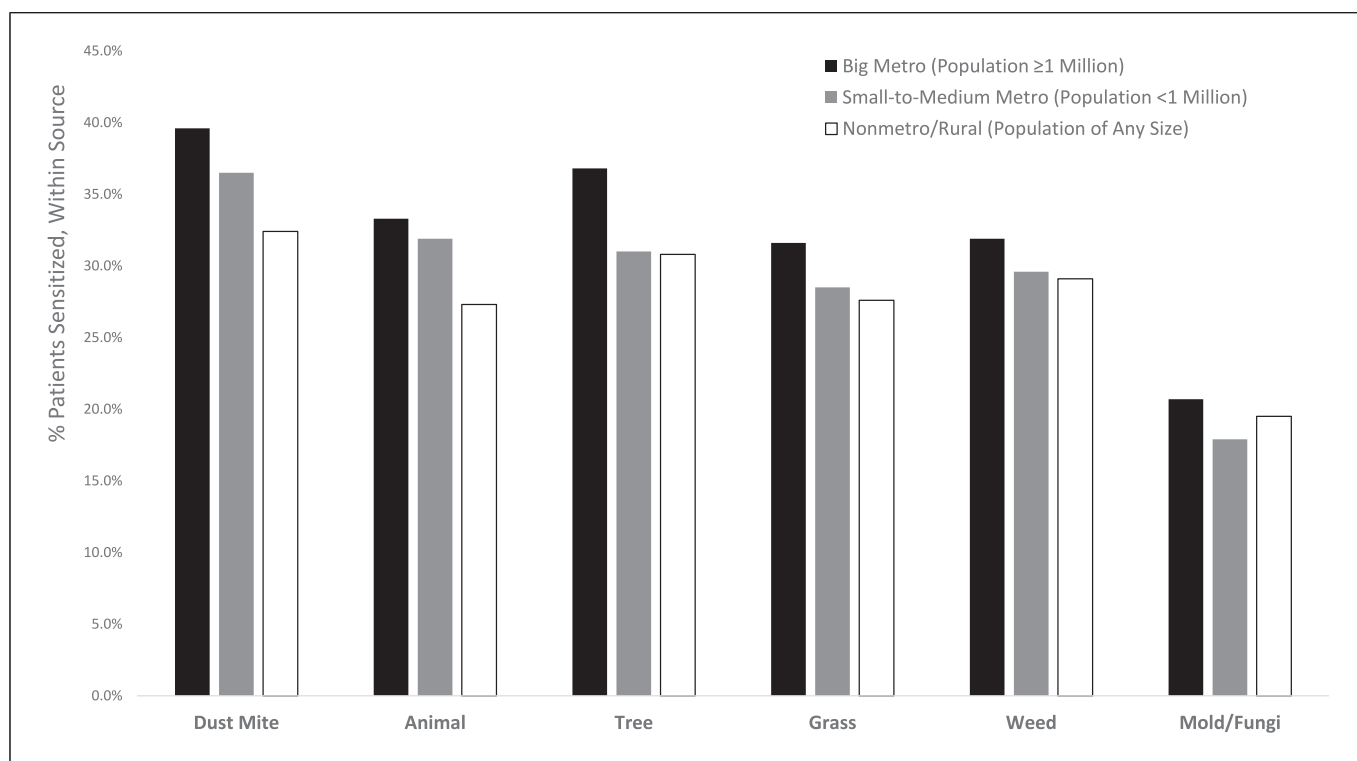


Fig. 3. Sensitization by level of urbanization, within a source. *p* value from chi-square test: all <0.0001.

seasonal allergen sensitization [27, 28]. Anecdotally, clinicians observed that allergy symptoms have increased in recent years [29]. Currently, a few small-scale reports show increased allergen sensitization over time [30, 31]. Quest Diagnostics reported in 2011 a 15.0% increase in ragweed and a 12.0% increase in mold sensitization over a 4-year period in a large non-peer-reviewed report involving a large cross-sectional analysis of the US population tested with sIgE tests [32]. A longitudinal study of a birth cohort of 651 Japanese children showed the prevalence of allergic rhinitis increased considerably over time (10.6%–31.2%) and the sensitization prevalence to allergen sIgE also increased from 57.8% at age 5 years to 74.8% at age 9 years [33]. We did not examine changes of allergen sensitization in our study, but we found similar geographic patterns of allergen sensitization compared to similar large studies performed 20–30 years ago (e.g., NHANES) [7, 8]. These data suggest that while sensitization rates may have increased in the last few decades due to climate change, these atmospheric effects have not influenced the general geographic distribution of inhalant allergen sensitization in the US. Our study did not examine whether the prevalence of sensitization within geographic regions

has changed over time and such studies are needed to answer this important question.

Many patients diagnosed with asthma and atopic dermatitis were more likely to be sensitized to seasonal and perennial allergens (Fig. 4). Detection of sIgE allergens does not automatically equate with clinical relevance to those antigens; however, it is generally accepted that sensitizing allergens play a pivotal role in pathogenesis of allergic disease [6]. In asthma and allergic rhinitis, allergic inflammation, driven by these antigens, decreases threshold of disease exacerbation in response to re-exposure to these allergens and non-specific triggers such as tobacco smoke, atmospheric changes, and air pollutants [6, 34]. Data from this study are highly congruent with results of other similar large studies. In a previous study examining fungal sensitization, we demonstrated that patients with asthma and atopic dermatitis were highly sensitized to seventeen unique fungal species compared to patients with rhinitis, chronic sinusitis and those with no ICD-10 coding of any allergic disease [14]. Our study did not show an association between rhinitis and allergic sensitization even though allergens play central role in the pathogenesis of allergic rhinitis [6, 35, 36]. This is most likely

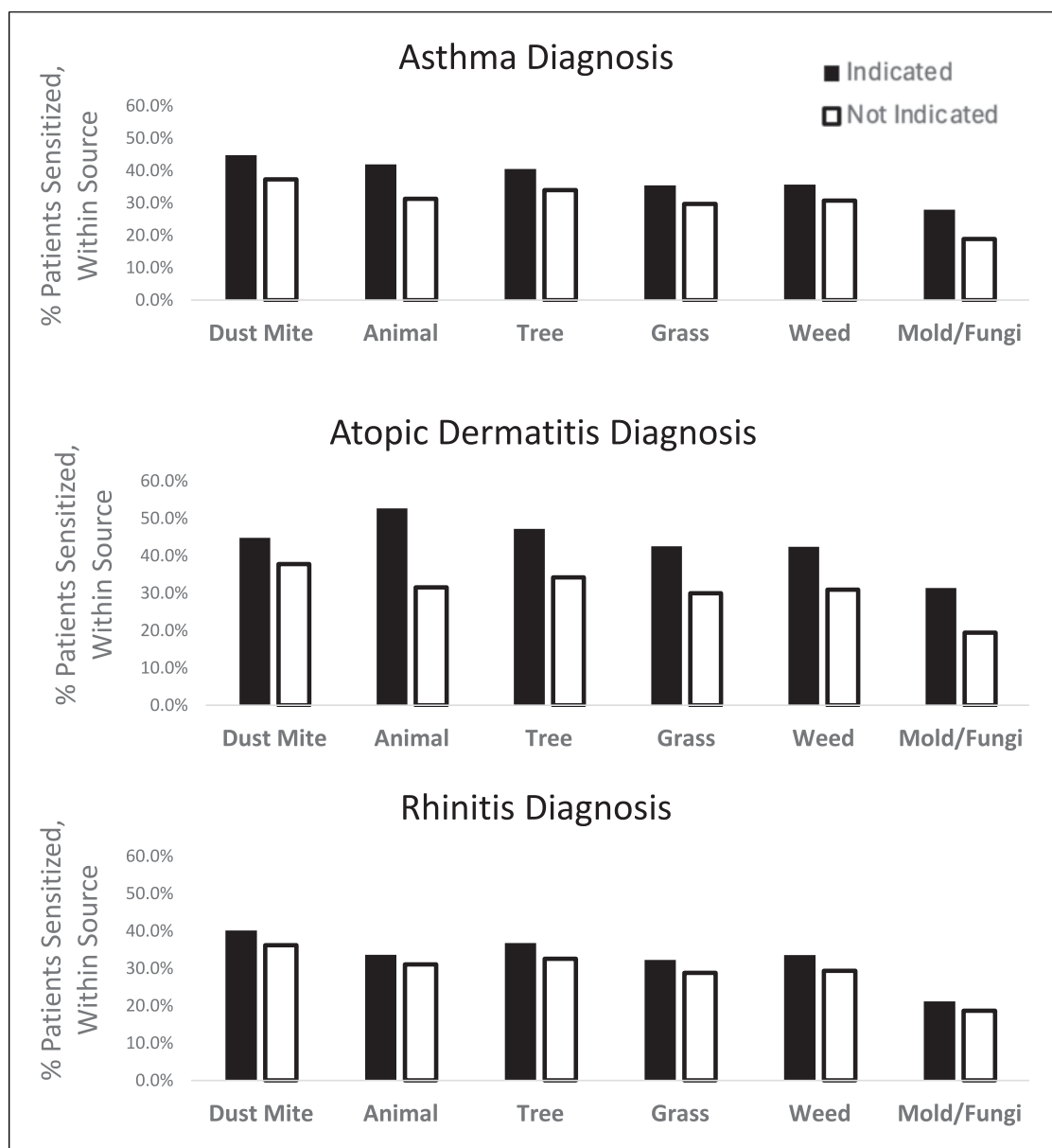


Fig. 4. Sensitization by allergic disease state, within a source. *p* value from chi-square test: all <0.0001.

due to our use of rhinitis ICD-10 codes that include patients with non-allergic forms of rhinitis such as upper respiratory tract infections and cholinergic gustatory rhinitis. Atopic dermatitis was highly associated with allergen sensitization even though atopy and allergic inflammation are not the only pathways in development and exacerbation of this skin disease [6, 36]. Allergen immunotherapy is not universally effective for patients with atopic dermatitis [37, 38]. High rates of sensitization in eczema patients may be ex-

plained by the loss of skin integrity in these patients, resulting in early onset exposure of allergens to the immune system with generation of sIgE in response to these perceived danger signals [6, 36].

In the US, providers often use pre-determined sets of “allergen panels” when testing for allergic desensitization in patient care, although as noted in the methods, this study excluded testing ordered as part of fixed regional panels. With the exception of food allergens, inhalant allergen panels are recommended by

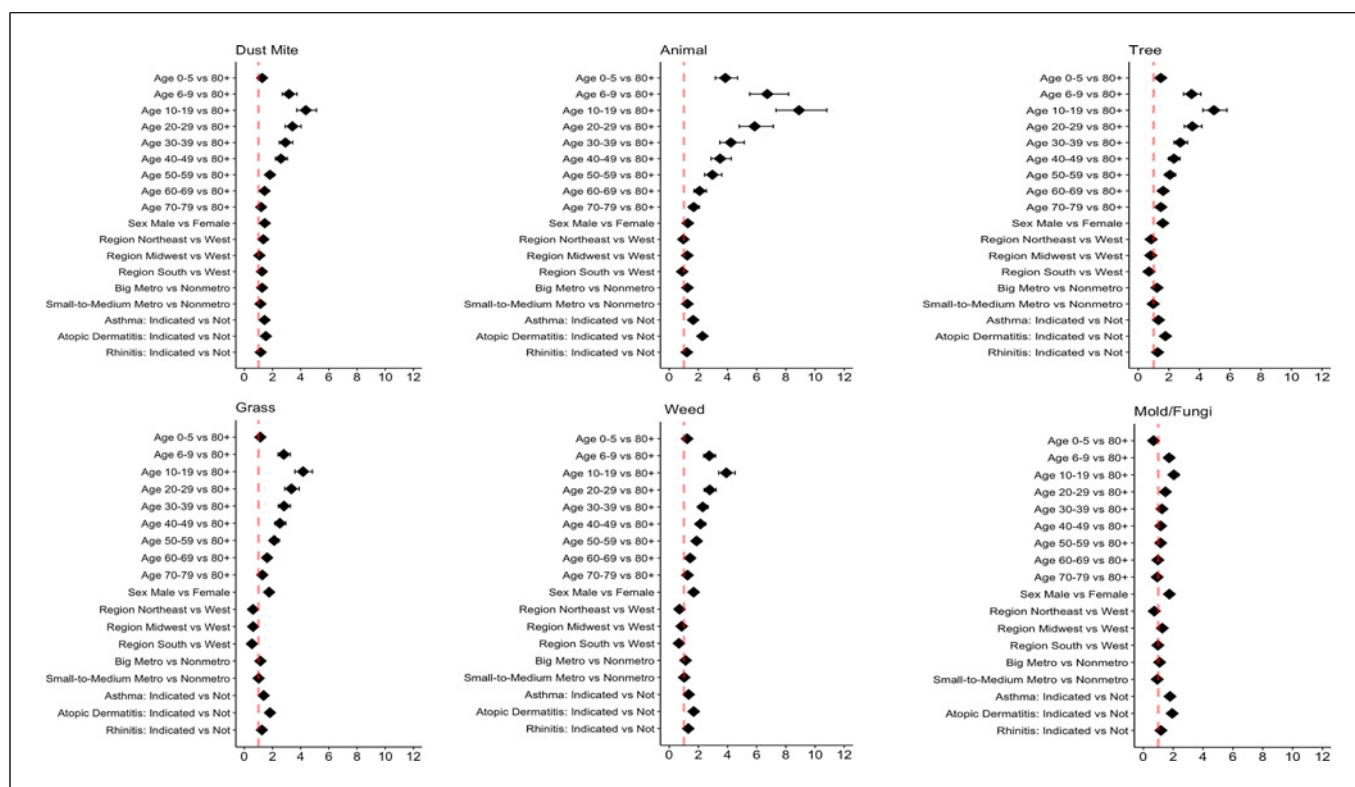


Fig. 5. Adjusted odds ratios for independent predictors of allergic sensitization to at least one allergen with each allergen source (95% CI) by allergen source, in multivariate logistic regression (modeling sensitized vs. not sensitized).

the US allergy guidelines to confirm sensitization in patients with findings consistent with atopy [5]. The number and types of allergens in panels, however, are based upon outdated botanical data. This and other studies show that there is high prevalence of allergic sensitization to inhalant allergens that are not regularly ordered by clinicians [11]. For instance, while most laboratory panels test for two species of dust mites, *Dermatophagoides farinae* and *Dermatophagoides pteronyssinus*, there is a high rate of sensitization to *Blomia tropicalis* and other mite species (online suppl. Fig. E1) [39]. In the LabCorp study, investigators found that practice guidelines recommended testing for only five fungi, missing high rates of sensitization to other fungal species [14]. This study confirms the finding wherein testing only *Aspergillus*, *Alternaria*, *Cladosporium*, *Penicillium*, and *Candida* missed many patients sensitized to other mold species (online suppl. Fig. E6). These data in combination with evidence of geographic variability of sensitization suggest that current inhalant allergen panels should be modified by

adding individual allergens guided by the parameters addressed by this study.

This study is limited to the US, but its findings have global implications. With a geographic area of 9 million km² and 15 broad level 1 eco regions, the US exhibits diverse patterns of allergic sensitization, suggesting that similar variations may exist in other regions worldwide [40, 41]. While specific allergens will be different, reflective of local flora and fauna, it is likely that the number of different allergen species will be similar to our study. To the best of our knowledge, most large global surveys of inhalant allergen sensitization have not analyzed as many allergens as ours [42, 43]. Expanding the number of allergens in global studies of inhalant antigen sensitization can therefore provide more information for clinicians in their management of allergic patients.

This study must be interpreted with consideration of associated limitations. First, this is a retrospective, uncontrolled cross-sectional analysis and may not be reflective of the general population. This limits the

comparison of results to other prospective studies that sampled large, randomized populations, such as NHANES 2005–2006 [8]. Second, regarding asthma and atopic dermatitis, we relied on provider-reported ICD-10 codes to identify patients; these may not reflect accurate, precise diagnoses. We did not differentiate disease severity, which may correlate with sensitization. It was not known when in the diagnostic process a diagnosis was made, so we cannot tell whether some patients' diagnoses were influenced by testing or whether testing was influenced by diagnoses. Finally, significant cross-reactivity between tree, fungi, and weed species exists, and patients with multiple allergen sensitization may not be allergic to multiple species within an allergen source. Use of resolved component testing may provide better insight into co-sensitization and clinical relevance.

In conclusion, many individuals in the US are sensitized to seasonal and perennial inhalant allergens. Sensitization to all allergens peaks in early adult years and, for most allergens, decreases with age; more males than females were sensitized at all ages. Fungal sensitization appears not to decrease into senescence. Patients with asthma and atopic dermatitis are highly sensitized to all allergens compared to patients with no atopic disease. Sensitization to different seasonal and perennial allergens varied by geography. This study yields valuable information in inhalant allergen sensitization in the US, particularly regarding demographic, geographic, and disease states. Diagnostic laboratories and payers should take these data into consideration in design of inhalant allergen panels for optimal detection of allergic sensitization in management of allergy patients.

References

- 1 Pate CA, Zahran HS, Malilay J, Hsu J. The shifting prevalence of asthma and allergic disease in US children. *Ann Allergy Asthma Immunol.* 2022;129(4):481–9. <https://doi.org/10.1016/j.anai.2022.06.030>
- 2 Akinbami LJ, Simon AE, Schoendorf KC. Trends in allergy prevalence among children aged 0–17 years by asthma status, United States, 2001–2013. *J Asthma.* 2016;53(4):356–62. <https://doi.org/10.3109/02770903.2015.1126848>
- 3 Dierick BJH, van der Molen T, Flokstra-de Blok BMJ, Muraro A, Postma MJ, Kocks JWH, et al. Burden and socioeconomics of asthma, allergic rhinitis, atopic dermatitis and food allergy. *Expert Rev Pharmacoecon Outcomes Res.* 2020;20(5):437–53. <https://doi.org/10.1080/14737167.2020.1819793>
- 4 Shamji MH, Valenta R, Jardetzky T, Verhasselt V, Durham SR, Würtzen PA, et al. The role of allergen-specific IgE, IgG and IgA in allergic disease. *Allergy.* 2021;76(12):3627–41. <https://doi.org/10.1111/all.14908>
- 5 Bernstein IL, Li JT, Bernstein DI, Hamilton R, Spector SL, Tan R, et al. Allergy diagnostic testing: an updated practice parameter. *Ann Allergy Asthma Immunol.* 2008;100(3 Suppl 3):S1–148. [https://doi.org/10.1016/s1081-1206\(10\)60305-5](https://doi.org/10.1016/s1081-1206(10)60305-5)
- 6 O'Hehir R, Holgate S, Sheikh A, Middleton E. Chapter 4. Middleton's allergy essentials essay: Elsevier; 2017.
- 7 Arbes SJ Jr, Gergen PJ, Elliott L, Zeldin DC. Prevalences of positive skin test responses to 10 common allergens in the US population: results from the third National Health and Nutrition Examination Survey. *J Allergy Clin Immunol.* 2005;116(2):377–83. <https://doi.org/10.1016/j.jaci.2005.05.017>
- 8 Salo PM, Arbes SJ Jr, Jaramillo R, Calatroni A, Weir CH, Sever ML, et al. Prevalence of allergic sensitization in the United States: results from the National Health and Nutrition Examination Survey (NHANES) 2005–2006. *J Allergy Clin Immunol.* 2014;134(2):350–9. <https://doi.org/10.1016/j.jaci.2013.12.1071>
- 9 Wong V, Wilson NW, Peele K, Hogan MB. Early pollen sensitization in children is dependent upon regional aeroallergen exposure. *J Allergy.* 2012;2012:583765. <https://doi.org/10.1155/2012/583765>

Statement of Ethics

This study protocol was reviewed and the need for approval was waived (deemed exempt) by the WCG Institutional Review Board based on federal regulation 45 CFR Parts 46 and 164. This study followed the Strengthening the Reporting of Observational Studies in Epidemiology (STROBE) reporting guideline for cross-sectional studies. The need for informed consent was waived (deemed exempt) by the WCG Institutional Review Board based on federal regulation 45 CFR Parts 46 and 164. Informed consent was not obtained because the data used in the study were already de-identified and presented as aggregate data.

Conflict of Interest Statement

L.H.H. and Z.C. are employees of Quest Diagnostics and may own its stock. L.S. declares no conflicts of interest. K.K. is consultant and independent contractor for ThermoFisher Scientific.

Funding Sources

This study was not supported by any sponsor or funder.

Author Contributions

K.K., L.H.H., Z.C., and L.S. were involved in study and writing of manuscript. L.H.H. and Z.C. were involved in acquisition of study data. Z.C. was involved in data analysis.

Data Availability Statement

Data for this study are sole property of Quest Diagnostics and are not publicly available. Further inquiries can be directed to the corresponding author.

- 10 Available from: <https://newsroom.questdiagnostics.com/Fact-sheet> (accessed December 12, 2024).
- 11 Thorpe M, Movérare R, Fischer C, Lidholm J, Rudengren M, Borres MP. History and utility of specific IgE cutoff levels: what is the relevance for allergy diagnosis? *J Allergy Clin Immunol Pract*. 2023;S2213-2198(23):00560-3.
- 12 USDA Economic Research Service. Rural urban continuum codes. 2013. <https://www.ers.usda.gov/data-products/rural-urban-continuum-codes/documentation/#DataSources>
- 13 von Elm E, Altman DG, Egger M, Pocock SJ, Gøtzsche PC, Vandenbroucke JP, et al. The Strengthening of Reporting of Observational Studies in Epidemiology (STROBE) statement: guidelines for reporting observational studies. *J Clin Epidemiol*. 2008; 61(4):344–9. <https://doi.org/10.1016/j.jclinepi.2007.11.008>
- 14 Kwong K, Robinson M, Sullivan A, Letovsky S, Liu AH, Valcour A. Fungal allergen sensitization: prevalence, risk factors, and geographic variation in the United States. *J Allergy Clin Immunol*. 2023;152(6):1658–68. <https://doi.org/10.1016/j.jaci.2023.09.010>
- 15 Sheehan WJ, Rangsitthienchai PA, Baxi SN, Gardynski A, Bharmanee A, Israel E, et al. Age-specific prevalence of outdoor and indoor aeroallergen sensitization in Boston. *Clin Pediatr*. 2010;49(6):579–85. <https://doi.org/10.1177/0009922809354326>
- 16 Shargorodsky J, Garcia-Esquinas E, Umanetskiy R, Navas-Acien A, Lin SY. Household pet exposure, allergic sensitization, and rhinitis in the U.S. population. *Int Forum Allergy Rhinol*. 2017;7(7):645–51. <https://doi.org/10.1002/alr.21929>
- 17 Bernstein DI, Würtzen PA, DuBuske L, Blaiss MS, Ellis AK, Weber RW, et al. Allergy to oak pollen in North America. *Allergy Asthma Proc*. 2021;42(1):43–54. <https://doi.org/10.2500/aap.2021.42.200089>
- 18 Sicherer SH, Sampson HA. Food allergy: a review and update on epidemiology, pathogenesis, diagnosis, prevention, and management. *J Allergy Clin Immunol*. 2018; 141(1):41–58. <https://doi.org/10.1016/j.jaci.2017.11.003>
- 19 Mathur SK. Allergy and asthma in the elderly. *Semin Respir Crit Care Med*. 2010;31(5): 587–95. <https://doi.org/10.1055/s-0030-1265899>
- 20 Roberts JW, Dickey P. Exposure of children to pollutants in house dust and indoor air. *Rev Environ Contam Toxicol*. 1995;143: 59–78. https://doi.org/10.1007/978-1-4612-2542-3_3
- 21 Bush RK, Portnoy JM, Saxon A, Terr AI, Wood RA. The medical effects of mold exposure. *J Allergy Clin Immunol*. 2006;117(2): 326–33. <https://doi.org/10.1016/j.jaci.2005.12.001>
- 22 Simon D, Straumann A, Dahinden C, Simon HU. Frequent sensitization to *Candida albicans* and profilins in adult eosinophilic esophagitis. *Allergy*. 2013;68(7):945–8. <https://doi.org/10.1111/all.12157>
- 23 Salvati L, Vitiello G, Parronchi P. Gender differences in anaphylaxis. *Curr Opin Allergy Clin Immunol*. 2019;19(5):417–24. <https://doi.org/10.1097/ACI.0000000000000568>
- 24 Fuseini H, Newcomb DC. Mechanisms driving gender differences in asthma. *Curr Allergy Asthma Rep*. 2017;17(3):19. <https://doi.org/10.1007/s11882-017-0686-1>
- 25 Pfefferle PI, Keber CU, Cohen RM, Garn H. The hygiene hypothesis: learning from but not living in the past. *Front Immunol*. 2021; 12:635935. <https://doi.org/10.3389/fimmu.2021.635935>
- 26 Brooks C, Pearce N, Douwes J. The hygiene hypothesis in allergy and asthma: an update. *Curr Opin Allergy Clin Immunol*. 2013; 13(1):70–7. <https://doi.org/10.1097/ACI.0b013e32835ad0d2>
- 27 Lin GC, Zacharek MA. Climate change and its impact on allergic rhinitis and other allergic respiratory diseases. *Curr Opin Otolaryngol Head Neck Surg*. 2012;20(3): 188–93. <https://doi.org/10.1097/MOO.0b013e3283524b14>
- 28 D'Amato G, D'Amato M. Climate change, air pollution, pollen allergy and extreme atmospheric events. *Curr Opin Pediatr*. 2023; 35(3):356–61. <https://doi.org/10.1097/MOP.0000000000001237>
- 29 Available from: <https://www.scientificamerican.com/article/why-climate-change-may-be-worsening-your-seasonal-allergies/> (accessed August 20, 2024).
- 30 Linneberg A, Gislum M, Johansen N, Husmoen LL, Jørgensen T. Temporal trends of aeroallergen sensitization over twenty-five years. *Clin Exp Allergy*. 2007;37(8): 1137–42. <https://doi.org/10.1111/j.1365-2222.2007.02760.x>
- 31 Beutner C, Forkel S, Gupta S, Fuchs T, Schön MP, Geier J, et al. Sex- and age-dependent changes in polysensitization to common aeroallergens over 20 years. *J Asthma Allergy*. 2020;13:725–30. <https://doi.org/10.2147/JAA.S280771>
- 32 Available from: <https://newsroom.questdiagnostics.com/press-releases?item=94740> (accessed December 12, 2024).
- 33 Yamamoto-Hanada K, Borres MP, Åberg MK, Yang L, Fukui T, Narita M, et al. IgE responses to multiple allergen components among school-aged children in a general population birth cohort in Tokyo. *World Allergy Organ J*. 2020;13(2):100105. <https://doi.org/10.1016/j.waojou.2020.100105>
- 34 Denlinger LC, Heymann P, Lutter R, Gern JE. Exacerbation-prone asthma. *J Allergy Clin Immunol Pract*. 2020;8(2):474–82. <https://doi.org/10.1016/j.jaip.2019.11.009>
- 35 Wise SK, Damask C, Roland LT, Ebert C, Levy JM, Lin S, et al. International consensus statement on allergy and rhinology: allergic rhinitis - 2023. *Int Forum Allergy Rhinol*. 2023;13(4):293–859. <https://doi.org/10.1002/alr.23090>
- 36 Bousquet J, Anto JM, Bachert C, Baiardini I, Bosnic-Anticevich S, Walter Canonica G, et al. Allergic rhinitis. *Nat Rev Dis Primers*. 2020;6(1):95. <https://doi.org/10.1038/s41572-020-00227-0>
- 37 Yepes-Núñez JJ, Guyatt GH, Gómez-Escobar LG, Pérez-Herrera LC, Chu AWL, Ceccaci R, et al. Allergen immunotherapy for atopic dermatitis: systematic review and meta-analysis of benefits and harms. *J Allergy Clin Immunol*. 2023;151(1):147–58. <https://doi.org/10.1016/j.jaci.2022.09.020>
- 38 Pessina B, Giovannini M, Mori F, Di Cara G, Novembre E, Chan S, et al. Is there room for allergen immunotherapy for the treatment of atopic dermatitis in the precision medicine era? *Front Pediatr*. 2022;10:1050560. <https://doi.org/10.3389/fped.2022.1050560>
- 39 Arlian LG, Bernstein D, Bernstein IL, Friedman S, Grant A, Lieberman P, et al. Prevalence of dust mites in the homes of people with asthma living in eight different geographic areas of the United States. *J Allergy Clin Immunol*. 1992;90(3 Pt 1): 292–300. [https://doi.org/10.1016/s0091-6749\(05\)80006-5](https://doi.org/10.1016/s0091-6749(05)80006-5)
- 40 Available from: <https://www.cia.gov/the-world-factbook/countries/united-states/#geography> (accessed March 7, 2025).
- 41 Available from: <https://www.epa.gov/ecoresearch/ecoregions-north-america> (accessed March 7, 2025).
- 42 Heinzerling LM, Burbach GJ, Edenharter G, Bachert C, Bindslev-Jensen C, Bonini S, et al. GA(2)LEN skin test study I: GA(2)LEN harmonization of skin prick testing: novel sensitization patterns for inhalant allergens in Europe. *Allergy*. 2009;64(10):1498–506. <https://doi.org/10.1111/j.1398-9995.2009.02093.x>
- 43 Burbach GJ, Heinzerling LM, Edenharter G, Bachert C, Bindslev-Jensen C, Bonini S, et al. GA(2)LEN skin test study II: clinical relevance of inhalant allergen sensitizations in Europe. *Allergy*. 2009;64(10):1507–15. [doi: 10.1111/j.1398-9995.2009.02089.x](https://doi.org/10.1111/j.1398-9995.2009.02089.x)