

Asthma, oculonasal symptoms, and skin test sensitivity across National Health and Nutrition Examination Surveys



Qingyu Meng, PhD^{*}; Sairaman Nagarajan, MD, MPH^{*}; Yeongkwon Son, PhD^{*}; Panagiotis Koutsoupas, BS^{*}; Leonard Bielory, MD^{†,‡,§}

^{*} School of Public Health, Rutgers University, Piscataway, New Jersey

[†] Rutgers University Center for Environmental Prediction, New Brunswick, New Jersey

[‡] STARx Allergy and Asthma Center, Springfield, New Jersey

[§] Robert Wood Johnson University Hospital, New Brunswick, New Jersey

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ABSTRACT

Background: The increasing prevalence of allergies and asthma has been reported. However, the progression of the prevalence of allergy (the “allergic diathesis progression”) has not been examined over time from skin test positivity to oculonasal symptoms to the development of asthma.

Objective: To investigate the change in the prevalences and associations of positive skin test reactions, oculonasal symptoms, and asthma during the Second and Third National Health and Nutrition Examination Surveys (NHANES II and NHANES III, respectively).

Methods: Data collected during NHANES II and III were used. The prevalence and associations of positive skin test reactions, oculonasal symptoms, and asthma and the linear trend of oculonasal symptoms and asthma prevalence across different cumulative positive skin test reactions were calculated for each NHANES period.

Results: From NHANES II to NHANES III, the prevalence of asthma doubled (2 times) and increased for positive skin test reactions (2.2 times), oculonasal symptoms (3.3 times), and concurrence of asthma, oculonasal symptoms, and positive skin test reactions (5.3 times). People were sensitive to an increasing number of allergens. Positive skin test reactions increased from 0.2% (NHANES II) to 2.7% (NHANES III) for people allergic to all 6 allergens.

Conclusion: Despite some methodologic differences in skin tests across NHANES II and III, this study demonstrated significant increases in allergen sensitivities (prevalence and number of allergens), oculonasal symptoms, and asthma over a 20-year course, indicating that increased sensitivity led to increased allergic symptoms and asthma during the 20 years from NHANES II to NHANES III.

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Introduction

Allergies and asthma are major disease burdens in the United States and have been increasing during the past 50 years.¹ Currently, allergic diseases affect approximately one third of the national population and appear to be increasing each year.²

The increasing prevalence of allergies and asthma appears to be multifactorial, including environmental exposures and lifestyle changes during the past quarter of a century.³ Studies have suggested that increased exposures to indoor and outdoor allergens over time lead to an increase in the risk of developing allergies and

asthma.⁴ Westernized lifestyles,⁵ obesity in the patient and potential impact of maternal obesity,⁶ microbiomes,⁷ antibiotic use,⁸ and altered gene–environment interactions in a changing environment also have been associated with the increased prevalence of asthma and allergies.⁹

The risk of developing allergies and asthma has been quantified in only a limited number of studies at the national level. Arbes et al¹⁰ described a doubling in the prevalence of allergen sensitivity in the United States from 1976 to 1994 using allergy skin test data from the Second and Third National Health and Nutrition Examination Surveys (NHANES II and NHANES III, respectively). This study noted that 54.3% of Americans were sensitized to at least 1 allergen and found that the prevalence of allergen sensitivity was 2.1 to 5.5 times higher in NHANES III (1988–1994) than in NHANES II (1976–1980). Other studies have used the 2005 to 2006 NHANES database to describe the prevalence of allergen-specific serum immunoglobulin E in the national population¹¹ and the prevalence

Reprints: Qingyu Meng, PhD, Rutgers School of Public Health, 683 Hoes Lane West, Piscataway, NJ 08854; E-mail: mengqi@sph.rutgers.edu.

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of asthma in the elderly and pediatric populations.¹² The studies mentioned earlier focused on a particular symptom measurement or a specific NHANES period. However, the progression of the prevalence of allergy (the “allergic diathesis progression”¹³) has not been examined over time from skin test positivity to oculonasal symptoms to the development of asthma.

The purpose of this study was to investigate the change in the prevalence of allergy and asthma using data collected from NHANES II and NHANES III, which were conducted from 1976 through 1980 and from 1988 through 1994, respectively. By examining responses to the medical history questionnaire and allergen skin test data across NHANES II and NHANES III, this study provides a better understanding of the potential progression of skin test positivity, oculonasal symptoms, and asthma associations and the changing prevalence of allergy and asthma over time.

Methods

NHANES Data

Data collected during the NHANES II and NHANES III were analyzed. NHANES II (1976–1980) and NHANES III (1988–1994) were conducted approximately 10 years apart and were designed to be nationally representative samples of the US population at the time. Data files were obtained from the public domain of the Center for Disease Control and Prevention. Data used in this work include demographic information, allergen skin test results, oculonasal symptoms, and asthma status of each NHANES participant.

Skin test results were assessed for 6 allergens common to NHANES II and NHANES III: cat, ragweed, perennial rye, oak, Bermuda grass, and *Alternaria alternata*. A skin test result was considered positive if the difference between the mean wheal length and skin test width and the negative control was greater than 3 mm. An individual was considered sensitized, or skin test positive, if he or she exhibited a positive reaction for at least 1 of the 6 allergens. There are methodologic differences between NHANES II and NHANES III in the conduction of skin tests.^{14,15} The differences include allergen extract standardization for potency, differences in inclusion and exclusion criteria for the 2 periods, different control (histamine) concentrations even within NHANES II, and skin test reading times. The impact of these differences on the present findings is discussed in the Discussion section.

Oculonasal symptoms were identified using survey responses from the medical history questionnaire. In NHANES II, participants were asked, “During the past 12 months not counting colds or the flu, have you frequently had trouble with: (1) Stuffy nose? (2) Itchy nose? (3) Watery discharge from nose? (4) Watery, itchy eyes?” An individual was considered to have oculonasal symptoms if he or she answered “yes” to any of items 1 to 3 (nasal symptom questions) and “yes” to item 4 (ocular symptom question). In NHANES III, participants were asked, “During the past 12 months, have you had any episodes of: (1) Stuffy, itchy, or runny nose? (2) Watery, itchy eyes?” An individual was considered to have oculonasal symptoms if he or she answered “yes” to the nasal symptom question (item 1) and the ocular symptom question (item 2). An individual was considered to have asthma if he or she had a history of the disease and still had the disease.

In addition, the prevalence of skin test positivity, oculonasal symptoms, and asthma was characterized and compared for 5 pairs of population groups across NHANES II and NHANES III (ie, comparing 1 age group of NHANES II to the following age group in NHANES III: group A, 6–10 years old in NHANES II and 16–19 years old in NHANES III; group B, 11–19 years old in NHANES II and 20–30 years old in NHANES III; group C, 20–30 years old in NHANES II and 31–40 years old in NHANES III; group D, 31–40 years old in NHANES II and 41–50 years old in NHANES III; group E, 41–50 years old in NHANES II and 51–60 years old in NHANES III).

As mentioned earlier, NHANES II and III were conducted approximately 10 years apart in different populations; however, the population of each NHANES period was chosen to be nationally representative at the time. Therefore, NHANES III can be viewed as a continuation of NHANES II. Comparing the prevalence of a disease for an NHANES III population with that of a 10-year younger NHANES II population can reflect the change in disease prevalence nationwide for that specific age-related population pair over time. This approach has been successfully applied to characterize the change in blood lead concentrations over time, for a population nationwide, across multiple NHANES surveys.¹²

Statistical Analysis

All statistical analyses were conducted with SAS 9.3 (SAS Institute, Cary, North Carolina), and the statistical significance level was .05 unless otherwise specified. The prevalence of skin test positivity, oculonasal symptoms, and asthma was calculated (frequency and percentage) within each NHANES period, and the differences in prevalence across NHANES periods were tested with χ^2 test. The strength of associations of skin test positivity, oculonasal symptoms, and asthma was expressed as correlation coefficients (ϕ for nominal variables, range -1 to 1),¹⁶ and the homogeneity of the associations across NHANES periods was tested with the Breslow–Day test. The linear trend of oculonasal symptoms and asthma prevalence across different cumulative numbers (range 0–6) of positive skin test reactions was examined with the Cochran–Armitage test.

Results

Prevalence of Skin Test Positivity, Oculonasal Symptoms, and Asthma across NHANES II and NHANES III

During NHANES II, allergy skin test results, oculonasal symptoms, and asthma status were collected from 11,044 people; during NHANES III, 10,833 people reported allergen-specific skin test results, oculonasal symptoms, and asthma status. The numbers of positive skin test reactions, oculonasal symptoms, and asthma cases were 2,144 (19.4%), 991 (9.0%), and 275 (2.5%), respectively, during NHANES II and 4,538 (41.9%), 3,242 (29.9%), and 547 (5.0%), respectively, during NHANES III. From NHANES II to NHANES III, the prevalence of asthma increased 2.0 times, that of skin test positivity increased 2.2 times, and that of oculonasal symptoms increased 3.3 times (Fig 1A). In contrast, the concurrent prevalence of asthma, oculonasal symptoms, and skin test positivity increased 5.3 times ($P < .0001$ by χ^2 test).

More skin test positivity, oculonasal symptoms, and asthma cases were observed in NHANES III than in NHANES II within each of the 5 pairs of population groups (Fig 1B). The increases in the prevalence of single symptoms and symptom combinations were statistically significant ($P < .001$ by χ^2 test). From NHANES II to NHANES III, the largest increases in the prevalence of single symptoms and combination of symptoms were observed for pediatric and adolescent populations (group A, 6–10 years old in NHANES II and 16–19 years old in NHANES III): asthma, oculonasal symptoms, and skin test positivity increased 1.7, 5.6, and 3.3 times, respectively; and the concurrence of all 3 symptoms increased 5.9 times. The middle-age population (group D, 31–40 years old in NHANES II and 41–50 years old in NHANES III) had the lowest prevalence of increases, ranging from 2.0 times for asthma to 3.6 times for the concurrence of all 3 symptoms. In addition, increases in oculonasal symptoms were usually greater than skin test positivity or asthma for each pair of population groups. From NHANES II to NHANES III, the prevalence increased from 2.7 to 5.6 times for oculonasal symptoms across the 5 population groups, from 1.6 to 2.1 times for asthma, and from 1.8 to 3.3 times for skin test

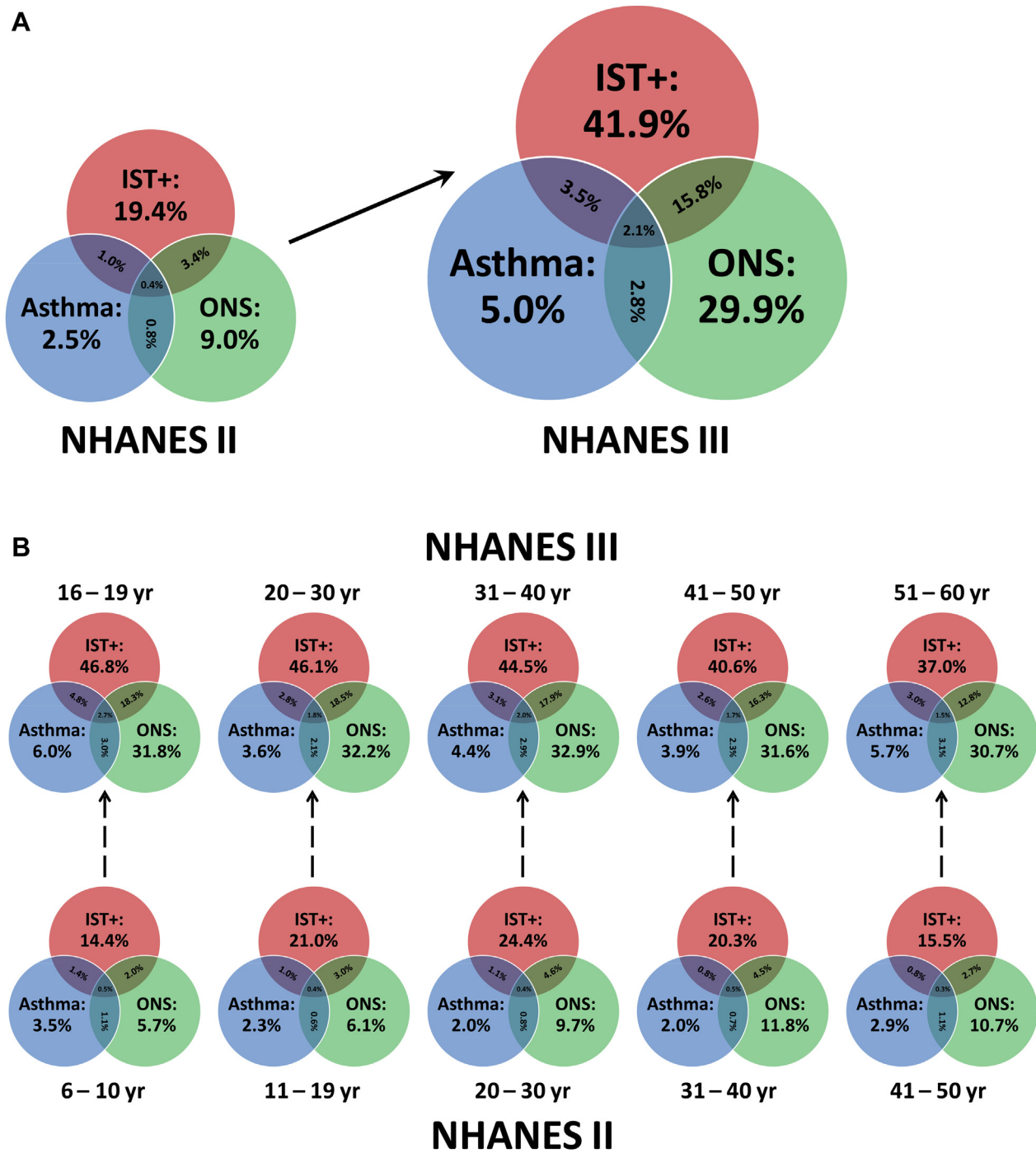


Figure 1. (A) Prevalence of asthma, oculonasal symptoms (ONS), intradermal skin test positivity (IST+) for at least 1 of the 6 common allergens, and symptom combinations during the Second and Third National Health and Nutrition Examination Surveys (NHANES II and NHANES III). (B) Prevalence of asthma, ONS, IST+, and symptom combinations for the specific age-related pair from NHANES II to NHANES III. Because NHANES II and NHANES III were approximately 10 years apart, test results in NHANES II for a certain age group were matched with the age group 10 years older in NHANES III.

positivity. The concurrence of asthma, oculonasal symptoms, and skin test positivity showed the greatest increase, ranging from 3.6 times (group D) to 5.9 times (group A).

Prevalence of Allergen-Specific Skin Test Positivity, Oculonasal Symptoms, and Asthma across NHANES II and NHANES III

For each of the 6 common allergens, the prevalence significantly increased ($P < .0001$ by χ^2 test) from NHANES II to NHANES III for skin test positivity alone, for skin test positivity and

oculonasal symptoms, and for the concurrence of skin test positivity, oculonasal symptoms, and asthma (Table 1). The largest prevalence increase from NHANES II to NHANES III was observed for cat, followed by Bermuda grass, *A alternata*, perennial rye, ragweed, and oak. For cat, the prevalence increased from 2.6% in NHANES II to 14.9% in NHANES III for skin test positivity, from 0.5% to 6.9% for the concurrence of skin test positivity and oculonasal symptoms, and from 0.1% to 1.2% for the concurrence of all 3. In addition, greater relative increases were observed for people with the concurrence of all 3: on average, a 9.6 times increase was

Table 1

Prevalence of skin test positivity, oculonasal symptoms, and asthma associated with each of the common allergens measured during NHANES II and NHANES III

Allergen	NHANES	Skin test positivity only			Skin test positivity and oculonasal symptoms			Skin test positivity, oculonasal symptoms, and asthma		
		Frequency ^a	% ^b	P value ^c	Frequency ^a	% ^b	P value ^c	Frequency ^a	% ^b	P value ^c
<i>Alternaria alternata</i>	II	434	3.9	<.0001	82	0.7	<.0001	12	0.1	<.0001
	III	1,516	14.0		625	5.8		117	1.1	
Bermuda grass	II	500	4.5	<.0001	107	1.0	<.0001	9	0.1	<.0001
	III	2,018	18.6		872	8.0		127	1.2	
Cat	II	289	2.6	<.0001	60	0.5	<.0001	10	0.1	<.0001
	III	1,619	14.9		749	6.9		126	1.2	
Oak	II	550	5.0	<.0001	120	1.1	<.0001	13	0.1	<.0001
	III	1,249	11.5		600	5.5		93	0.9	
Ragweed	II	1,217	11.0	<.0001	232	2.1	<.0001	26	0.2	<.0001
	III	2,830	26.1		1,156	1.7		162	1.5	
Perennial rye	II	1,191	1.8	<.0001	233	2.1	<.0001	24	0.2	<.0001
	III	2,905	26.8		1,168	1.8		158	1.5	

Abbreviation: NHANES, National Health and Nutrition Examination Survey.

^aThe number of people with skin test positivity alone, skin test positivity and oculonasal symptoms, and skin test positivity, oculonasal symptoms, and asthma associated with a specific allergen within a given NHANES period.^bThe percentage of skin test positivity alone, skin test positivity and oculonasal symptoms, and skin test positivity, oculonasal symptoms, and asthma cases for a specific allergen within a given NHANES period.^cP value by χ^2 test showing statistically significant difference in the prevalence of skin test positivity alone, skin test positivity and oculonasal symptoms, and skin test positivity, oculonasal symptoms, and asthma for each allergen from NHANES II to NHANES III.

observed for the prevalence of the concurrence of all 3, followed by a 7.3 times increase for the concurrence of skin test positivity and oculonasal symptoms and a 3.4 times increase for skin test positivity alone.

A similar increasing prevalence from NHANES II to NHANES III was observed for each of the 5 pairs of population groups. Figure 2 illustrates population pair-specific increases in the prevalence of skin test positivity only, with oculonasal symptoms, and all 3 for each of the 6 common allergens. All prevalence increases were statistically significant ($P < .001$ by χ^2 test). Among the 5 pairs of population groups, group A showed the greatest increase in the prevalence of skin test positivity alone and the concurrence of multiple symptoms: the prevalence of skin test positivity alone increased from 4.0 to 13.4 times across the 6 allergens; the prevalence of the concurrence of skin test positivity and oculonasal symptoms increased from 12.4 to 33.9 times; and the prevalence of

the concurrence of all 3 increased from 8.7 to 22.4 times. Across different population groups, the concurrence of multiple symptoms showed 2 to 3 times greater prevalence increase than positive skin test reactions alone.

The prevalence of oculonasal symptoms and asthma in populations with skin test positivity and negativity for each allergen is presented in Table 2. The prevalence of oculonasal symptoms and asthma increased significantly ($P < .0001$ by χ^2 test) from NHANES II to NHANES III not only in the skin test positive population but also in the skin test negative population for each of the 6 common allergens. Across the 6 common allergens, the prevalence of oculonasal symptoms and asthma increased 2.1 and 1.8 times, respectively, from NHANES II to NHANES III for the skin test positive population and increased 3.3 and 1.6 times, respectively, for the skin test negative population. Similar results were observed for each pair of population groups (eTable 1). Larger increases in the

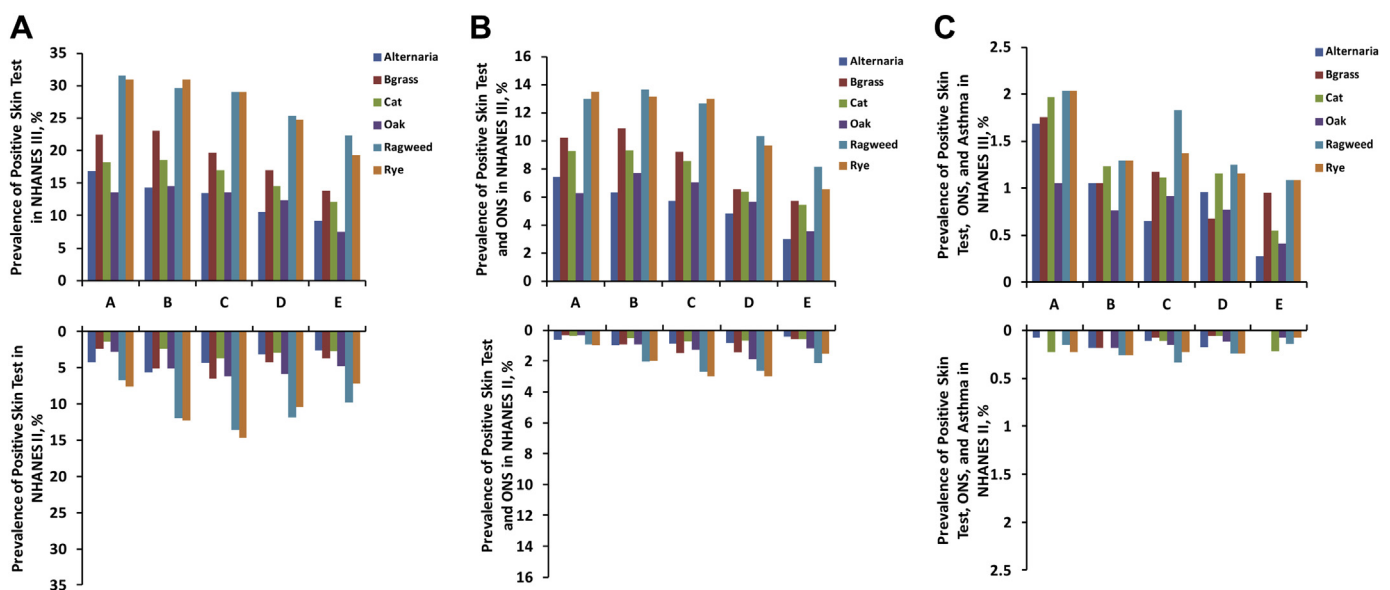


Figure 2. (A) Prevalence of skin test positivity for each common allergen during the Second and Third National Health and Nutrition Examination Surveys (NHANES II and NHANES III). (B) Prevalence of oculonasal symptoms (ONS) with allergen-specific positive skin test reactions. (C) Prevalence of asthma with ONS and with allergen-specific positive skin test reactions. Five age groups were investigated: A, 6 to 10 years old in NHANES II and 16 to 19 years old in NHANES III; B, 11 to 19 years old in NHANES II and 20 to 30 years old in NHANES III; C, 20 to 30 years old in NHANES II and 31 to 40 years old in NHANES III; D, 31 to 40 years old in NHANES II and 41 to 50 years old in NHANES III; E, 41 to 50 years old in NHANES II and 51 to 60 years old in NHANES III.

Table 2

Prevalence of oculonasal symptoms and asthma for skin test positive and negative populations for each allergen during NHANES II and NHANES III

Allergen	NHANES	Prevalence of oculonasal symptoms ^a						Prevalence of asthma ^b					
		Skin test positive population			Skin test negative population			Skin test positive population			Skin test negative population		
		n	%	P value	n	%	P value	n	%	P value	n	%	P value
<i>Alternaria alternata</i>	II	82	18.9	<.0001	909	8.6	<.0001	37	8.5	.01	238	2.2	<.0001
	III	625	41.2		2,617	28.1		199	13.1		348	3.7	
Bermuda grass	II	107	21.4	<.0001	884	8.4	<.0001	24	4.8	2E-04	251	2.4	<.0001
	III	872	43.2		2,370	26.9		204	1.1		343	3.9	
Cat	II	60	2.8	<.0001	931	8.7	<.0001	23	8.0	.032	252	2.3	<.0001
	III	749	46.3		2,493	27.1		200	12.4		347	3.8	
Oak	II	120	21.8	<.0001	871	8.3	<.0001	29	5.3	<.0001	246	2.3	<.0001
	III	600	48.0		2,642	27.6		152	12.2		395	4.1	
Ragweed	II	232	19.1	<.0001	759	7.7	<.0001	62	5.1	<.0001	213	2.2	<.0001
	III	1,156	4.8		2,086	26.1		270	9.5		277	3.5	
Perennial rye	II	233	19.6	<.0001	758	7.7	<.0001	60	5.0	<.0001	215	2.2	<.0001
	III	1,168	4.2		2,074	26.2		262	9.0		285	3.6	
≥1 Positive reaction ^c	II	371	17.3	<.0001	620	7.0	<.0001	109	5.1	<.0001	166	1.9	7E-04
	III	1,713	37.7		1,529	24.3		378	8.3		169	2.7	

Abbreviation: NHANES, National Health and Nutrition Examination Survey.

^aThe prevalence of ocular and nasal symptoms, including frequency (number) and percentage, for the skin test positive population and skin test negative population during NHANES II and NHANES III for each of the 6 common allergens. A χ^2 test (*P* value) was conducted to test prevalence differences across NHANES II and III.^bThe prevalence of asthma, including frequency (number) and percentage, for the skin test positive population and skin test negative population during NHANES II and NHANES III for each of the 6 common allergens. A χ^2 test (*P* value) was conducted to test prevalence differences across NHANES II and III.^cIn this category, skin test positive population means the skin test reaction is positive for at least 1 of the 6 common allergens, and skin test negative population means all skin test reactions are negative for the 6 common allergens.

prevalence of oculonasal symptoms and asthma were usually observed for younger groups (groups A and B) than for older groups (groups C–E).

Polysensitivity

From NHANES II to NHANES III, people had become sensitive to an increasing number of allergens. Table 3 presents the prevalence of skin test positivity for different cumulative numbers (range 0–6) of allergens, for the overall population, for the population with oculonasal symptoms, and for the population with oculonasal symptoms and asthma. Table 3 presents a clear pattern showing that a larger portion of the population was sensitive to an increasing number of allergens. During NHANES II, the prevalence of skin test positivity ranged from 0.2% for people allergic to all 6 allergens to 9.6% for people allergic to a single allergen. In contrast,

during NHANES III, the prevalence increased and ranged from 2.7% for people allergic to all 6 allergens to 14.1% for people allergic to a single allergen. All increases were statistically significant ($P < .0001$ by χ^2 test). The proportion of people allergic to all 6 allergens increased 15 times from NHANES II to NHANES III ($P < .0001$ by χ^2 test). There were no people with asthma and oculonasal symptoms allergic to all 6 allergens during NHANES II vs 13.3% during NHANES III ($P = .0002$ by χ^2 test).

A similar pattern of the change in polysensitivity was observed for each of the 5 pairs of population groups (Fig 3). From NHANES II to NHANES III, the prevalence of skin test positivity for people allergic to 5 or 6 allergens increased from 0.2% to 9.2% for group A, from 0.9% to 9.3% for group B, from 1.0% to 7.8% for group C, from 1.0% to 6.0% for group D, and from 0.5% to 4.1% for group E. All increases were statistically significant ($P < .001$ by χ^2 test).

Table 3

Prevalence of a cumulative number of skin test positivity during NHANES II and NHANES III for the overall population, the population with oculonasal symptoms, and the population with asthma and oculonasal symptoms

Positive skin test reactions, n	NHANES	Overall population			Population with oculonasal symptoms			Population with asthma and oculonasal symptoms		
		Frequency ^a	% ^b	P value ^c	Frequency ^a	% ^b	P value ^c	Frequency ^a	% ^b	P value ^c
0	II	8,900	8.6	<.0001	620	62.6	<.0001	48	52.7	<.0001
	III	6,295	58.1		1,529	47.2		76	25.3	
1	II	1,064	9.6	<.0001	140	14.1	.981	16	17.6	.234
	III	1,527	14.1		459	14.2		38	12.7	
2	II	507	4.6	<.0001	101	1.2	.301	12	13.2	.696
	III	899	8.3		295	9.1		35	11.7	
3	II	292	2.6	<.0001	57	5.8	.003	8	8.8	.28
	III	701	6.5		283	8.7		39	13.0	
4	II	196	1.8	<.0001	50	5.0	.0007	5	5.5	.029
	III	637	5.9		269	8.3		42	14.0	
5	II	67	.6	<.0001	17	1.7	<.0001	2	2.2	.017
	III	483	4.5		246	7.6		30	1.0	
6	II	18	.2	<.0001	6	0.6	<.0001	0	.0	.0002
	III	291	2.7		161	5.0		40	13.3	

Abbreviation: NHANES, National Health and Nutrition Examination Survey.

^aThe number of people with a certain number (from 0 to 6) of positive skin test reactions within the overall population, the population with oculonasal symptoms, and the population with asthma and oculonasal symptoms.^bThe percentage of people with a certain number (from 0 to 6) of positive skin test reactions during NHANES II or III within the overall population, the population with oculonasal symptoms, and the population with asthma and oculonasal symptoms.^c*P* value by χ^2 test showing statistical significance between NHANES II and NHANES III for each cumulative number of positive skin test reactions.

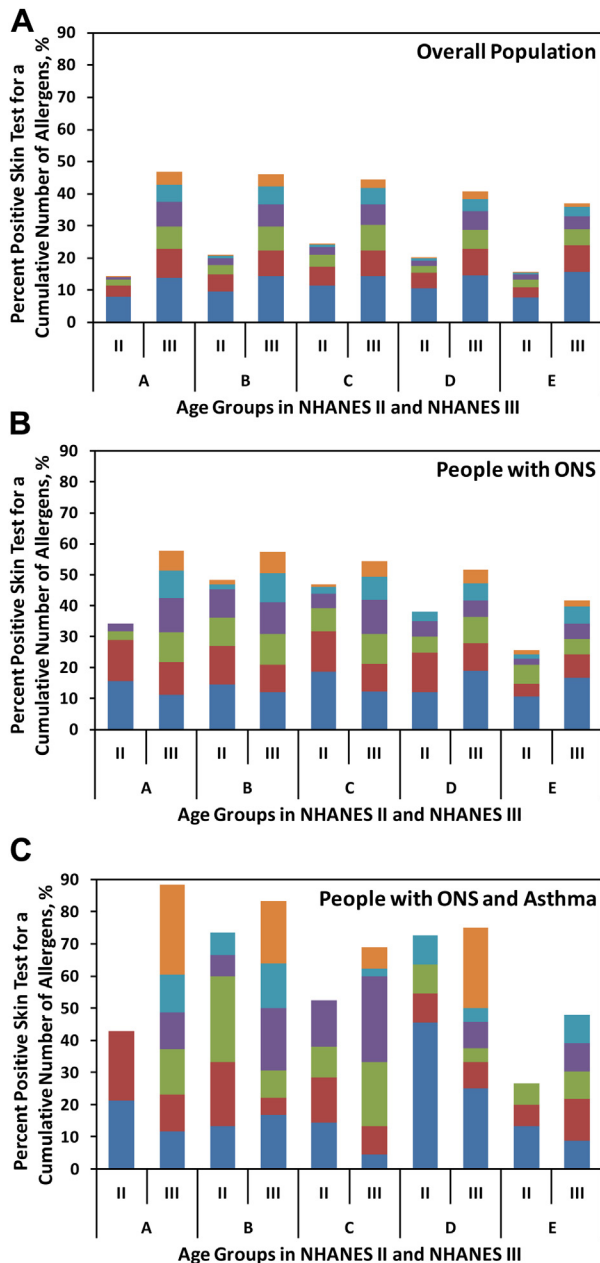


Figure 3. Prevalence of skin test positivity for a cumulative number of allergens during the Second and Third National Health and Nutrition Examination Surveys (NHANES II and NHANES III) for (A) the overall population, (B) people with oculonasal symptoms (ONS), and (C) people with ONS and asthma. Five age groups were investigated: A, 6 to 10 years old in NHANES II and 16 to 19 years old in NHANES III; B, 11 to 19 years old in NHANES II and 20 to 30 years old in NHANES III; C, 20 to 30 years old in NHANES II and 31 to 40 years old in NHANES III; D, 31 to 40 years old in NHANES II and 41 to 50 years old in NHANES III; E, 41 to 50 years old in NHANES II and 51 to 60 years old in NHANES III.

The prevalence of oculonasal symptoms, asthma, and concurrence of oculonasal symptoms and asthma increased from NHANES II to NHANES III for people with the same cumulative number of positive skin test reactions (range 0–6; Fig 4). Although most increases for asthma and the concurrence of asthma and oculonasal symptoms were not statistically significant, the prevalence of oculonasal symptoms was 2 to 3 times higher in NHANES III than in NHANES II, and all increases in oculonasal symptoms were statistically significant ($P < .0001$; except for people allergic

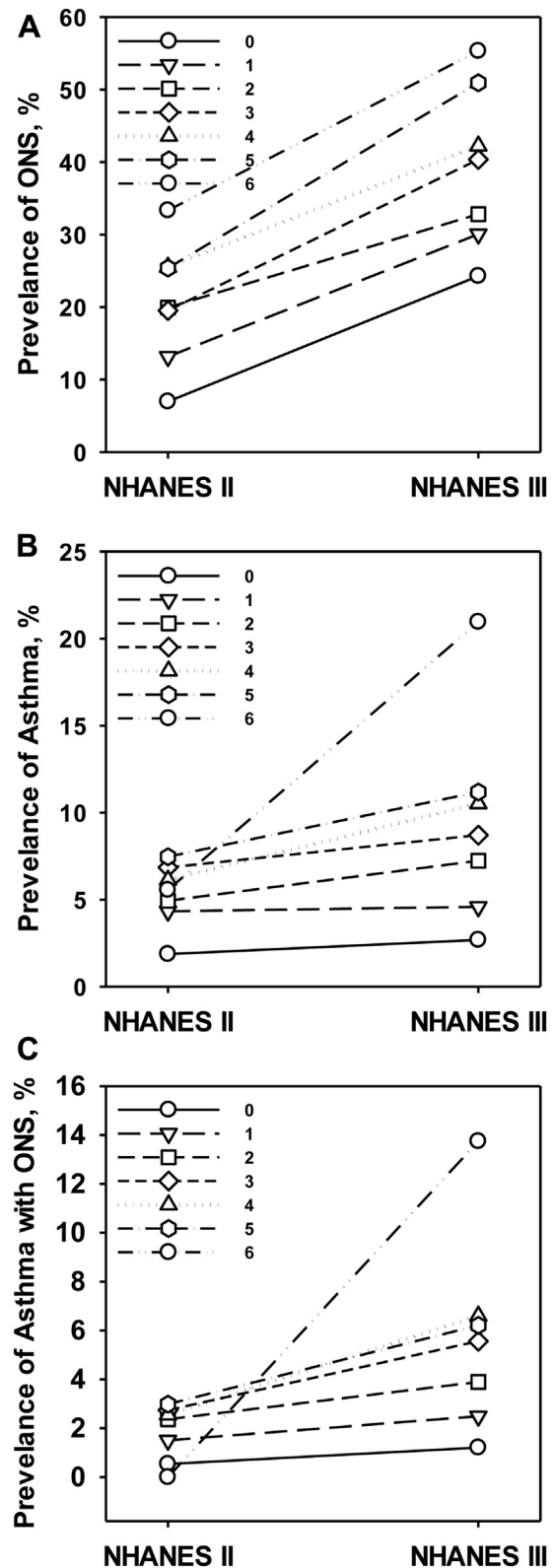


Figure 4. Prevalence of (A) oculonasal symptoms (ONS), (B) asthma, and (C) asthma and ONS during the Second and Third National Health and Nutrition Examination Surveys (NHANES II and NHANES III) within the population with different cumulative numbers (range 0–6) of skin test positivity to the 6 common allergens.

to all 6 allergens, $P = .069$ by χ^2 test). A similar pattern of prevalence increases was observed for each of the 5 population groups (eTable 2).

Associations among Skin Test Positivity, Oculonasal Symptoms, and Asthma

The correlation coefficients among skin test positivity, oculonasal symptoms, and asthma are presented in Table 4. Within each NHANES, the correlation coefficients among positive skin test reactions, oculonasal symptoms, and asthma, although small, were statistically significant because of the large sample. Stronger correlation coefficients among all 3 were observed in NHANES III compared with NHANES II. Correlation coefficients between asthma and positive skin test reactions doubled or tripled in NHANES III (eg, 0.04 in NHANES II vs 0.12 in NHANES III for oak). A similar pattern was observed for each of the 5 populations groups (groups A–E; eTable 3). In addition, a significant linear association ($P < .0001$ by Cochran–Armitage test) was observed between the cumulative number of positive skin test reactions (range 0–6) and the prevalence of oculonasal symptoms or asthma, and this linear association was stronger during NHANES III.

Discussion

This study provides insights into the progression of asthma and allergic disease (the “allergic diathesis progression”) in a changing population milieu from the 1970s through the 1990s. First, during the 20-year course of NHANES II and NHANES III, the prevalences of skin test positivity, oculonasal symptoms, asthma, and their concurrence increased. Second, the associations among skin test positivity, oculonasal symptoms, and asthma changed over time from NHANES II to NHANES III, suggesting a change of the association of skin test reaction, oculonasal symptoms, and asthma over time. The associations between skin tests and oculonasal symptoms and asthma were stronger in NHANES III than in NHANES II, suggesting that oculonasal symptoms and asthma might have developed more often from positive skin test reactions during NHANES III compared with NHANES II. The change in the association among skin test reaction, oculonasal symptoms, and asthma complicates the projection of public health in the future because it appears that the prediction for the future public health burden of allergic diseases will not be linear,^{17,18} indicating that the current associations among skin test reactions, oculonasal symptoms, and asthma change with changing environments and lifestyles. Third, people were becoming more sensitized to an increasing number of allergens. The prevalence of skin test positivity to all 6 allergens increased from 0.2% in NHANES II to 2.7% in NHANES III ($P < .0001$), which demonstrates an increased propensity for allergen polysensitivity. Fourth, the prevalence of allergies of 1 age group to

another 10 years older in the 2 populations from NHANES II to NHANES III was charted. The prevalence in skin test positivity, oculonasal symptoms, and asthma and the tendency for polysensitivity increased for each of the 5 population groups.

The increased prevalence of skin test positivity could be attributed to methodologic differences in the conduction of allergen-specific skin tests in NHANES II and III.^{19–22} A major difference was the lack of consistent allergen extract standardization. This and minor differences, such as medical exclusion criteria, control (histamine) concentrations, and skin test reading times in the 2 periods, might have caused variability in individual reactivity and could make comparisons suspect. However, previous studies have scrutinized these methodologic differences¹⁰ and have provided convincing evidence and reasonable interpretations that the increased prevalences are likely to be true, despite methodologic differences, although caution should be used to interpret the results.

The increased prevalence of atopic diseases observed in this study also is consistent with the findings from other developed countries^{5,23} and can be attributed to multiple factors, including environmental exposures, westernized lifestyles, obesity, microbiomes, antibiotic use, and altered gene–environment interactions. Changes in environmental factors affect allergen exposure and allergenicity.¹⁷ For instance, increasing levels of carbon dioxide and ozone change the allergen content of the atmosphere, leading to increased sensitization and exacerbation of existing allergic airway disease.^{24,25} In addition, plant productivity and airborne pollen levels have been increasing in outdoor environments as a result of climate change.^{3,26} Poor ventilation rates, stable indoor temperatures, and humidity levels promote the growth of perennial indoor allergens such as molds and fungi.³ Poor indoor air quality increases the risk of developing allergic diseases, especially in urban substandard housing.^{18,27,28} These changes affect allergen production and allergenicity in indoor and outdoor environments.

Changes in lifestyle and indoor and outdoor environments during the past quarter of the 20th century are purported to be risk factors in the development and progression of the atopic phenotype, including asthma.²⁹ Modifiable risk factors, such as sedentary lifestyles (home and workplace), during that period led to increased exposures to indoor allergens, such as mold, cat, cockroach, dust mite, and endotoxins.²⁴ Previous studies have described a dose-to-response relation between obesity and allergy.¹ Obesity and allergy reached epidemic proportions in the 1990s and have plateaued since. Westernized lifestyles and residence in a developed country also have been linked to increased occurrence of allergic disease through as yet unidentified mechanisms.^{30,31} In

Table 4
Associations between skin test sensitivity and oculonasal symptoms and between skin test sensitivity and asthma for each of the 6 common allergens during NHANES II and NHANES III

Intradermal skin testing	NHANES	Associations between skin test sensitivity and oculonasal symptoms		Associations between skin test sensitivity and Asthma	
		Correlation coefficient (ϕ) ^a	P value ^b	Correlation coefficient (ϕ) ^a	P value ^b
<i>Alternaria alternata</i>	II	0.07	<.0001	0.08	<.0001
	III	0.10	<.0001	0.15	<.0001
Bermuda grass	II	0.09	<.0001	0.03	.0007
	III	0.14	<.0001	0.11	<.0001
Cat	II	0.07	<.0001	0.06	<.0001
	III	0.15	<.0001	0.14	<.0001
Oak	II	0.10	<.0001	0.04	<.0001
	III	0.14	<.0001	0.12	<.0001
Ragweed	II	0.12	<.0001	0.06	<.0001
	III	0.14	<.0001	0.12	<.0001
Perennial rye	II	0.13	<.0001	0.06	<.0001
	III	0.14	<.0001	0.11	<.0001

Abbreviation: NHANES, National Health and Nutrition Examination Survey.

^aThe ϕ correlation coefficients reflect the strength of association between 2 nominal variables.

^bP value by χ^2 test showing the statistical significance of the association (ϕ) within each NHANES.

addition, various epigenetic mechanisms underlying gene–environment interactions appear to be responsible for the skewing of T-helper cell types (T_H) 1 and 2 in developed nations, which contributes to the increased prevalence of an atopic status, whereas there has been a trend of decreasing infectious triggers in the past century. For most people who have clinically documented allergic responses, allergens specifically stimulate T_H2 cells to produce specific cytokines (ie, interleukin-4, interleukin-5, and interleukin-13) rather than the cytokines produced by T_H1 cells (interferon- γ and interleukin-2). Thus, the allergic phenotype demonstrates an unbalanced T_H2 skewing with its resultant cytokine cascade compared with T_H1 . Obesity also contributes more to a T_H2 inflammatory cascade, among other mechanisms. In contrast, T_H1 activation is commonly seen in developing countries with many prevalent infectious diseases. The lack of infectious diseases and obesogenic environments of the West and the different life-style factors described appear to act synergistically to cause an increase in allergy prevalence.

This study had several strengths. In this study, for the first time, the prevalences of positive skin test reactions, oculonasal symptoms, and asthma and the associations among skin test positivity, oculonasal symptoms, and asthma were studied over 20 years using NHANES II and NHANES III data. Second, allergen-specific skin test results were objectively recorded and had minimal observer bias in the end point. Third, the use of a nationally representative dataset makes significant population inferences possible from the results. The difference between this study and other studies that also use NHANES is innovative because previous studies examined patients within the NHANES at the time when the study was conducted. There was no follow-up to the present time. In other words, other studies have examined only the incidence of asthma during the period of the study. One major uncertainty of this study was the methodologic differences in the conduction of allergen-specific skin tests in NHANES II and III, which was discussed earlier.

Despite the limitations, this study highlights the need for continued surveillance of allergic disease to promote public health and decrease the clinical and economic burden of allergies and asthma, especially with changing environments and lifestyles over time. Future longitudinal studies with better exposure assessments and allergen allergenicity quantification are needed to improve the prediction of the disease burden of allergies and asthma. A better understanding of personal exposure to indoor and outdoor allergens and their aero-allergenicity will help identify vulnerable populations. The importance of exposure mitigation in the primordial prevention of atopic sensitization has been established. Studies have suggested that 39% of physician-diagnosed cases of asthma in the United States could be avoided by eliminating different environmental exposures.³² Eliminating potential sources of early life personal exposure could attenuate the prevalence of atopic sensitization, whereby a large percentage of asthma and allergic disease can be prevented. In later life, ubiquitous allergen avoidance has been helpful to ameliorate asthma exacerbations.

Supplementary Data

Supplementary data related to this article can be found at <http://dx.doi.org/10.1016/j.anai.2015.11.006>.

References

- [1] Redd SC. Asthma in the United States: burden and current theories. *Environ Health Perspect*. 2002;110:556–557.
- [2] Bielory L, Lyons K, Goldberg R. Climate change and allergic disease. *Curr Allergy Asthma Rep*. 2012;12:485–494.
- [3] Institute of Medicine. *Clearing the Air: Asthma and Indoor Air Exposures*. Washington, DC: The National Academies Press; 2000.
- [4] Ogden CL, Carroll MD, Kit BK, Flegal KM. Prevalence of childhood and adult obesity in the United States, 2011–2012. *JAMA*. 2014;311:806–814.
- [5] Hahm MI, Chae Y, Kwon HJ, et al. Do newly built homes affect rhinitis in children? The ISAAC phase III study in Korea. *Allergy*. 2014;69:479–487.
- [6] Hampton T. Studies probe links between childhood asthma and obesity. *JAMA*. 2014;311:1718–1719.
- [7] Haahtela T, Holgate S, Pawankar R, et al. The biodiversity hypothesis and allergic disease: World Allergy Organization position statement. *World Allergy Organ J*. 2013;6:3.
- [8] Yang S-I, Lee E, Jung Y-H, et al. Effect of antibiotic use and mold exposure in infancy on allergic rhinitis in susceptible adolescents. *Ann Allergy Asthma Immunol*. 2014;113:160–165.
- [9] Sears MR. Trends in the prevalence of asthma. *Chest*. 2014;145:219–225.
- [10] 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;116:377–383.
- [11] Salo PM, Calatroni A, Gergen PJ, et al. Allergy-related outcomes in relation to serum IgE: results from the National Health and Nutrition Examination Survey 2005–2006. *J Allergy Clin Immunol*. 2011;127:1226–1235.e7.
- [12] US Environmental Protection Agency. *Integrated Science Assessment for Lead (Final Report)*. Washington, DC: US Environmental Protection Agency; 2013.
- [13] Bousquet J, Vignola AM, Demoly P. Links between rhinitis and asthma. *Allergy*. 2003;58:691–706.
- [14] Bryant-Stephens T. Asthma disparities in urban environments. *J Allergy Clin Immunol*. 2009;123:1199–1206.
- [15] Centers for Disease Control and Prevention. *Training Manual for Allergy Component. National Health and Nutrition Examination Survey III*. Atlanta, GA: Centers for Disease Control and Prevention; 1988.
- [16] Privitera GJ. *Statistics for the Behavioral Sciences*. Thousand Oaks, CA: Sage Publications; 2014.
- [17] Zhang Y, Isukapalli SS, Bielory L, Georgopoulos PG. Bayesian analysis of climate change effects on observed and projected airborne levels of birch pollen. *Atmos Environ*. 2013;68:64–73.
- [18] Morello-Frosch R, Zuk M, Jerrett M, Shamasunder B, Kyle AD. Understanding the cumulative impacts of inequalities in environmental health: implications for policy. *Health Aff*. 2011;30:879–887.
- [19] Norrman G, Fälth-Magnusson K. Adverse reactions to skin prick testing in children—prevalence and possible risk factors. *Pediatr Allergy Immunol*. 2009;20:273–278.
- [20] Karila C. Allergen skin prick tests in asthmatic infants and young children. *Trends Asthma Res*. 2005;67–78.
- [21] van Ree R. Indoor allergens: relevance of major allergen measurements and standardization. *J Allergy Clin Immunol*. 2007;119:270–277. quiz 278–279.
- [22] Chapman MD, Ferreira F, Villalba M, et al. The European Union CREATE project: a model for international standardization of allergy diagnostics and vaccines. *J Allergy Clin Immunol*. 2008;122:882–889.e2.
- [23] Downs SH, Marks GB, Sporik R, Belosouva EG, Car NG, Peat JK. Continued increase in the prevalence of asthma and atopy. *Arch Dis Child*. 2001;84:20–23.
- [24] Singer BD, Ziska LH, Frenz DA, Gebhard DE, Straka JG. Increasing Amb a 1 content in common ragweed (*Ambrosia artemisiifolia*) pollen as a function of rising atmospheric CO₂ concentration. *Funct Plant Biol*. 2005;32:667–670.
- [25] Schelegle ES, Miller LA, Gershwin LJ, et al. Repeated episodes of ozone inhalation amplifies the effects of allergen sensitization and inhalation on airway immune and structural development in Rhesus monkeys. *Toxicol Appl Pharmacol*. 2003;191:74–85.
- [26] Busse PJ, Cohn RD, Salo PM, Zeldin DC. Characteristics of allergic sensitization among asthmatic adults older than 55 years: results from the National Health and Nutrition Examination Survey, 2005–2006. *Ann Allergy Asthma Immunol*. 2013;110:247–252.
- [27] Rauh VA, Chew GL, Garfinkel RS. Deteriorated housing contributes to high cockroach allergen levels in inner-city households. *Environ Health Perspect*. 2002;110:323–327.
- [28] Antonny B, Audhya J, I Bagnat M, et al. Directing traffic into the future. *Dev Cell*. 2013;27:480–484.
- [29] Beggs PJ. Climate change and plant food allergens. *J Allergy Clin Immunol*. 2009;123:271–272.
- [30] Ho SM. Environmental epigenetics of asthma: an update. *J Allergy Clin Immunol*. 2010;126:453–465.
- [31] Herbert OC, Barnetson RS, Weninger W, Kramer U, Behrendt H, Ring J. Western lifestyle and increased prevalence of atopic diseases: an example from a small Papua New Guinean island. *World Allergy Organ J*. 2009;2:130–137.
- [32] Lanphear BP, Aligne CA, Auinger P, Weitzman M, Byrd RS. Residential exposures associated with asthma in US children. *Pediatrics*. 2001;107:505–511.

eTable 1

Prevalence of oculonasal symptoms and asthma for skin test positive and negative populations for each allergen during NHANES II and NHANES III, stratified by age groups

Population ^a	Allergen	NHANES	Prevalence of oculonasal symptoms ^b						Prevalence of asthma ^c					
			Skin test positive population			Skin test negative population			Skin test positive population			Skin test negative population		
			n	%	P value	n	%	P value	n	%	P value	n	%	P value
A	<i>Alternaria alternata</i>	II	8	14.3	<.0001	68	5.3	<.0001	10	17.9	.95	36	2.8	.214
		III	106	44.2	<.0001	347	29.3		42	17.5	.95	44	3.7	
	Bermuda grass	II	4	12.9	5E-04	72	5.5	<.0001	1	3.2	.093	45	3.5	.659
		III	145	45.5	5E-04	308	27.9		44	13.8	.093	42	3.8	
	Cat	II	5	27.8	.057	71	5.4	<.0001	4	22.2	.417	42	3.2	.266
		III	132	51.0	.057	321	27.6		39	15.1	.417	47	4.0	
	Oak	II	4	1.8	<.0001	72	5.6	<.0001	2	5.4	.132	44	3.4	.095
		III	89	46.1	<.0001	364	29.6		28	14.5	.132	58	4.7	
	Ragweed	II	12	13.5	<.0001	64	5.2	<.0001	7	7.9	.258	39	3.1	.853
		III	185	41.2	<.0001	268	27.5		54	12.0	.258	32	3.3	
B	Perennial rye	II	13	12.9	<.0001	63	5.1	<.0001	8	7.9	.316	38	3.1	.458
		III	192	43.5	<.0001	261	26.6		50	11.3	.316	36	3.7	
	≥1 Positive reaction ^d	II	26	13.6	<.0001	50	4.4	<.0001	18	9.4	.75	28	2.5	.909
		III	261	39.2	<.0001	192	25.4		68	1.2	.75	18	2.4	
	<i>Alternaria alternata</i>	II	26	17.1	<.0001	140	5.5	<.0001	12	7.9	.427	50	2.0	.223
		III	108	44.4	<.0001	440	3.2		25	1.3	.427	37	2.5	
	Bermuda grass	II	25	18.0	<.0001	141	5.5	<.0001	9	6.5	.873	53	2.1	.225
		III	185	47.1	<.0001	363	27.7		27	6.9	.873	35	2.7	
	Cat	II	14	21.5	<.0001	152	5.7	<.0001	3	4.6	.203	59	2.2	.873
		III	159	5.3	<.0001	389	28.1		30	9.5	.203	32	2.3	
C	Oak	II	25	18.2	<.0001	141	5.5	<.0001	7	5.1	.142	55	2.1	.272
		III	131	53.0	<.0001	417	28.7		23	9.3	.142	39	2.7	
	Ragweed	II	55	17.0	<.0001	111	4.6	<.0001	17	5.3	.387	45	1.9	.365
		III	232	46.0	<.0001	316	26.4		34	6.7	.387	28	2.3	
	Perennial rye	II	53	16.0	<.0001	113	4.7	<.0001	15	4.5	.162	47	2.0	.639
		III	224	42.5	<.0001	324	27.6		36	6.8	.162	26	2.2	
	≥1 positive reaction ^d	II	80	14.1	<.0001	86	4.0	<.0001	28	4.9	.401	34	1.6	.921
		III	315	4.1	<.0001	233	25.4		47	6.0	.401	15	1.6	
	<i>Alternaria alternata</i>	II	23	19.8	<.0001	239	9.3	<.0001	10	8.6	.971	45	1.7	2E-04
		III	87	42.2	<.0001	417	31.5		18	8.7	.971	49	3.7	
D	Bermuda grass	II	39	22.3	<.0001	223	8.9	<.0001	6	3.4	.029	49	1.9	.009
		III	141	46.8	<.0001	363	29.5		26	8.6	.029	41	3.3	
	Cat	II	19	19.4	<.0001	243	9.4	<.0001	9	9.2	.66	46	1.8	.01
		III	131	5.4	<.0001	373	29.3		28	1.8	.66	39	3.1	
	Oak	II	34	2.2	<.0001	228	9.0	<.0001	10	6.0	.044	45	1.8	.006
		III	108	51.9	<.0001	396	29.9		25	12.0	.044	42	3.2	
	Ragweed	II	72	19.7	<.0001	190	8.2	<.0001	18	4.9	.019	37	1.6	.104
		III	194	43.6	<.0001	310	28.5		41	9.2	.019	26	2.4	
	Perennial rye	II	80	2.3	<.0001	182	7.9	<.0001	18	4.6	.135	37	1.6	.002
		III	199	44.8	<.0001	305	28.1		31	7.0	.135	36	3.3	
E	≥1 positive reaction ^d	II	123	18.7	<.0001	139	6.8	<.0001	29	4.4	.049	26	1.3	.035
		III	274	4.2	<.0001	230	27.1		47	6.9	.049	20	2.4	
	<i>Alternaria alternata</i>	II	14	26.9	.024	183	11.3	<.0001	4	7.7	.636	29	1.8	.02
		III	50	45.5	.024	278	29.9		11	1.0	.636	30	3.2	
	Bermuda grass	II	24	33.8	.477	173	1.8	<.0001	3	4.2	.533	30	1.9	.014
		III	68	38.6	.477	260	3.1		11	6.3	.533	30	3.5	
	Cat	II	11	22.4	.008	186	11.4	<.0001	2	4.1	.166	31	1.9	.141
		III	66	43.7	.008	262	29.5		16	1.6	.166	25	2.8	
	Oak	II	31	31.6	.031	166	1.5	<.0001	4	4.1	.255	29	1.8	.014
		III	59	45.7	.031	269	29.6		10	7.8	.255	31	3.4	
	Ragweed	II	44	22.1	<.0001	153	1.4	<.0001	7	3.5	.118	26	1.8	.063
		III	107	4.7	<.0001	221	28.5		18	6.8	.118	23	3.0	
	perennial rye	II	50	28.6	.027	147	9.8	<.0001	7	4.0	.394	26	1.7	.016
		III	100	38.9	.027	228	29.2		15	5.8	.394	26	3.3	
	≥1 positive reaction ^d	II	75	22.1	<.0001	122	9.1	<.0001	14	4.1	.168	19	1.4	.178
		III	169	4.0	<.0001	159	25.8		27	6.4	.168	14	2.3	
	<i>Alternaria alternata</i>	II	6	16.7	.086	143	1.5	<.0001	0	.0	.022	40	2.9	.023
		III	22	32.4	.086	204	3.6		9	13.2	.022	33	4.9	
	Bermuda grass	II	8	15.7	.002	141	1.5	<.0001	2	3.9	.084	38	2.8	.045
		III	42	41.2	.002	184	29.1		13	12.7	.084	29	4.6	
	Cat	II	8	21.1	.011	141	1.4	<.0001	4	1.5	.786	36	2.7	.003
		III	40	44.9	.011	186	28.8		8	9.0	.786	34	5.3	
	Oak	II	16	24.2	.008	133	1.0	<.0001	4	6.1	.204	36	2.7	.005
		III	26	47.3	.008	200	29.4		7	12.7	.204	35	5.1	
	Ragweed	II	30	21.9	.006	119	9.5	<.0001	7	5.1	.131	33	2.6	.031
		III	60	36.6	.006	166	29.1		16	9.8	.131	26	4.6	

(continued on next page)

eTable 1 (continued)

Population ^a	Allergen	NHANES	Prevalence of oculonasal symptoms ^b						Prevalence of asthma ^c					
			Skin test positive population			Skin test negative population			Skin test positive population			Skin test negative population		
			n	%	P value	n	%	P value	n	%	P value	n	%	P value
	Perennial rye	II	21	21.0	.03	128	9.9	<.0001	5	5.0	.166	35	2.7	.024
		III	48	33.8	.03	178	3.0		14	9.9	.166	28	4.7	
		≥1 positive reaction ^d	38	17.6	<.0001	111	9.4	<.0001	11	5.1	.191	29	2.5	.047
		III	94	34.6	<.0001	132	28.5		22	8.1	.191	20	4.3	

Abbreviation: NHANES, National Health and Nutrition Examination Survey.

^aFive age groups were investigated: A, 6 to 10 years old in NHANES II and 16 to 19 years old in NHANES III; B, 11 to 19 years old in NHANES II and 20 to 30 years old in NHANES III; C, 20 to 30 years old in NHANES II and 31 to 40 years old in NHANES III; D, 31 to 40 years old in NHANES II and 41 to 50 years old in NHANES III; E, 41 to 50 years old in NHANES II and 51 to 60 years old in NHANES III.

^bThe prevalence of oculonasal symptoms, including frequency (number) and percentage, for the skin test positive population and skin test negative population during NHANES II and NHANES III for each of the 6 common allergens. A χ^2 test (*P* value) was conducted to test prevalence differences across NHANES II and III.

^cThe prevalence of asthma, including frequency (number) and percentage, for the skin test positive population and skin test negative population during NHANES II and NHANES III for each of the 6 common allergens. A χ^2 test (*P* value) was conducted to test prevalence differences across NHANES II and III.

^dIn this category, skin test positive population means the skin test reaction is positive for at least 1 of the 6 common allergens, and skin test negative population means all skin test reactions are negative for the 6 common allergens.

eTable 2

Prevalence of oculonasal symptoms, asthma, and asthma and oculonasal symptoms during NHANES II and NHANES III within the population with different numbers of positive skin test reactions (range 0–6) to the 6 common allergens for each age group

Population ^a	Cumulative number of positive skin test reactions	NHANES	Prevalence of oculonasal symptoms ^b			Prevalence of asthma ^c			Prevalence of asthma and oculonasal symptoms ^d		
			n	%	P value	n	%	P value	n	%	P value
A	0	II	50	4.4	<.0001	28	2.5	.9088	8	.7	.9126
		III	192	25.4		18	2.4		5	.7	
	1	II	12	11.2	.0029	10	9.3	.0955	3	2.8	.879
		III	51	25.6		9	4.5		5	2.5	
	2	II	10	22.2	.0618	5	11.1	.6161	3	6.7	.4482
		III	48	37.5		11	8.6		5	3.9	
	3	II	2	7.7	.0007	2	7.7	.8227	0	.0	.1983
		III	43	43.4		9	9.1		6	6.1	
	4	II	2	2.0	.0978	0	.0	.2661	0	.0	.4869
		III	51	47.2		12	11.1		5	4.6	
	5	II	0	.0	.3014	0	.0	.6788	0	.0	.7894
		III	39	52.0		11	14.7		5	6.7	
B	0	II	0	.0	.1572	1	5.0	.5009	0	.0	.4672
		III	29	5.9		16	28.1		12	21.1	
	1	II	86	4.0	<.0001	34	1.6	.9209	4	.2	.0378
		III	233	25.4		15	1.6		6	.7	
	2	II	24	9.1	<.0001	9	3.4	.8643	2	.8	.1237
		III	66	27.2		9	3.7		6	2.5	
	3	II	21	14.5	<.0001	10	6.9	.214	3	2.1	.6865
		III	48	34.5		5	3.6		2	1.4	
	4	II	15	19.5	.0005	4	5.2	.4657	4	5.2	.2813
		III	55	43.3		4	3.1		3	2.4	
	5	II	15	25.9	.0053	3	5.2	.3317	1	1.7	.2042
		III	56	47.9		11	9.4		7	6.0	
C	0	II	3	16.7	.0027	2	11.1	.723	1	5.6	.9674
		III	52	55.3		8	8.5		5	5.3	
	1	II	2	28.6	.1305	0	.0	.2634	0	.0	.3608
		III	38	58.5		10	15.4		7	1.8	
	2	II	139	6.8	<.0001	26	1.3	.035	10	.5	.0018
		III	230	27.1		20	2.4		14	1.6	
	3	II	49	15.9	.0005	10	3.2	.743	3	1.0	.9463
		III	62	28.3		6	2.7		2	.9	
	4	II	34	21.8	.0085	4	2.6	.3147	3	1.9	.4949
		III	45	36.0		6	4.8		4	3.2	
	5	II	20	19.2	.0009	9	8.7	.7375	2	1.9	.0558
		III	48	39.7		9	7.4		9	7.4	
D	0	II	12	19.0	<.0001	4	6.3	.1572	3	4.8	.1067
		III	56	57.7		13	13.4		12	12.4	
	1	II	6	26.1	.0432	2	8.7	.9017	0	.0	.5803
		III	38	5.0		6	7.9		1	1.3	
	2	II	2	66.7	.7385	0	.0	.4539	0	.0	.6402
		III	25	56.8		7	15.9		3	6.8	
	3	II	122	9.1	<.0001	19	1.4	.1777	3	.2	.0234
		III	159	25.8		14	2.3		6	1.0	
	4	II	24	13.3	<.0001	9	5.0	.7227	5	2.8	.5606
		III	62	4.5		9	5.9		6	3.9	
	5	II	25	32.5	.7825	1	1.3	.0693	1	1.3	.612
		III	29	34.5		6	7.1		2	2.4	
E	0	II	10	25.6	.0487	1	2.6	.8488	1	2.6	.7383
		III	28	45.2		2	3.2		1	1.6	
	1	II	10	4.0	.3714	2	8.0	.3546	0	.0	.3556
		III	18	3.0		2	3.3		2	3.3	
	2	II	6	4.0	.6836	1	6.7	.825	1	6.7	.4746
		III	18	46.2		2	5.1		1	2.6	
	3	II	0	.0	.0566	0	.0	.3261	0	.0	.3261
		III	14	58.3		6	25.0		6	25.0	
	4	II	111	9.4	<.0001	29	2.5	.0469	11	.9	.0102
		III	132	28.5		20	4.3		12	2.6	
	5	II	16	15.0	.0019	5	4.7	.8634	2	1.9	.935
		III	38	32.8		6	5.2		2	1.7	
F	0	II	6	13.0	.0584	2	4.3	.8753	1	2.2	.4492
		III	17	28.3		3	5.0		3	5.0	
	1	II	9	28.1	.9395	3	9.4	.8729	1	3.1	.6599
		III	11	28.9		4	1.5		2	5.3	
	2	II	3	12.5	.0299	1	4.2	.2172	0	.0	.1818
		III	11	39.3		4	14.3		2	7.1	

(continued on next page)

eTable 2 (continued)

Population ^a	Cumulative number of positive skin test reactions	NHANES	Prevalence of oculonasal symptoms ^b			Prevalence of asthma ^c			Prevalence of asthma and oculonasal symptoms ^d		
			n	%	P value	n	%	P value	n	%	P value
5		II	2	4.0	.4381	0	.0	.3811	0	.0	.4835
		III	13	59.1		3	13.6		2	9.1	
6		II	2	10.0	.1967	0	.0	.4292			
		III	4	5.0		2	25.0				

Abbreviation: NHANES, National Health and Nutrition Examination Survey.

^aFive age groups were investigated: A, 6 to 10 in NHANES II and 16 to 19 years old in NHANES III; B, 11 to 19 years old in NHANES II and 20 to 30 years old in NHANES III; C, 20 to 30 years old in NHANES II and 31 to 40 years old in NHANES III; D, 31 to 40 years old in NHANES II and 41 to 50 years old in NHANES III; E, 41 to 50 years old in NHANES II and 51 to 60 years old in NHANES III.

^bThe prevalence of oculonasal symptoms, including frequency (number) and percentage, within each population with different cumulative numbers of skin test reactions during NHANES II and NHANES III for each of the 6 common allergens. A χ^2 test (*P* value) was conducted to test prevalence differences across NHANES II and III.

^cThe prevalence of asthma, including frequency (number) and percentage, within each population with different cumulative numbers of positive skin test reactions during NHANES II and NHANES III for each of the 6 common allergens. A χ^2 test (*P* value) was conducted to test prevalence differences across NHANES II and III.

^dThe prevalence of concurrence of asthma and oculonasal symptoms, including frequency (number) and percentage, within each population with different cumulative numbers of positive skin test reactions during NHANES II and NHANES III for each of the 6 common allergens. A χ^2 test (*P* value) was conducted to test prevalence differences across NHANES II and III.

eTable 3

Associations between skin test sensitivity and oculonasal symptoms and between skin test sensitivity and asthma for each subpopulation during NHANES II and NHANES III

Population ^a	Allergen	NHANES	Associations between skin test sensitivity and oculonasal symptoms		Associations between skin test sensitivity and asthma	
			Correlation coefficient (ϕ) ^b	P value	Correlation coefficient (ϕ) ^b	P value
A	<i>Alternaria alternata</i>	II	0.08	.0048	0.17	<.0001
		III	0.12	<.0001	0.22	<.0001
	Bermuda grass	II	0.05	.0813	0.00	.9422
		III	0.16	<.0001	0.17	<.0001
	Cat	II	0.11	<.0001	0.12	<.0001
		III	0.19	<.0001	0.18	<.0001
	Oak	II	0.04	.1761	0.02	.5117
		III	0.12	<.0001	0.14	<.0001
	Ragweed	II	0.09	.0011	0.06	.0186
		III	0.14	<.0001	0.17	<.0001
B	Perennial rye	II	0.09	.0013	0.07	.0108
		III	0.17	<.0001	0.15	<.0001
	<i>Alternaria alternata</i>	II	0.11	<.0001	0.09	<.0001
		III	0.11	<.0001	0.14	<.0001
	Bermuda grass	II	0.12	<.0001	0.07	.0007
		III	0.17	<.0001	0.09	<.0001
	Cat	II	0.10	<.0001	0.02	.2037
		III	0.19	<.0001	0.15	<.0001
	Oak	II	0.12	<.0001	0.04	.0233
		III	0.18	<.0001	0.12	<.0001
C	Ragweed	II	0.17	<.0001	0.07	.0001
		III	0.19	<.0001	0.11	<.0001
	Perennial rye	II	0.15	<.0001	0.06	.0037
		III	0.15	<.0001	0.11	<.0001
	<i>Alternaria alternata</i>	II	0.07	.0002	0.10	<.0001
		III	0.08	.0022	0.08	.001
	Bermuda grass	II	0.11	<.0001	0.03	.1797
		III	0.15	<.0001	0.10	<.0001
	Cat	II	0.06	.001	0.10	<.0001
		III	0.17	<.0001	0.14	<.0001
D	Oak	II	0.09	<.0001	0.07	.0002
		III	0.16	<.0001	0.15	<.0001
	Ragweed	II	0.13	<.0001	0.08	<.0001
		III	0.15	<.0001	0.15	<.0001
	Perennial rye	II	0.15	<.0001	0.07	.0001
		III	0.16	<.0001	0.08	.0014
	<i>Alternaria alternata</i>	II	0.08	.0006	0.07	.0026
		III	0.10	.0009	0.11	.0006
	Bermuda grass	II	0.14	<.0001	0.03	.1627
		III	0.07	.0269	0.05	.085
E	Cat	II	0.06	.0185	0.03	.2808
		III	0.11	.0005	0.14	<.0001
	Oak	II	0.15	<.0001	0.04	.1214
		III	0.11	.0002	0.07	.0177
	Ragweed	II	0.12	<.0001	0.04	.0946
		III	0.11	.0002	0.09	.0052
	Perennial rye	II	0.18	<.0001	0.05	.0413
		III	0.09	.0035	0.06	.0728
	<i>Alternaria alternata</i>	II	0.03	.2403	−0.03	.2959
		III	0.01	.7634	0.10	.005
	Bermuda grass	II	0.03	.2401	0.01	.6473
		III	0.09	.0139	0.12	.001
	Cat	II	0.06	.0362	0.08	.0042
		III	0.11	.002	0.05	.1557
	Oak	II	0.10	.0003	0.04	.112
		III	0.10	.0058	0.09	.0198
	Ragweed	II	0.12	<.0001	0.04	.0986
		III	0.07	.0661	0.09	.0114
	Perennial rye	II	0.09	.0005	0.04	.1859
		III	0.03	.3799	0.09	.0178

Abbreviation: NHANES, National Health and Nutrition Examination Survey.

^aFive age groups were investigated: A, 6 to 10 years old in NHANES II and 16 to 19 years old in NHANES III; B, 11 to 19 years old in NHANES II and 20 to 30 years old in NHANES III; C, 20 to 30 years old in NHANES II and 31 to 40 years old in NHANES III; D, 31 to 40 years old in NHANES II and 41 to 50 years old in NHANES III; E, 41 to 50 years old in NHANES II and 51 to 60 years old in NHANES III.^bCorrelation coefficients reflect the strength of the association between 2 nominal variables.