

The Relationship Between a Specific IgE Level and Asthma Outcomes: Results from the 2005-2006 National Health and Nutrition Examination Survey

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What is already known about this topic? Absolute specific IgE may be predictive of asthma outcomes in the absence of exposure data.

What does this article add to our knowledge? This analysis demonstrated that, in a general population, there may be a dose-response relationship between total IgE and specific IgE to certain allergens and asthma outcomes in adults and children.

How does this study impact current management guidelines? The absolute level of specific IgE to certain allergens may be a more relevant and useful clinical tool than an arbitrary sensitized or nonsensitized cut-point value in the prediction of severe asthma outcomes.

BACKGROUND: Allergen exposure is associated with increased specific IgE (sIgE), and allergen exposure plus sensitization is predictive of asthma outcomes. However, it is not known if sIgE is predictive of asthma outcomes in the absence of exposure data.

OBJECTIVE: To investigate whether IgE to indoor allergens is predictive of and has a dose-response relationship with asthma emergency department (ED) visits and wheeze.

METHODS: In the 2005-2006 National Health and Nutrition Examination Survey, 351 children and 390 adults reported current asthma. Continuous sIgE to 9 indoor allergens were considered. Asthma morbidity in the past year was measured by wheezing. Health care utilization was defined as any asthma ED visits in the past year.

RESULTS: Analyses were adjusted for race, age, education, poverty index ratio and (in adults) tobacco use. In children, ED visits were associated with cockroach (odds ratio [OR] 1.5 [95% CI, 1.1-2.1]), rat (OR 1.9 [95% CI, 1.2-2.8]), and *Aspergillus* (OR 1.6 [95% CI, 1.001-2.60]). Continuous *Aspergillus* (OR 1.5 [95% CI, 1.04-2.1], *Alternaria* (OR 1.4 [95% CI, 1.1-1.6]), and total IgE (OR 1.2 [95% CI, 1.1-1.4]) were associated with

wheeze in children. Adult ED visits were associated with sIgE for dust mites (*Dermatophagoides pteronyssinus* OR 1.6 [95% CI, 1.3-2.1]; *Dermatophagoides farinae* OR 1.6 [95% CI, 1.3-1.9]), total IgE (OR 1.4 [95% CI, 1.04-1.9]), and the sum of sIgEs (OR 1.6 [95% CI, 1.2-2.2]).

CONCLUSIONS: Sensitization to particular indoor environmental allergens was found to be a risk factor for wheeze and asthma ED visits. These outcomes increased as the concentration of sIgE to these allergens increased. © 2013 American Academy of Allergy, Asthma & Immunology (J Allergy Clin Immunol: In Practice 2013;1:501-8)

Key words: Asthma; Allergy; Immunoglobulin E; NHANES; Asthma Outcomes; Asthma Morbidity; Cockroach; Rat; Dust mites; Sensitization; Hypersensitivity

IgE levels in persons with asthma are higher than levels in the general population.¹⁻⁵ Measurement of allergen-specific IgE (sIgE) from serum is used in the clinical setting to identify sensitization in the context of allergic disease and is usually dichotomized as present versus absent at a sIgE level ≥ 0.35 kU/L. Quantitative sIgE values correlate with the likelihood of clinically relevant food allergy and are currently used in the diagnostic process.^{6,7} It is hypothesized that quantitative sIgE to indoor aeroallergens may also correlate with asthma outcomes and provides a useful clinical management tool, although studies that examined this relationship are limited.^{8,9}

The quantity of sIgE may be a marker of environmental exposure to an antigen. In children with asthma, there is a positive relationship between the magnitude of exposure to specific aeroallergens and IgE titers.¹⁰⁻¹⁷ It also has been demonstrated that exposure in children with sensitization to indoor allergens is associated with adverse asthma outcomes.^{10,18,19} If exposure plus sensitization is predictive of asthma morbidity and health care utilization and if the sIgE level is indicative of exposure, then the absolute level of IgE sensitization to indoor allergens may be

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Abbreviations used

CI- Confidence interval

Der f- *Dermatophagoides farinae*Der p- *Dermatophagoides pteronyssinus*

ED- Emergency department

HDM- House dust mites

IgE- Immunoglobulin E

NHANES- National Health and Nutrition Examination Survey

OR- Odds ratio

PIR- Poverty index ratio

sIgE- Specific immunoglobulin E

predictive of asthma outcomes. Use of sIgE as a predictor of health care utilization and asthma morbidity would be a valuable tool to clinicians in the treatment and management of asthma in lieu of, typically unavailable, allergen exposure data.

Few studies have assessed the relationship between the level of sIgE and asthma outcomes and those that have were performed in select populations, eg, inner-city children or among people with asthma who are sensitized to at least 1 study allergen. Furthermore, the results of these studies are inconsistent.^{10,17,20-22} Additional research is needed on the relationship of sIgE quantity and asthma morbidity, and health care utilization for both children and adults, particularly from the general population to maximize the generalizability of findings for use in clinical practice.

The National Health and Nutritional Examination Survey (NHANES) presents a unique opportunity to investigate the role of IgE in asthma morbidity and health care utilization in the general population. Previous analyses of NHANES data examined the relationships between food allergy and asthma,²³ sIgE and allergy-related outcomes,²⁴ and the prevalence of asthma and total IgE.²⁵ None have addressed the association between sIgE and asthma outcomes. The objective of this analysis was to test whether sensitization (modeled as continuous sIgE) to indoor environmental allergens is predictive of asthma morbidity or health care utilization, and to assess whether there is a dose-response relationship in both children and adults. The secondary objective was to test whether sIgE treated as a dichotomous variable is associated with these asthma outcomes.

METHODS

NHANES is a national survey designed to assess the health and nutritional status of those in the United States. It uses a complex multistage design to sample the civilian, noninstitutionalized US population. Particular groups, such as persons with low income, adolescents, the elderly, and African Americans, are oversampled to ensure adequate sample sizes, detailed elsewhere.²⁶ NHANES 2005-2006 added an allergy component, which included total and specific IgE levels to 19 allergens, to its yearly questions on asthma morbidity and health care utilization. These allergens included 4 food allergens, 6 outdoor aeroallergens, and 9 indoor aeroallergens.

Study population

The present analysis includes all 2005-2006 NHANES survey participants who reported having current asthma (n = 741). NHANES defines current asthma as a positive response to the following 2 questions (NHANES question numbers are in parentheses): (1) has a physician or other health professional ever

told you that you had asthma (MCQ.010), and (2) do you still have asthma (MCQ.035)?

Because asthma outcomes are different in adults and children, all results are presented separately.^{27,28} The study population includes 351 children (≤ 17 years) and 390 adults. NHANES 2005-2006 was approved by the National Center for Health Statistics Research Ethics Review Board, and all participants provided written informed consent.²⁹ A detailed description of the survey design and implementation can be found online at <http://www.cdc.gov/nchs/nhanes.htm>.²⁶

IgE measurement

The participants were tested for total IgE and a panel of 9 indoor environmental allergens. These included sIgE levels to house dust mites (HDM) (*Dermatophagoides farinae* [Der f] and *Dermatophagoides pteronyssinus* [Der p]), cat dander, dog dander, cockroach [*Blattella germanica*], and *Alternaria alternata*. For those older than 6 years of age, sIgE levels to *Aspergillus fumigatus*, mouse urine proteins, and rat urine proteins were also measured. Total and sIgE antibodies were analyzed by using the Pharmacia Diagnostics ImmunoCAP 1000 System (Kalamazoo, Mich). The lower limit of detection for total IgE was 2.00 kU/L, and the lower limit of detection for each sIgE was 0.35 kU/L. For those below the limit of detection, NHANES assigned a value 0.25 kU/L. Any sample that exceeds the upper limit of detection for sIgE (1000 kU/L) was assigned a value of 1000 kU/L. No samples exceeded the upper limit of detection for total IgE. Details of the laboratory methods and procedures can be found elsewhere.³⁰

Outcome measurement

Asthma morbidity was defined as a positive response to the question "In the past 12 months, have you had wheezing or whistling in your chest (RDQ070)?" Health care utilization was defined as a positive response to the question "During the past 12 months, have you had a visit to the emergency room or urgent care center because of asthma (MCQ.050)?" This question was asked only among persons with active asthma, those with a positive response to the question "during the past 12 months, have you had an episode of asthma or an asthma attack (MCQ040)?"

Covariables

Additional variables associated with asthma were considered in the analysis. These include age, sex, race or ethnicity, household education level, and poverty status. For children, age was categorized as 1-5 years, 6-11 years, and 12-17 years. Adult ages were categorized as follows: 18-39 years, 40-59 years, and 60+ years. Race and ethnicity were combined into 1 race category defined as non-Hispanic white, non-Hispanic black, Hispanic, and other. The poverty index ratio (PIR) represents the family income to poverty ratio as defined by the US Census Bureau. The PIR was used to measure poverty status and was divided into commonly used categories of <1.3 , 1.3-3.5, and >3.5 . PIR values below 1.3 are below the poverty threshold, and the 1.3 and 3.5 thresholds are used to establish eligibility for US food assistance programs.³¹ Household education was defined as the highest education level obtained by the household reference person, usually the head of the household.²³

Statistical methods

All analyses were performed with SAS statistical software (version 9.2; SAS Institute Inc, Cary, NC). SAS survey procedures were used to account for the complex sampling design of

TABLE I. Demographic, allergic, and asthma characteristics of 741 persons with current asthma in the National Health and Nutrition Examination Survey 2005-2006

Variable	Children (1-17 y)		Adult (18+ y)	
	Current asthma counts (n = 351)	Weighted % $\pm$ SE	Current asthma counts (n = 390)	Weighted % $\pm$ SE
Sex				
Male	197	54.5 $\pm$ 4.3	155	37.6 $\pm$ 2.8
Female	154	45.5 $\pm$ 4.3	235	62.4 $\pm$ 2.8
PIR				
<1.3	133	26.4 $\pm$ 3.2	123	23.5 $\pm$ 2.0
1.3-3.5	129	38.5 $\pm$ 3.1	143	36.2 $\pm$ 2.3
>3.5	81	35.1 $\pm$ 4.5	107	40.3 $\pm$ 3.9
Household education				
<12th grade	104	17.4 $\pm$ 2.2	96	17.1 $\pm$ 2.3
12th grade	79	25.0 $\pm$ 3.6	86	24.9 $\pm$ 2.8
>12th grade	159	57.7 $\pm$ 4.9	193	58.0 $\pm$ 3.9
Race				
Non-Hispanic white	100	63.0 $\pm$ 4.3	209	76.0 $\pm$ 2.7
Non-Hispanic black	131	17.1 $\pm$ 2.8	109	12.4 $\pm$ 2.0
Hispanic	103	16.1 $\pm$ 2.6	58	6.4 $\pm$ 1.6
Other	17	3.8 $\pm$ 1.4	14	5.3 $\pm$ 1.6
Age				
1-5 y	82	18.1 $\pm$ 2.6		
6-11 y	96	35.2 $\pm$ 3.3		
12-17 y	173	46.7 $\pm$ 2.9		
18-39 y			167	35.8 $\pm$ 4.0
40-59 y			118	43.9 $\pm$ 3.1
60+ y			105	20.4 $\pm$ 3.0
Used tobacco in the past 5 d			99	25.7 $\pm$ 3.1
IgE sensitized (sIgE $\geq$ 0.35 kU/L)				
Sensitized to at least 1 allergen*	179	63.3 $\pm$ 3.5	218	56.3 $\pm$ 2.4
Sensitized to at least 1 allergen†	31	44.5 $\pm$ 6.1		
Der p	119	33.3 $\pm$ 2.4	139	35.7 $\pm$ 3.8
Der f	120	35.0 $\pm$ 2.5	136	32.7 $\pm$ 3.7
Cat	100	32.9 $\pm$ 5.0	104	30.2 $\pm$ 1.6
Dog	113	33.6 $\pm$ 5.2	127	35.9 $\pm$ 3.1
Cockroach	74	15.9 $\pm$ 3.0	78	16.6 $\pm$ 2.3
<i>Alternaria</i>	104	28.6 $\pm$ 3.2	77	18.2 $\pm$ 1.7
Mouse (6+ y only)	24	5.1 $\pm$ 1.5	18	4.2 $\pm$ 1.0
Rat (6+ y only)	21	4.4 $\pm$ 1.4	16	2.1 $\pm$ 0.8
<i>Aspergillus</i> (6+ y only)	82	26.2 $\pm$ 3.9	66	13.3 $\pm$ 1.9
ED for asthma in the past year	69	28.3 $\pm$ 3.7	57	25.8 $\pm$ 4.1
Wheeze	235	69.4 $\pm$ 4.5	267	73.4 $\pm$ 2.7
Total IgE (kU/L)	99.3 (Median)	36.2-318.0 (IQR)	77.6 (Median)	21.3-249.0 (IQR)

Der f, *Dermatophagoides farinae*; *Der p*, *Dermatophagoides farinae*; ED, emergency department; IQR, interquartile range; PIR, poverty index ratio; sIgE, specific IgE.

*Children ages 6-17 years old and adults.

†Children ages 1-5 years old.

NHANES. Appropriate weight and design variables were applied to all analyses. The sIgE levels were classified as sensitized (≥ 0.35 kU/L) or not sensitized (< 0.35 kU/L) for all dichotomous analyses. Total and sIgE levels were log transformed for quantitative analyses to account for the skewed distribution. Data were stratified by adults and children for all analyses. ORs and 95% CIs were obtained by using logistic regression for each variable and outcome. The decision was made *a priori* to include demographic variables known to be associated with asthma in the multivariable analysis, regardless

of whether they were significant in the univariate analysis. These variables included race, household education level, PIR, age, and tobacco use (for adults). Multivariable logistic regression was performed for each sIgE treated as a dichotomous variable for continuous log-transformed values of sIgE, total IgE, and the sum of the 9 sIgE levels for the outcomes wheeze and emergency department (ED) visits. ORs for continuous IgE represent a 1-unit change in the natural log of IgE. *Aspergillus*, mouse, and rat allergen models only included participants ages 6 years old and older. Predicted probability plots were obtained by using

TABLE II. ORs between IgE (dichotomous and continuous) and asthma outcomes among person with current asthma in National Health and Nutrition Examination Survey 2005-2006

Variable	Child ^a		Adult ^a	
	ED visit for asthma, OR (95% CI)	Wheeze, OR (95% CI)	ED visit for asthma, OR (95% CI)	Wheeze, OR (95% CI)
IgE sensitized dichotomous				
Der p	1.7 (0.58-4.76)	1.1 (0.74-1.79)	3.6 (1.31-9.72)*	0.9 (0.51-1.59)
Der f	2.0 (0.69-6.05)	1.3 (0.79-2.21)	2.5 (0.99-6.07)	1.0 (0.62-1.44)
Cat	2.3 (0.86-6.01)	1.2 (0.64-2.25)	2.9 (1.27-6.81)*	1.3 (0.80-2.21)
Dog	1.5 (0.40-5.70)	1.6 (0.88-3.05)	1.5 (0.60-3.51)	0.8 (0.40-1.67)
Mouse†	0.6 (0.08-5.02)	1.5 (0.62-3.83)	0.2 (0.02-1.10)	1.4 (0.24-8.46)
Rat†	8.8 (2.39-32.27)‡	0.3 (0.08-1.41)	0.6 (0.05-7.35)	5.3 (0.51-54.36)
Cockroach	5.0 (1.37-18.34)*	1.5 (0.79-2.92)	1.2 (0.33-4.64)	1.2 (0.44-3.03)
<i>Aspergillus</i> †	2.9 (0.62-13.60)	2.6 (0.86-7.54)	1.8 (0.36-8.63)	0.4 (0.16-1.01)
<i>Alternaria</i>	1.2 (0.32-4.17)	2.2 (0.96-4.92)	1.2 (0.30-5.12)	0.2 (0.09-0.50)‡
IgE continuous (log transformed)				
Total IgE	1.5 (0.90-2.68)	1.2 (1.05-1.41)*	1.4 (1.04-1.91)*	1.0 (0.86-1.17)
Sum specific IgE	1.4 (0.97-1.91)	1.1 (0.95-1.33)	1.6 (1.18-2.16)‡	0.9 (0.78-1.09)
Der p	1.1 (0.86-1.30)	1.0 (0.89-1.16)	1.6 (1.30-2.08)§	0.9 (0.78-1.01)
Der f	1.1 (0.89-1.43)	1.0 (0.89-1.21)	1.6 (1.30-2.05)§	0.9 (0.78-1.02)
Cat	1.2 (0.96-1.45)	1.1 (0.97-1.29)	1.2 (0.95-1.41)	1.1 (0.88-1.39)
Dog	1.1 (0.88-1.49)	1.1 (0.84-1.32)	1.1 (0.79-1.42)	1.0 (0.80-1.35)
Mouse†	1.0 (0.56-1.81)	1.0 (0.79-1.36)	0.5 (0.13-1.66)	1.4 (0.65-2.93)
Rat†	1.9 (1.24-2.78)‡	0.8 (0.44-1.43)	1.2 (0.46-3.06)	2.2 (0.51-9.30)
Cockroach	1.5 (1.12-2.13)‡	1.3 (0.96-1.64)	1.2 (0.70-2.05)	1.1 (0.74-1.70)
<i>Aspergillus</i> †	1.6 (1.00-2.60)*	1.5 (1.04-2.10)*	1.2 (0.58-2.32)	0.8 (0.47-1.26)
<i>Alternaria</i>	1.2 (0.85-1.84)	1.4 (1.09-1.64)‡	1.1 (0.64-1.90)	0.6 (0.45-0.77)§

Der f, *Dermatophagoides farinae*; Der p, *Dermatophagoides pteronyssinus*; ED, emergency department; OR, odds ratio.

* $P < .05$.

†Only participants age 6 y and older were included in the analysis.

‡ $P < .01$.

§ $P < .0001$.

^aLogistic regression models were adjusted for household education, age, poverty index ratio, race, and tobacco use (among adults only).

logistic regression for allergens, with a significant relationship between continuous IgE and ED visits.

RESULTS

A total of 10,348 adults and children were interviewed in NHANES 2005-2006, of whom 8336 had total IgE measured. Of these, 351 children and 390 adults who reported current asthma were included in this analysis. After adjusting for the complex survey design, among children, 54.5% were boys, 63% non-Hispanic white, 26.4% had a PIR < 1.3 , and 17.4% had a household education level < 12 th grade. Among children, nearly 60% were sensitized to at least 1 indoor environmental allergen, wheeze was reported by 69.4%, and 28.3% had at least 1 asthma ED visit in the previous year (Table I). Among adults 18 years old and older, 37.6% were men, 76% were non-Hispanic white, 23.5% had a PIR < 0.3 , 17.1% had a household education level < 12 th grade, and 25.7% reported tobacco use in the past 5 days. In adults, 56.3% were sensitized to at least 1 indoor allergen, 73.4% had wheeze in the past year, and 25.8% had an asthma ED visit. The median total IgE was 99.3 kU/L for children and 77.6 kU/L for adults (Table I).

In children, allergy to both cockroach and rat allergens was strongly associated with asthma ED visits in both the dichotomous (OR 5.0 [95% CI, 1.4-18.3] and OR 8.8 [95% CI,

2.4-32.3], respectively) and continuous (OR 1.5 [95% CI, 1.1-2.1] and OR 1.9 [95% CI, 1.2-2.8], respectively) models. *Aspergillus* was not associated with ED visits in the dichotomous model but was when modeled continuously (OR 1.6 [95% CI, 1.001-2.60]). In the continuous model, mold sensitization (*Aspergillus* OR 1.5 [95% CI, 1.04-2.1]; *Alternaria* OR 1.2 [95% CI, 1.05-1.4]) and total IgE (OR 1.2 [95% CI, 1.05-1.4]) remained significantly associated with wheeze in children. For adults, sensitization to HDM (*Der p* OR 3.6 [95% CI, 1.3-9.7]; *Der f* OR 2.5 [95% CI, 1.0-6.1], and cat (OR 2.9 [95% CI, 1.3-6.8]) were positively associated with ED visits in the dichotomous model. HDM remained significantly associated in the continuous model (*Der p* OR 1.6 [95% CI, 1.3-2.1]; *Der f* OR 1.6 [95% CI, 1.3-2.05]). In addition, the sum of the specific IgE (OR 1.6 [95% CI, 1.2-2.2] and the total IgE (OR 1.4 [95% CI, 1.04-1.9]) were also significantly associated with ED visits in this model (Table II).

To further explore the dose-response relationships between continuous sIgE and asthma ED visits, predicted probability graphs (Figure 1, A-C and Figure 2, A-D) were produced. The probability of an asthma ED visit increased significantly as sIgE to rat and cockroach and *Aspergillus* increased in children. An increased probability of an ED visit was also seen in adults as sIgE to HDM, the sum of the sIgE and the total IgE increased. In children, these increased probabilities corresponded to an OR

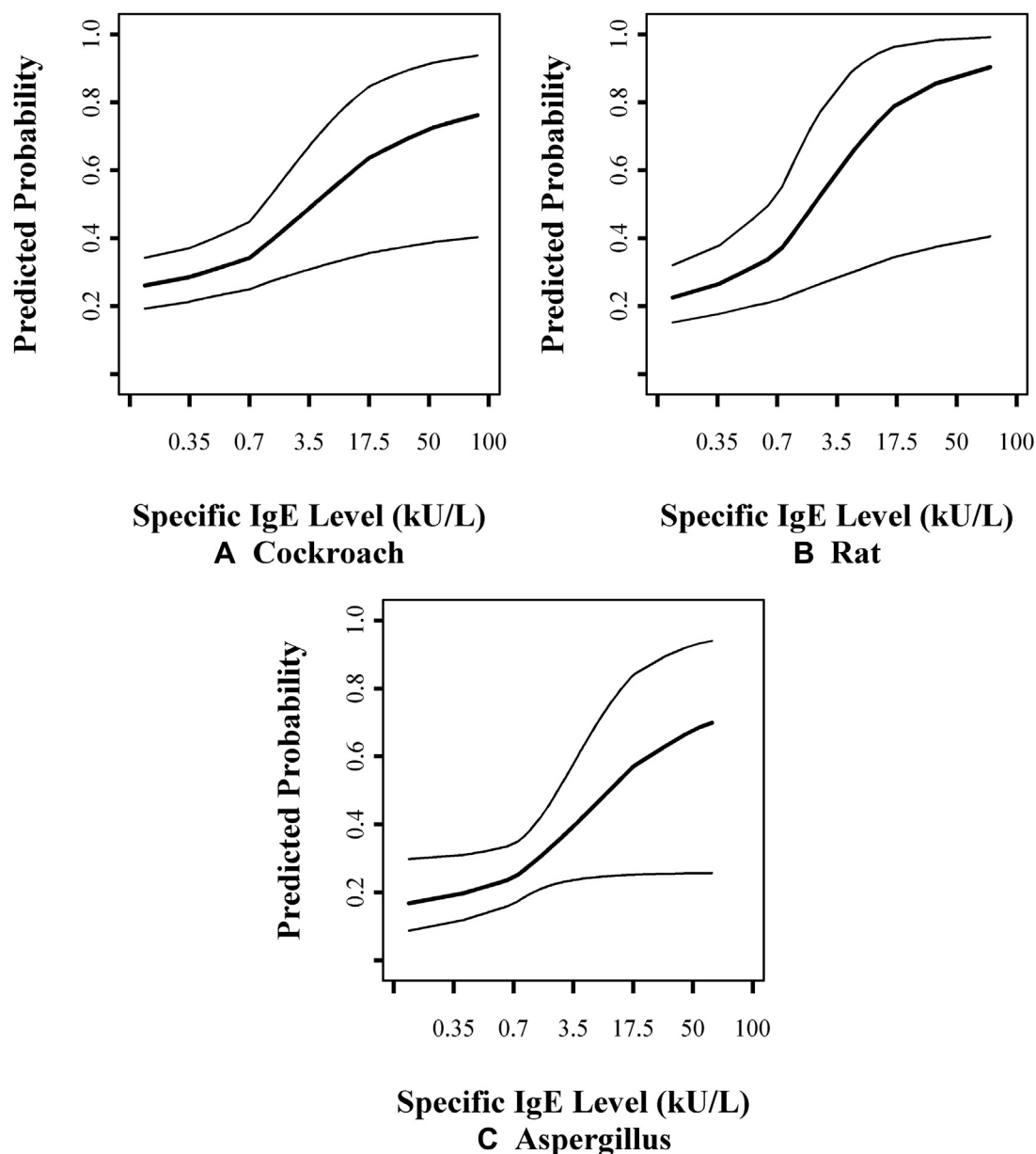


FIGURE 1. Predicted probability of emergency department visits for continuous specific IgE in children (with 95% confidence intervals), National Health and Nutrition Examination Survey 2005-2006.

of 2.7 for a 10 kU/L increase in sIgE to cockroach and an OR of 4.4 for a 30 kU/L increase. Elevated sIgE to rat allergen in children corresponded to an OR of 4.1 for a 10 kU/L increase and an OR of 8.1 for a 30 kU/L increase. In adults, an OR of 3.1 corresponded with a 10 kU/L increase in sIgE to HDM (der p) and an OR of 5.4 for a 30 kU/L increase (Table III).

DISCUSSION

This analysis of NHANES 2005-2006 data is, to our knowledge, the first to examine the relationship between sIgE and asthma outcomes in a general, unselected population of persons with asthma. The analysis expands upon previous research conducted in specialized populations by documenting that

sensitization alone, in the absence of exposure data, to particular indoor environmental allergens is a risk factor for wheeze and asthma ED visits. In addition, we found a dose-response relationship; the association increased as the concentration of sIgE increased. Interestingly, the allergens associated with asthma outcomes differed for adults and children. For children, sIgE sensitization to rat allergen and cockroach allergen were strongly associated with ED visits for asthma and showed a dose-response relationship, which indicated that the absolute level of sIgE for rat and cockroach may be of more clinical value than a dichotomous designation of sensitized or not sensitized. Although the percentage of children sensitized to cockroach and rat allergens was low in this general population sample (15.9% and 4.4%, respectively), this corresponds to a large number of children. The

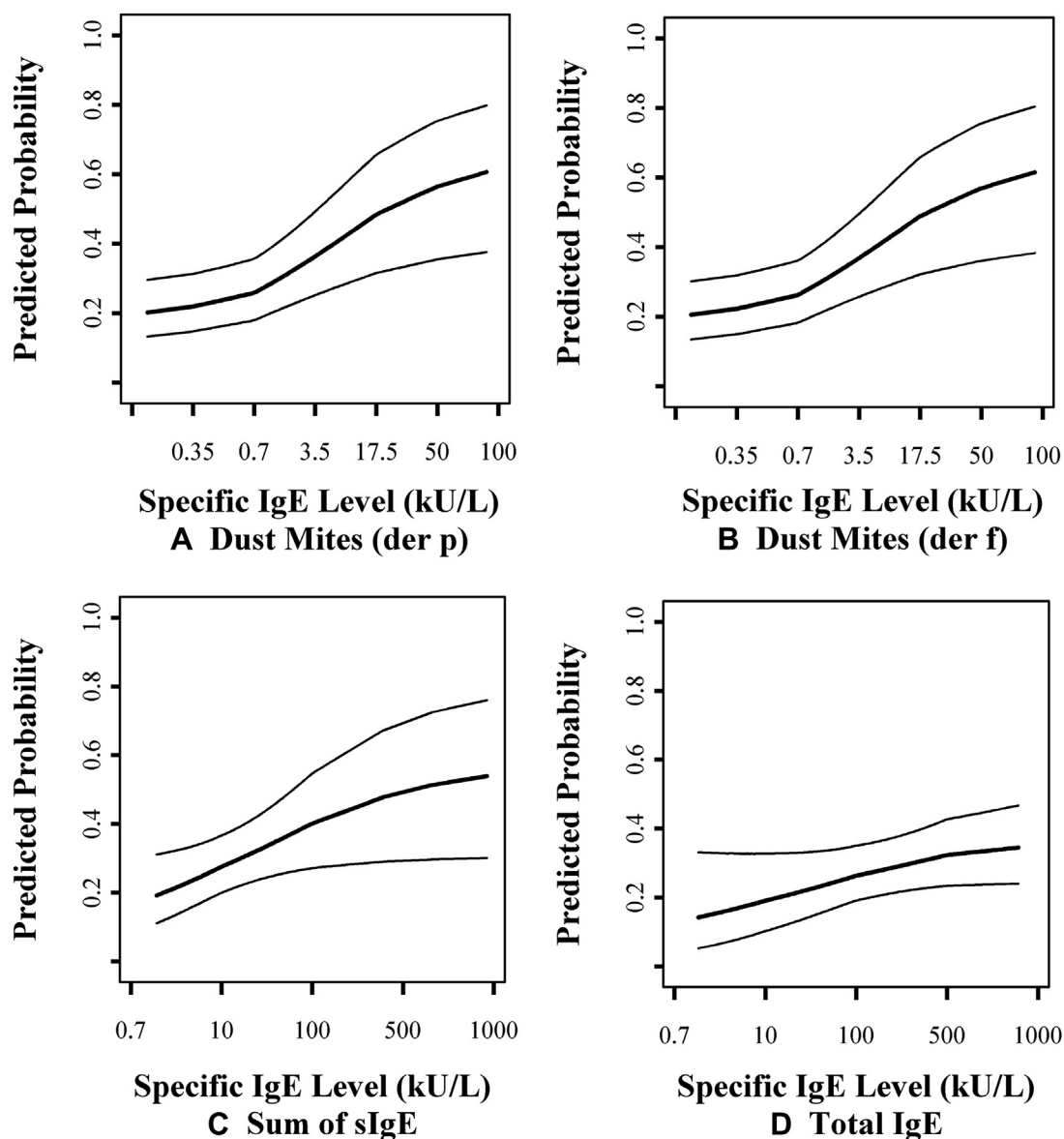


FIGURE 2. Predicted probability of emergency department visits for continuous specific IgE, sum of sIgE and total IgE in adults (with 95% confidence intervals), National Health and Nutrition Examination Survey 2005-2006.

Centers for Disease Control and Prevention reports that, in the United States, there are 7.1 million children with asthma,³² which results in 1.1 million children sensitized to cockroaches and 312,000 sensitized to rats. Furthermore, vulnerable populations, such as inner-city children, bear a higher burden of asthma than the general population, with estimated 50% or more sensitized to cockroaches^{12,18} and up to 20% sensitized to rats.³³ Allergy testing for cockroach and rat may be important in clinical practices that treat inner-city children with asthma.

Among sensitization to HDM and cat were positively associated with asthma ED visits. Quantitative sIgE levels to HDM and cat dander, along with total IgE and the sum of the 9 sIgEs, were positively related to ED visits, which exhibited a significant dose-response relationship. The differences between adults and children may reflect the fact that there are differences in the clinical characteristics of adult and childhood asthma.^{34,35}

Analysis of the predicted probability plots suggests that, for sIgE to rat, cockroach, and *Aspergillus* in children, and sIgE to HDM in adults, any cut point used to determine sensitization may be arbitrary because the probability of asthma ED visits increases with increasing sIgE level. When analyzed by IgE class, these allergens showed a nonsignificant increase in OR as IgE class increased (data not shown).

Our findings corroborate the findings of several other studies conducted in specialized populations in recent years. In a population-based cohort study of 521 five-year-old children, Simpson et al²⁰ observed a positive association between dichotomous sIgE antibodies to cat, dog, and HDM allergen, and wheezing. Wang et al,¹⁰ in a study of 506 inner-city children ages 4-9 years old found that sensitization to cockroach, HDM, and mold were associated with hospitalizations and steroid use, whereas HDM sensitization was associated with any unscheduled

TABLE III. ORs for emergency department visits due to asthma at corresponding kU/L increases in total and specific IgE in children and adults, National Health and Nutrition Examination Survey 2005-2006

	2.7 kU/L, OR (95% CI)*	10 kU/L, OR (95% CI)*	30 kU/L, OR (95% CI)*	100 kU/L, OR (95% CI)*
Children				
Rat	1.9 (1.24-2.78)	4.1 (1.63-10.49)	8.1 (2.06-32.26)	17.1 (2.65-109.94)
Cockroach	1.5 (1.12-2.13)	2.7 (1.29-5.69)	4.4 (1.45-13.07)	7.3 (1.65-32.39)
<i>Aspergillus</i>	1.61 (1.001-2.60)	3.0 (1.002-8.97)	5.1 (1.003-25.59)	8.98 (1.004-80.37)
Adults				
Der p	1.6 (1.30-2.08)	3.1 (1.82-5.42)	5.4 (2.41-12.15)	9.8 (3.29-29.32)
Der f	1.6 (1.30-2.05)	3.1 (1.82-5.22)	5.3 (2.42-11.51)	9.5 (3.30-27.27)
Sum sIgE	1.6 (1.18-2.16)	2.9 (1.46-5.87)	4.9 (1.75-13.69)	8.6 (2.13-34.46)
Total IgE	1.4 (1.04-1.91)	2.2 (1.10-4.43)	3.2 (1.15-9.03)	4.9 (1.20-19.65)

Der f, *Dermatophagoides farinae*; Der p, *Dermatophagoides pteronyssinus*; OR, odds ratio; sIgE, specific IgE.

*Logistic regression models were adjusted for household education, age, poverty index ratio, race, and tobacco use (among adults only).

asthma visits in the past year. A dose-response relationship with sIgE to cockroach, HDM, and total IgE, and asthma outcomes was found. A positive association between categorical total IgE and dichotomous sIgE to cockroach, HDM, cat and mouse allergens, and health care utilization was found by Rotsides et al¹⁷ in a study of 453 inner-city preschoolers. Other studies have had contradictory findings. Matsui et al²¹ studied 546 participants between the ages of 12 and 20 years old, and did not find a relationship between sIgE to cockroach and asthma exacerbation or hospitalization when modeled continuously. In a study of inner-city adults, Wisnivesky et al²² found no association between dichotomously categorized sIgE to cockroach, HDM, cat, mouse, or mold, and several measures of asthma outcomes. In studies that found a positive relationship between sIgE level and asthma outcomes, the more objective outcome of health care utilization tended to be significant as opposed to the more subjective outcomes of wheeze or symptom days.

There may be several reasons for the disparate results among studies. A smaller sample size could have prevented Wisnivesky et al²² and the current analysis from seeing the small effects reported in other studies. For studies that considered sIgE as a dichotomous variable, several sensitization cut points were used. Matsui et al²¹ used a sensitization level of ≥ 0.10 kU/L, Simpson et al²⁰ used ≥ 0.20 kU/L and the remaining (including this analysis) used ≥ 0.35 kU/L. In addition, asthma outcomes and time frames were defined differently across the studies with health care utilization assessed over the previous 3 months,¹⁰ the previous year,²⁰⁻²² as in the current analysis, and the previous 5 years.¹⁷ Wheeze was defined as any wheeze in the past 2 weeks¹⁰ and any wheeze in the past year²⁰ (including the current analysis). These differences in classification and outcome assessment could easily account for the differences seen in study results. Finally, the present analysis was population based as opposed to the selected populations examined in previous studies and relationships may differ among these groups.

The consistency between results for asthma ED visits in the unadjusted (data not shown) and adjusted models, and in the dichotomous and continuous analyses led us to believe that they reflected a true underlying association. However, there are several limitations to this cross-sectional analysis. The most important limitation is the sample size. Furthermore, current asthma is self-reported in the NHANES survey as are wheeze and ED visits. This may have limited the ability to detect significance in weaker associations. We modeled asthma events that occurred in the

previous year. Therefore, an important assumption underlying this analysis is that IgE levels to these chronic household exposures are unlikely to vary widely over the course of 1 year.^{36,37}

Other asthma prediction models³⁸⁻⁴⁰ have been presented in recent years, and the use of sIgE level to cockroach, rat, and HDM to help predict future severe asthma outcomes, as presented in this analysis, could be a valuable addition to these models in the clinical management of asthma. Use of the absolute value of food sIgE is currently used in the clinical setting in the diagnosis of symptomatic allergy to egg, milk, peanut, and fish (among other foods). For many food allergens, the likelihood of a clinically relevant food allergy increases with increasing sIgE level.^{6,7} Findings from this analysis suggest that absolute sIgE levels to certain indoor environmental allergens may have similar clinical significance in predicting ED visits and wheeze. Moreover, the level of sIgE could be used to determine which allergens a patient may be most exposed to in the home and to recommend exposure remediation, which makes it a useful tool for clinicians. Additional studies are needed to confirm these findings and to pursue the study of alternate cut points. Studies that include the analysis of continuous values of sIgE levels along with standardized outcome assessments would improve the ability to compare findings across studies.

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