

The Role of Cockroach Exposure in Asthma Exacerbation

Felicia Rabito, PhD



Background

- An estimated 7 million US children currently have asthma.
 - Highest burden borne by low-income black children living in urban environments.
- Severe asthma outcomes constitute a health disparity.
 - Annual asthma hospitalization rate for black children is 2.2 times greater than the rate for white children.

Background (2)

- Strong evidence links allergen exposure and sensitization to the diagnosis of asthma.
- Allergen avoidance is a major component of asthma control advocated by physicians.
 - Effectiveness of allergen reduction techniques have been mixed.
- Conflicting evidence as to whether current exposure is associated with morbidity.

Background (3)

- Exposure to household dust mites (HDM) is independently associated with allergic sensitization.
 - However, exposure to HDM has not been found to be independently associated with clinical asthma endpoints.
- Evidence also confirms exposure to cockroach allergen is independently associated with allergic sensitization.
 - Unlike HDM data, there seems to be a positive relationship between cockroach exposure and asthma morbidity.
 - Only a few studies have addressed this association.

Background (4)

- Studies assessing cockroach exposure and asthma exacerbation.
 1. The National Cooperative Inner-City Asthma Study *
 - Children sensitized and exposed to cockroach allergen at greater than 8 U/g had increased hospitalization and morbidity rates.
 - Findings were not adjusted for medication use, smoking or income.

* Rosenstreich, 1997

Background (5)

2. Inner-City Asthma Study*

- Children sensitized and exposed to cockroach at greater than 2 U/g had significantly greater asthma-related morbidity, but not higher hospitalization rate in adjusted analysis.

* Gruchalla, 2005

Background (6)

- Sarpong and Karrison (1997)
 - Found an association between cockroach sensitization and hospitalization.
 - Significance was lost after controlling for sociodemographic factors.

Background Summary

- Cockroach allergens may independently be driving higher rates of asthma morbidity and hospitalization seen in inner city populations, however few studies have looked at this association.
- The apparent differences in clinical outcomes for asthmatic patients regarding house dust mites and cockroach allergens are perplexing and warrant further study.

Background Summary

- Successful asthma management depends partly upon effective allergen avoidance strategies.
- Designing an effective allergen avoidance strategy depends upon an improved understanding of the relation between current exposure and clinical outcomes.

New Orleans Healthy Homes Study

- The purpose of the study was to examine the relationship between house dust mite and cockroach exposure, asthma morbidity, and healthcare utilization in inner-city children.
- Results provide further data upon which effective intervention strategies targeted to atopic asthmatic children in the inner city can be developed and tested.

Methods

- Cross-sectional study
- Asthmatic children, ages 4-17 recruited from allergy clinics serving low-income children in New Orleans.
 - Physician-diagnosed asthma, record of positive skin test for indoor allergen, kept their previous 2 clinic appointments.

Methods (2)

- Outcome Data
 - Health Care Utilization
 - 1 or more visit to the emergency department (ED) for asthma.
 - 1 or more overnight stay at the hospital for asthma.
 - 1 or more urgent trip to a physician's office for asthma.
 - Asthma Morbidity
 - 16 or more days with wheezing episodes during the previous 4 months.

Methods (3)

- Survey Data
 - Questionnaires on sociodemographics, home characteristics, and a modified children respiratory health questionnaire.
- Environmental Sampling and Measurement
 - 5 vacuum dust samples taken
 - Kitchen dust sample used as the exposure variable for cockroaches, bedroom sample used as the exposure variable for dust mites.
- IgE Analysis
 - Blood samples collected via venipuncture at the time of environmental sample and survey data collection.

Results

Demographic Characteristics	n	%
	86	
Age of Child		
4 to 11 years	64	74.4%
12 to 17 years	20	23.3%
Male gender	55	64.7%
Household Income		
<\$10,000	51	59.3%
Sensitivity		
Dust Mite	71	83.5%
Cockroach	46	54.1%
Allergen Exposure		
Bla g 1 > 2.0 U/g	38	44.2%
Def f 1 or Der p 1 > 2.0 µg/g	34	39.5%

Results (2)

Associations Between Measures of Asthma Morbidity and Health Care Utilization and Participant Characteristics

Characteristics	≥ 1 ER visit n = 48 OR (95% CI)	≥ 1 Hospital Admission n = 21 OR (95% CI)	16+ days with Wheezing n = 10 OR (95% CI)
Exposure			
Bla g 1 exposure ≥2 U/g (kitchen floor)	1.81 (0.70, 4.7)	4.53 (1.49,13.80)	3.61 (0.65,19.99)
Der p 1 exposure ≥2 µg/g (bedroom bed)	0.70 (0.25, 2.01)	1.13 (0.35, 3.67)	1.60 (0.37, 6.94)
Der f 1 exposure ≥2 µg/g (bedroom bed)	0.79 (0.29, 2.14)	2.32 (0.79, 6.78)	1.31 (0.31, 5.60)
Sensitization			
Bla g 1 ≥0.35 ku/L	1.99 (0.82, 4.84)	1.45 (0.54,3.92)	1.53 (0.41,5.75)
Der p 1 ≥0.35 ku/L	0.84 (0.31,2.23)	0.60 (0.21,1.76)	3.44 (0.41,28.81)
Exposure & Sensitization**			
Bla g 1 exposed ≥2 U/g AND sensitized	1.54 (0.53,4.46)	3.12 (1.04, 9.41)	2.16 (0.44,10.66)
Der p 1 exposed ≥2 µg/g AND sensitized	0.70 (0.25, 2.01)	1.13 (0.35,3.67)	1.60 (0.37,6.94)
Der f 1 exposed ≥2 µg/g AND sensitized	0.62 (0.21,1.80)	1.86 (0.58, 5.85)	1.81 (0.41,7.88)

Statistically significant in bold, **sensitized and exposed vs all other categories

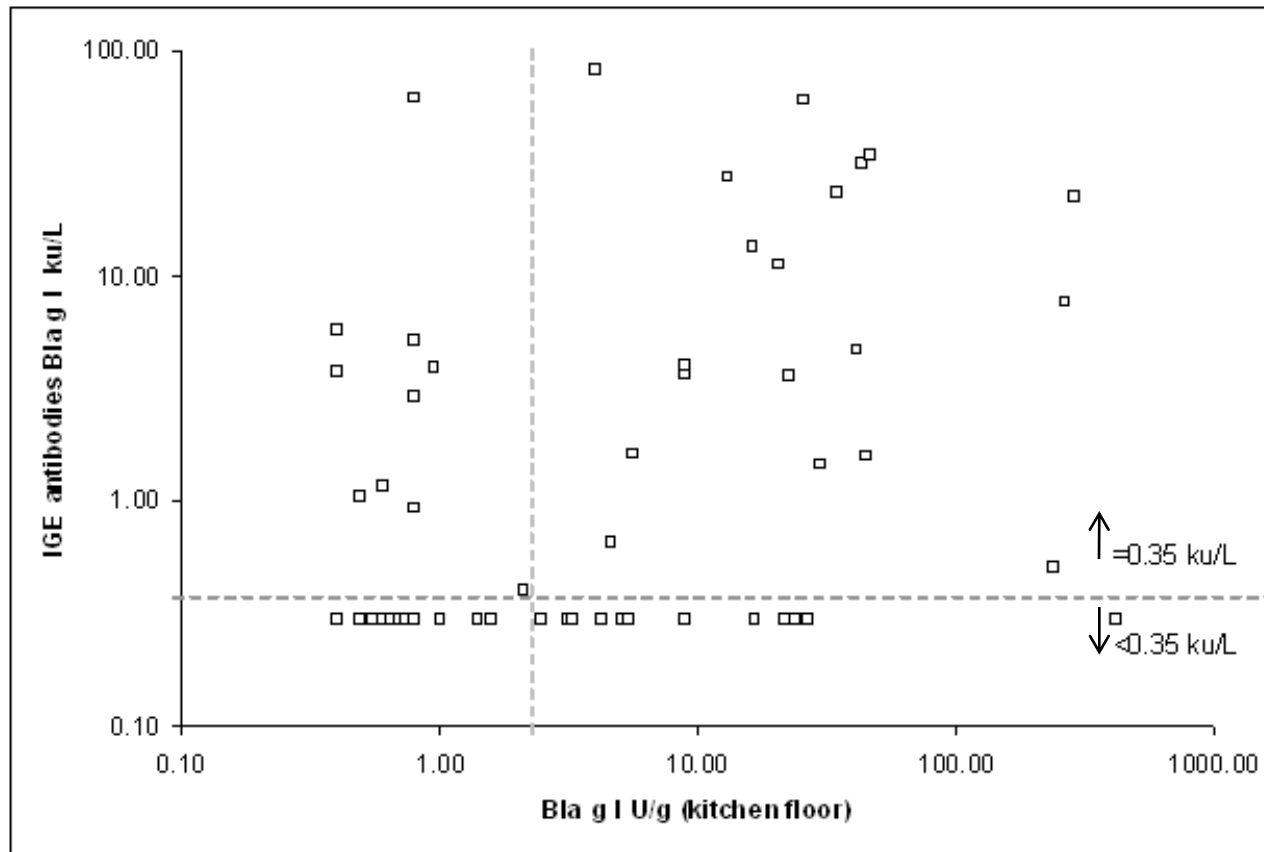
Results (3)

Associations Between Measures of Asthma Morbidity and Health Care Utilization and Participant Characteristics (cont.)

Characteristics	≥ 1 ER visit n = 48 OR (95% CI)	≥ 1 Hospital Admission n = 21 OR (95% CI)	16+ days with Wheezing n = 10 OR (95% CI)
Medication Use / Morbidity			
Oral steroid use (at least 1 x daily)	5.3 (0.6,45.9)	9.8 (1.8, 55.5)	7.71 (1.43, 41.65)
Daily Beta-2 agonist use (at least 1 x daily)	1.54 (0.57,4.19)	0.88 (0.28, 2.77)	1.29 (0.30, 5.47)
Daily ICS use (at least 1 x daily)	1.06 (0.45, 2.49)	1.58 (0.58, 4.31)	0.85 (0.23, 3.19)
Missed asthma medication in last 2 wks	1.75 (0.45, 6.81)	0.97 (0.33, 2.87)	1.75 (0.45, 6.81)
Ever admitted to the ICU for asthma	2.42 (0.83,7.03)	3.31 (1.39, 9.63)	1.38 (0.32,5.90)
Home and Demographic Characteristics			
Sibling with asthma	0.96 (0.35, 2.62)	1.45 (0.48, 4.45)	2.50 (0.63, 9.94)
Owens a dog or cat	0.99 (0.35, 2.81)	0.86 (0.25, 2.96)	0.94 (0.18,4.86)
1 or more smokers in the home	0.65 (0.24, 1.74)	0.26 (0.05, 1.20)	0.75 (0.15, 3.84)
Annual income ≤ \$15,000 per year	2.03 (0.79, 5.86)	1.29 (0.37, 4.48)	†
Age 12 to 17 years	0.74 (0.27, 2.00)	1.04 (0.33, 3.32)	0.33 (0.04, 2.81)
Male gender	1.25 (0.51, 3.08)	1.53 (0.56, 4.21)	2.00 (0.53, 7.56)
Sibling with asthma	0.96 (0.35, 2.62)	1.45 (0.48, 4.45)	2.50 (0.63, 9.94)

Statistically significant in bold, † undefined estimate due to reduced cell size

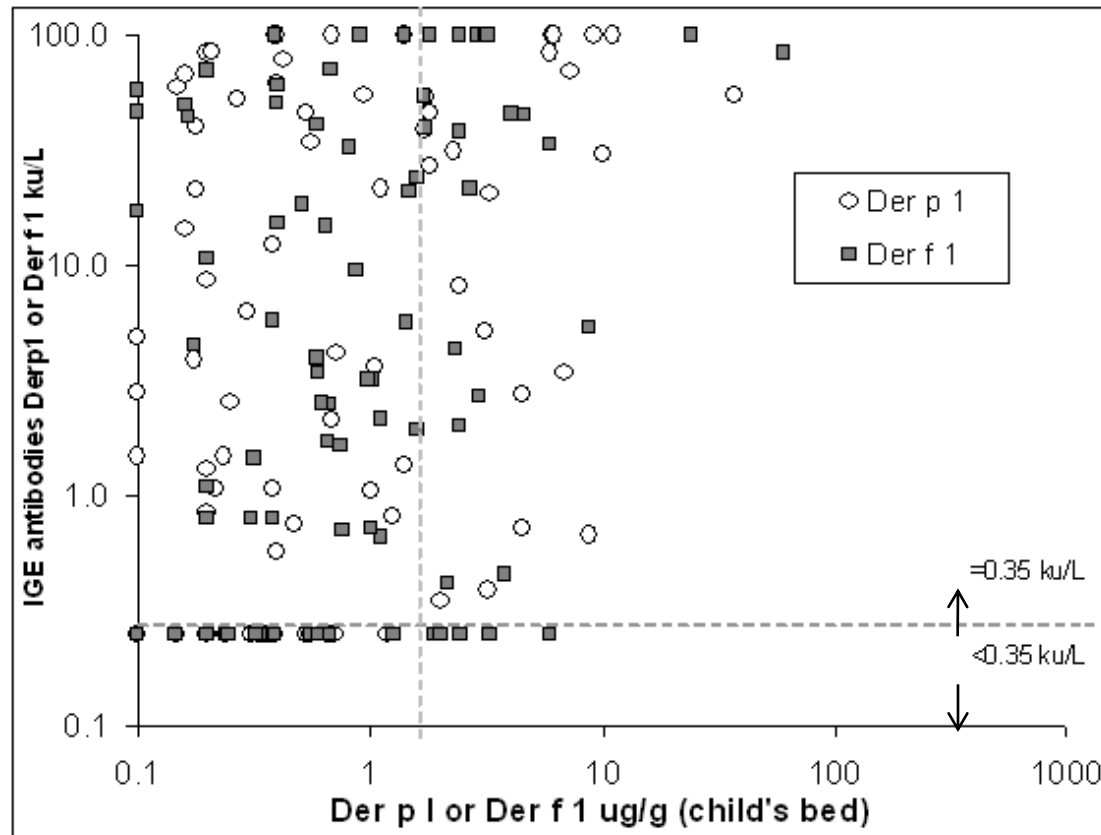
Results (4)



Spearman's $r = 0.430$ $p = 0.0001$

Circulating IgE Antibodies (kU/L) to cockroach (Bla g 1) and concentration of Bla g 1 dust sampled from the Kitchen Floor. *Dotted lines represent traditional cutoff levels for sensitization and exposure level.*

Results (5)



Spearman's $r=0.279$ $p=0.0115$ (Der p 1) and $r=0.198$ $p=0.0714$ (Der f 1)
Circulating IgE antibodies (kU/L) to house dust mite (Der p 1 and Der f 1) allergen and concentration of Der p 1 or Der f 1 in dust sampled from child's bed mattress *Dotted lines represent traditional cutoff levels for sensitization and exposure level.*

Results (6)

Exposure	Dust Allergen Levels, median (IQR)		
	≥ 1 ED visit (n = 48)	≥ 1 hospital admissions (n = 21)	≥ 16 days with wheezing (n = 10)
Bla g 1, U/g (kitchen floor)	2.1 (1.0 – 23.0)	7.2 (1.2 – 24.5) ^a	5.6 (0.6 – 8.8)
Dust mite allergen (µg/g) ^b	2.2 (0.7 – 5.5)	2.5 (0.7 – 3.3)	2.7 (1.7 – 3.2)

^a p < .05 by Wilcoxon rank sum test

^b Highest of either Der f 1 or Der p 1 from bedroom samples.

Results (7)

Characteristic	Crude OR (95% CI)		
	≥ 1 ED visit	≥ 1 hospital admissions	≥ 16 days with wheezing
Exposure			
Bla g 1 > 2 U/g	1.8 (0.7 – 4.7)	4.5 (1.4 – 13.8) ^a	3.6 (0.7 – 19.99)
Der p 1 > 2 µg/g	0.7 (0.3 – 2.0)	1.1 (0.4 – 3.7)	1.6 (0.4 – 6.9)
Der f 1 > 2 µg/g	0.8 (0.3 – 2.1)	2.3 (0.8 – 6.8)	1.3 (0.3 – 5.7)
Exposed and Sensitization			
Bla g 1 > 2 U/g	1.5 (0.5 – 4.5)	3.1 (1.04 – 9.4) ^a	2.2 (0.4 – 10.7)
Der p 1 > 2 µg/g	0.7 (0.3 – 2.0)	1.1 (0.4 – 3.7)	1.6 (0.4 – 6.9)
Der f 1 > 2 µg/g	0.6 (0.2 – 1.8)	1.9 (0.6 – 5.9)	1.8 (0.4 – 7.9)

^a Statistically significant ($p < .05$)

^b Sensitized/exposed vs all other categories combined

Results (8)

Multivariable Regression of Children Who Were Hospitalized for Asthma vs Those with No Hospitalization

	Adjusted OR (95% CI)	
	Model 1 ^a	Model 2 ^b
Bla g 1 > 2 U/g	5.4 (1.1 – 25.6)	4.2 (1.2 – 14.2)
Bla g 1 > 2 U/g and sensitized	0.7 (0.1 – 3.3)	NA

^a Model 1 controlling for variables found to be significant in the univariate analysis (oral corticosteroid use, ever admitted to ICU for asthma)

^b Model 2 includes variables selected using forward and backward selection

Discussion

- The rate of hospital admissions in children exposed to cockroach allergen levels greater than 2 U/g was **4 to 5 times greater** than children unexposed to cockroach, in both unadjusted and adjusted models.
- Rate of hospital admission was not associated with exposure to house dust mite (Der f 1 or Der p 1).

Discussion (2)

- Unexpected finding of a strong association between cockroach exposure and hospitalization independent of sensitization status.
 - The major cockroach allergens are environmentally stable. Retention of protease activity may account for their tendency to provoke an immune response even when patient does not have allergic sensitization.
 - Alternatively, clinical effects may be caused by T-Cells. Studies to date have been limited to IgE sensitization because of the difficulty evaluating T-cell sensitization.
 - Studies show black children are at higher risk than whites only among the very poor. Therefore, differential social and environmental conditions, leading to increased disorder and stress may be driving factors – although care was taken to control for these factors at both the design and analysis phase.

Discussion (3)

- Limitations of the study
 - Small Sample Size
 - May have limited ability to detect and HDM effect, though results are consistent with other research.
 - Despite small sample size, the association with cockroach exposure was pronounced.
 - Unknown causal mechanism

Conclusions

- Exposure to cockroach allergens is strongly associated with hospital admissions for asthmatic children.
- May be the factor driving high rates of asthma morbidity seen in inner-city children.

Path Forward

- Controlled trials of isolated cockroach abatement in urban homes using clinical outcomes are needed.
- We have just launched a controlled trial testing the single intervention of cockroach abatement with hospitalization/asthma morbidity as outcomes.

Childhood Asthma and the Home Environment: A Summary of Current Knowledge

Track 7: Just the Facts

Päivi Salo, PhD - NIEHS/NIH, Environmental
Cardiopulmonary Diseases Group, RTP, NC



HOMES, FAMILIES, AND COMMUNITIES

NATIONAL HEALTHY
HOMES CONFERENCE

COLORADO CONVENTION CENTER • JUNE 20-23, 2011



U.S. Department of Health and Human Services
National Institute of Health
National Institute of Environmental Health Sciences

▶ Chronic inflammatory disorder of the airways

- Characterized by
 - Airway hyperresponsiveness
 - Mucus production
 - Epithelial damage
 - Inflammation
 - Increased cytokine production

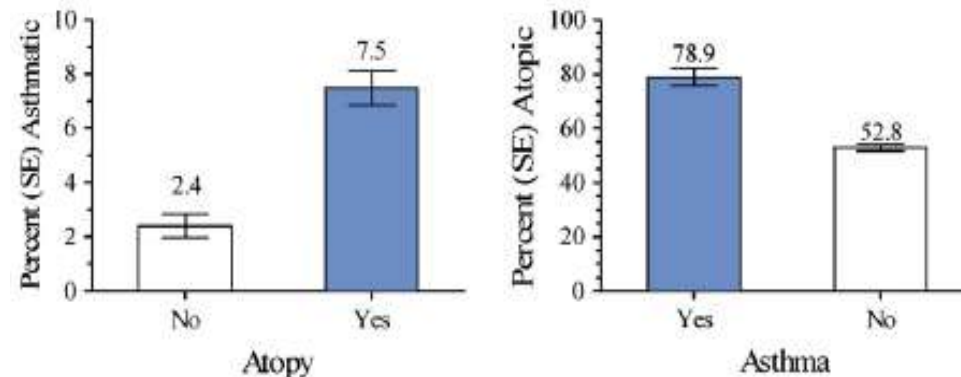


Stephan Mottessier / AP

▪ Leads to airway obstruction

- Wheezing
- Breathlessness
- Chest tightness
- Cough

▪ Association with atopy



Childhood Asthma

- ▶ **Asthma is a multifactorial disease**
- ▶ **Risk factors**
 - **Genetic**
 - **Environmental**
 - **Indoor particulates (e.g., indoor allergens, ETS, microbes and microbial products)**
 - **Ambient air pollutants (e.g., DEPs, O₃, NO₂)**
 - **Lifestyle**
 - **Early-life exposures (e.g., breastfeeding, daycare attendance, improved hygiene)**
 - **Diet and physical activity**

Asthma Prevalence in the U.S.

- ▶ **Current asthma affects 24.6 million people (8.2%)**
 - **Prevalence higher females, children, non-Hispanic blacks and Puerto Ricans, individuals below poverty level**

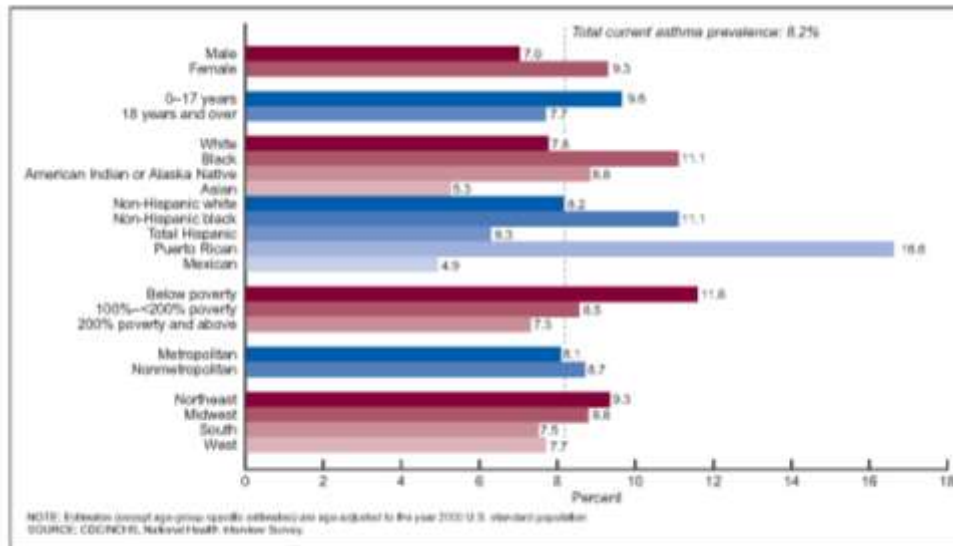


Figure 2. Prevalence of current asthma, by selected characteristics: United States, 2008

Morbidity and Mortality

- ▶ **School and work absence due to asthma**
 - 10.5 million school days
 - 14.2 million work days

- ▶ **Health care use**
 - 1.75 million asthma-related emergency department visits, 13.9 million outpatient visits
 - 456,000 hospitalizations

- ▶ **Increasing medical expenses \$48.6 billion (2002) to \$50.1 billion (2007)**

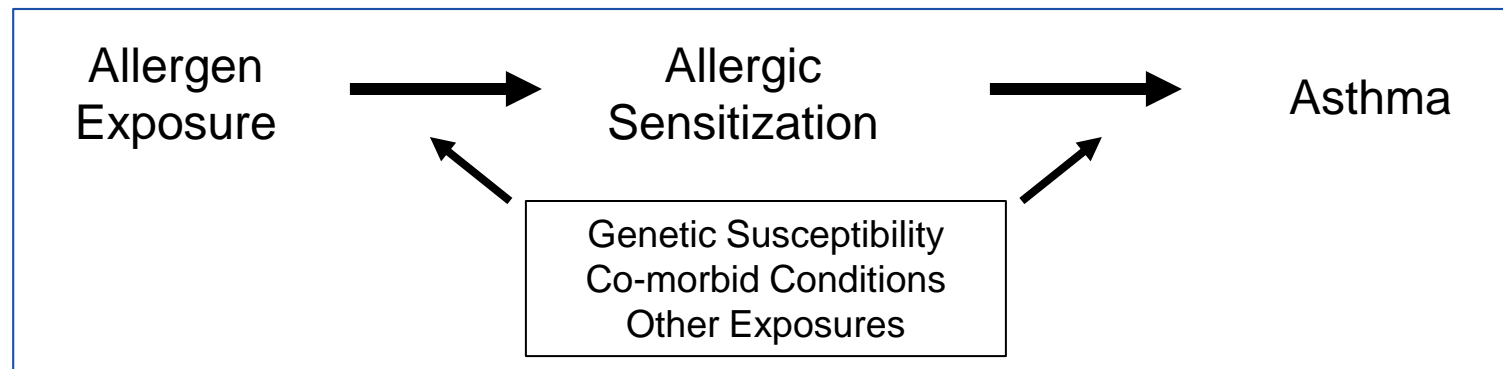
- ▶ **Asthma linked to 3,447 deaths (2007)**

- ▶ **Large cross-sectional survey**
 - ~ 10,000 participants / survey cycle
 - Nationally representative sample
 - Environmental and clinical data
 - Prevalence and risk factors of major diseases
 - National standards (height, weight, blood pressure etc.)
 - National data for public health policies
- ▶ **Conducted by the NCHS, CDC**
- ▶ **Components**
 - Questionnaire
 - Medical examination
 - Laboratory testing



Asthma and Allergy Component

- ▶ To estimate nationwide prevalence of indoor allergen and endotoxin exposures
- ▶ To estimate nationwide prevalence of allergic sensitization to indoor, outdoor and food allergens
- ▶ To estimate nationwide prevalence of allergic diseases including asthma
- ▶ To investigate the complex relationships between allergen and endotoxin exposures, allergic sensitization and allergic diseases



Assessment of Allergy

- ▶ Serum IgE (total, 19 specific) measured using Pharmacia- CAP System™
 - LLOD: 0.35 kU/L (sIgEs); 2.00 kU/L (total IgE)



D. farinae*
D. pteronyssinus*
Cat epithelium/dander*
Dog dander*
German cockroach*
Rat urine proteins
Mouse urine proteins

*Alternaria alternata**
Aspergillus fumigatus
Bermuda grass
White oak
Birch
Russian thistle
Common ragweed
Ryegrass

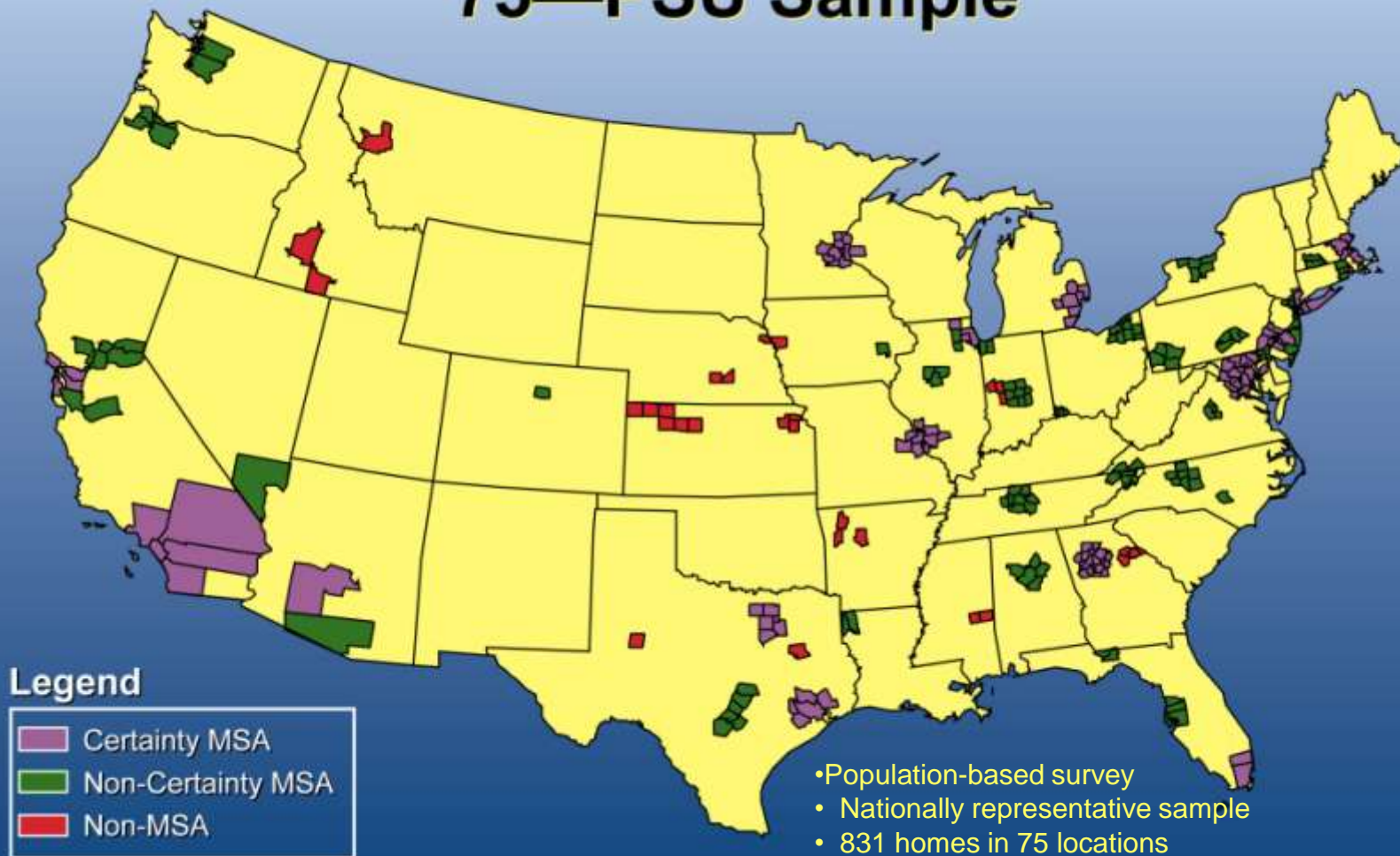
Peanut*
Shrimp
Egg*
Milk*



* 1 ≤ Age < 6

Detailed description of the survey design and implementation of NHANES 2005-2006 can be found online at <http://www.cdc.gov/nchs/nhanes.htm>

75—PSU Sample



- Population-based survey
- Nationally representative sample
- 831 homes in 75 locations
- 2456 occupants
- Sampling in 1998-1999

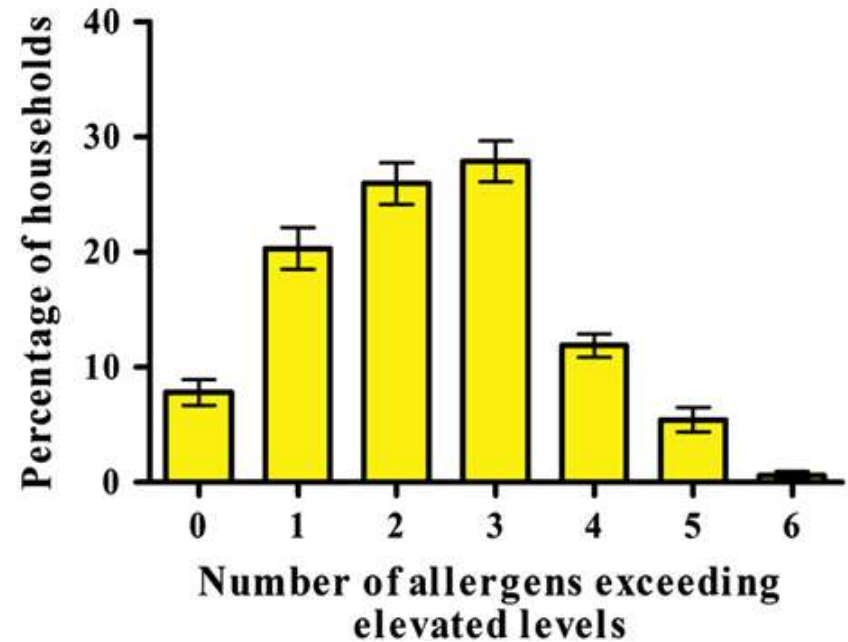
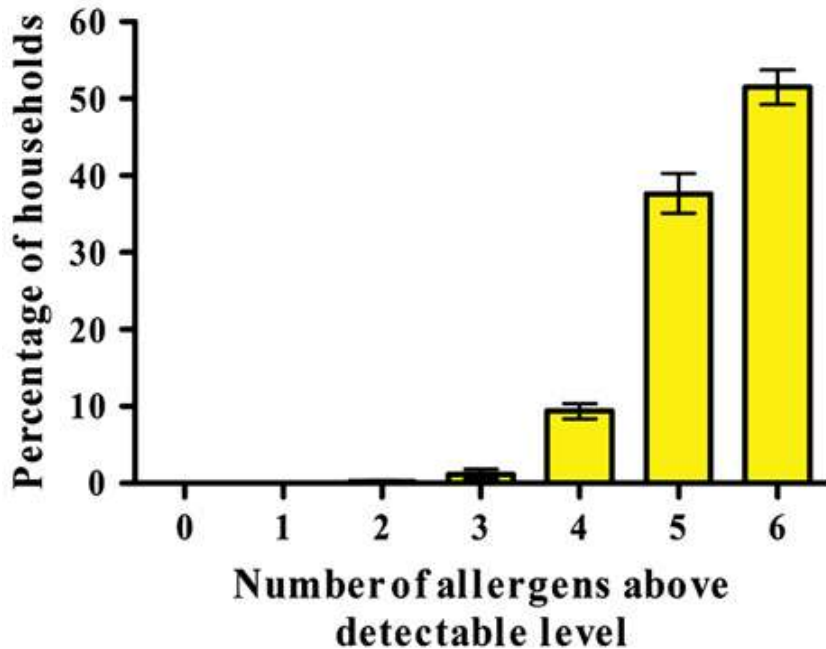
(Vojta et al., EHP 2002;101:527-32)

TABLE I. Estimated distributions of detectable and increased allergen levels in US homes by sampling location*

Allergen levels	Percentage (SE) of households by sampling location					
	Bedroom bed	Bedroom floor	Kitchen floor	Living room floor	Living room upholstery	Any location
<i>A alternata</i>						
Detectable	92.9 (1.4)	99.6 (0.2)	98.1 (0.5)	98.7 (0.4)	98.6 (0.5)	99.9 (0.1)
>7 µg/g	10.4 (1.6)	30.4 (2.4)	24.0 (2.4)	38.8 (1.9)	24.6 (2.2)	56.5 (2.3)
<i>Bla g 1</i>						
Detectable	6.1 (0.8)	17.6 (1.6)	28.5 (1.9)	44.4 (2.1)	38.4 (2.0)	62.7 (1.8)
>8 U/g	0.5 (0.2)	3.2 (0.7)	9.5 (1.0)	2.7 (0.7)	1.1 (0.4)	10.2 (1.1)
<i>Can f 1</i>						
Detectable	93.8 (1.1)	95.6 (0.9)	82.6 (2.4)	94.9 (0.9)	98.0 (0.5)	99.2 (0.3)
>10 µg/g	28.9 (1.9)	30.3 (2.0)	27.2 (3.9)	34.6 (2.0)	37.7 (2.0)	42.2 (2.1)
<i>Der f 1</i>						
Detectable	82.3 (2.0)	80.7 (2.1)	42.8 (3.5)	73.5 (2.2)	78.3 (2.2)	89.5 (1.8)
>10 µg/g	17.4 (2.1)	24.2 (2.5)	1.1 (0.6)	15.6 (1.6)	15.3 (2.2)	35.5 (2.6)
<i>Der p 1</i>						
Detectable	68.7 (2.7)	70.3 (2.2)	39.0 (4.4)	63.6 (3.0)	72.1 (3.0)	85.9 (2.2)
>10 µg/g	8.4 (0.9)	11.6 (1.5)	1.0 (0.5)	8.6 (1.1)	14.6 (1.7)	22.1 (1.5)
<i>Fel d 1</i>						
Detectable	96.7 (0.6)	96.9 (0.8)	83.5 (2.0)	96.0 (0.8)	97.9 (0.5)	99.7 (0.2)
>8 µg/g	30.9 (1.9)	28.3 (1.6)	22.3 (2.2)	26.9 (1.8)	40.2 (1.8)	43.4 (1.7)
MUP						
Detectable	41.2 (2.2)	50.0 (2.1)	57.0 (2.2)	40.7 (2.5)	37.4 (2.4)	82.3 (1.6)
>1.6 µg/g	8.4 (1.2)	13.5 (1.2)	21.6 (2.1)	12.1 (1.4)	7.9 (1.2)	34.6 (2.3)

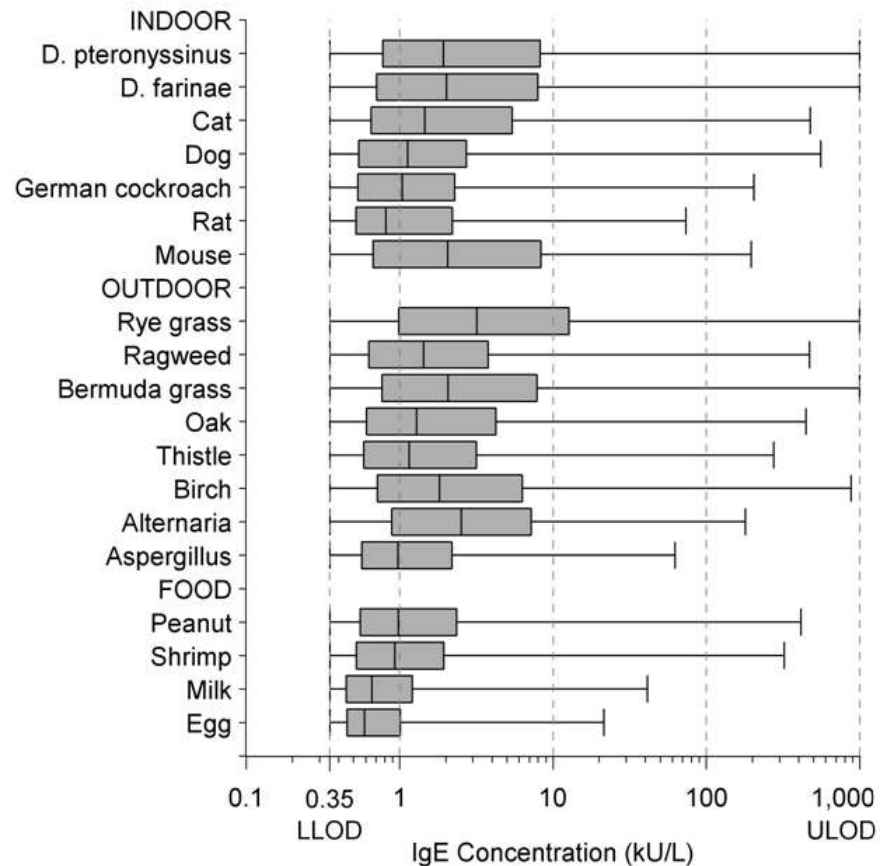
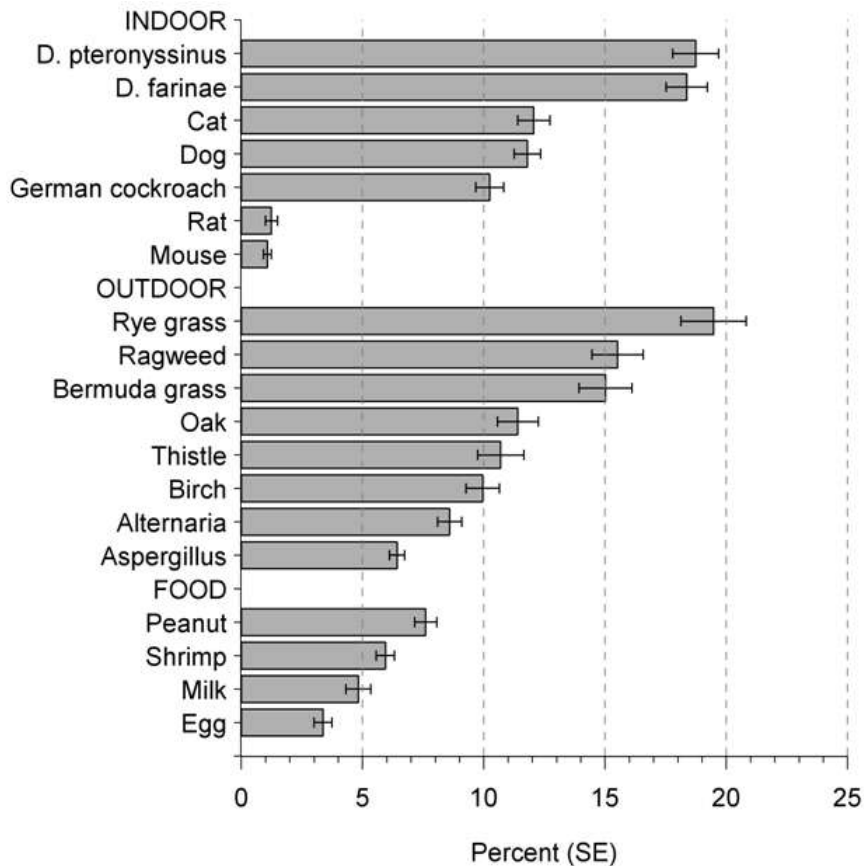
*Allergen measurements were available from at least 1 room for 99% (n = 822) of the households.

Prevalence of Allergen Exposure - NSLAH

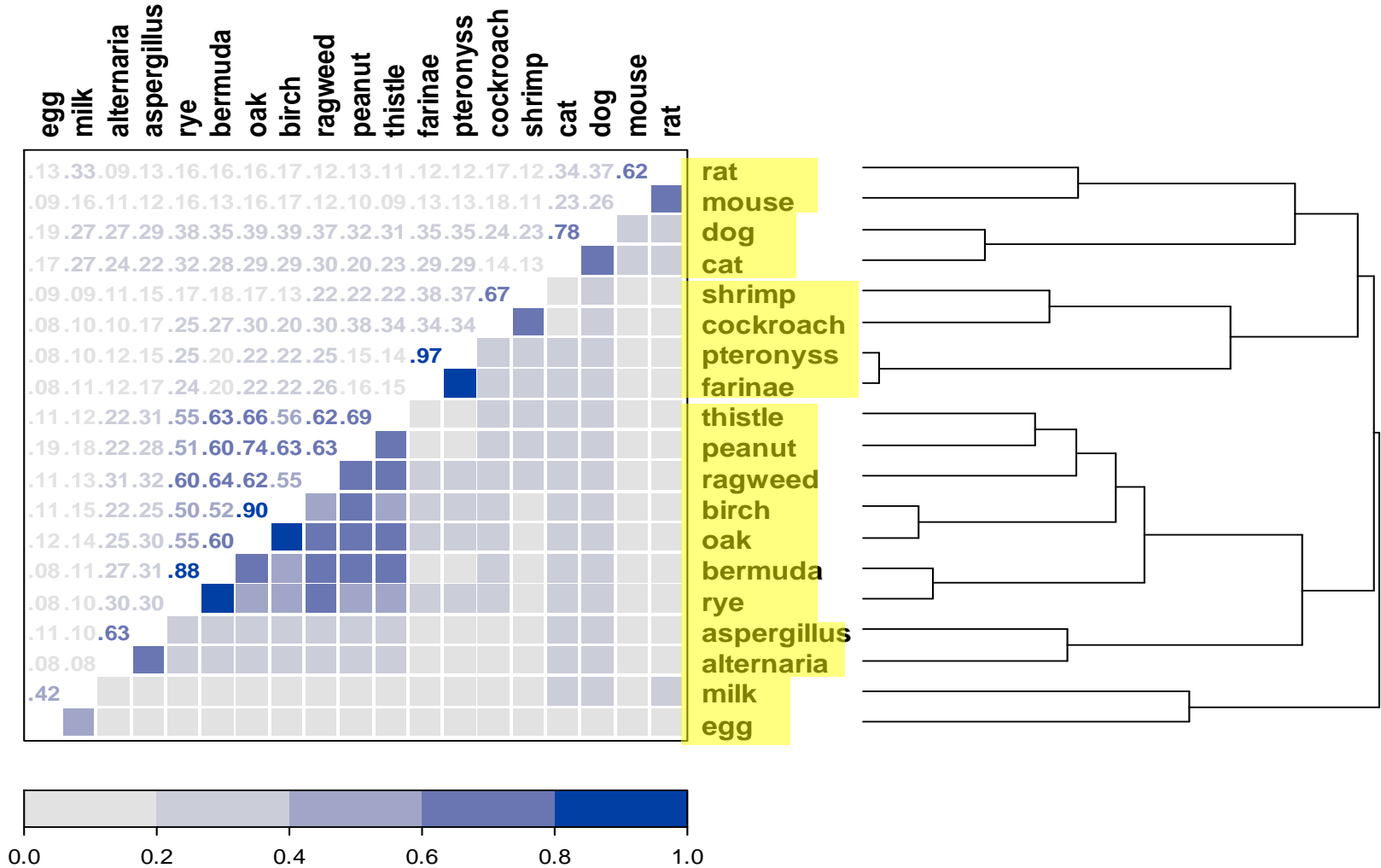


- ▶ **Exposure to multiple indoor allergens was common in U.S. households**
 - **51.5% of households had at least 6 detectable allergens**
 - **45.8% of households had 3 or more allergens at increased levels**

Prevalence and Distributions of Allergen-Specific IgEs



Clustering of Specific IgEs – NHANES 2005-2006



▶ Current asthma

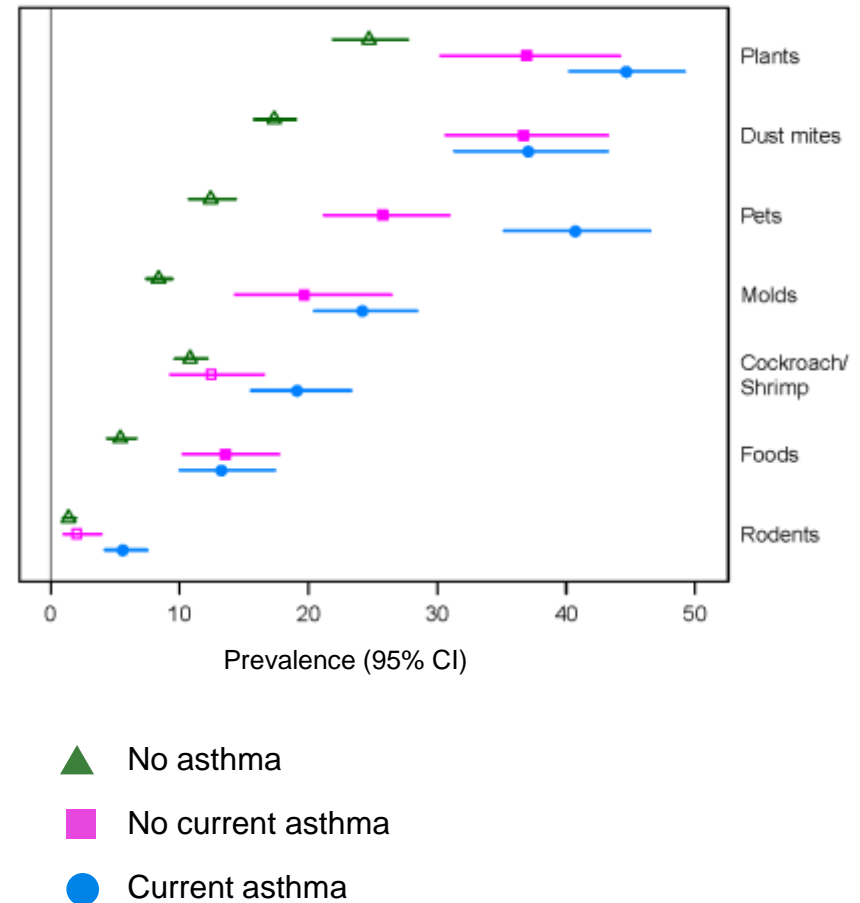
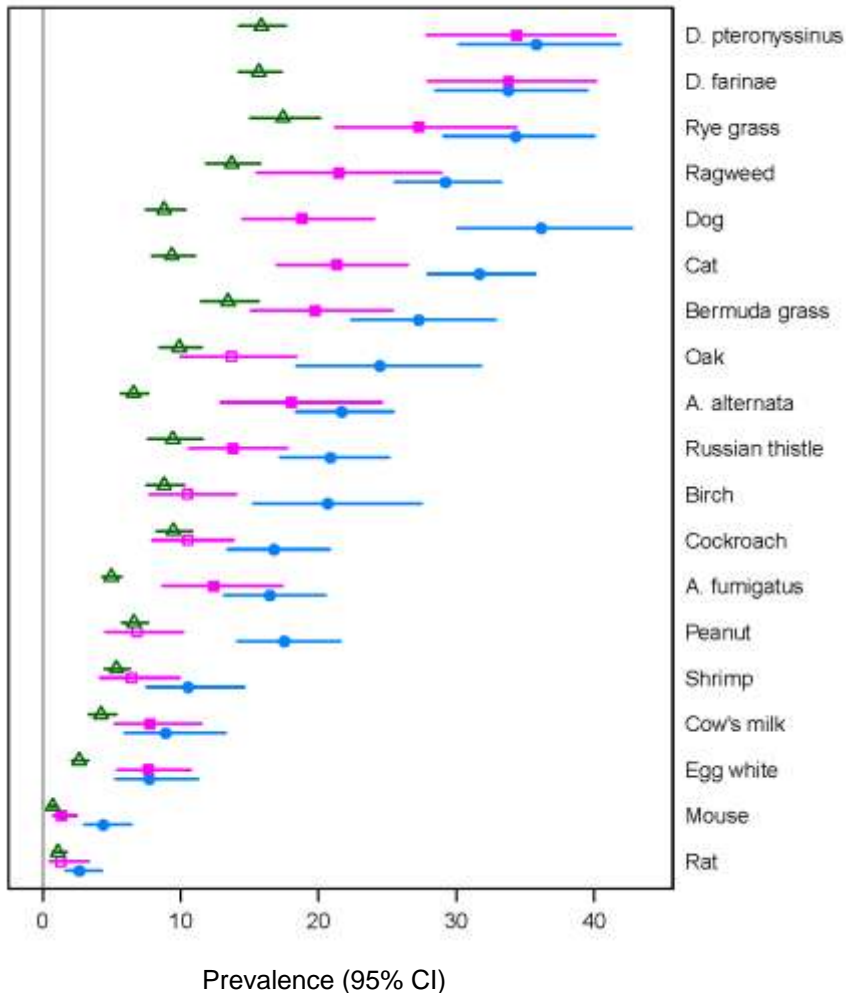
- Has a doctor or other health professional ever told you that you have asthma?
- Do you still have asthma?

▶ Prevalence of asthma

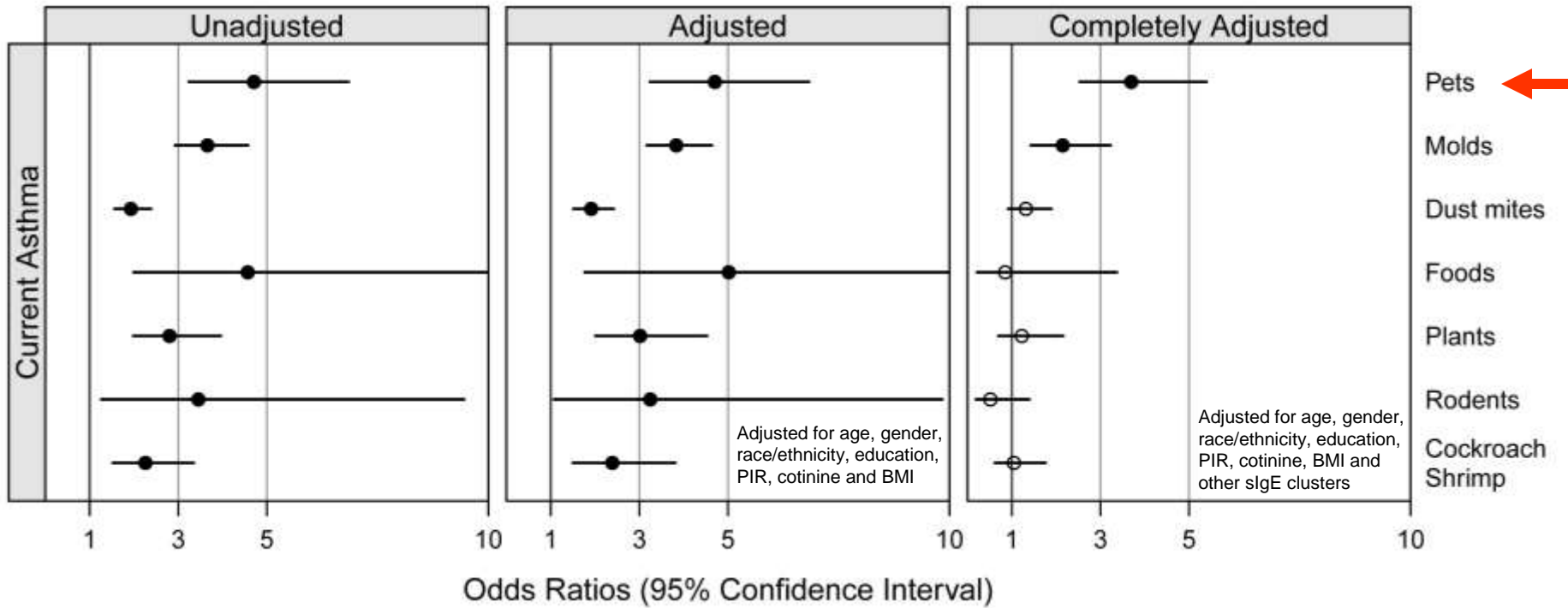
- Children (aged 6-17 yrs)
 - Diagnosed asthma 17.1%
 - Current asthma 11.9%
- Adults (aged 18 and older)
 - Diagnosed asthma 14.0%
 - Current asthma 8.2%

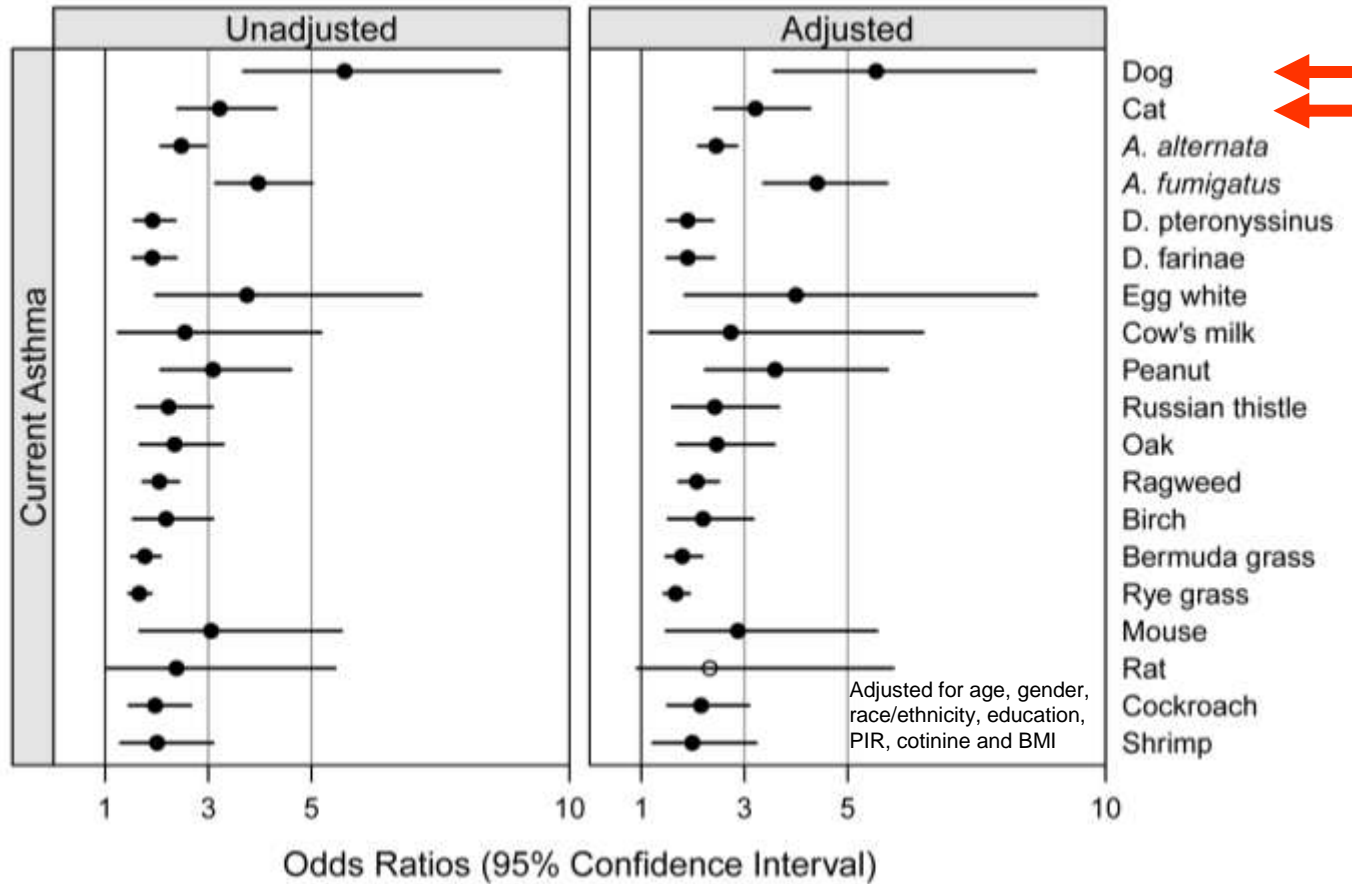
Asthma - Prevalence of Sensitization

► The majority of the asthmatics (62.1%) were atopic (Gergen et al., J Allergy Clin Immunol 2009)

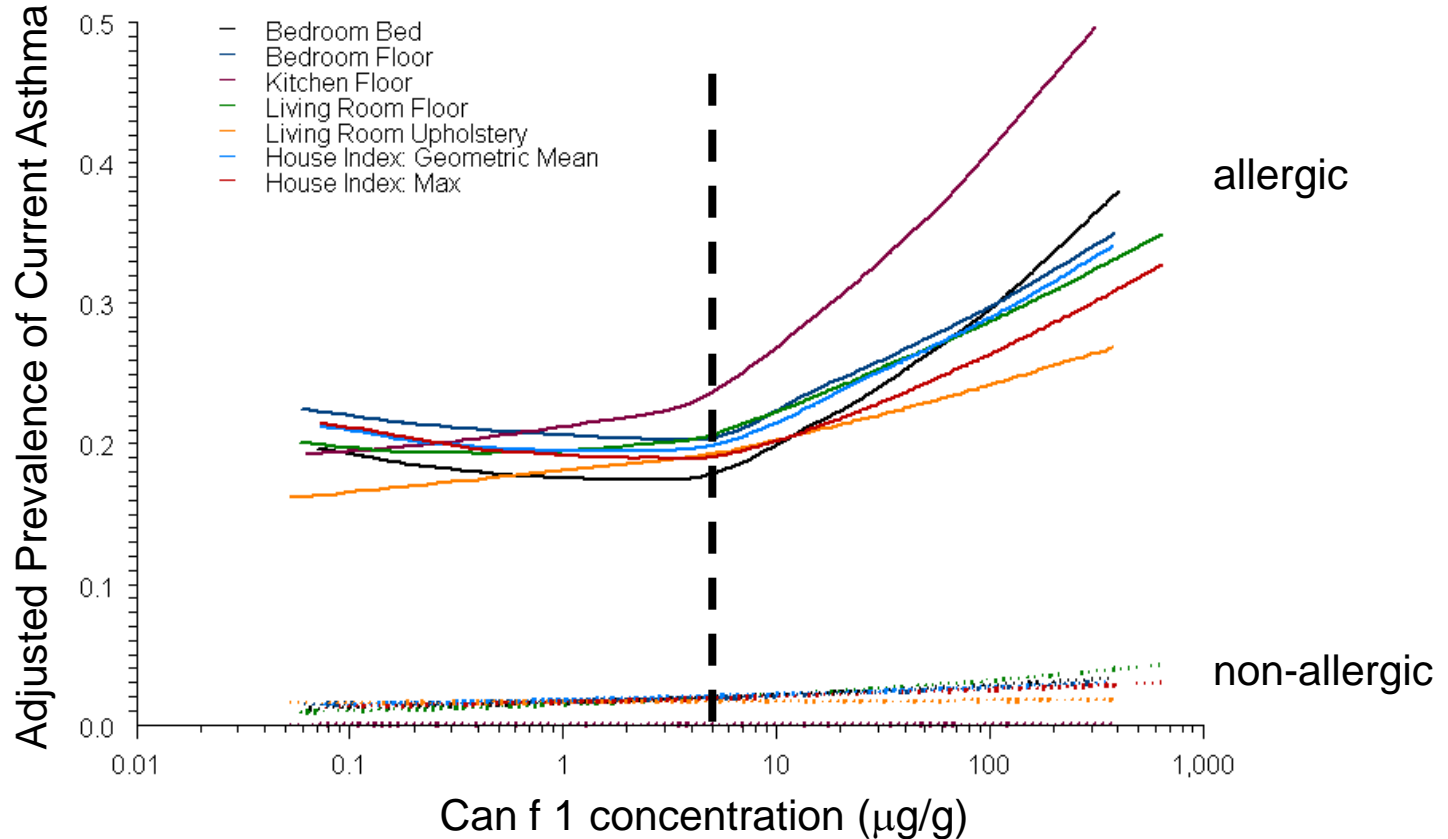


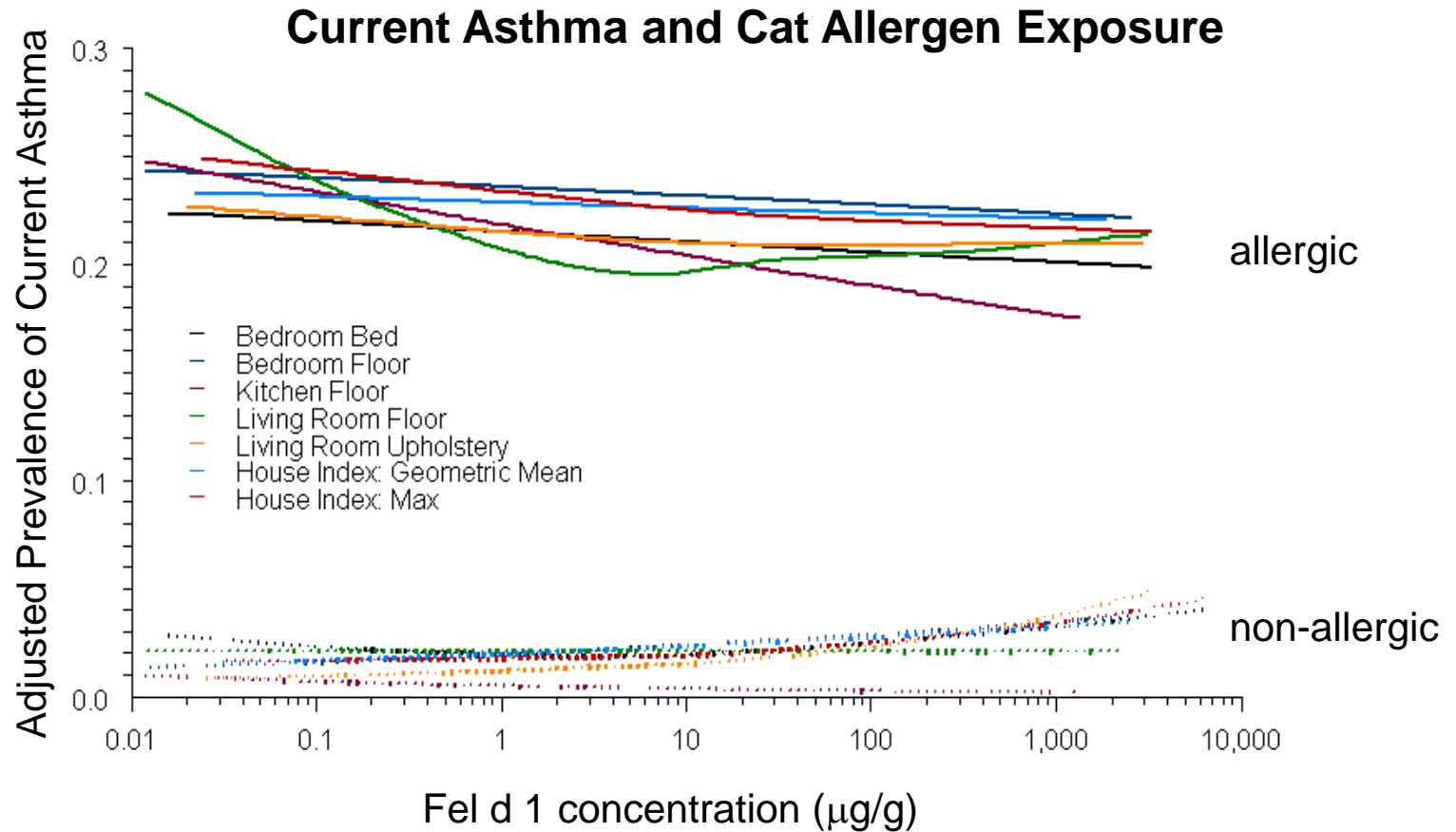
(Salo et al., Unpublished)

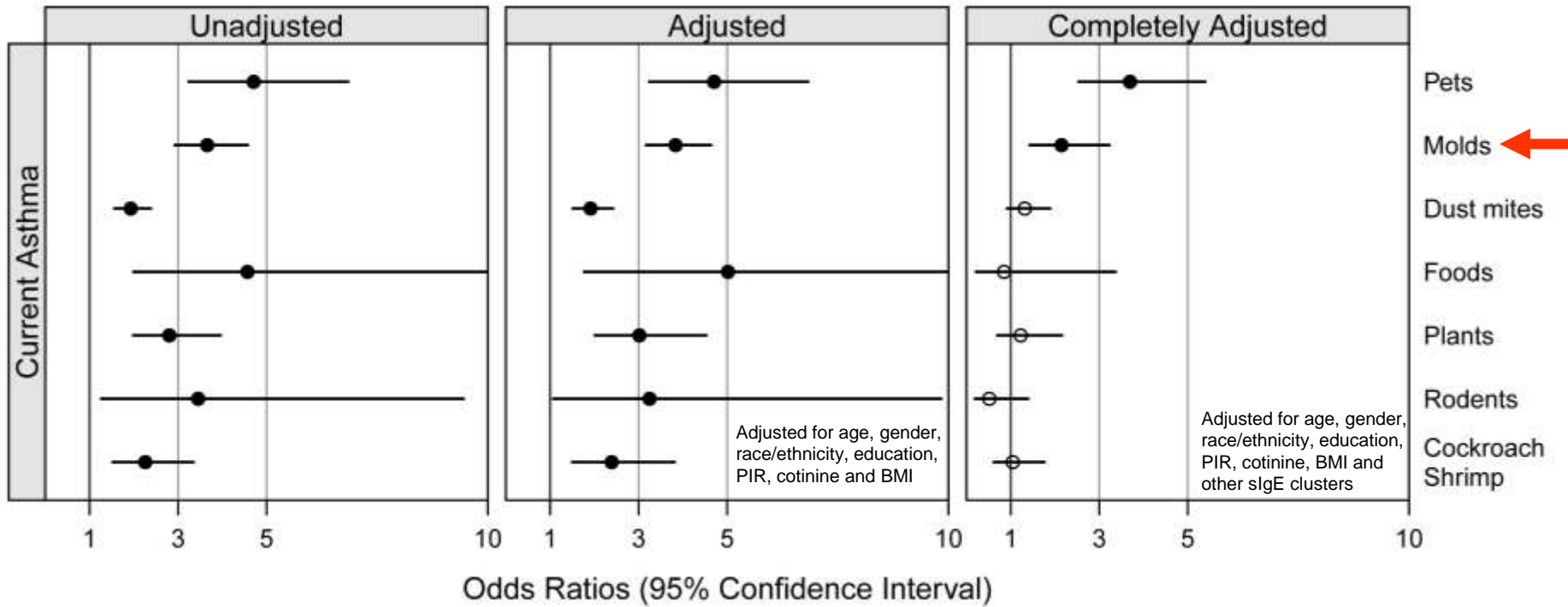


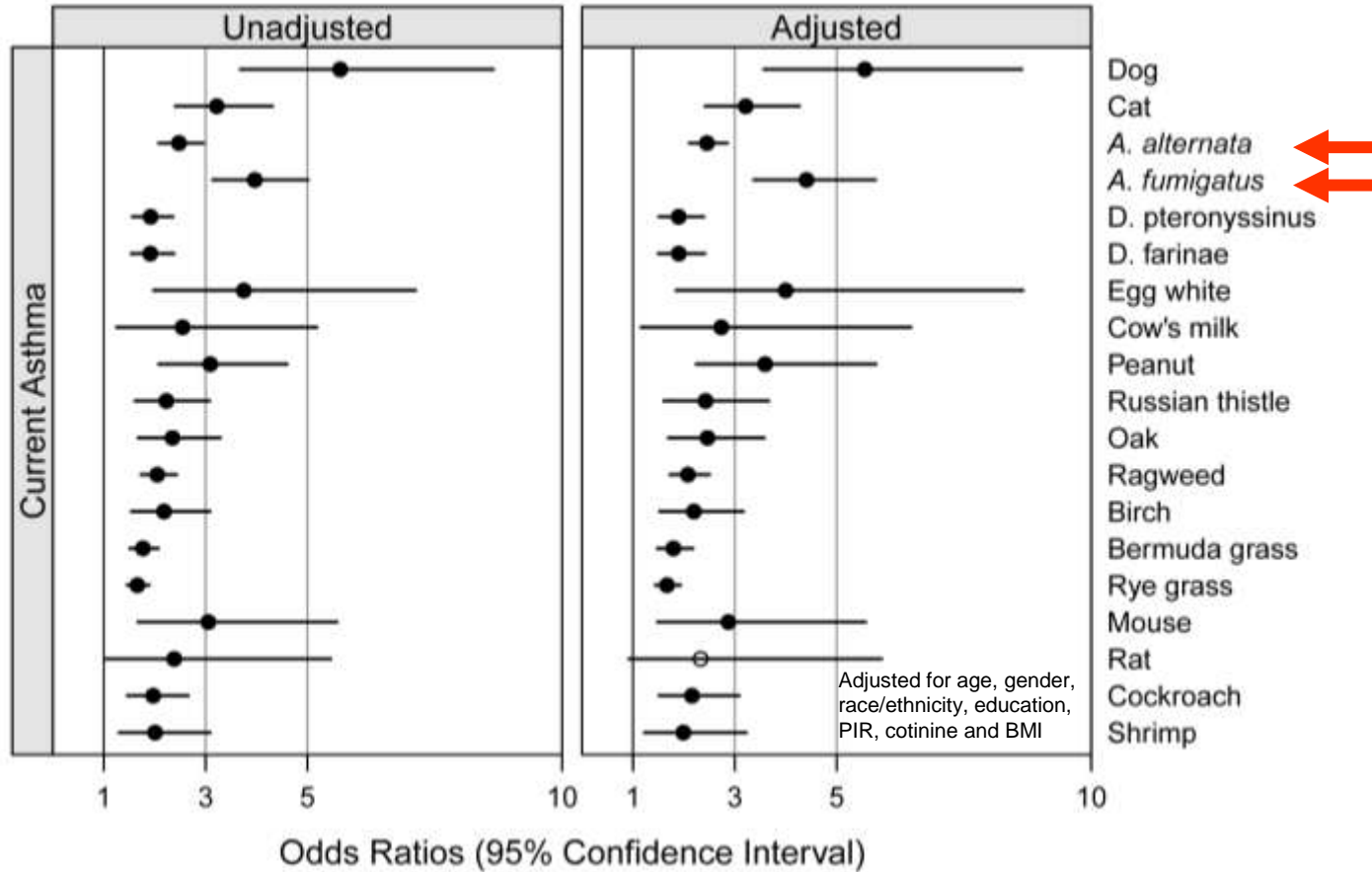


Current Asthma and Dog Allergen Exposure

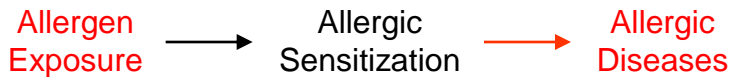
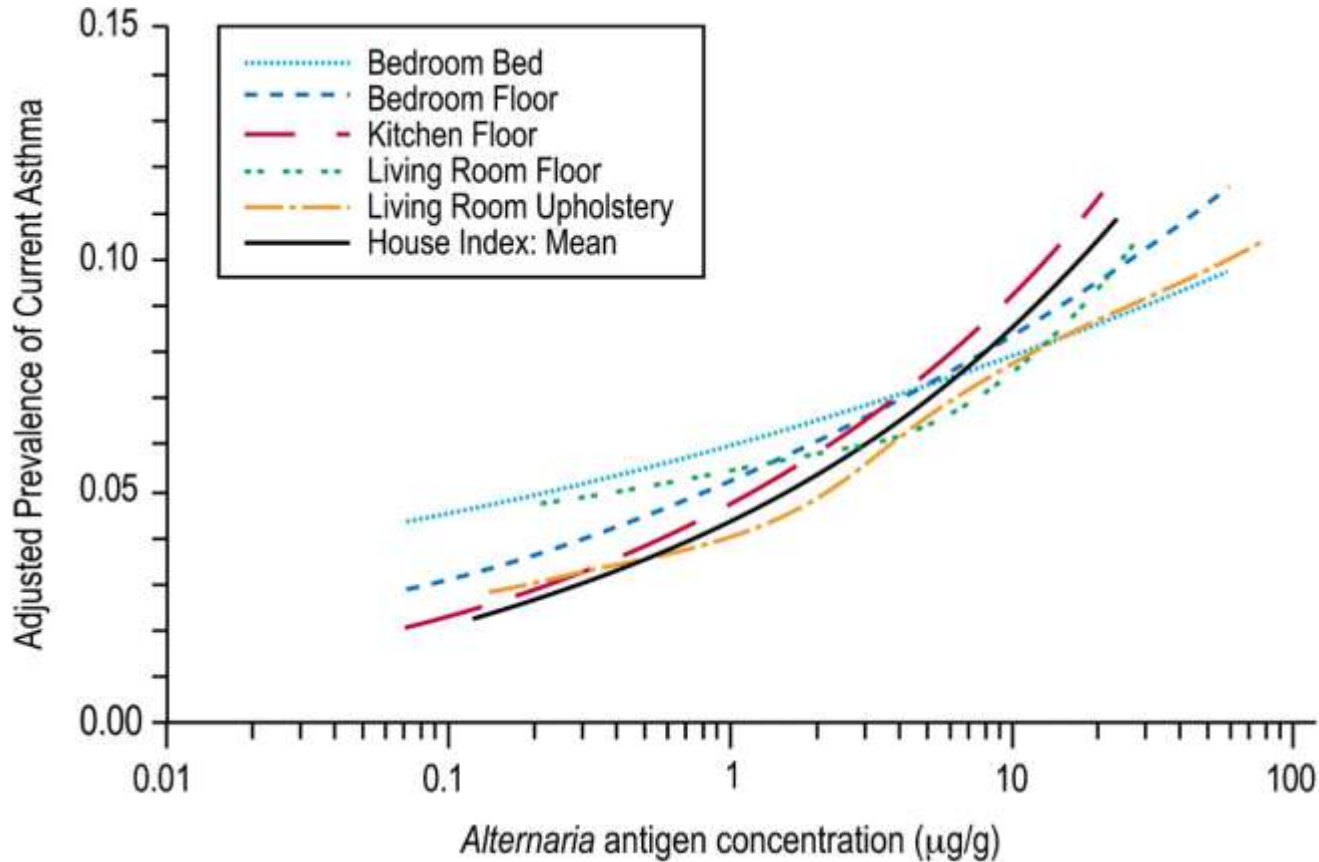






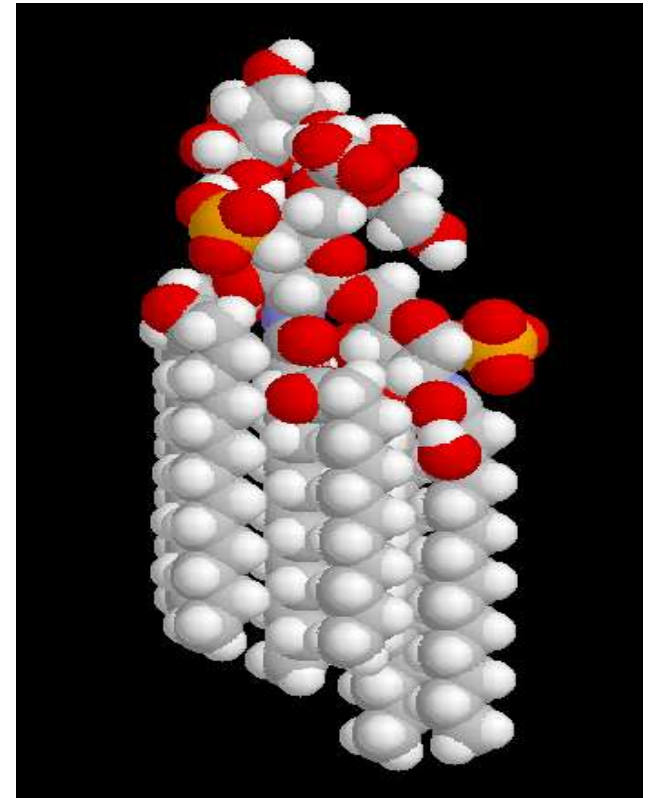


Current Asthma and Mold Exposure- NSLAH



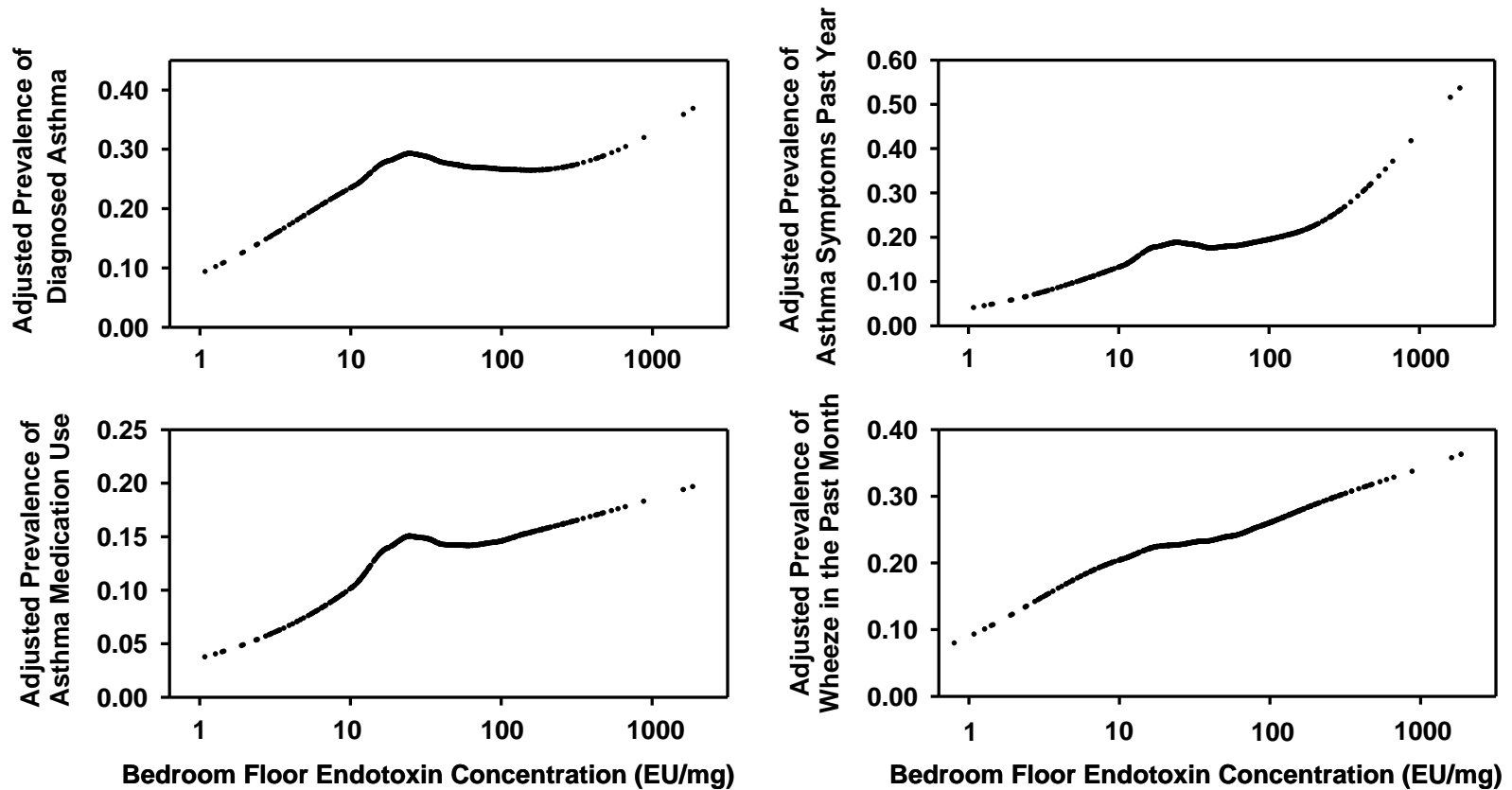
(Salo et al., J Allergy Clin Immunol 2006)

- Lipopolysaccharide molecules come from gram negative bacteria
- Ubiquitous in the environment and indoors
- Trigger inflammatory responses in the lung
- Also have immunomodulatory effects (hygiene hypothesis)
- The role of endotoxin as a risk factor for asthma is controversial; timing of exposure is critical
- Endotoxin exposure known to exacerbate asthma symptoms



(Thorne et al., Amer J Resp Crit Care Med 2005;
Thorne et al., Environ Health Perspect, 2009)

Association Between Endotoxin Exposure and Asthma in US Homes



Summary

- ▶ **Allergen exposure is common in U.S. homes; most homes have >6 allergens above detectable levels and 2-3 allergens that exceed presumptive thresholds**
- ▶ **Allergic sensitization is also common in the U.S.; approximately half of the population is sensitive to at least to one allergen**
- ▶ **Asthma is most consistently associated with pet- and mold-specific sensitization**
- ▶ **Relationship between allergen exposure, allergic sensitization and asthma is complex and varies by allergen type**
- ▶ **Endotoxin exposure is associated with asthma morbidity**

Conclusions

- ▶ **Exposure to allergens and endotoxin in the environment is important in asthma pathogenesis**
- ▶ **Reducing exposure to environmental triggers should be considered an integral part of any asthma management plan in sensitized individuals**



Thank you!