

Disclosure Slide

- **Employment**
 - University of Wisconsin
- **Financial Interests**
 - Advisory Boards: Merck
 - Consultant: Amgen, Novartis, GlaxoSmithKline, MedImmune, Genentech
- **Data Monitoring Boards and Study Oversight Committees**
 - Boston Scientific
 - Genentech
 - Icon
- **Research Interests**
 - NHLBI, NIAID,
- **Organizational Interests**
 - AAAAI, ATS, AAP, ACAAI, AAI, ACP, CIM
- **Gifts**
 - Nothing to Disclose
- **Other Interests**
 - Nothing to Disclose

Why Focus on Inner City Asthma in Children and Adolescents?

- Asthma is both more common and more severe in U.S. inner cities
- High allergen loads
 - Cockroach
 - Mouse
 - House dust mite
- Given the likely importance of allergen – IgE interactions to disease, particularly in the inner city, it was hypothesized that asthma control would improve by modulating IgE-dependent contributions to asthma

**Randomized Trial of Omalizumab
(Anti-IgE) for Asthma in Inner-City
Children. Busse WW, Morgan WJ, et
al. N Engl J Med 2011; 364:1005-15**

Enrollment characteristics

- 6 to 20 years of age with a diagnosis of persistent asthma
- Allergy to a perennial allergen
- Inner-city resident
- At recruitment, participants had uncontrolled asthma
- Weight and total serum IgE levels were suitable for omalizumab dosing

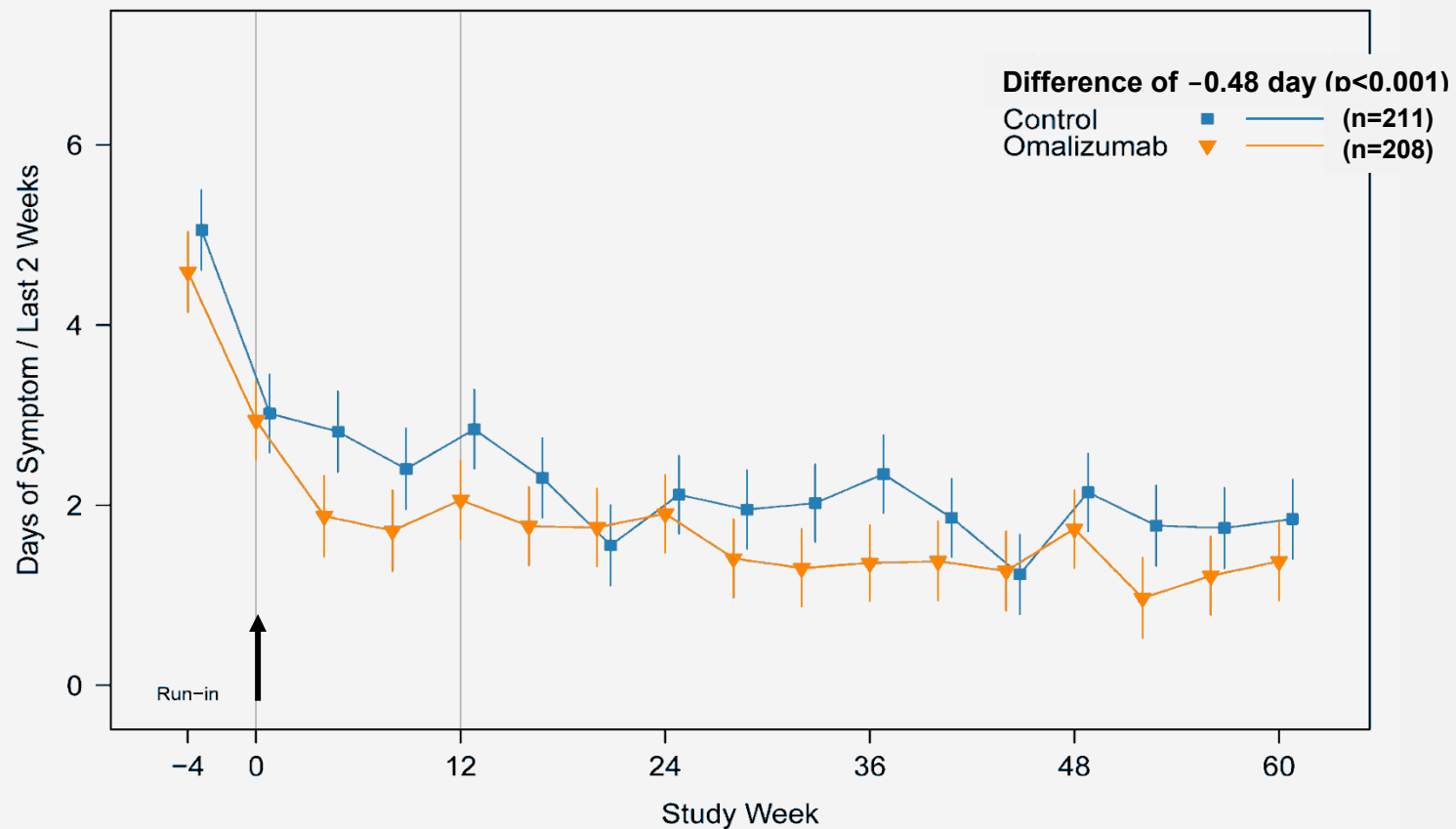
Study design

- Enrollment (4 weeks)
 - asthma control assessed
 - using a guidelines-based algorithm, treatment was begun or adjusted to achieve asthma control
- Randomization and treatment (60 weeks)
 - following an adjustment of asthma medications during enrollment, participants were randomized to receive omalizumab or placebo every 2–4 weeks for 60 weeks

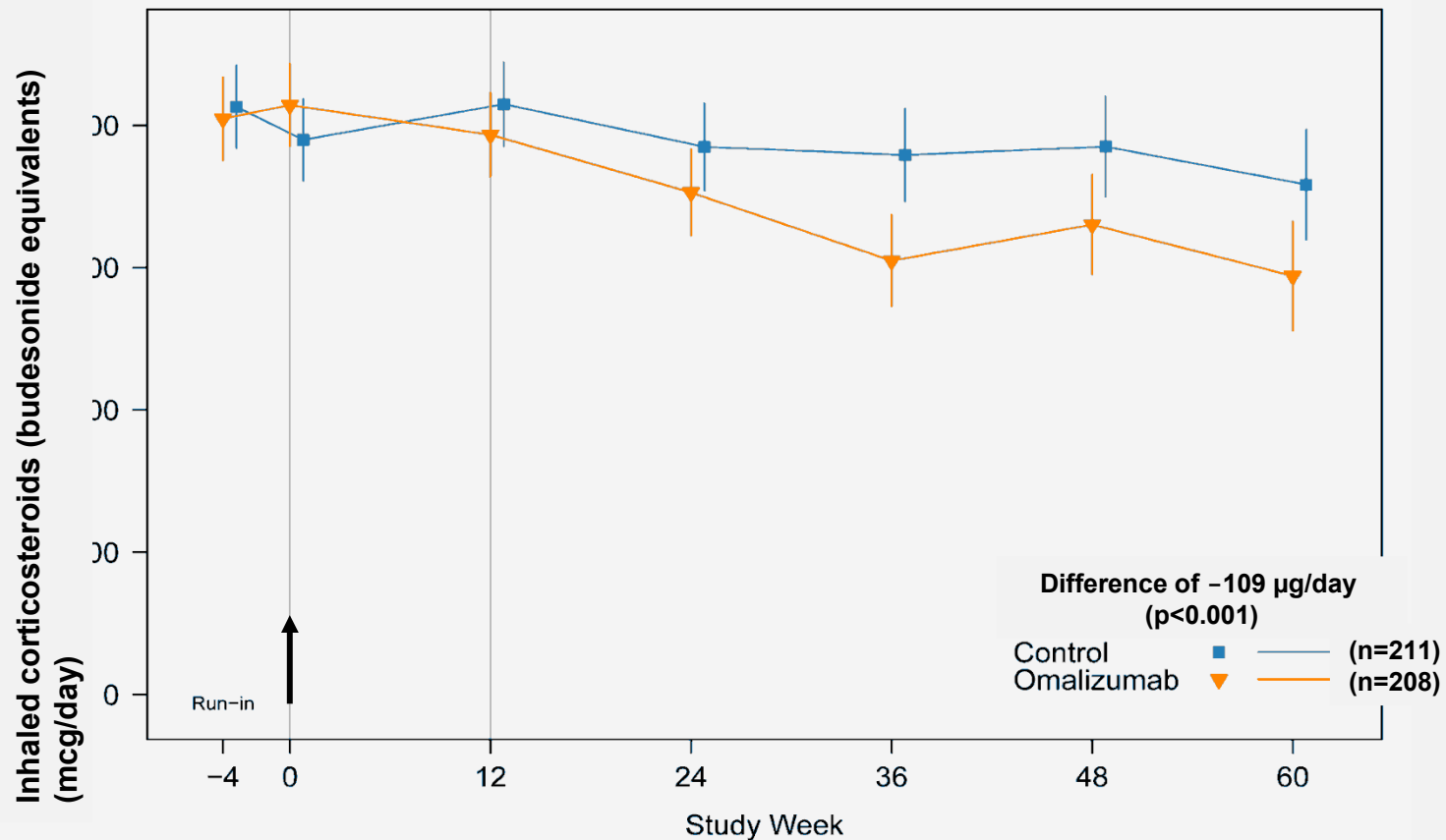
Asthma control of participants at enrollment (n=419)

- Days of asthma symptoms the previous 2 weeks 4.9±4.2
- Childhood ACT[®] score in the last month (4–11 years) 18.9±4.1
- ACT[®] score (12 years and over) 18.8±4.2
- FEV₁ (% predicted value) 92.1±17.1
- FEV₁/FVC 77.1±9.9
- ≥1 Hospitalization/past year 25%
- ≥1 Unscheduled visit/ past year 78%
- Male subjects 58%

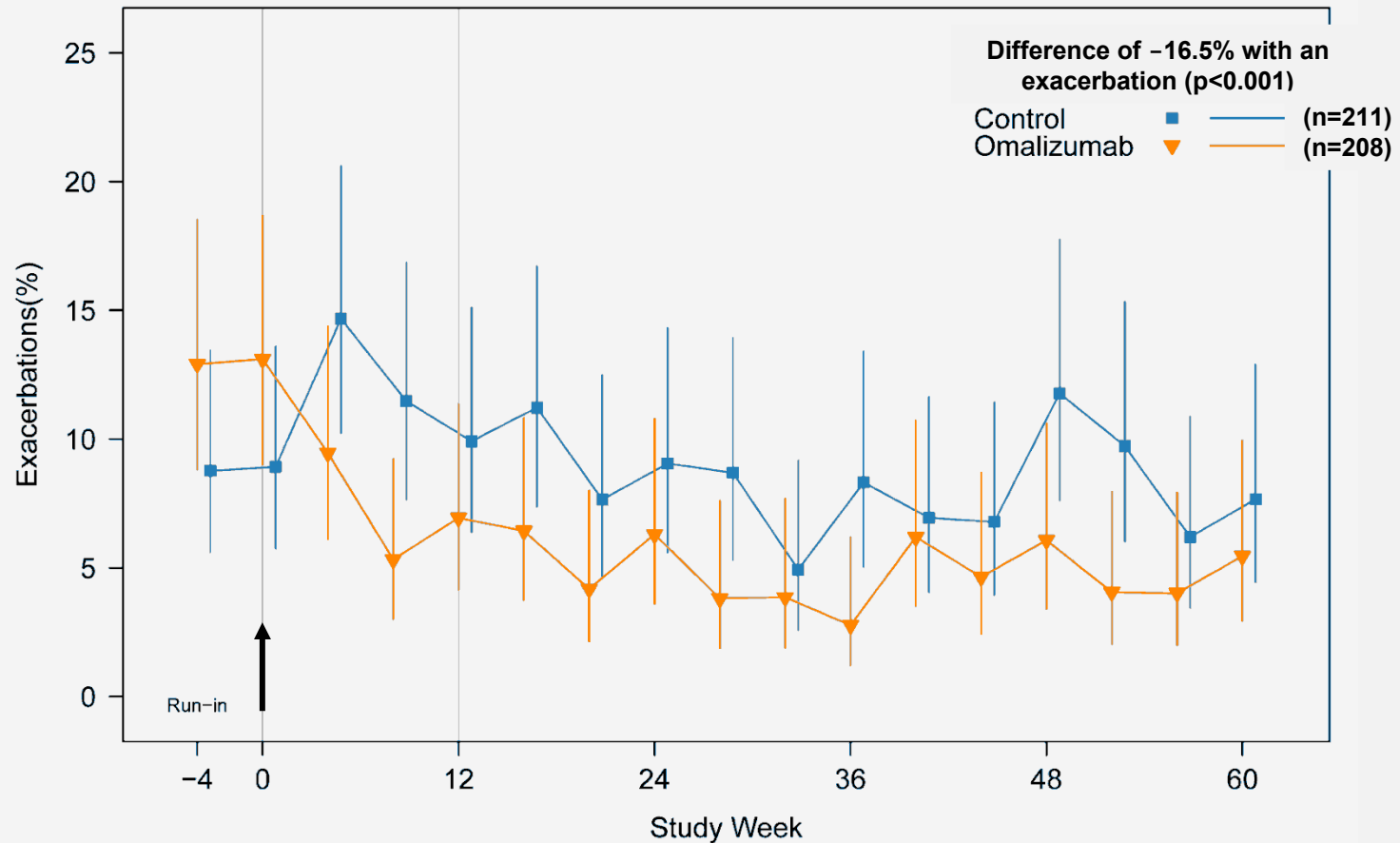
What were the effects of omalizumab on the number of days with asthma symptoms in the last 2 weeks?



What were the effects of omalizumab on the daily dose of inhaled corticosteroids (budesonide equivalents [$\mu\text{g}/\text{day}$])?



What were the effects of omalizumab on exacerbations?



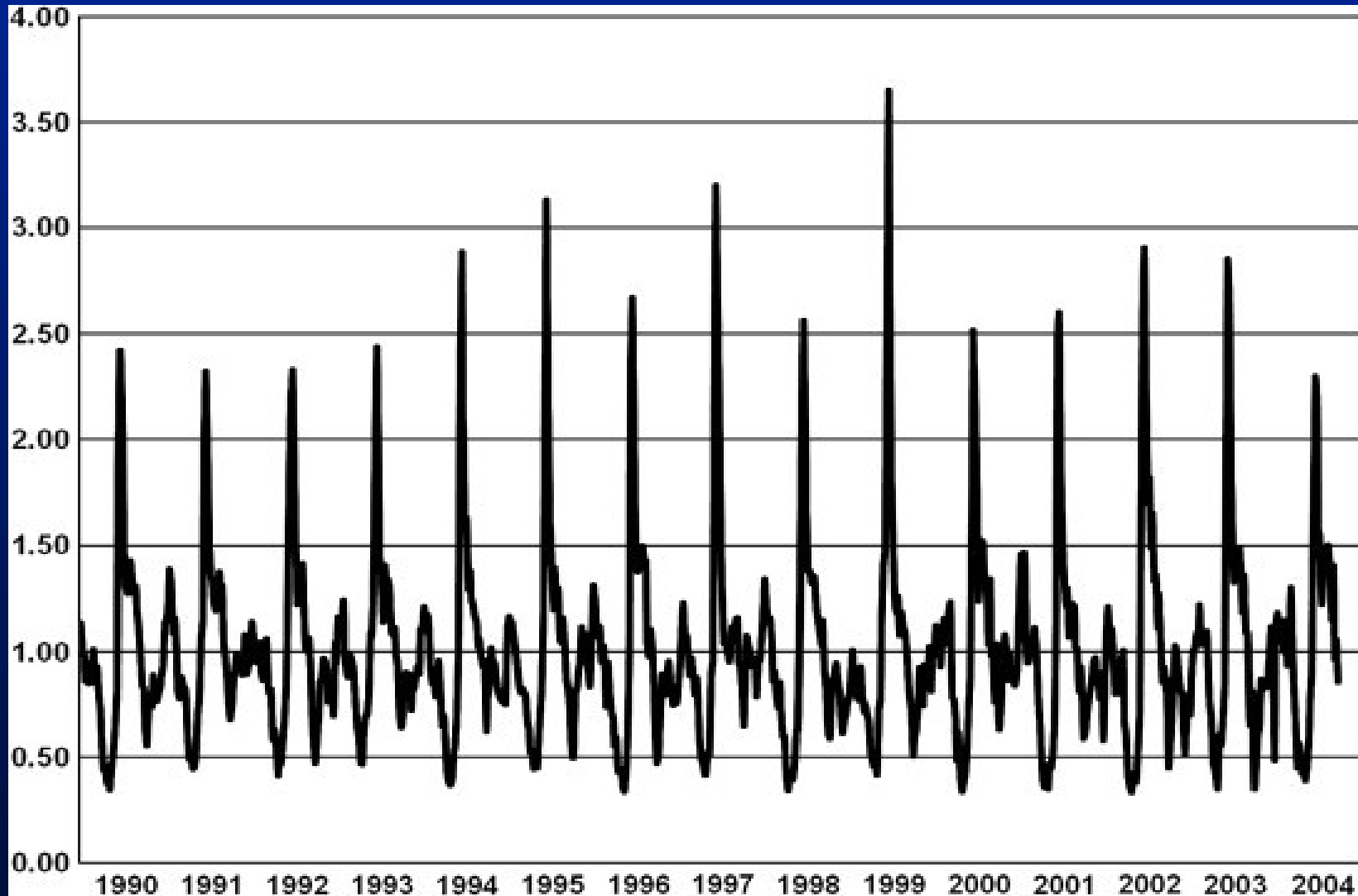
**Asthma exacerbations also
have seasonal patterns**

The September Epidemic of Asthma Exacerbations

Johnston N et al, JACI 117:557-62, 2006

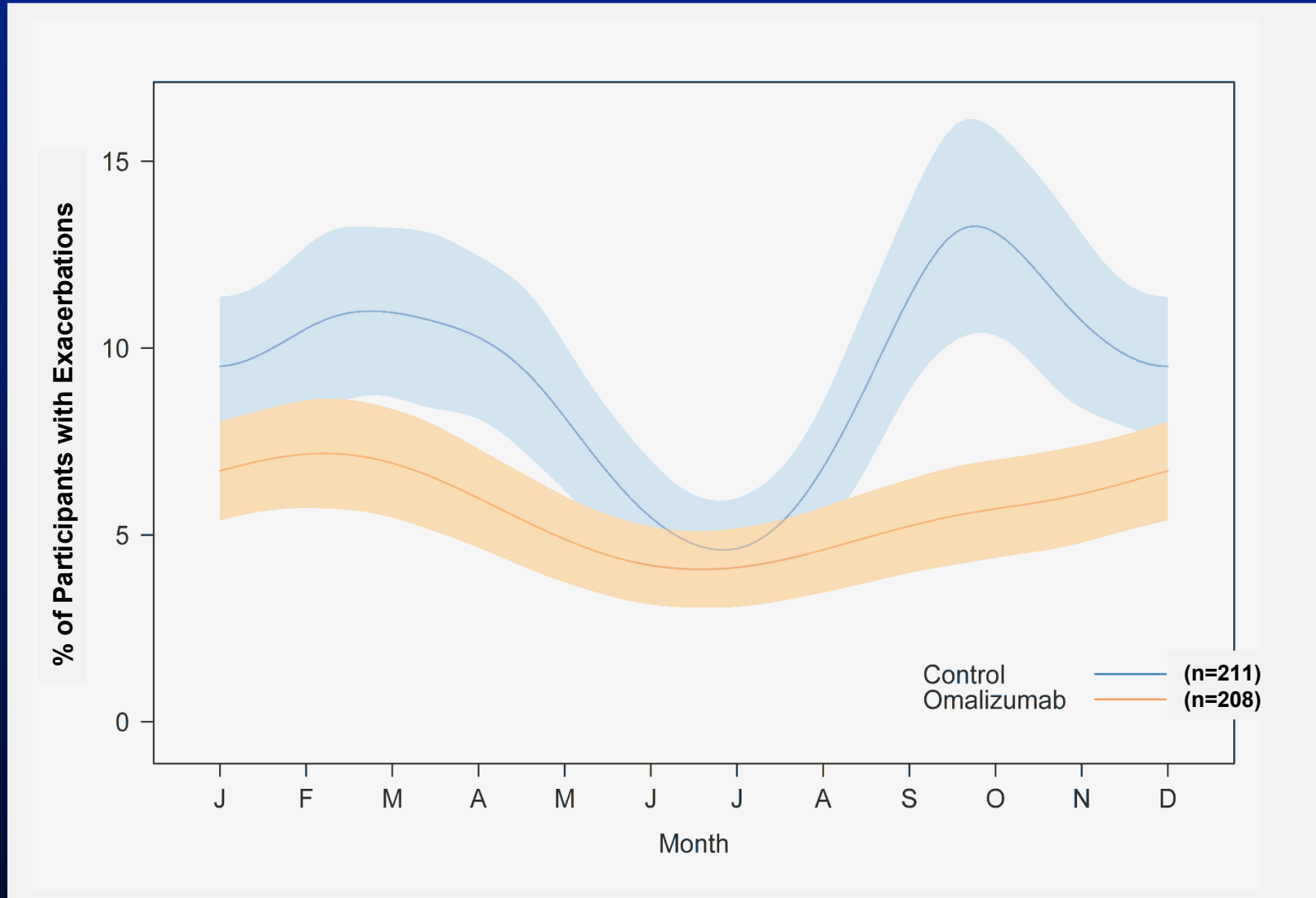
- Canadian asthma hospitalization admission data
- Timing and magnitude of peaks in asthma hospitalization
 - 5-15 y/o children: 17.7 days after Labor Day
 - Preschoolers 1.7 days later
 - Adults 6.3 days later
- Peak season for:
 - HRV
 - Some allergens (*Alternaria*, ragweed)

Asthma Hospitalization Rates Ages 5-15 Yrs

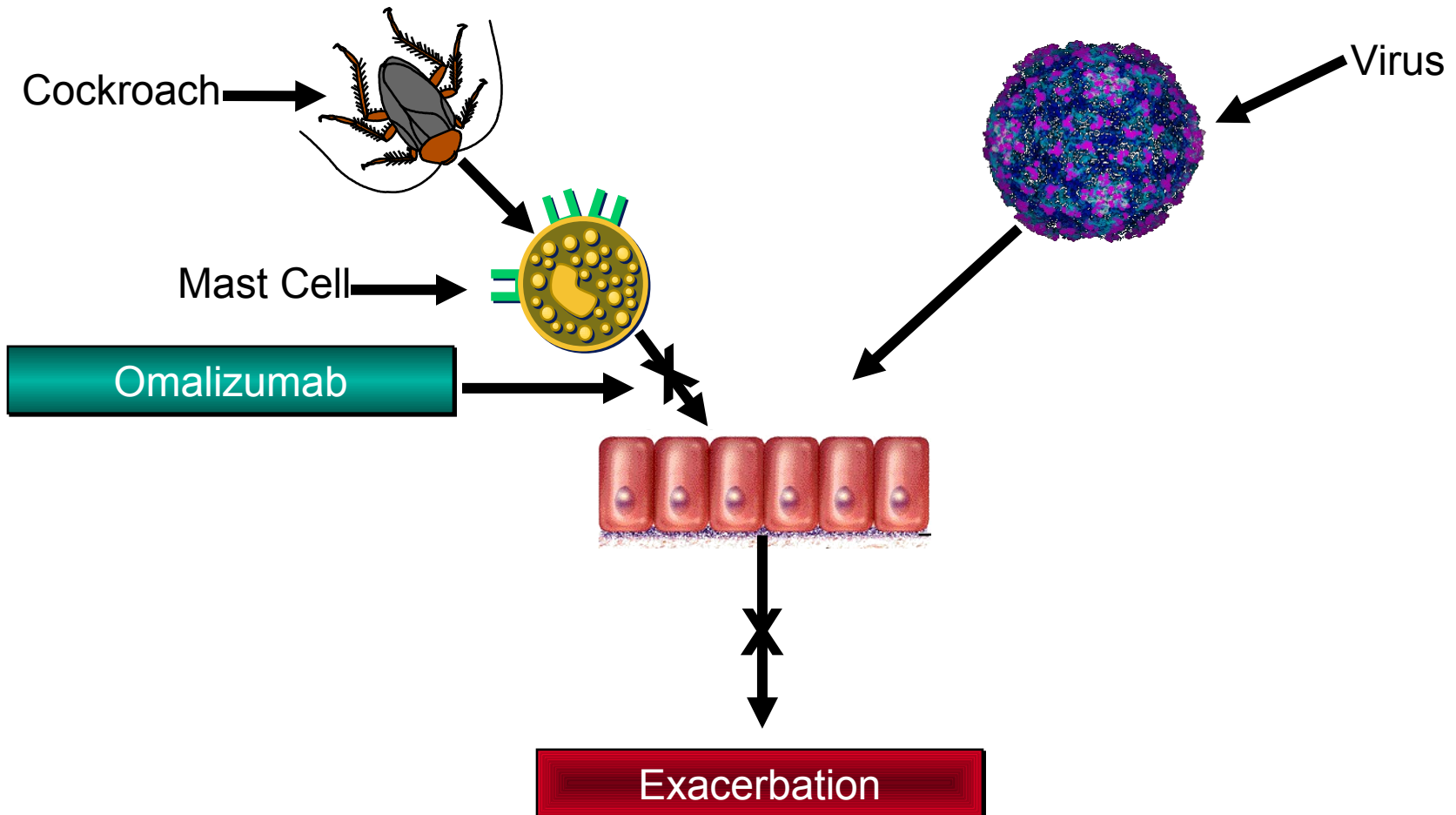


Johnston N, et al. JACI 117:557-62, 2006

What are the effects of omalizumab on the percentage of participants experiencing exacerbations over the year?



The importance of IgE and allergic sensitization in virus-provoked asthma exacerbations

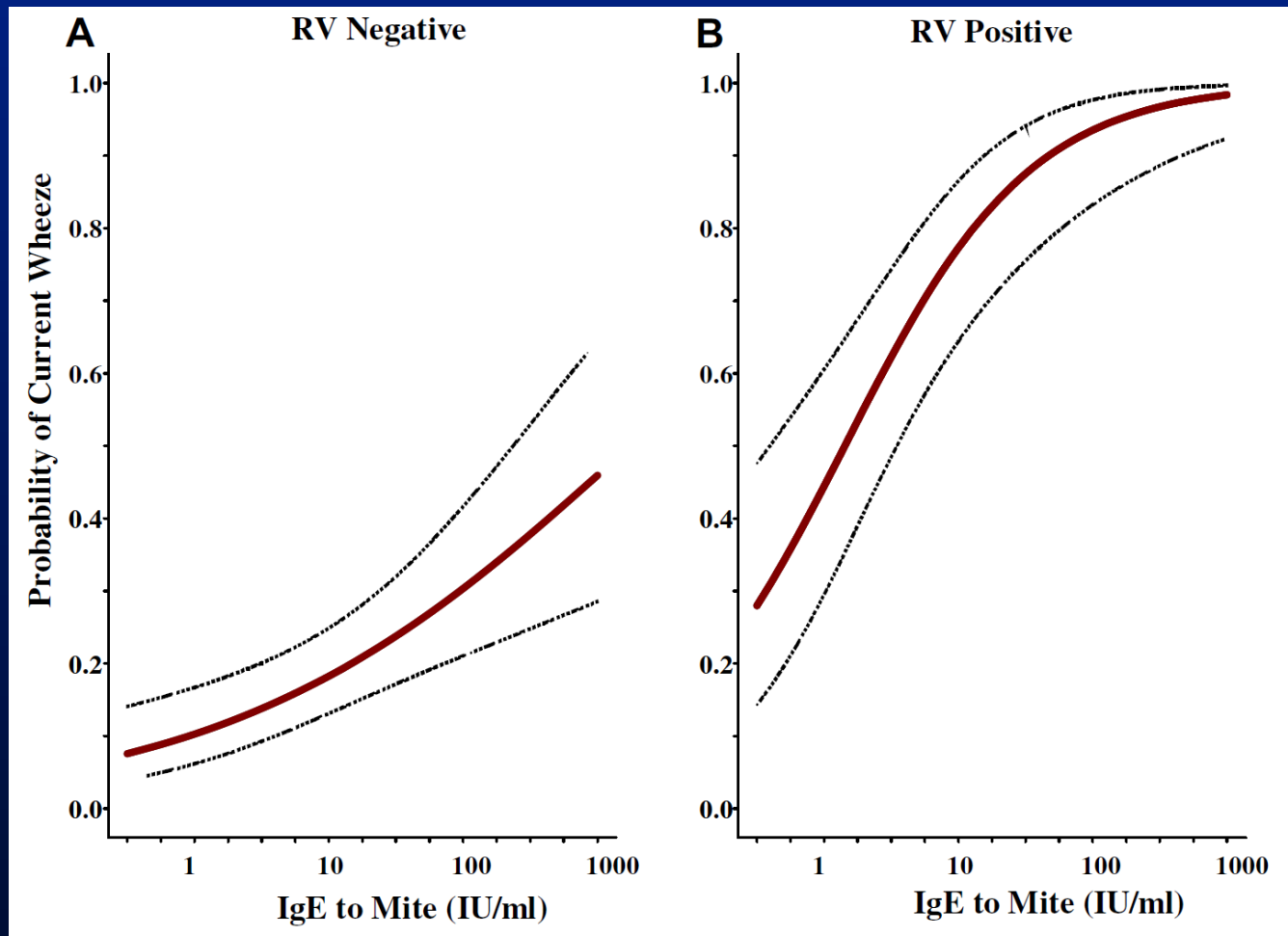


What role does IgE play in asthma exacerbations?

Soto-Quiros et al. High titers of IgE antibody to dust mite allergen and risk for wheezing among asthmatic children infected with rhinovirus. J Allergy Clin Immunol 2012;129:1499-1505.

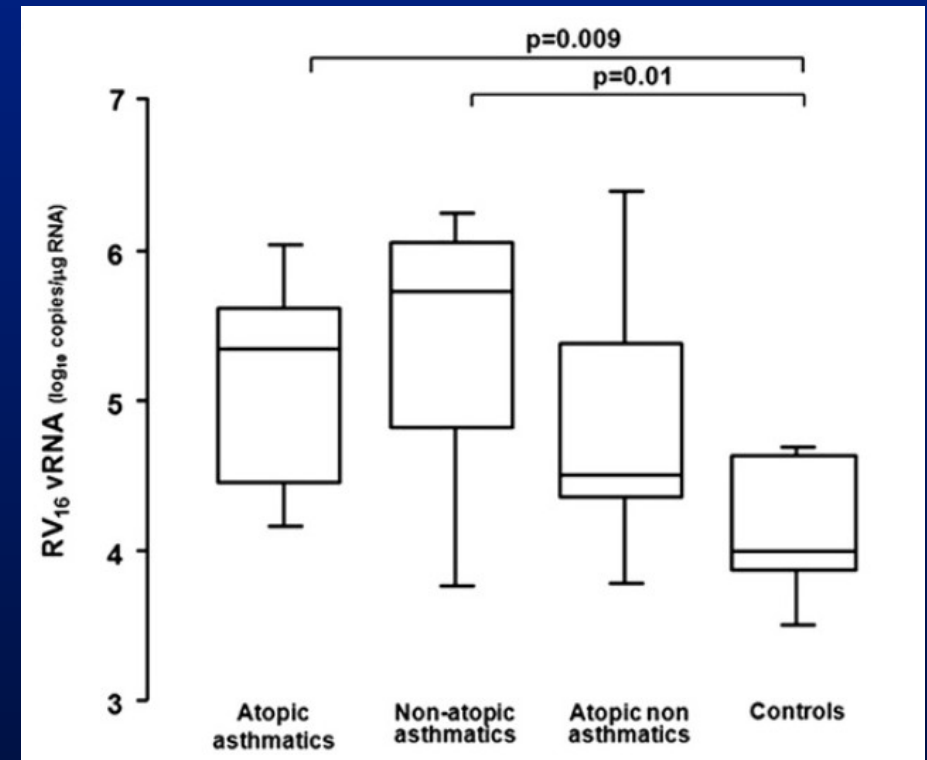
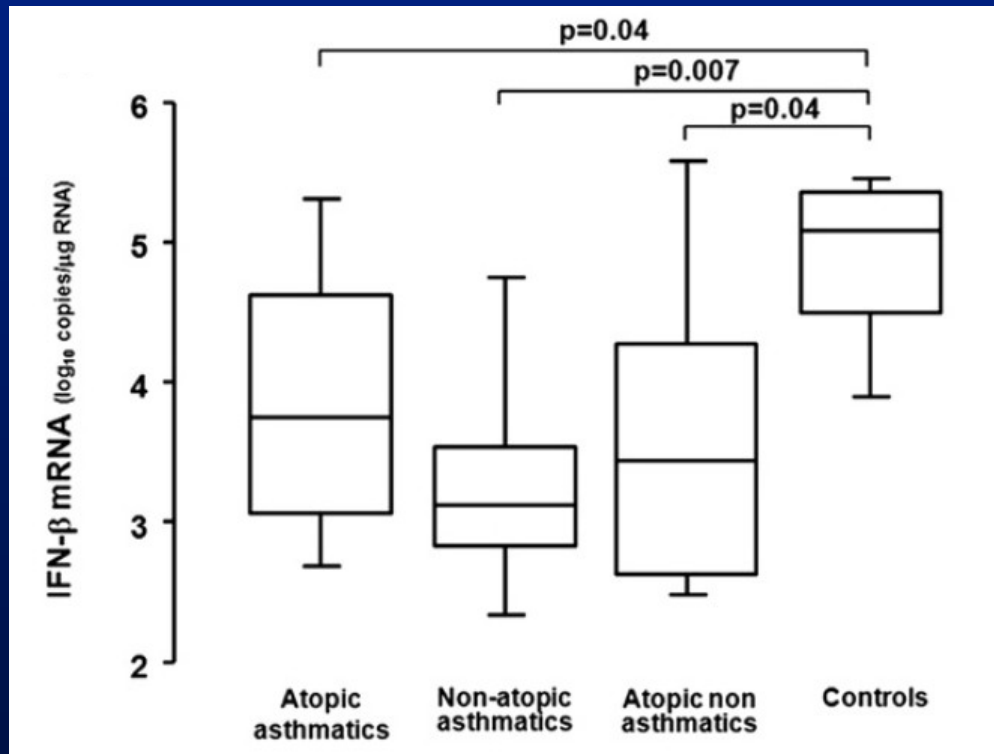
- Evaluated the contribution of rhinovirus infections and atopic status to wheezing episodes in children (7 to 12 years old) in Costa Rica
- 287 Children
 - 96 with acute wheezing
 - 65 stable asthma
 - 126 non-asthmatic control subjects

Probability of current wheezing based on increasing titers of IgE antibodies to *D pteronyssinus* in children with negative test results for rhinovirus by using real-time PCR (A) compared with children with positive test results for rhinovirus (B).



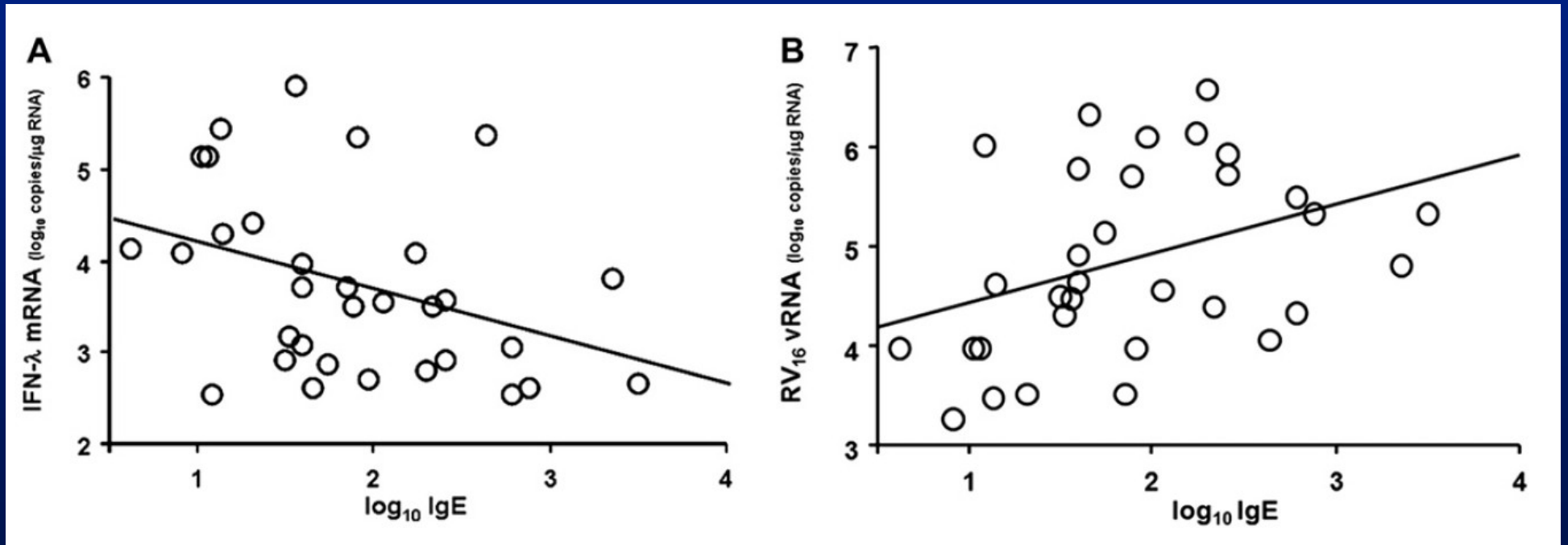
Soto-Quiros, et al. J Allergy Clin Immunol 2012;129:1499-1505.

Does IgE affect interferon induction to rhinovirus and its replication?



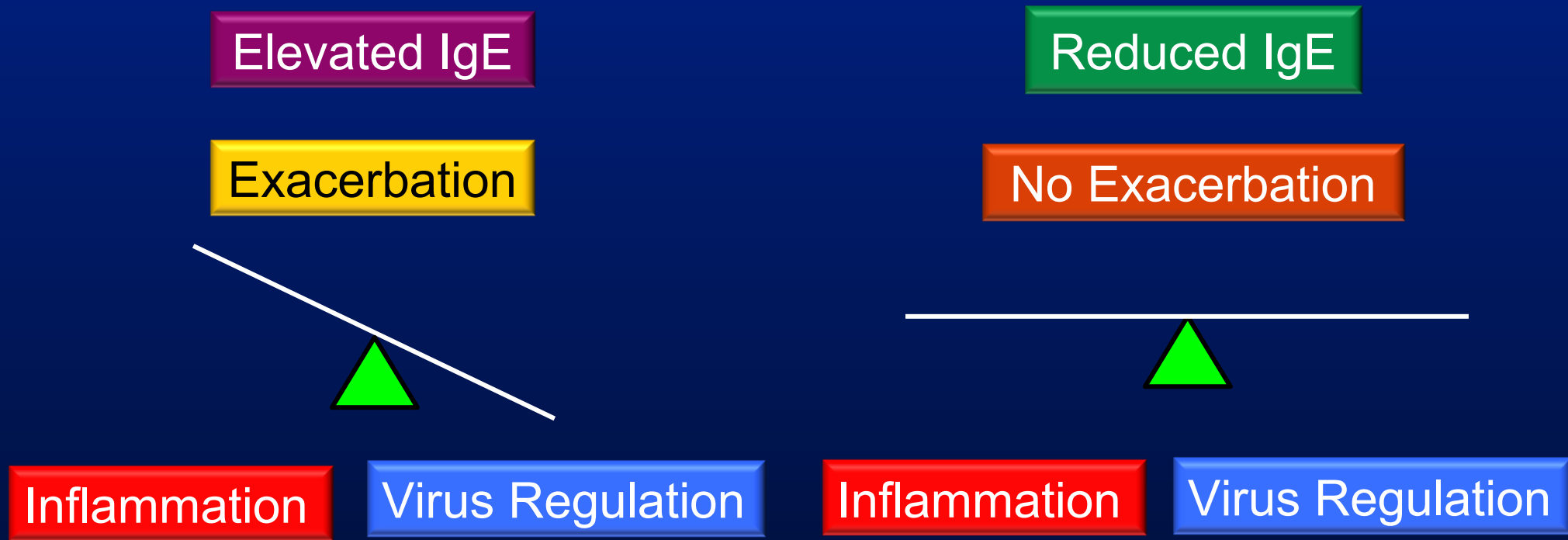
Baraldo et al. J Allergy Clin Immunol 2012; 130:1307-1314.

Total Serum IgE Levels

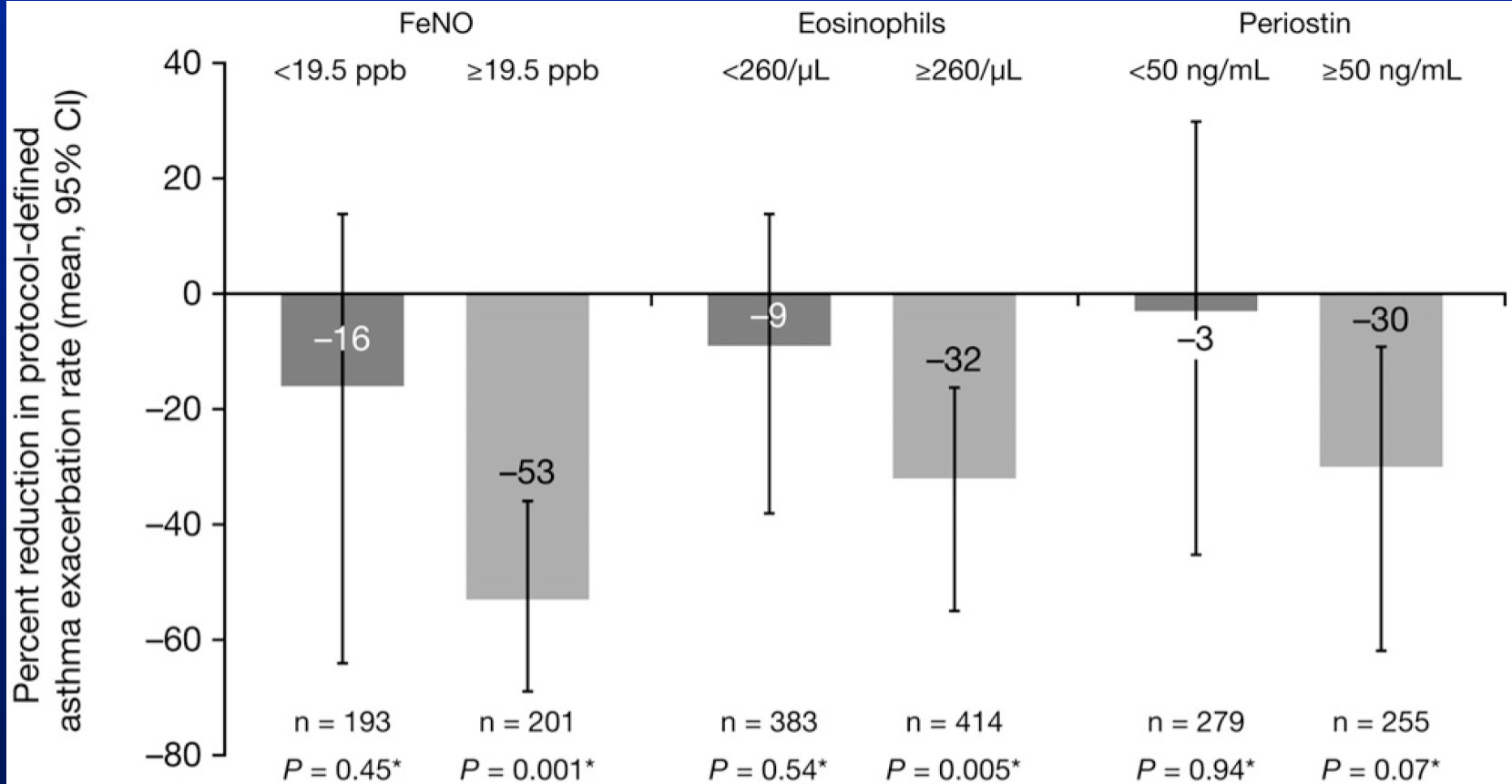


Baraldo et al. J Allergy Clin Immunol 2012; 130:1307-1314.

What contribution does IgE make to a respiratory virus provoked asthma exacerbation?



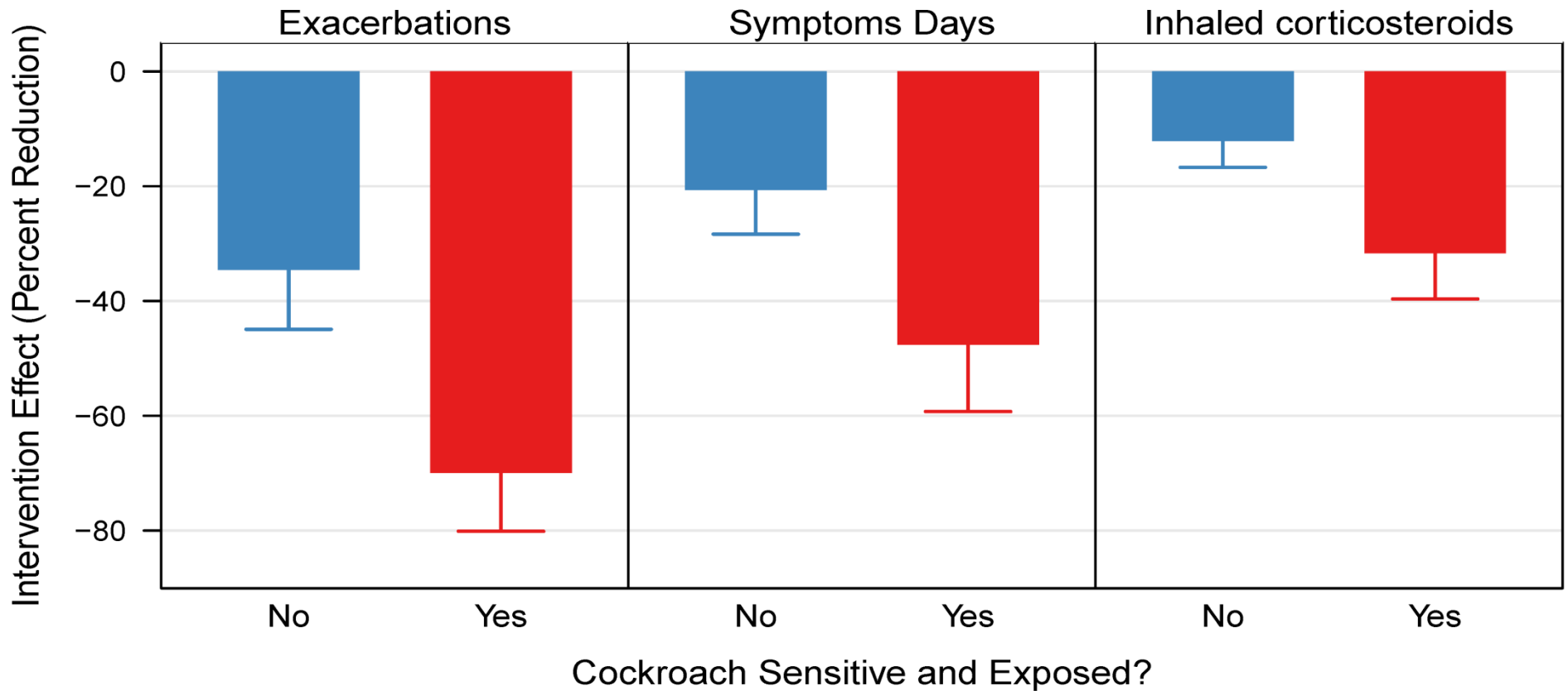
Who are the candidates for the most favorable response to omalizumab?



Exacerbation rates						
	Low FeNO at baseline	High FeNO at baseline	Low eosinophils at baseline	High eosinophils at baseline	Low periostin at baseline	High periostin at baseline
Omalizumab	0.60	0.50	0.65	0.70	0.73	0.66
Placebo	0.71	1.07	0.72	1.03	0.72	0.93

Hanania NA, et al. Am J Respir Crit Care Med 2013;187:804-811.

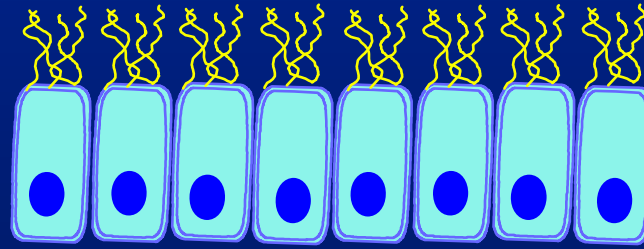
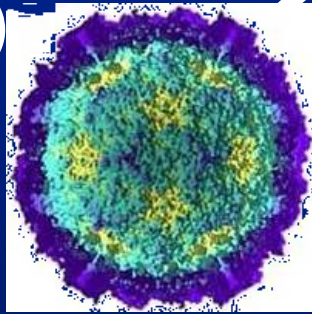
Cockroach Sensitization & Exposure's Effect on Omalizumab Efficacy



What factors contribute to whether a respiratory infection provokes asthma and how might IgE fit into this process?

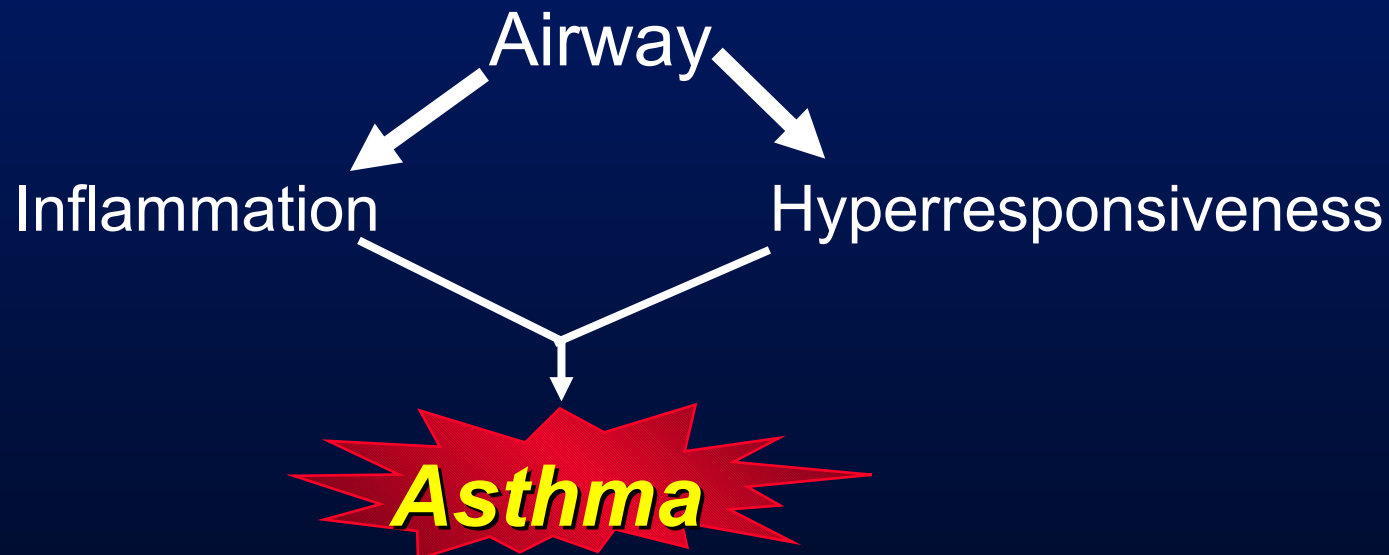
Seed (Virus)

RV-subclasses
(Class A and C)



Soil (Host)

Allergic Inflammation
Innate immune
response



Acknowledgements: Inner City Asthma Consortium

- **Investigators and sites**

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