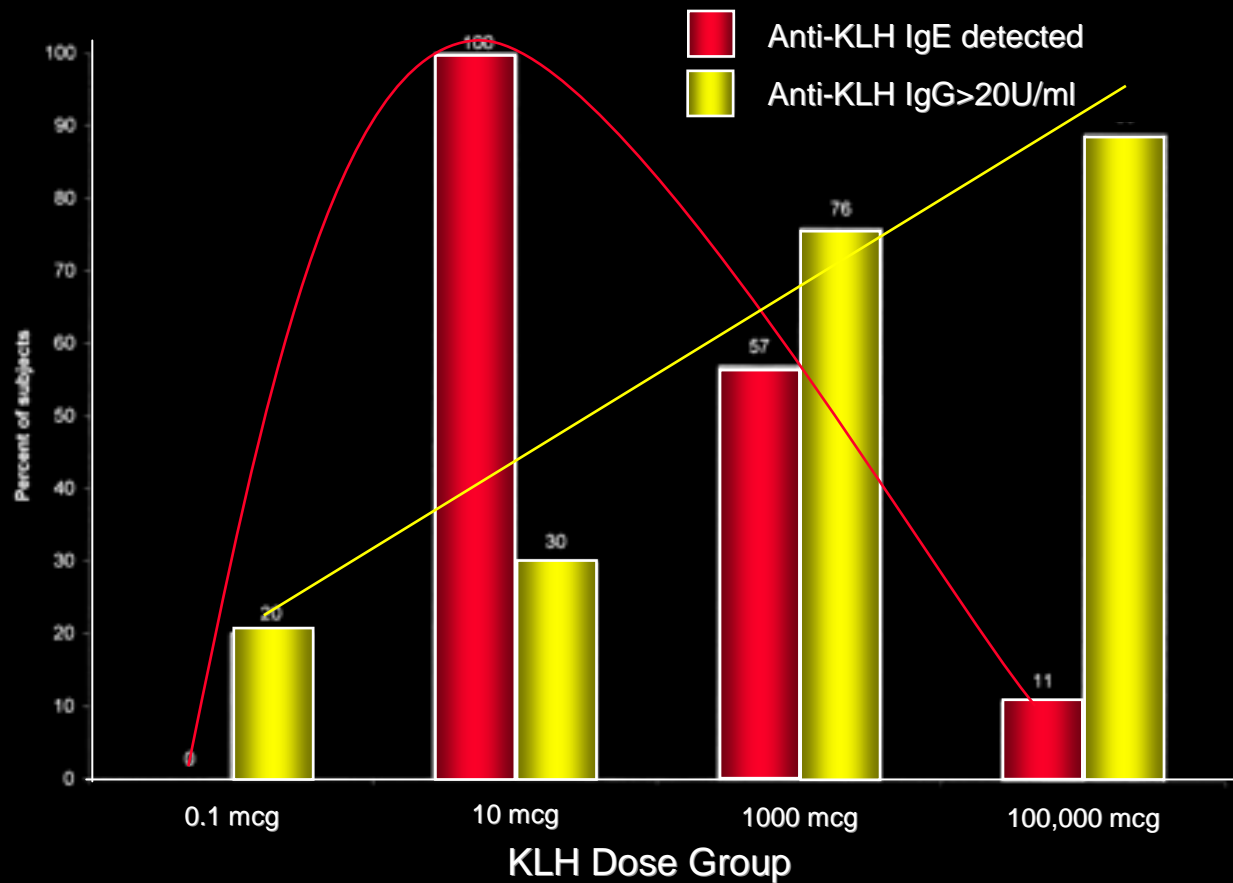


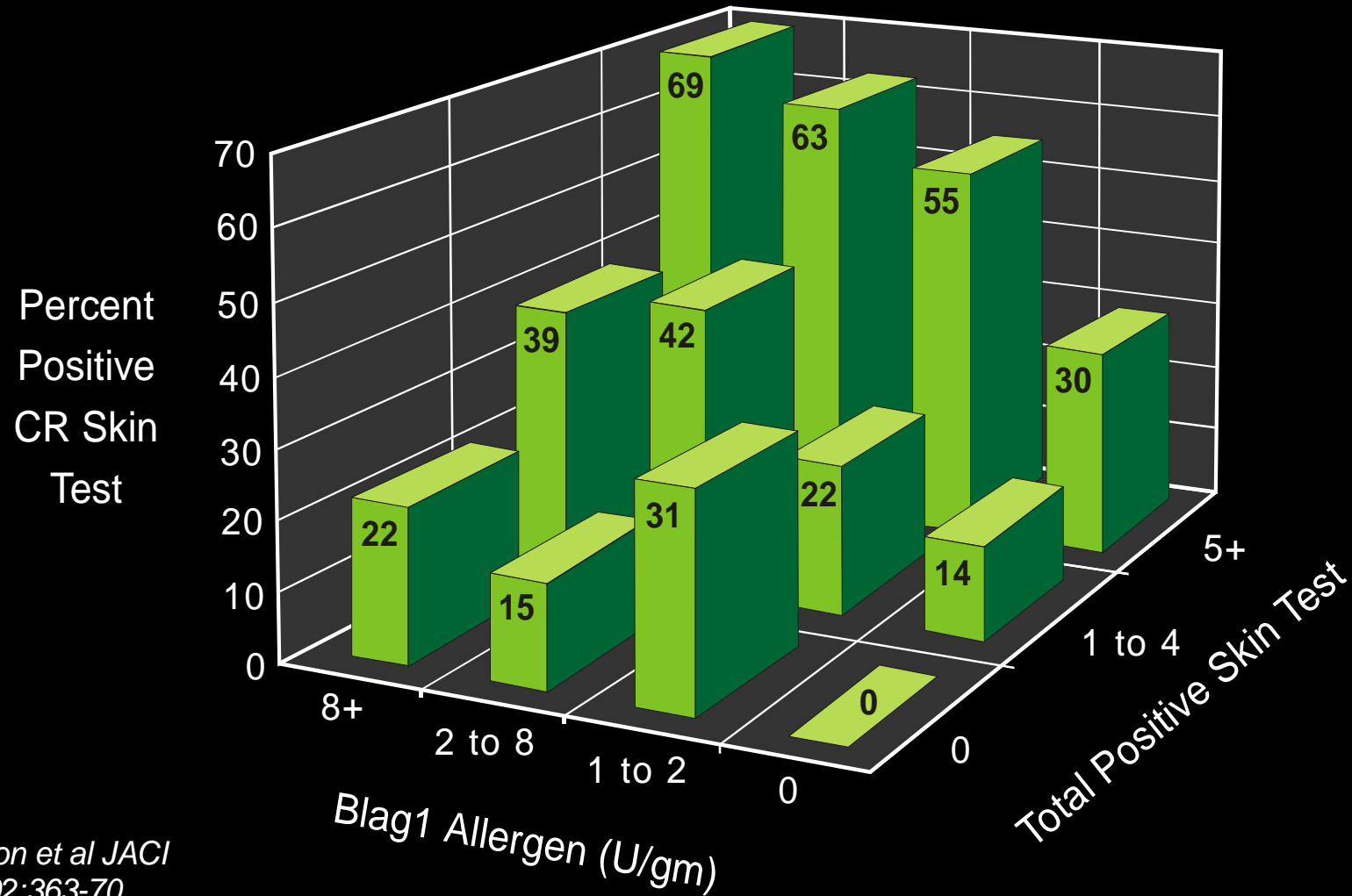
# Is Early Exposure to Allergens Protective?

Adnan Custovic MSc DM MD PhD  
Professor of Allergy  
North West Lung Centre  
Manchester, UK

# Highest Sensitisation Rate With Moderate Dose Antigen Exposure



# Interrelationship of Exposure, Atopic Status and Frequency of Sensitization to Cockroach Allergen



Eggleston et al JACI  
1998;102:363-70

# Paradoxical Effects Of Exposure To Domestic Animals

## Decreased sensitization to cat amongst cat owners

- Hesselmar, Bjorksten *et al* Sweden CEA 1999
- Roost *et al* ECRHS JACI 1999
- Sporik *et al* USA Thorax 1999
- Custovic *et al* UK JACI 2002

## Production of IgG and IgG4 (without IgE):

- Platts-Mills *et al* Lancet 2001
- Erwin *et al* JACI 2003

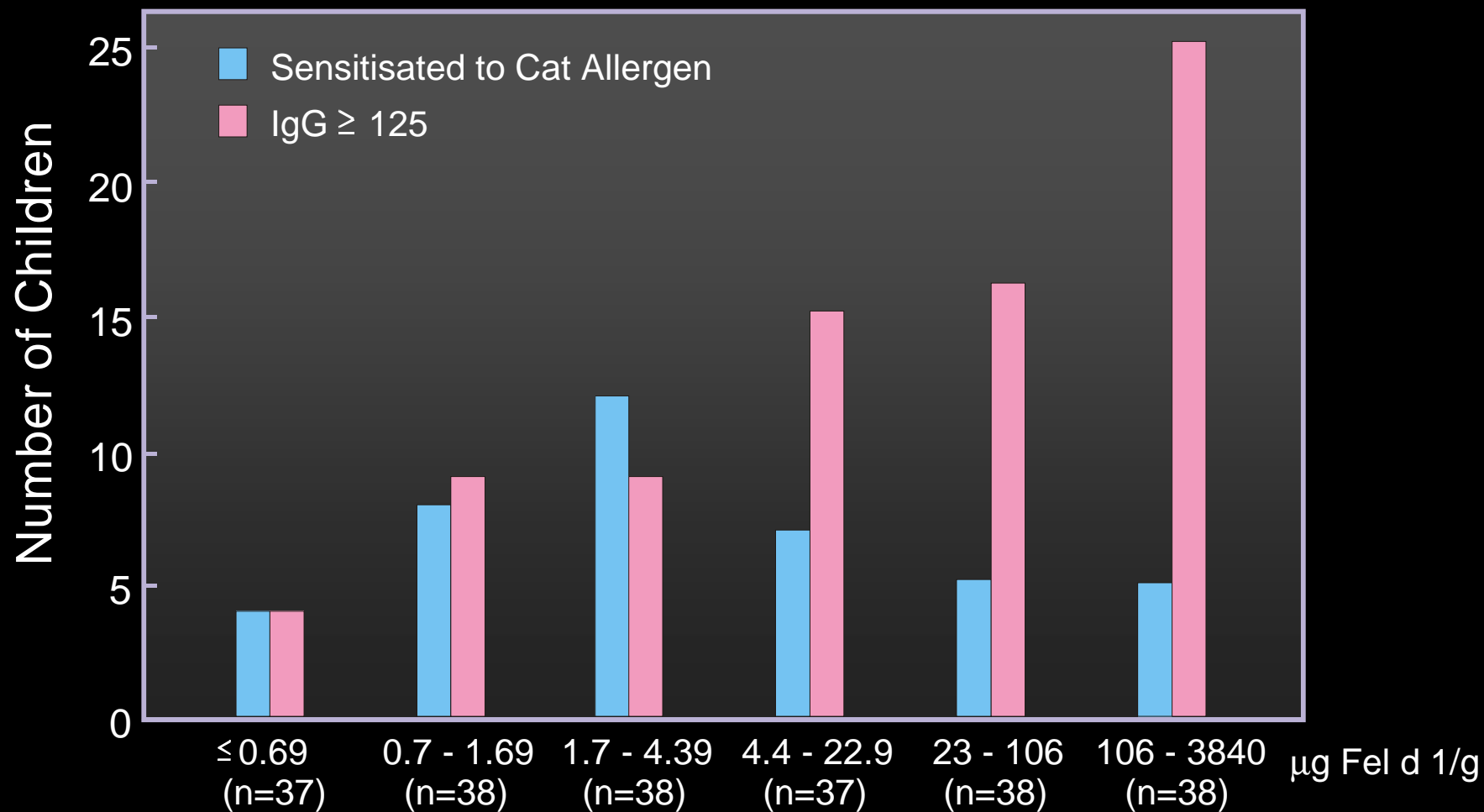
## Non-specific effects on other allergens:

- Ownby *et al*\* USA JAMA 2002
- Perzanowski *et al* Sweden AJRCCM 2002

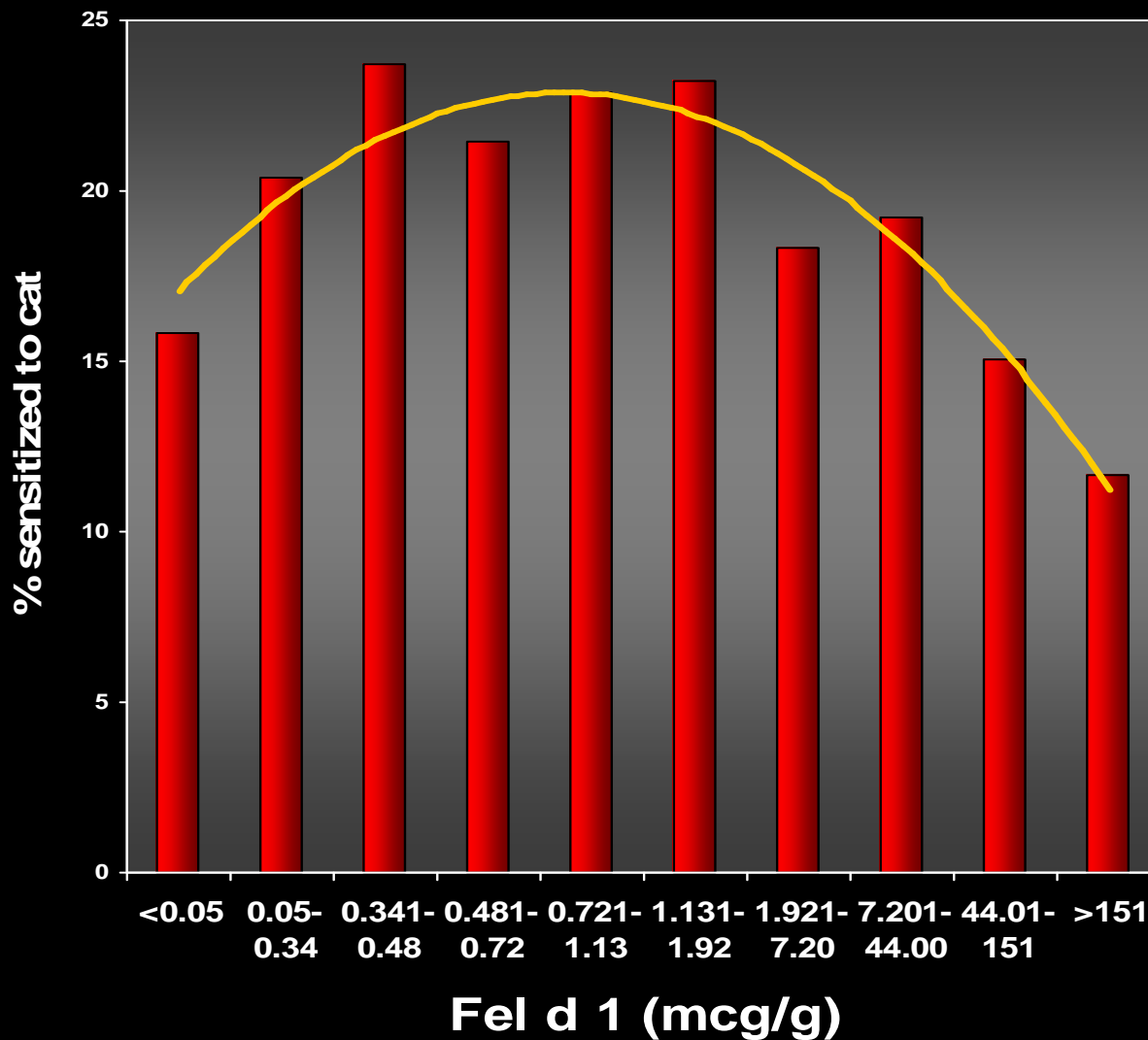
\* More than one animal.



## Decreased Risk of Sensitisation to Cat With High Exposure to Cat Allergen

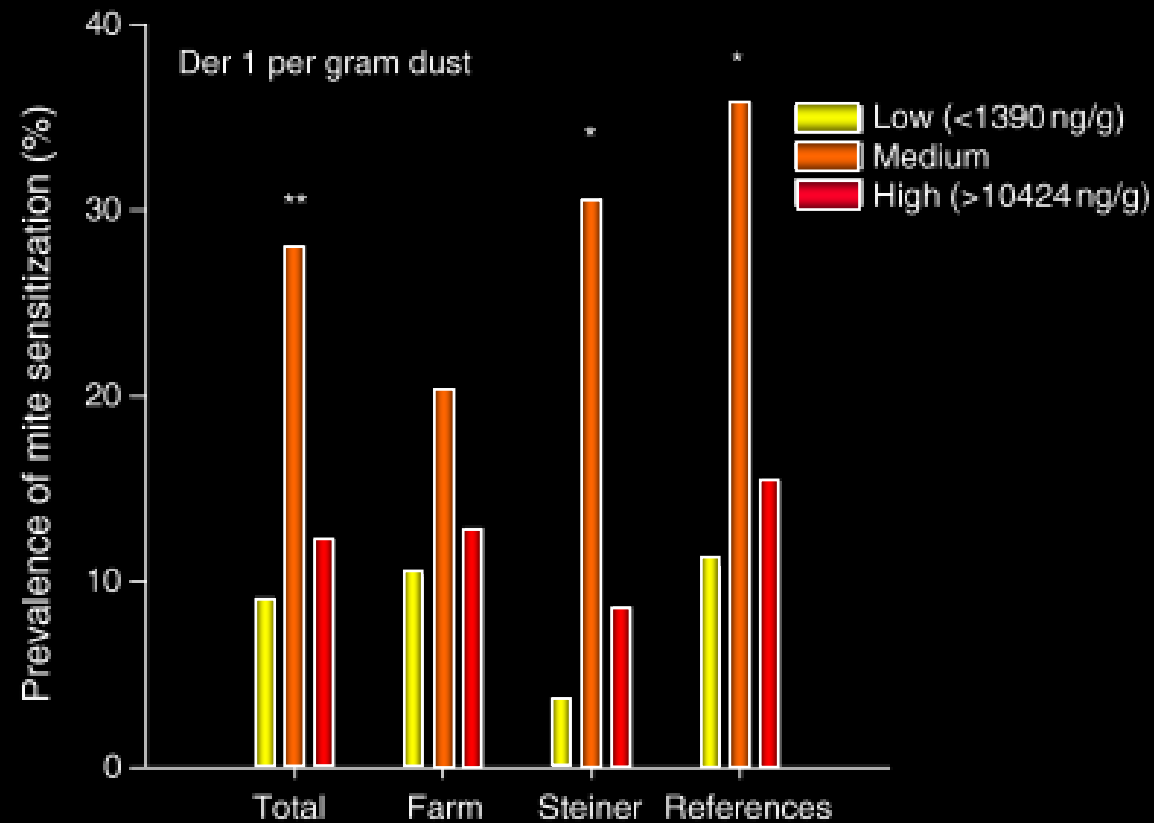


# Decreased Risk of Sensitisation to Cat With High Exposure to Cat Allergen

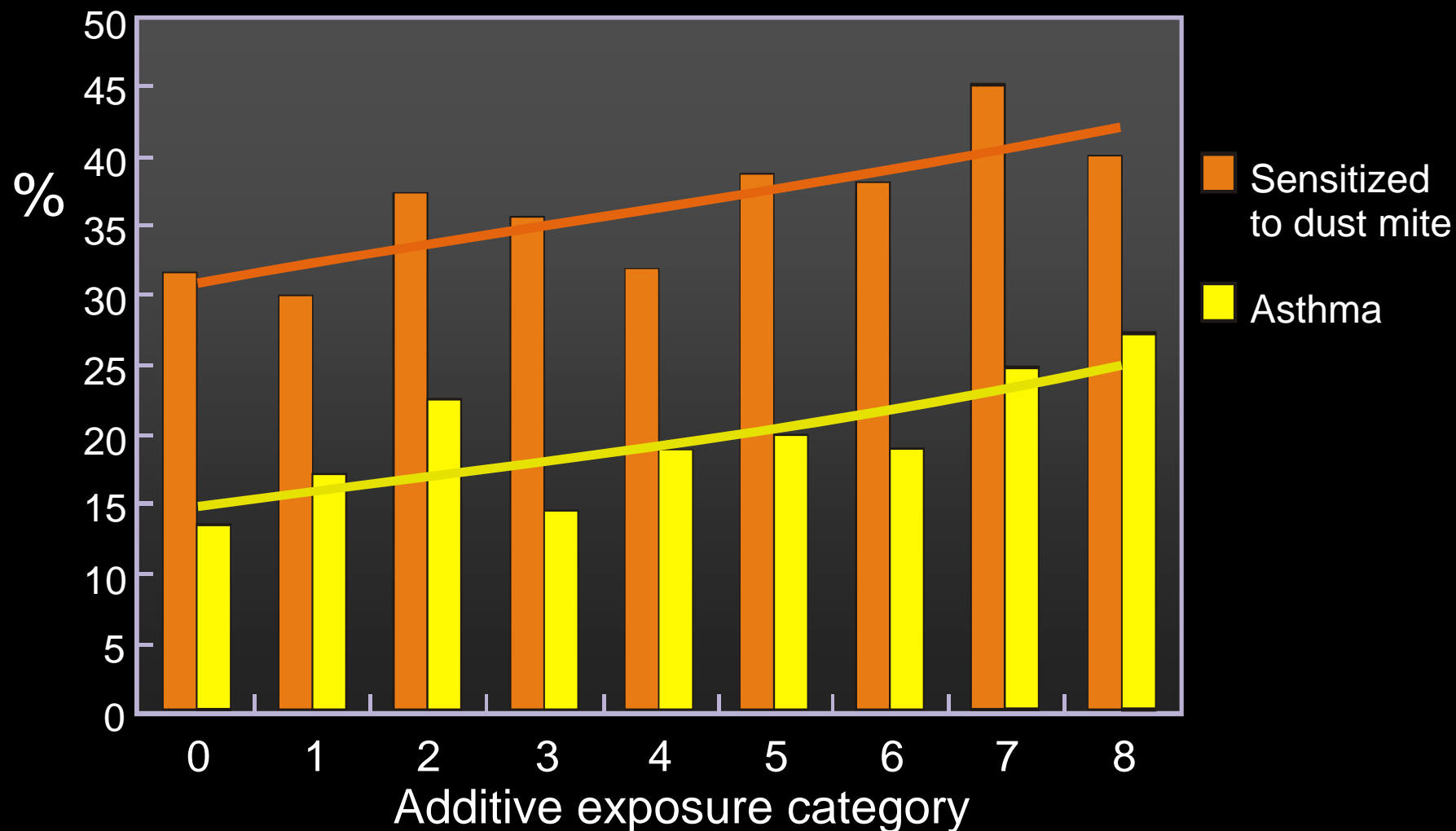


*Custovic et al.  
J Allergy Clin  
Immunol 2001; 108:  
537-9*

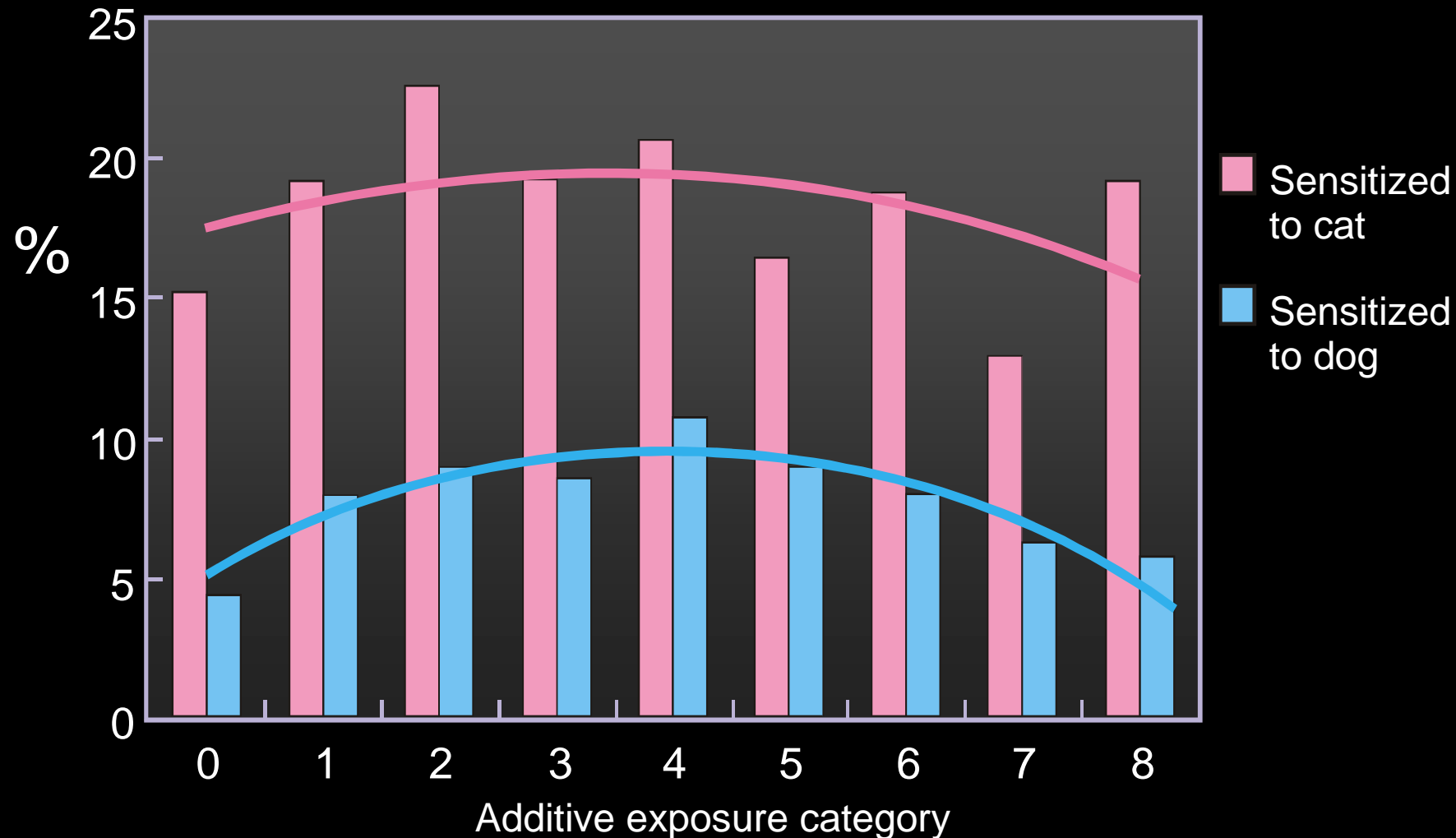
## PARSIFAL: Prevalence of Mite Sensitization by Tertiles of Der 1 Levels



# Additive Exposure to Indoor Allergens and Sensitisation in 2200 Adults



# Additive Exposure to Indoor Allergens and Sensitisation in 2200 Adults



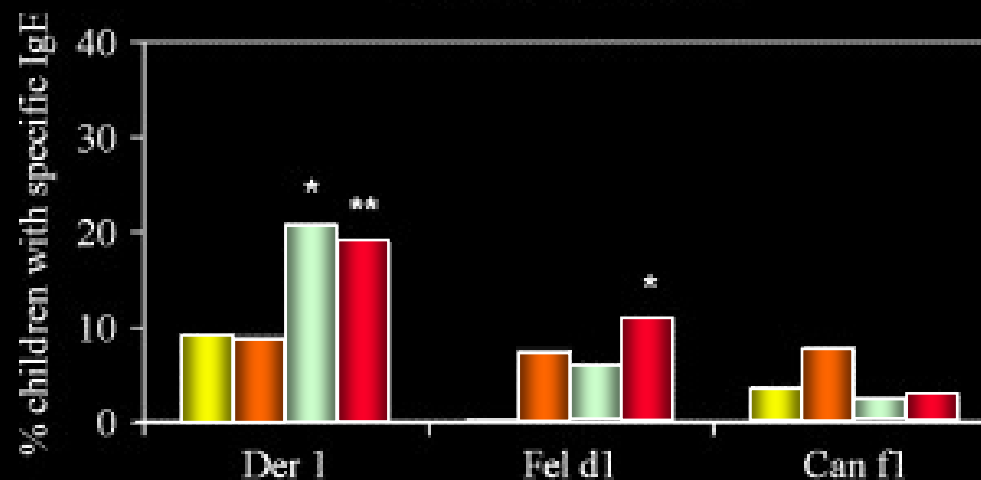
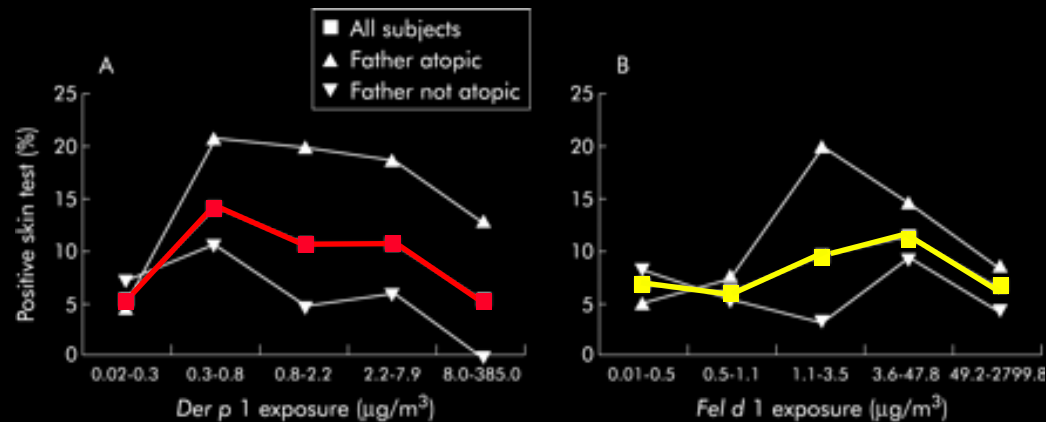
# Allergen Exposure, Sensitisation and Wheeze

- Ashford cohort (Cullinan et al, Thorax 2004; 59: 855–861)
  - No significant relationships between Der p 1 and Fel d 1 and either sensitisation or wheeze
  - Exposure-response relationships for both allergens and for each outcome rose steeply at low levels and were attenuated at high levels
  - **These patterns were modified by paternal atopy and by birth order**
  - No linear relationships between early allergen exposure and the induction of childhood respiratory allergy

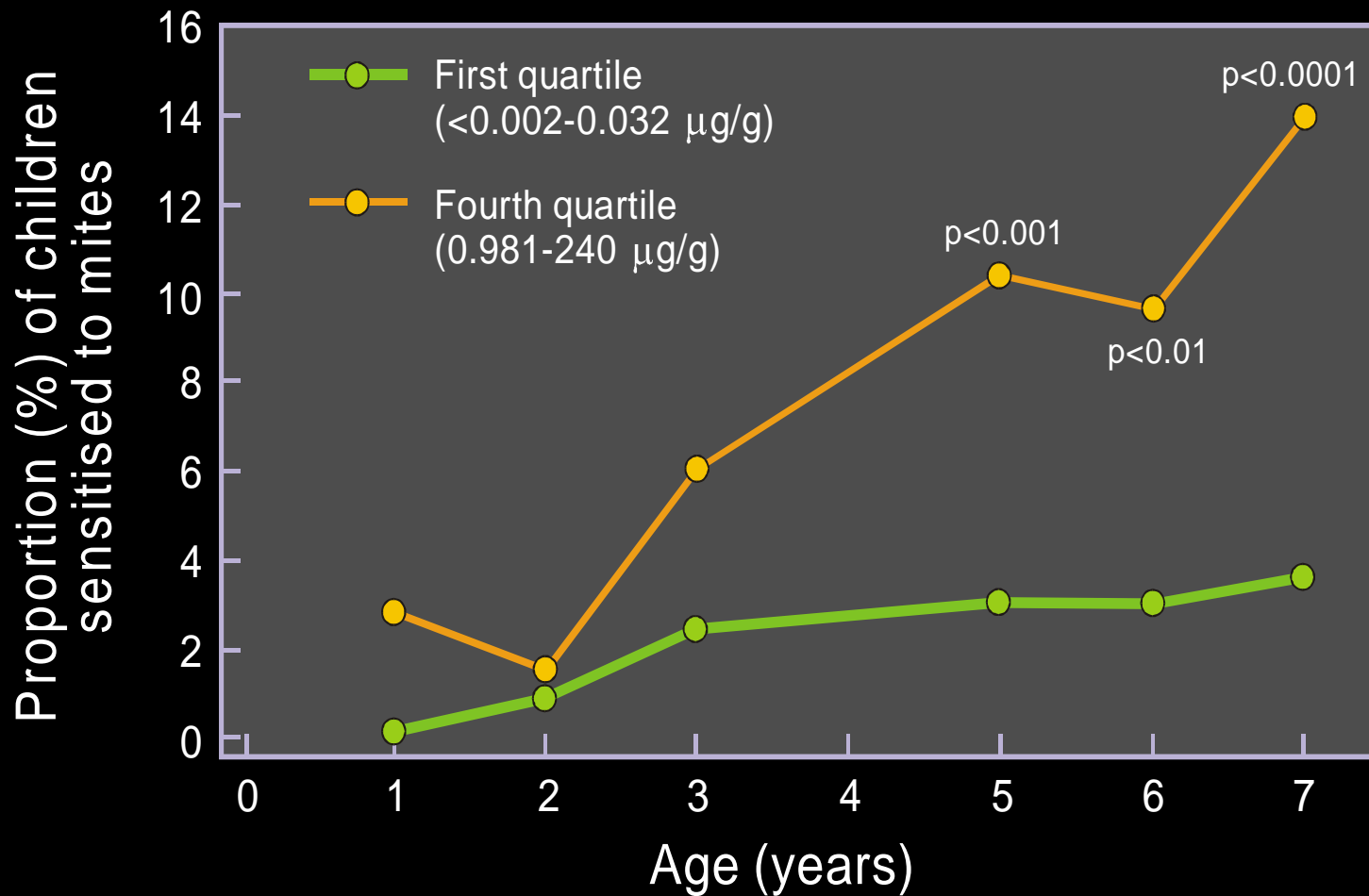
# Allergen Exposure, Sensitisation and Wheeze

- PIAMA (Brussee et al, JACI 2005; 115: 946-52)
  - Der p 1 and Fel d 1 exposure in infancy associated with an increased risk of sensitization at age 4 years
  - Borderline associations between Fel d 1 exposure and persistent wheeze (all subjects) & between Can f 1 exposure and persistent wheeze (children with non-atopic mother)
  - Indication of a positive association between Der p 1 and physician-diagnosed asthma (children with atopic mother)

# AMICS and PIAMA: Differences in the Effect of Allergen Exposure



# Sensitisation to House Dust Stratified by Highest and Lowest Quartiles of House-Dust-Mite Exposure at Age 6 Months

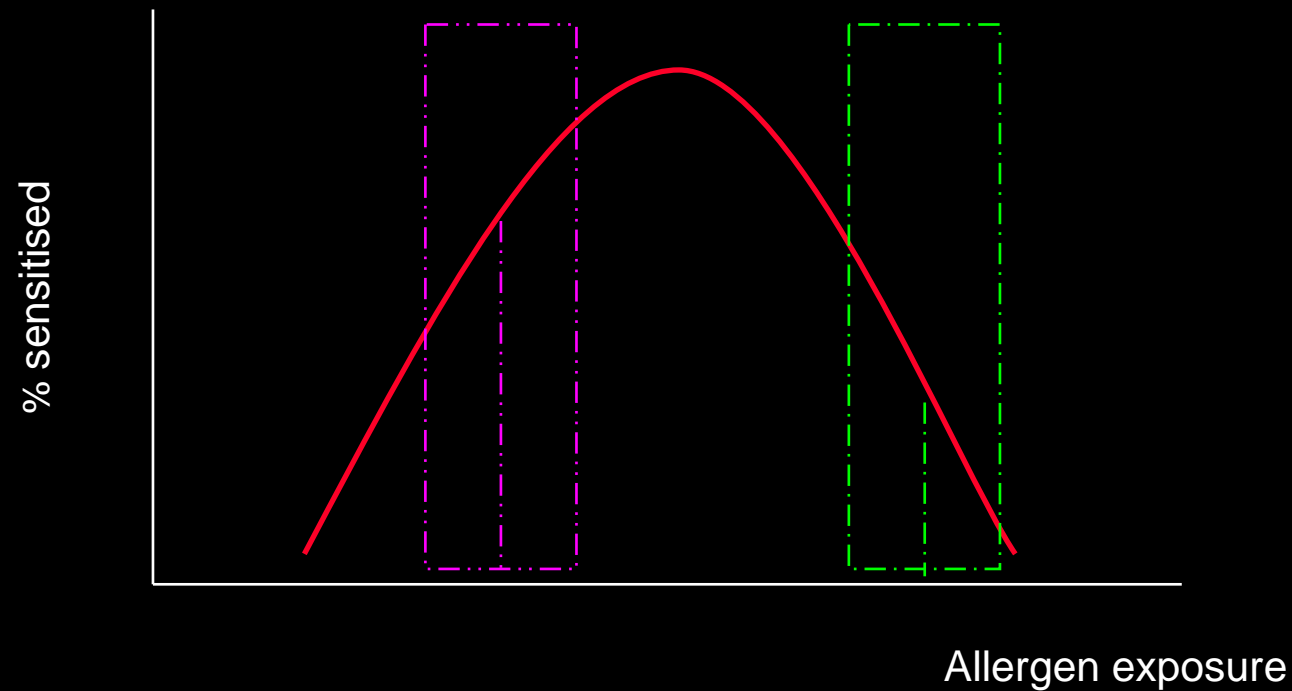


# Mite Allergen Exposure Increases the Risk of Specific Sensitisation

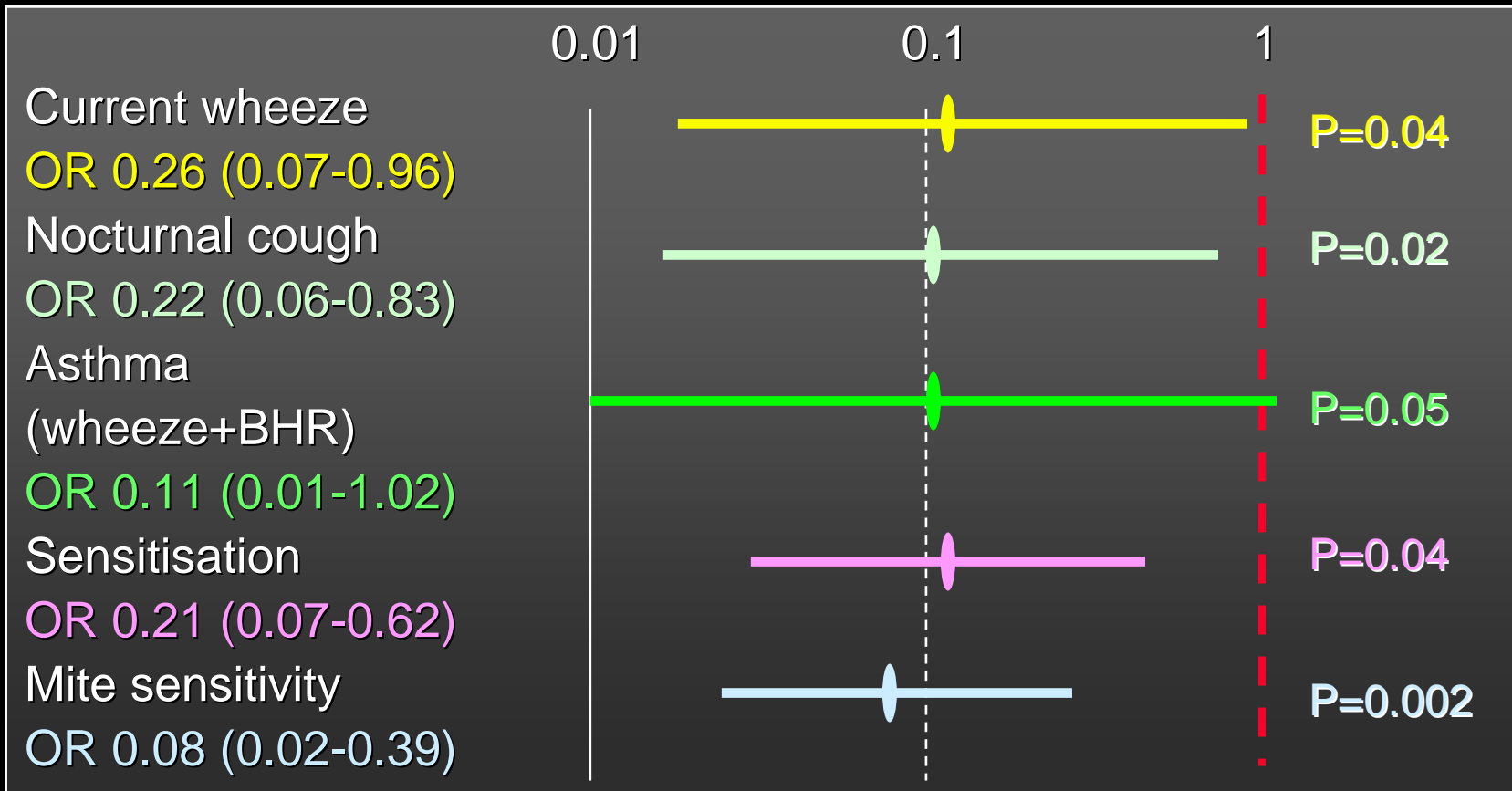


# WHAT CAN WE LEARN FROM INTERVENTION STUDIES?

# Hypothetical Scenarios on the Outcomes of Environmental Control

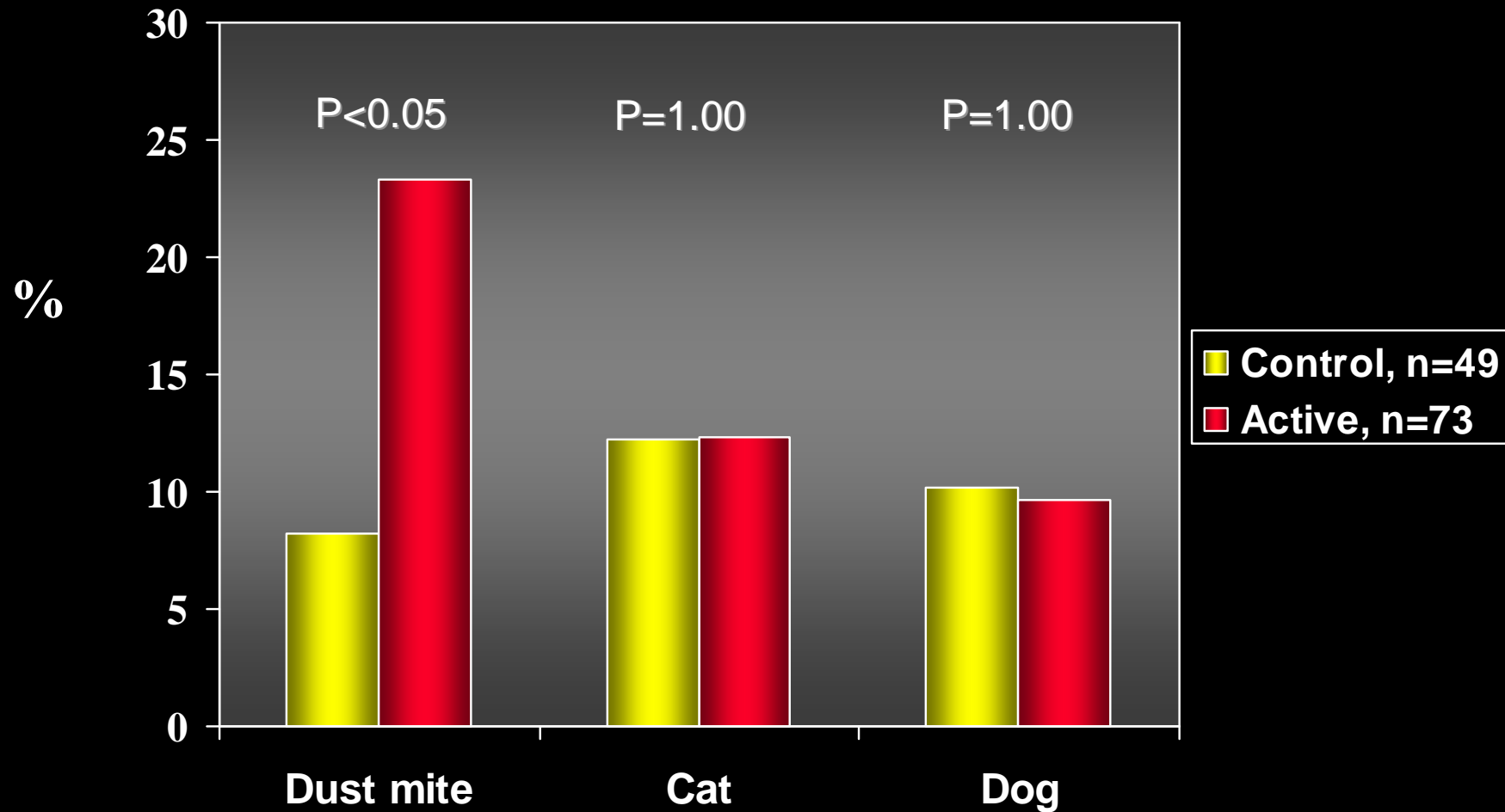


# Isle of Wight Study: At 8 Years Reduction in Respiratory Symptoms and Atopy

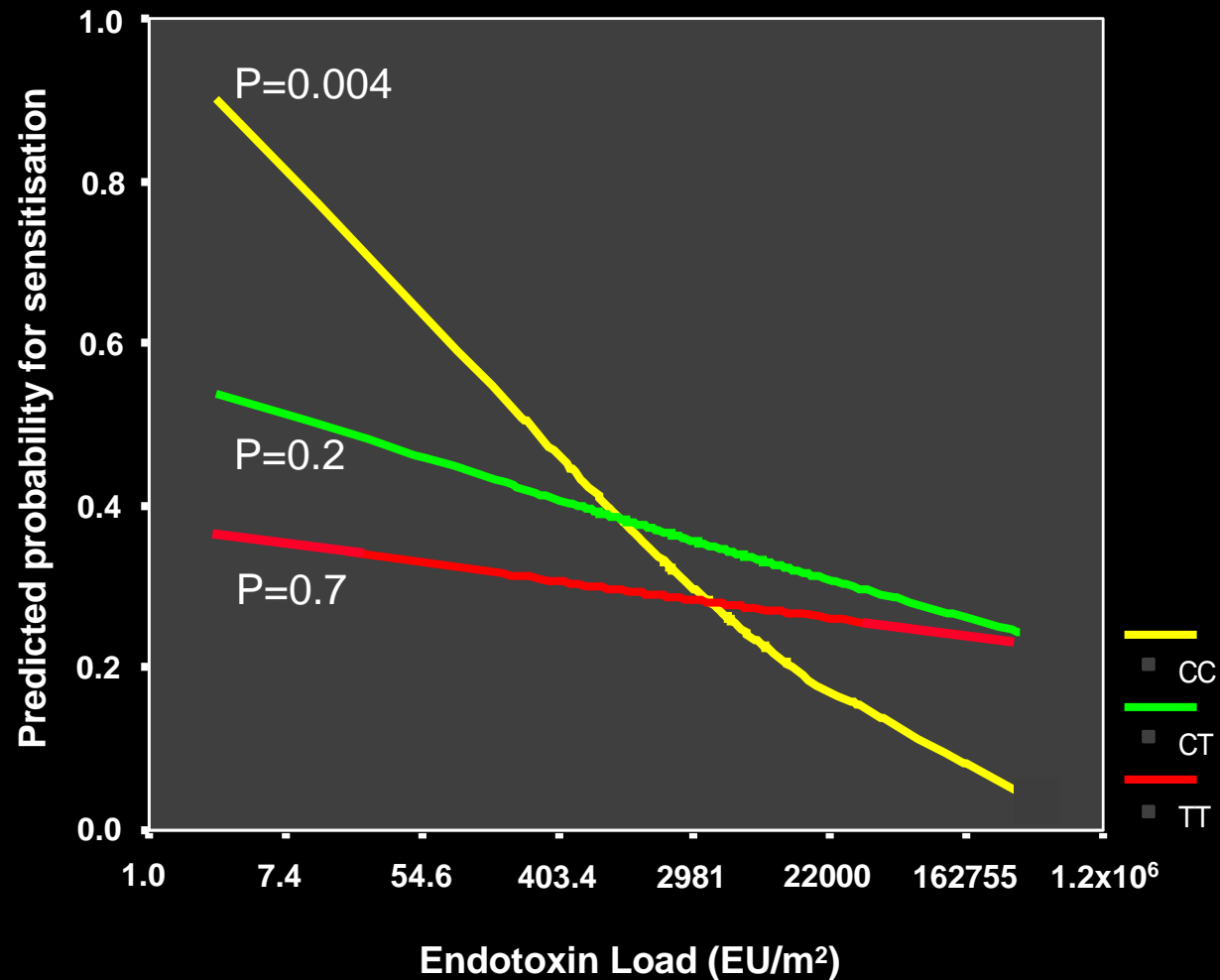




# Age Three Years: Effect of Environmental Control on Sensitisation (IgE)



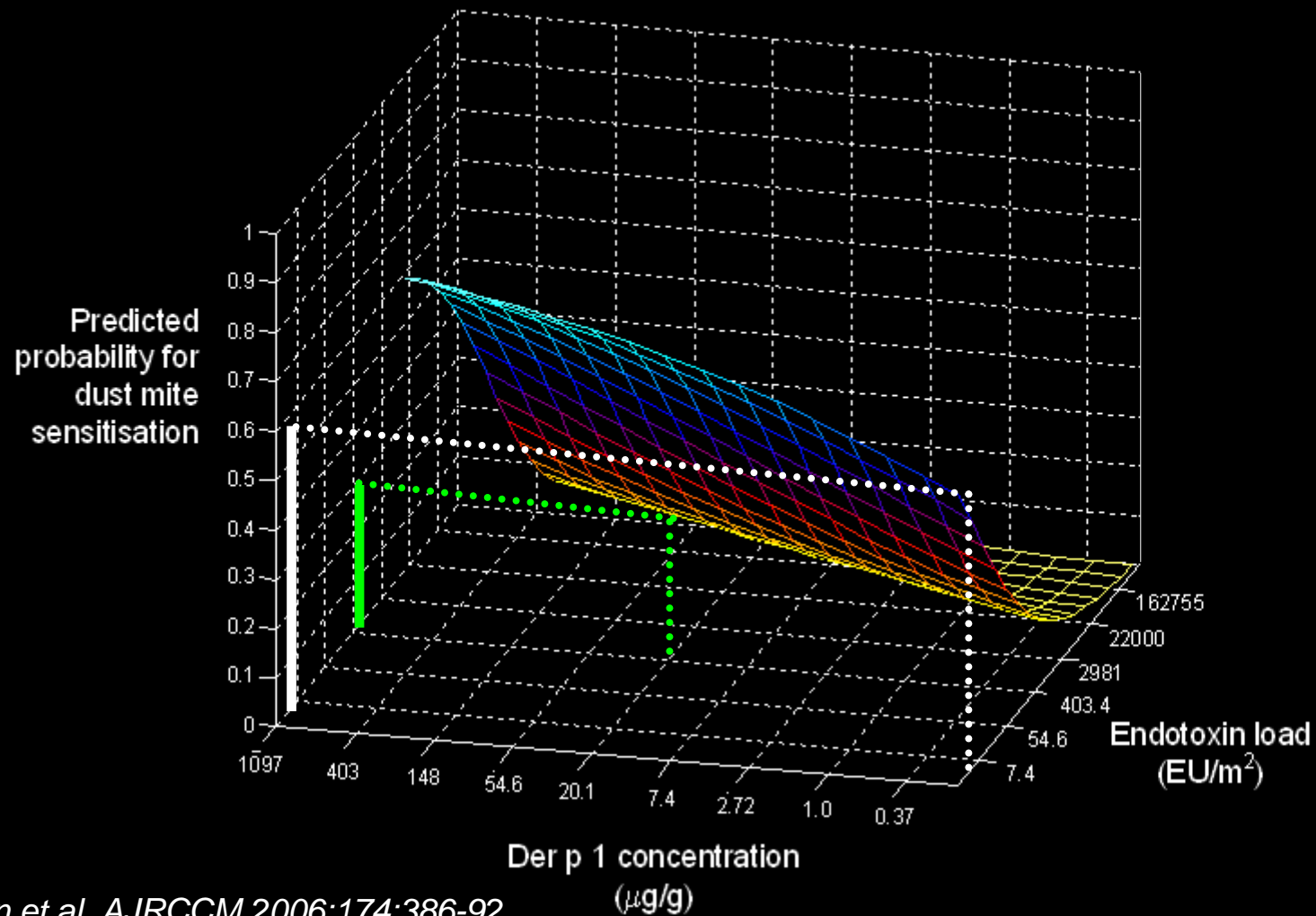
# CD 14 Promoter Polymorphism, Endotoxin Exposure and Sensitization



Simpson et al, AJRCCM 2006;174:386-92

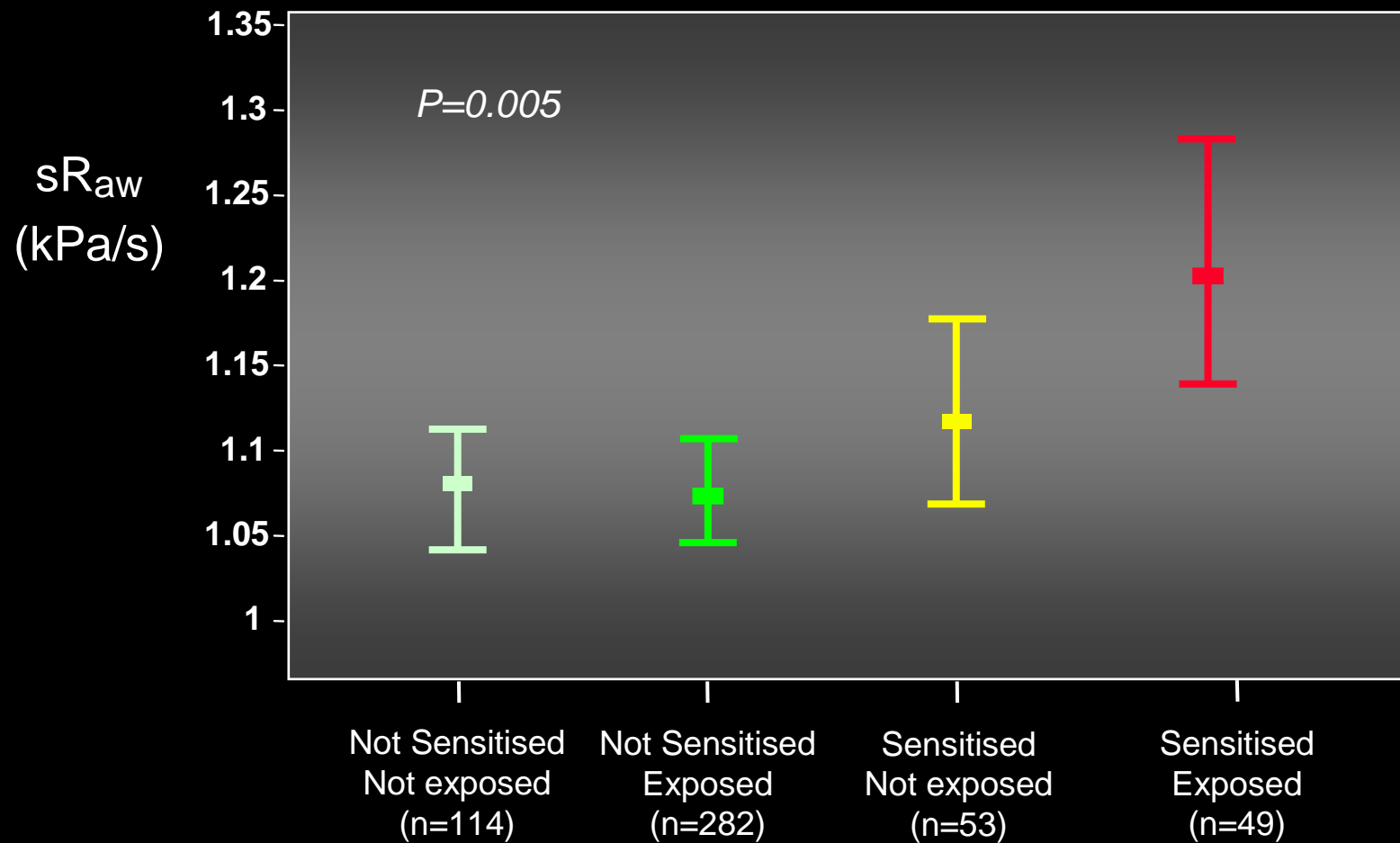


# Endotoxin and Der p 1 Exposure and Probability for Mite Sensitisation in Children With *CD14 -159 CC* Genotype

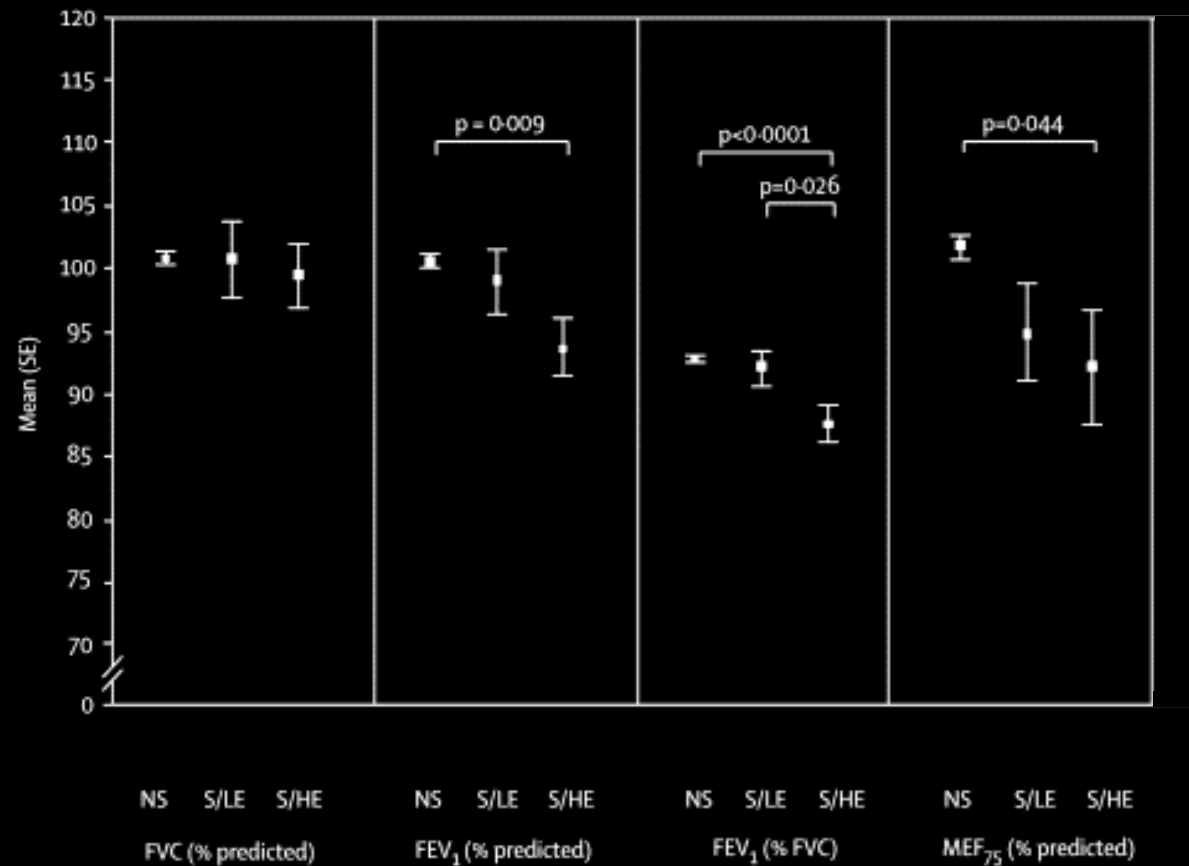


Simpson et al, AJRCCM 2006;174:386-92

# Allergen Sensitisation, Exposure and Lung Function at Age 3 Years



## Allergen Sensitisation and Exposure at $\leq 3$ Years and Lung Function at Age 7 Years



## Conclusions

- Exposure to sensitising allergen increases asthma severity amongst allergic asthmatics
- The relationship between allergen exposure and the development of IgE-mediated sensitisation and the symptoms of allergic disease is complex
- Individual susceptibility critical in determining the effect of environmental exposures

# Conclusions

- What is the effect of high early allergen exposure on the development of sensitisation?
    - Increases the risk
    - Protects
    - Does not matter
- } Depending on allergen and individual susceptibility
- The selection of subjects for primary prevention and the treatment using environmental control needs to be refined
    - Identify genetic polymorphisms which confer an increase in risk
  - This will result in tailor made approaches for individuals