LEIDEN UNIVERSITY MEDICAL CENTER

Food and Respiratory Allergy in Ghana

Insights from population studies among children

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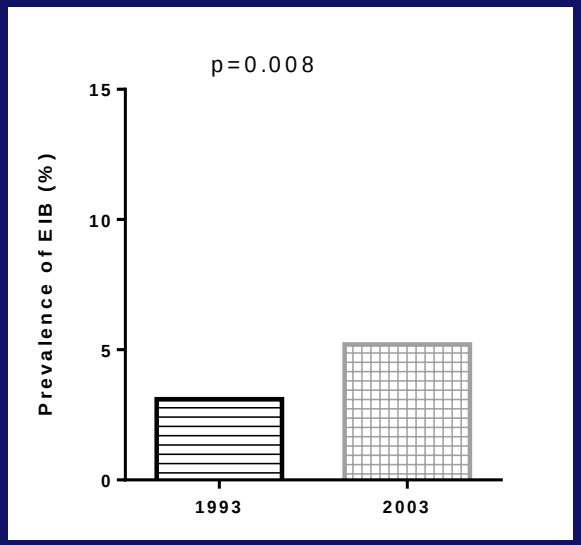
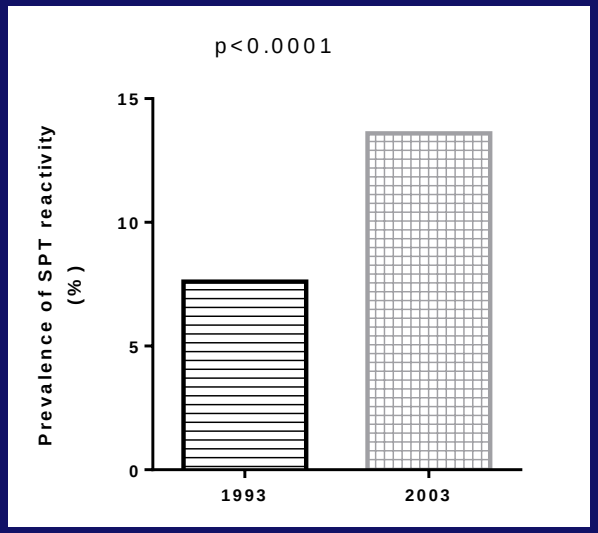
Background: Allergies in Ghana

- Studies indicate that allergies are on the rise in Ghana
- Two surveys conducted 10 years apart in children (aged 9-16 years) in one area showed an increase in markers of allergy

Exercise-Induced Bronchospasm



Skin Prick Test Reactivity



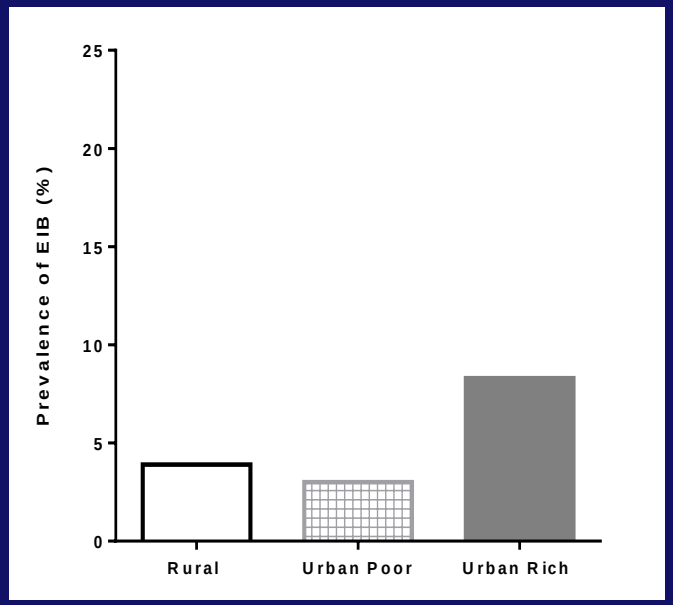
Addo-Yobo *et al*, *Plos Med* 2007

Urban-rural differences in allergy outcomes

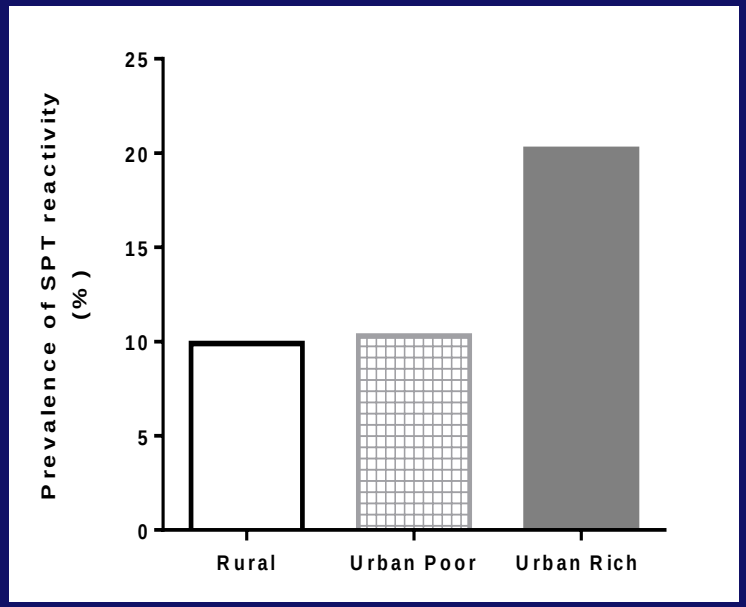
- Distinct urban-rural differences in allergy outcomes
- Within urban area differences in allergy outcomes based on socioeconomic status

2003 Data

Exercise-Induced Bronchospasm



Skin Prick Test Reactivity



Addo-Yobo *et al.*, Plos Med 2007

Factors associated with the rural to urban gradient in allergy

RURAL → **URBAN POOR** → **URBAN RICH**

DECREASE IN INFECTION

INCREASE IN POLLUTION

INCREASE IN ALLERGY

DIETARY CHANGES (RURAL DIET TO FAST-FOOD)

Adapted from van Ree and Yazdanbakhsh, 2007

Objectives

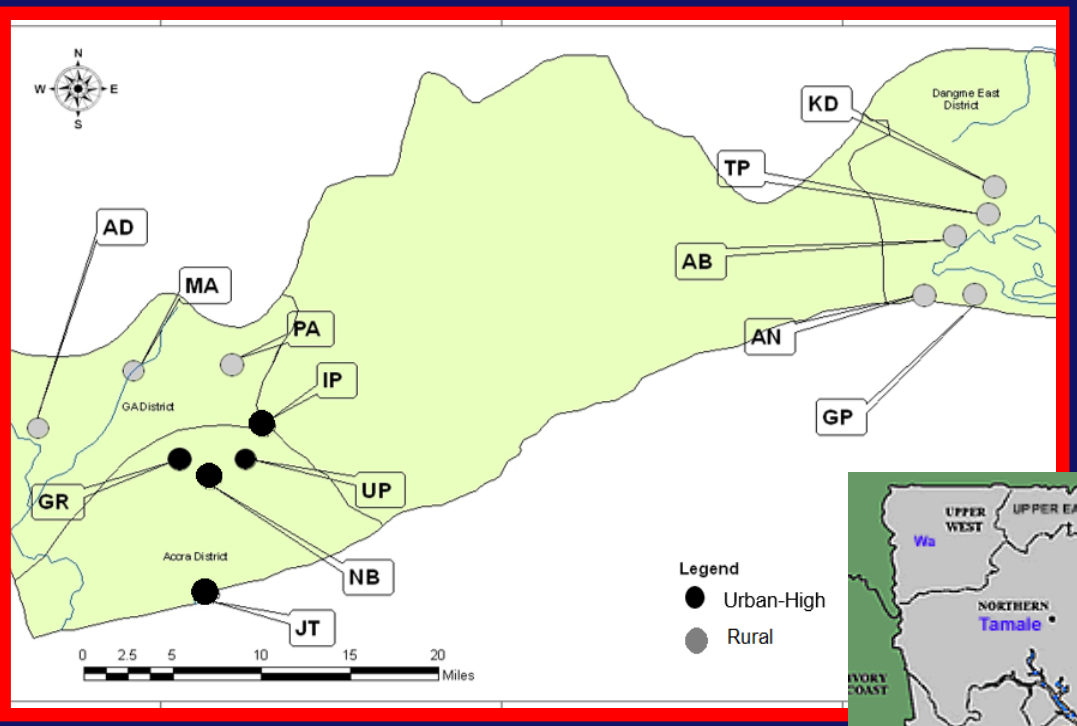
i. To determine urban-rural differences in the prevalence of aero-allergy in Southern Ghana

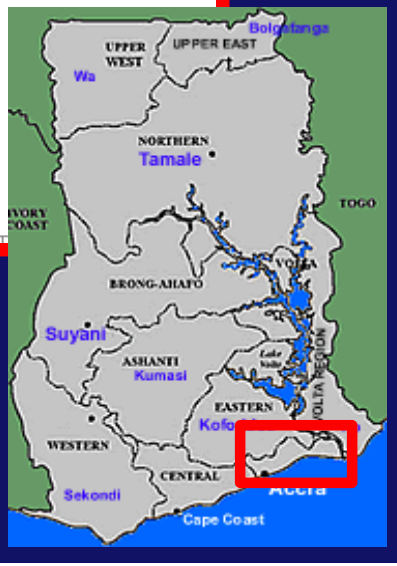
ii. To determine urban-rural differences in the prevalence of food allergy in Southern Ghana

iii. To examine associations between parasitic worm infections and allergy outcomes

Study area and population

Greater Accra Region





School-based cross-sectional study

- 13 Schools
  - 8 Rural
  - 5 Urban
- Target age-range: 5-16 years
- N= 2,331 recruited

Study Methodology: Allergic sensitization based on serum-specific IgE levels

ImmunoCap® /RAST

Allergen-specific IgE

- Mite (Der p)
- Cockroach (Bla g)
- Peanut (Ara h)

Sensitization cut-off :
$\geq$0.35 kU/L

Study Methodology: Allergic sensitization by skin prick testing







Skin prick test positivity cut-off
Average wheal size ≥ 3mm

Allergen panel

- Negative control
- Mite extract
- Cockroach extract
- Peanut extract
- 6 fresh fruits
- Positive control

Aero-allergens

Food Allergens

Study Methodology: Reported Symptoms

- Standardized questionnaire administered to parents or guardians of study subjects
- Symptoms of asthma & other allergic disorders:
  - Adapted from the International Study of Asthma and Allergies in Childhood
    - Weinmayr et al, Allergy 2010
    - Weinmayr et al, Eur Respir J 2008
- Symptoms of adverse reactions to food:
  - Adapted from EuroPrevall study
    - Kummeling et al, Allergy 2009
    - Wong et al, Allergy 2009
    - Mills et al, Allergy 2007
- Demographic and socioeconomic parameters

Study Methodology: Parasitological assessment

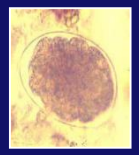
Urine

Urine filtration

S. haematobium

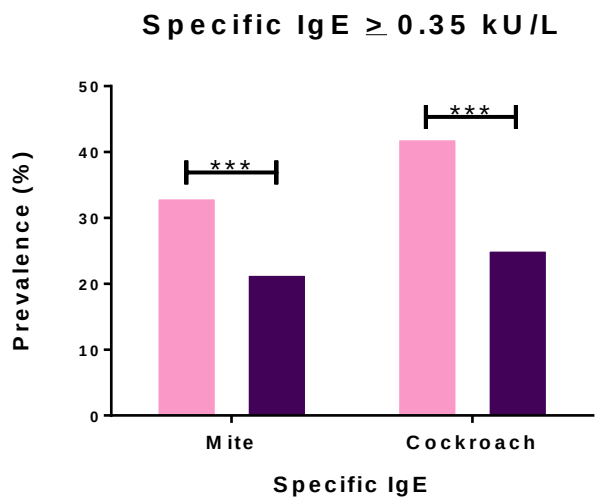
Stool

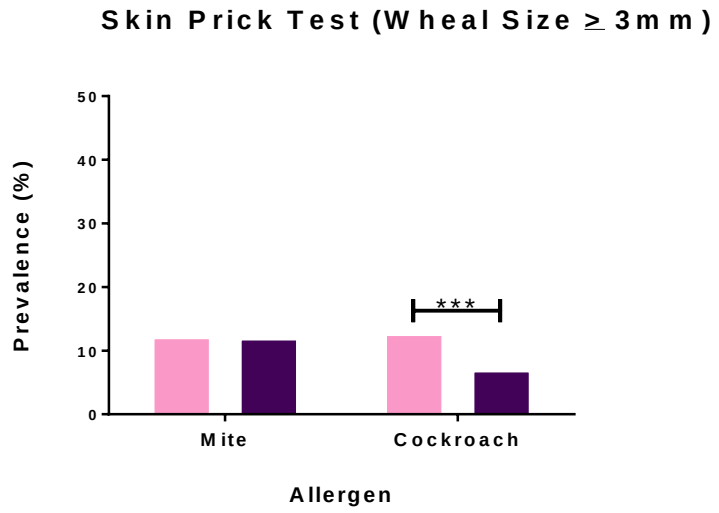
Kato-Katz

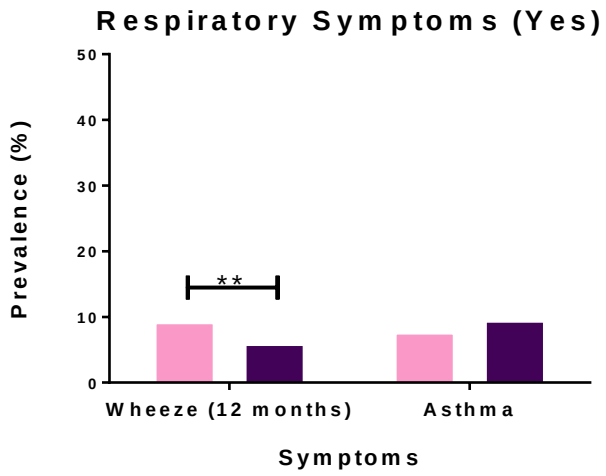


Intestinal helminths

Results: Aero-allergy outcomes stratified by area (N=1385)



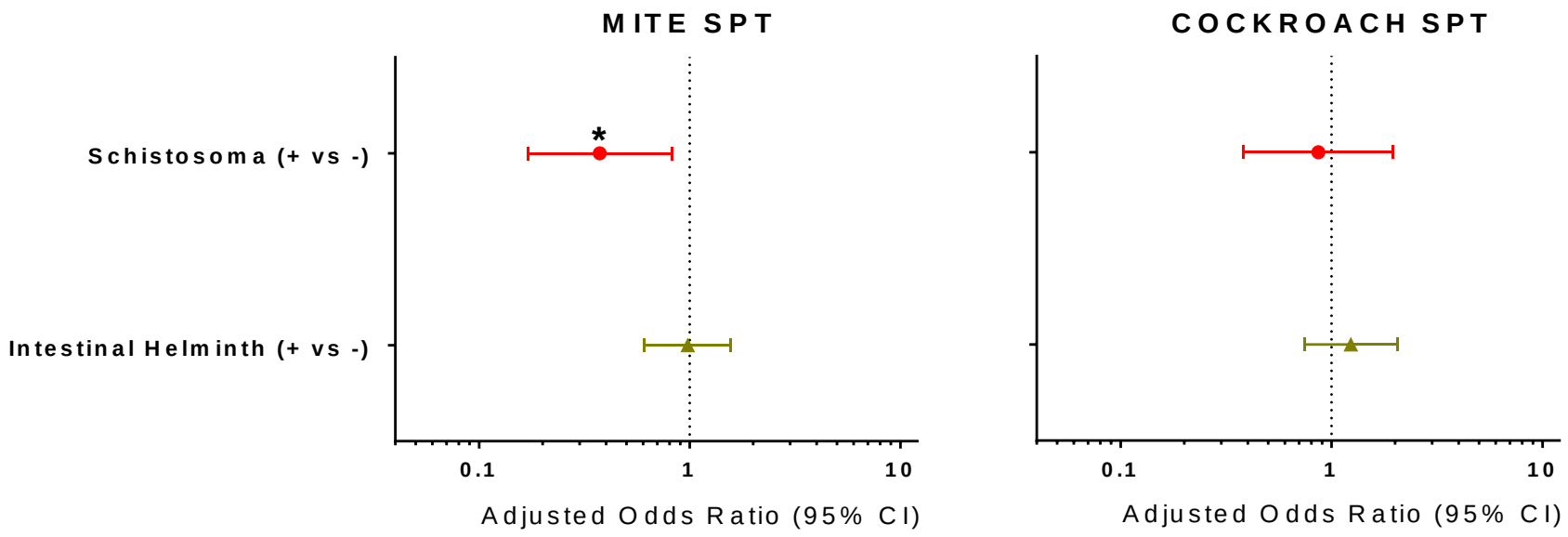




RURAL
URBAN

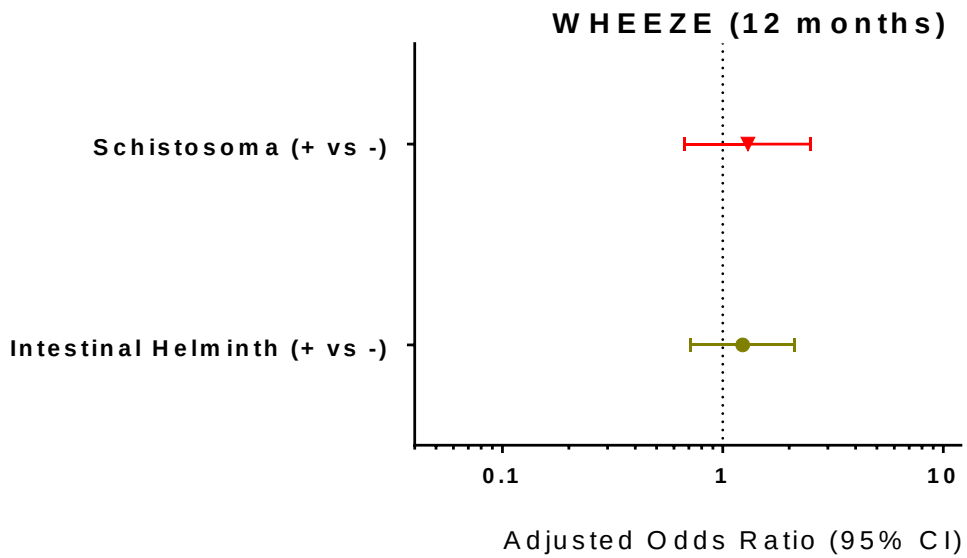
* p <0.05
** p <0.01
*** p<0.001

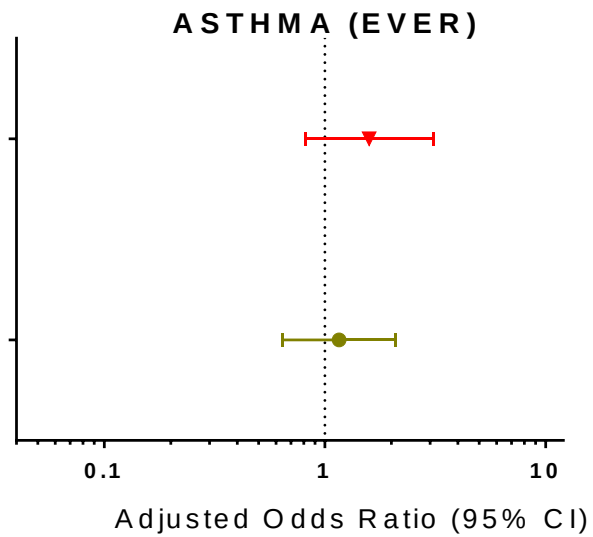
Worm infection and Skin Prick Test reactivity



Logistic regression models adjusted for age, gender and area
Wald's Test : * P<0.05

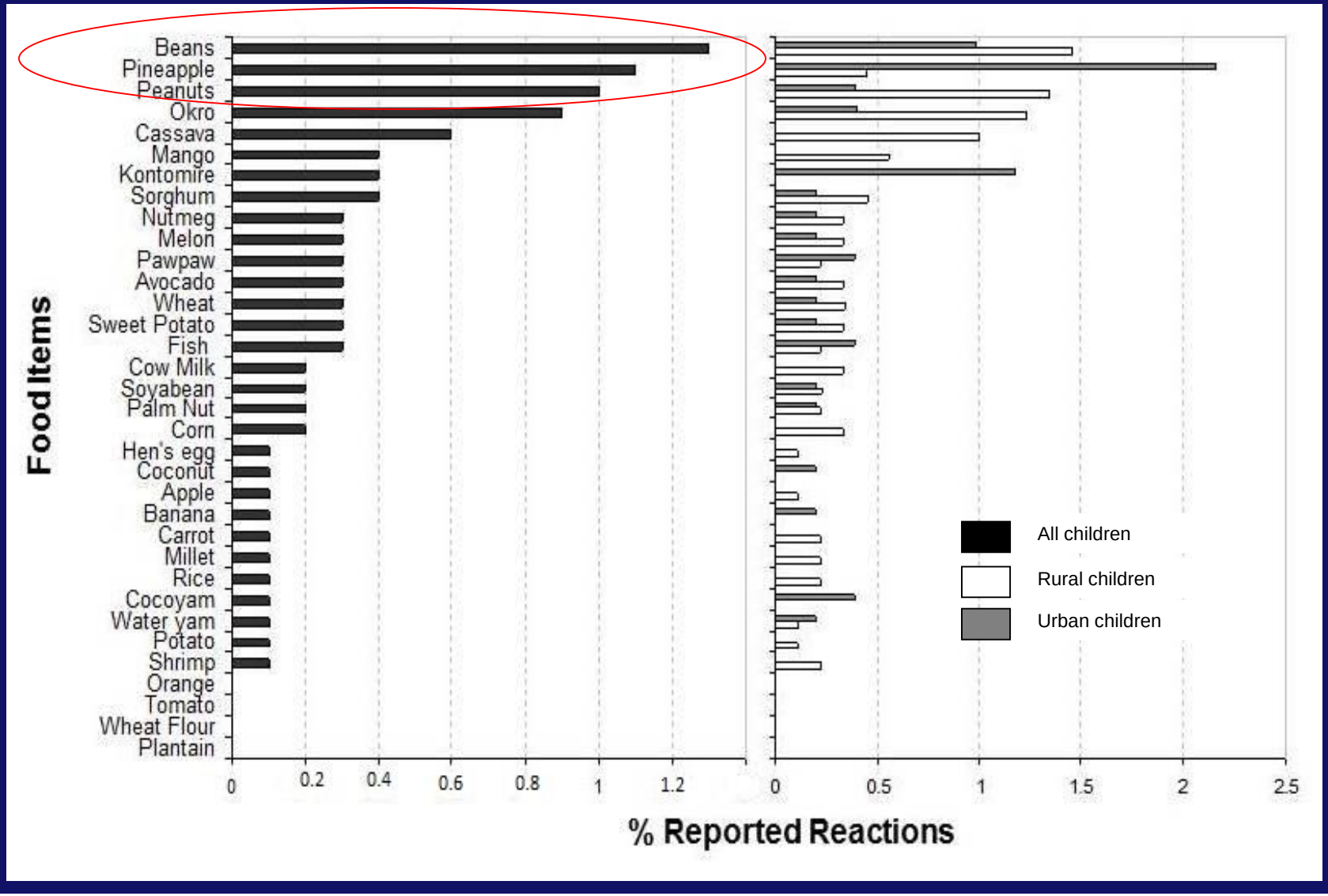
Worm infection and respiratory allergy symptoms



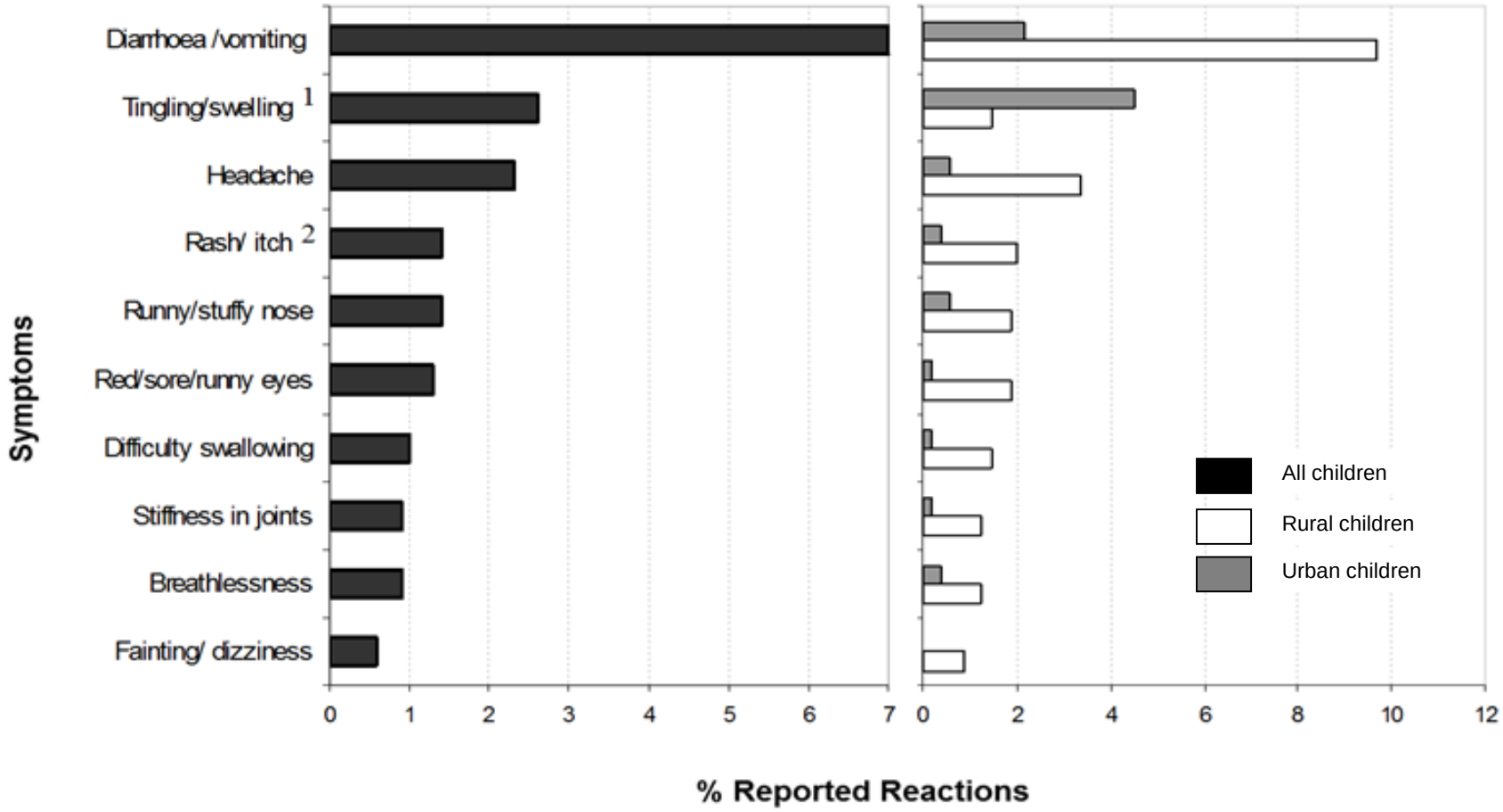


Logistic regression models adjusted for age, gender and area
Wald's Test : * P<0.05

Reported adverse reactions to food (N=1407)



Reported symptoms of adverse reactions to food (N=1407)

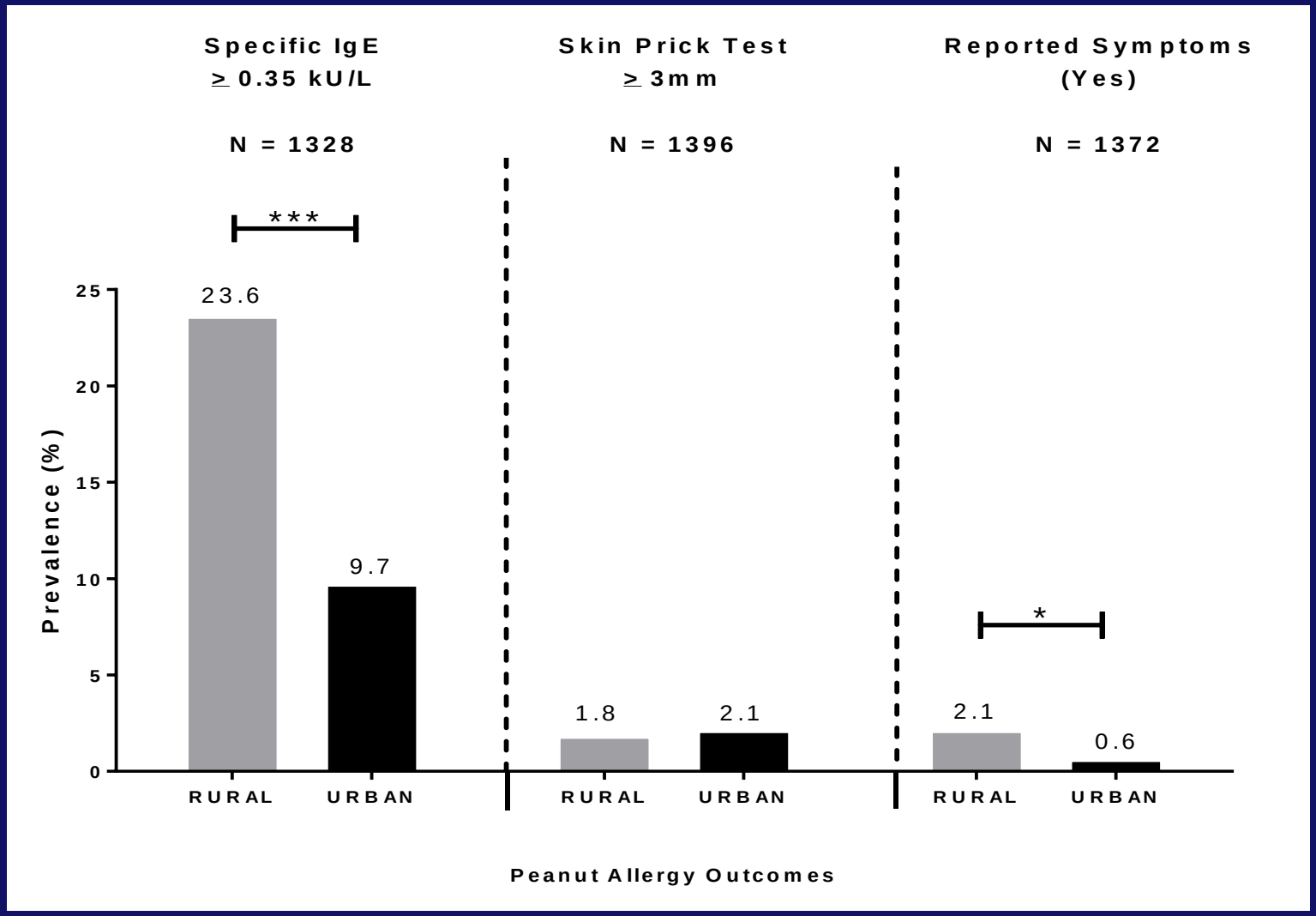


1 'Tingling/swelling = swelling of the mouth, lips or throat'
2 'Rash/itch = itching of the skin including nettle sting-like rash'

Ghana and peanuts (groundnuts)

- High peanut consumption
- Relatively few reports of adverse reactions to peanut
- Lack of avoidance of peanuts during pregnancy
- Early introduction of peanut as part of weaning foods

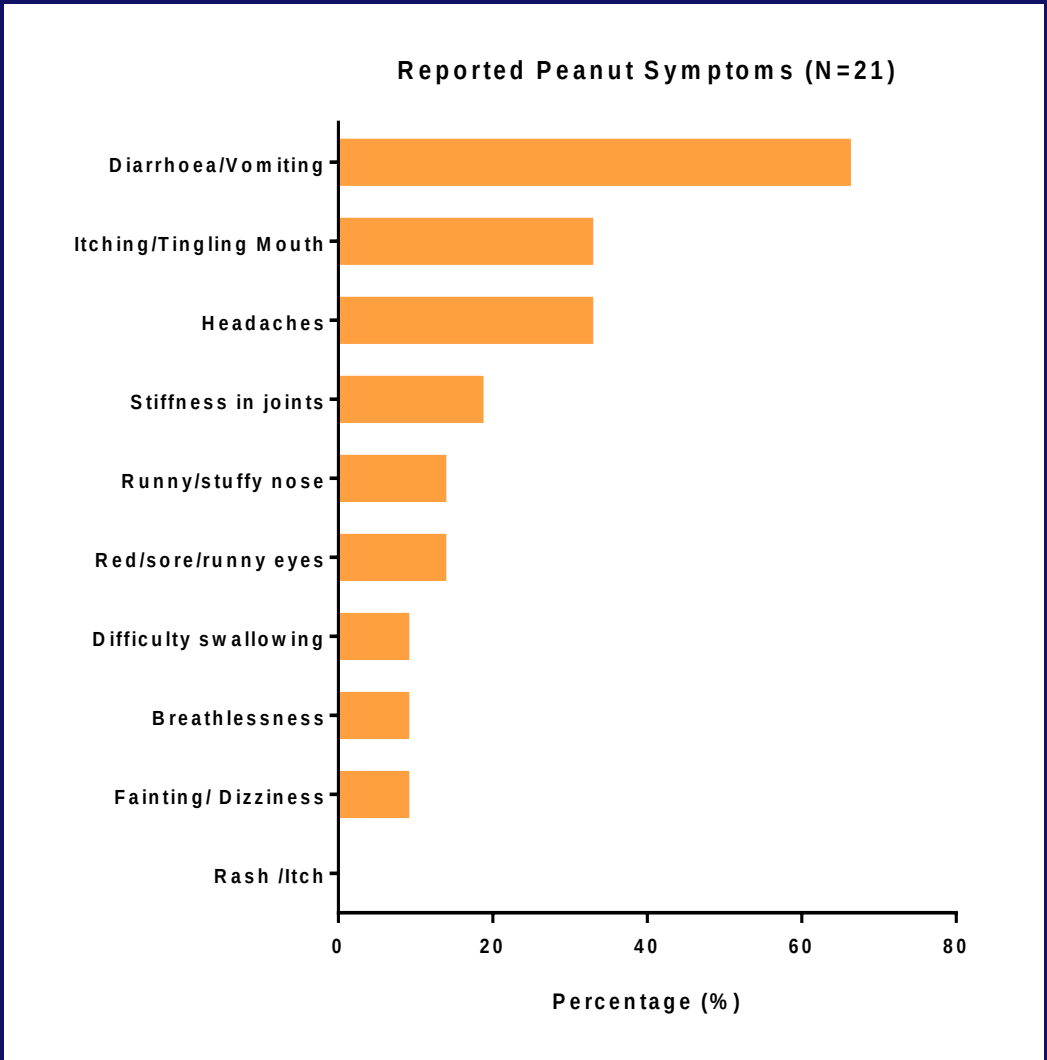
Peanut allergy outcomes among urban and rural children in Ghana

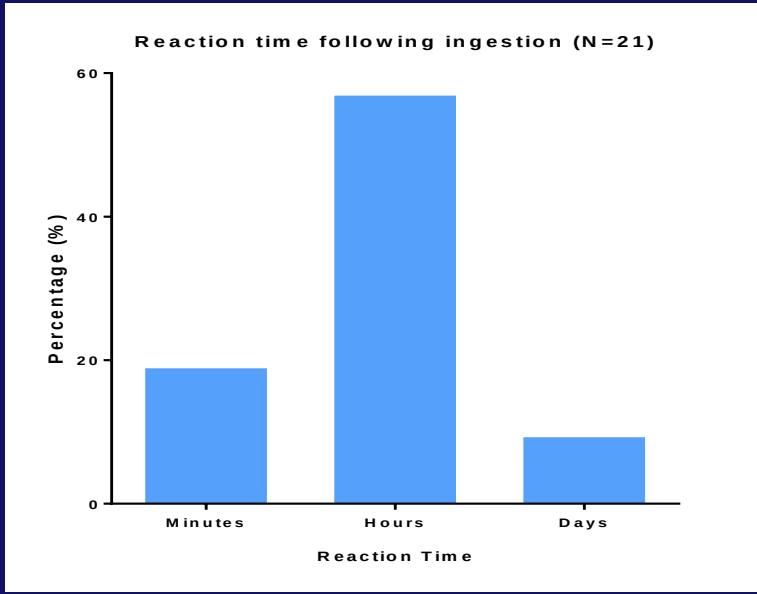


RURAL
URBAN

* $p < 0.05$
** $p < 0.01$
*** $p < 0.001$

Subjects reporting adverse reactions to peanut (N=21)



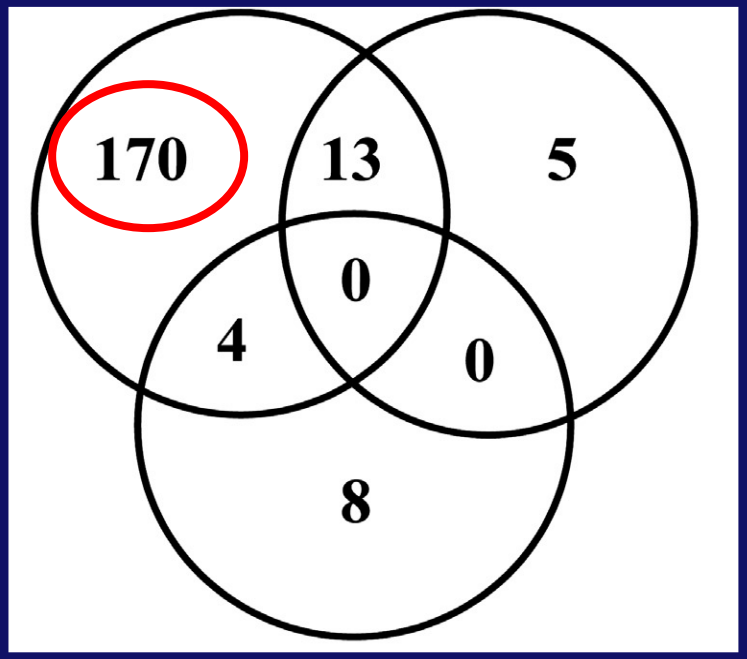


Peanut allergy outcomes (complete data, N=1004)

Peanut Specific IgE

IgE ImmunoCap®

Cut-off : ≥0.35 Ku/L

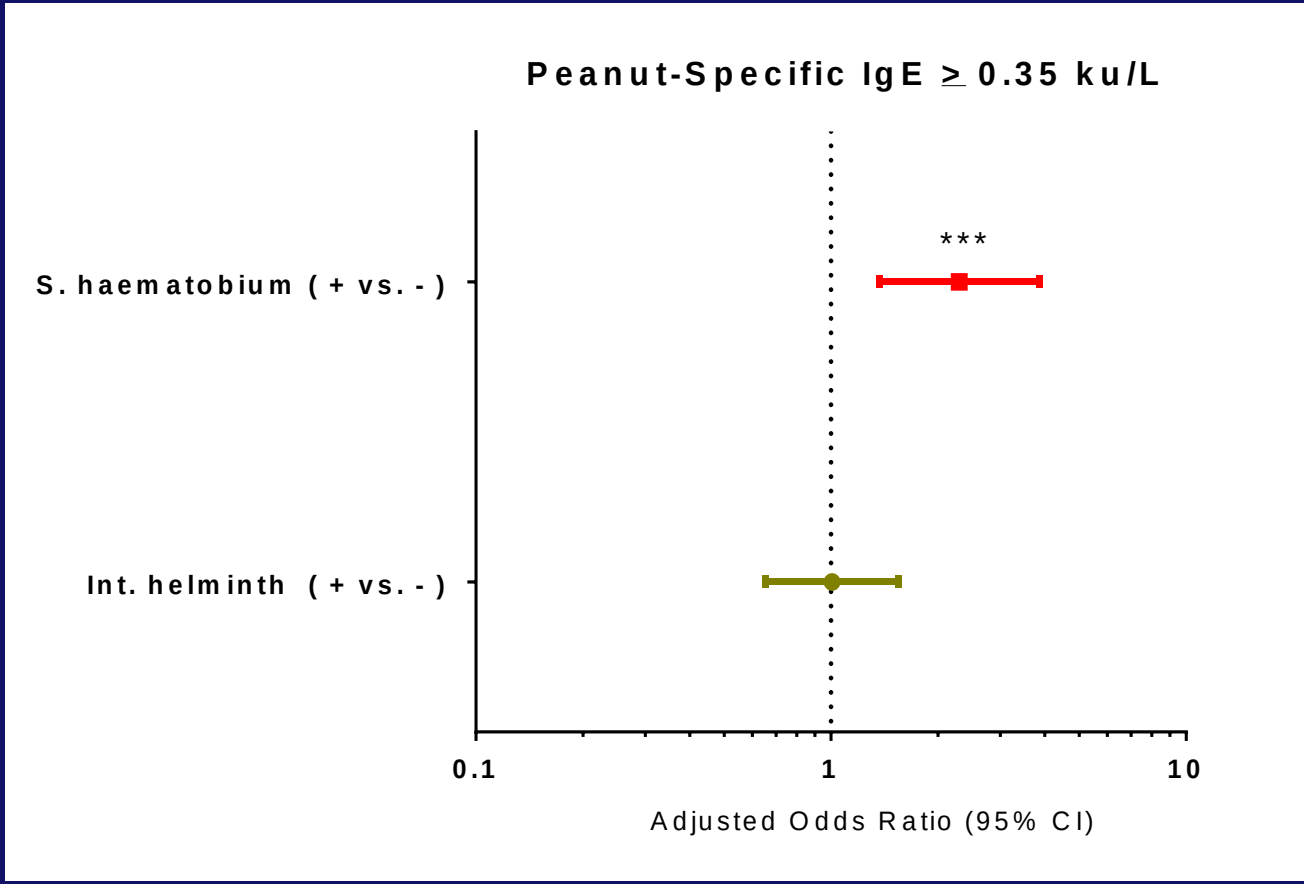


Reported Symptoms to Peanut Questionnaire

Peanut SPT Reactivity

Cut-off : ≥ 3mm

Worm infection and peanut-specific IgE sensitization

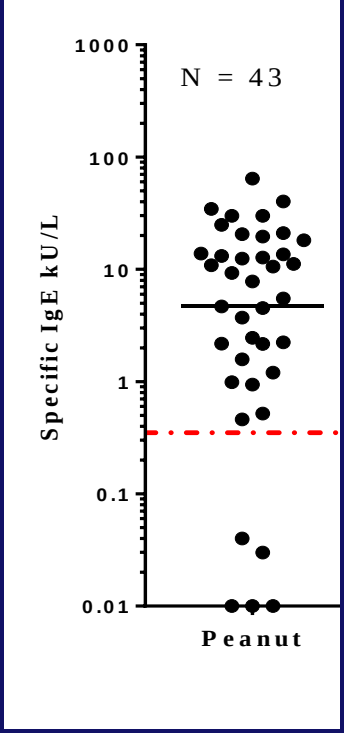


Logistic regression model adjusted for age, gender and area
Wald's Test : *** P<0.001

Peanut-specific IgE: recombinant peanut allergen responses

Additional sera measurements in a subset (N=43):

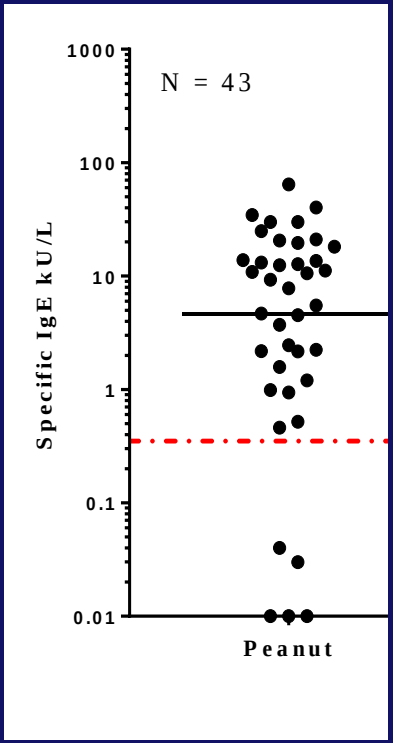
- Specific IgE responses to purified peanut allergens Ara h 1, 2, 3 (seed storage proteins)
- Recombinant non-glycosylated allergen produced in an *E. coli* strain



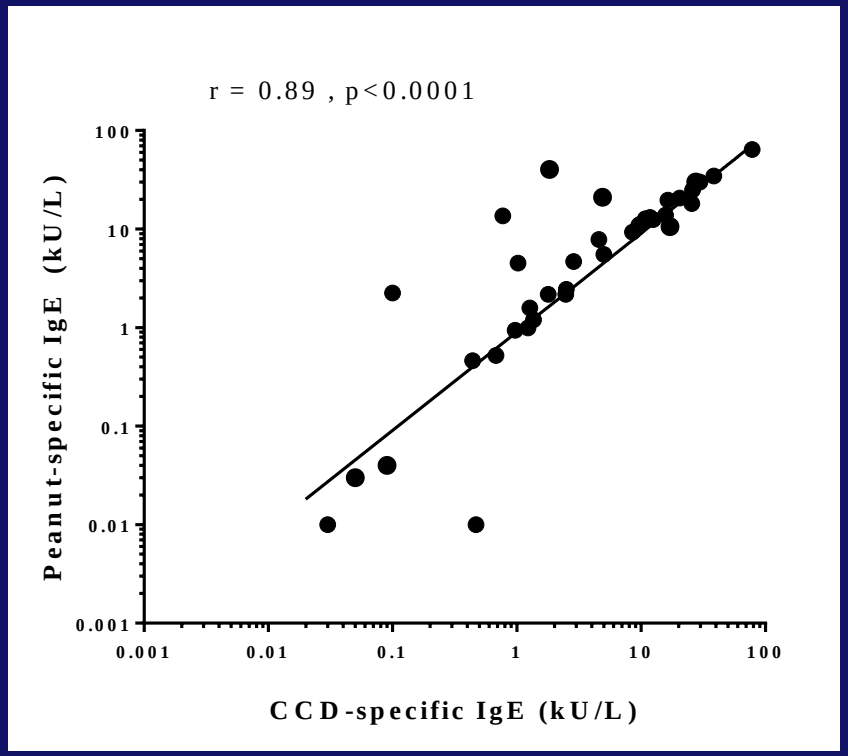
Peanut-specific IgE: Cross-reactive carbohydrate determinants

Additional sera measurements in a subset (N=43)

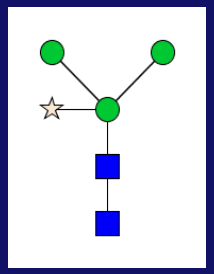
- Specific IgE responses to bromelain as a marker of cross-reactive carbohydrate determinants (CCDs) which are carbohydrate epitopes on glycoproteins



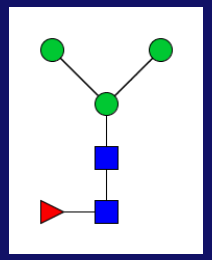
N-glycan induced IgE cross-reactivity



- Indications of the presence of IgE recognizing epitopes common to both peanut and bromelain
- Possible cross-reactivity due to N-glycan epitopes commonly found in plants and helminths

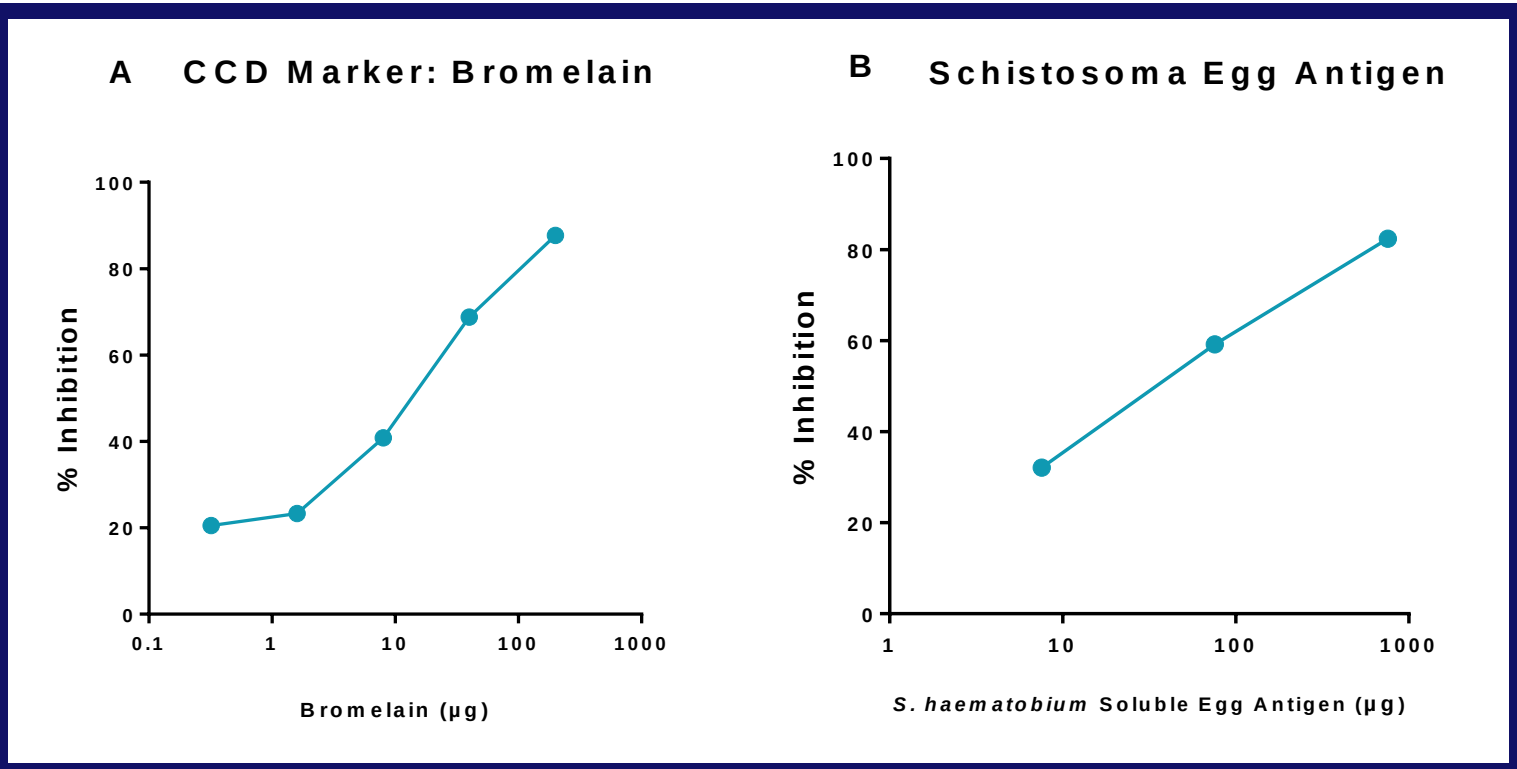


Core β(1,2)-xylose



Core α(1,3)-fucose

Inhibition of IgE binding to peanut by bromelain & Schistosoma SEA

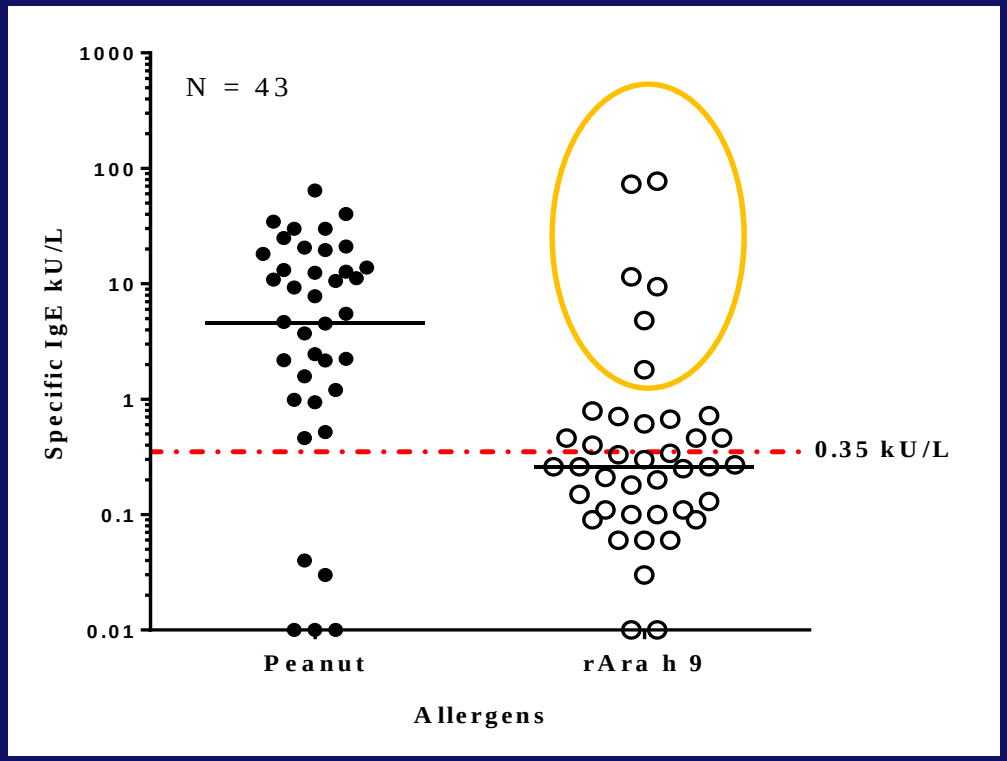


- More than 80% inhibition with both bromelain and Schistosoma soluble egg antigen
- High levels of peanut-specific IgE as a result of carbohydrate cross-reactivity

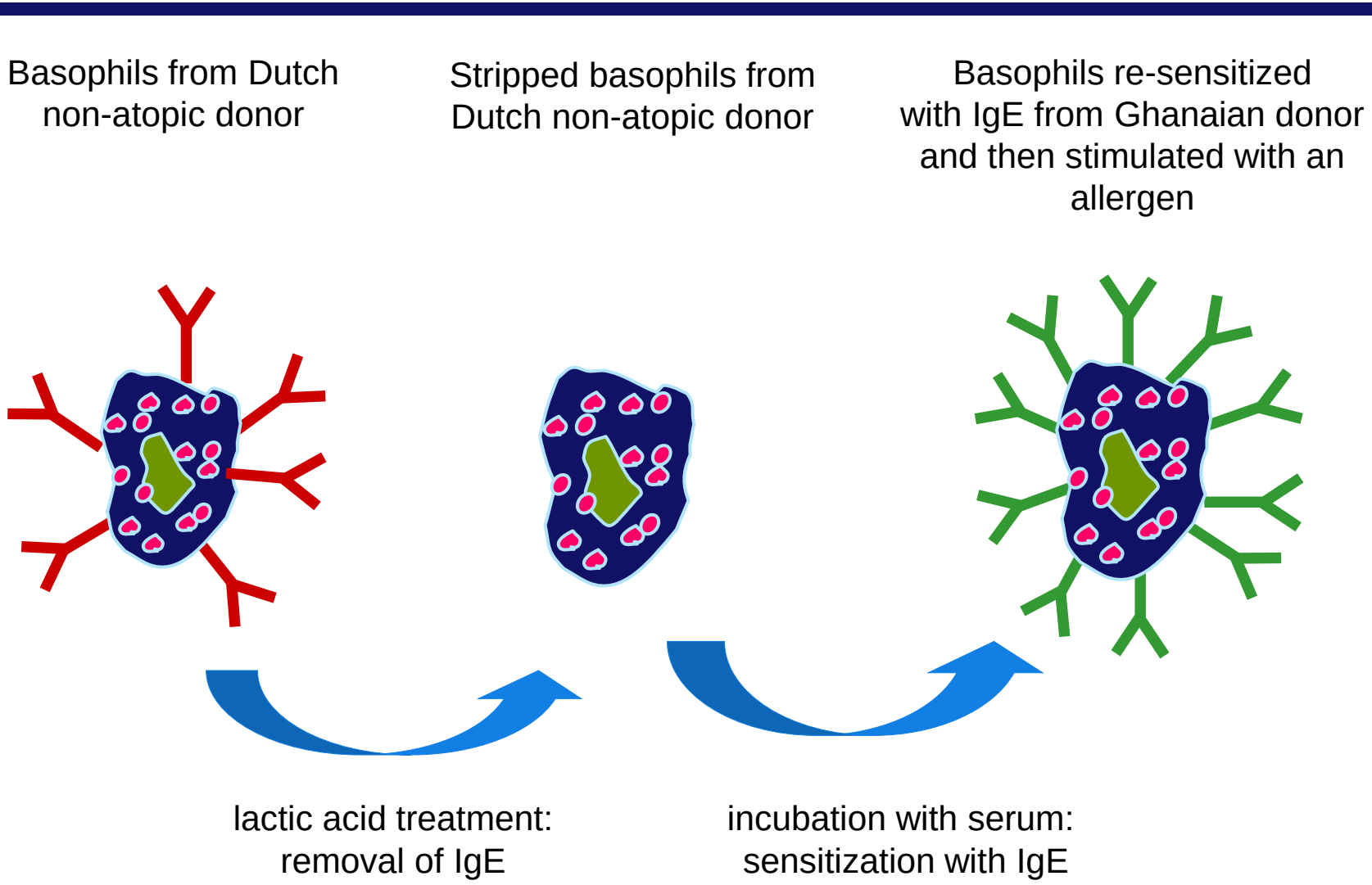
Peanut-specific IgE: responses to recombinant Ara h 9

Additional sera measurements in a subset (N=43)

- Specific IgE responses to purified peanut allergen Ara h 9 (lipid transfer protein)
- Recombinant non-glycosylated allergen produced in an *E. coli* strain



Stripped basophil histamine release assay



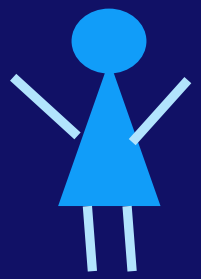
Source: Ronald van Ree

Basophil histamine release- Ara h 9 & whole peanut

Donor #1

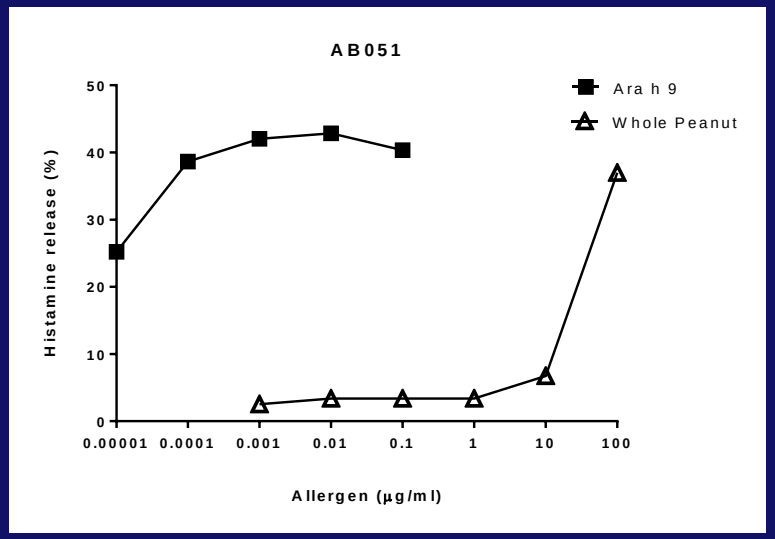
ID	AB051
Area	RURAL
IgE to whole peanut	40.2 kU/L
IgE to CCD	1.8 kU/L
IgE to rAra h 9	72.8 kU/L

Donor #2

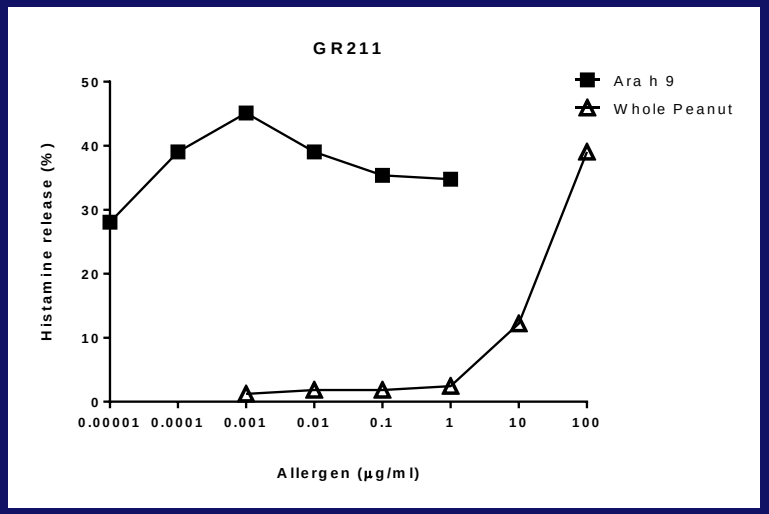


ID	GR211
Area	URBAN
IgE to whole peanut	21.0 kU/L
IgE to CCD	4.9 kU/L
IgE to rAra h 9	77.4 kU/L

Basophil histamine release- Ara h 9 & whole peanut



IgE to whole peanut	40.2 kU/L
IgE to CCD	1.8 kU/L
IgE to rAra h 9	72.8 kU/L
SPT to peanut	-
Reported Symptoms	Yes



IgE to whole peanut	21.0 kU/L
IgE to CCD	4.9 kU/L
IgE to rAra h 9	77.4 kU/L
SPT to peanut	+
Reported Symptoms	No

Conclusions

- Significant urban-rural differences in allergy outcomes
- Schistosoma infection negatively associated with mite SPT reactivity
  - Indications of a protective effect
- High levels of allergen-specific IgE as a result of carbohydrate cross-reactivity
  - Possible helminth involvement in inducing cross-reactivity
- Little evidence of IgE-mediated peanut allergy
- Biologically active IgE to Ara h 9 observed
  - Factors associated with Ara h 9 sensitization in Ghana are currently unknown

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ORIGINAL ARTICLE Epidemiology of Allergic Disease

Schistosome infection is negatively associated with mite atopy, but not wheeze and asthma in Ghanaian Schoolchildren

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Food Allergy in Ghanaian Schoolchildren: Data on Sensitization and Reported Food Allergy

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Peanut-specific IgE antibodies in asymptomatic Ghanaian children possibly caused by carbohydrate determinant cross-reactivity

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