

Sub-populations at risk: age and co-morbidity as risk factors for developing food allergy

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Disclosures 2012

- **Employment**
 - UCC, HSE, Ireland
- **Research funding**
 - EU FP7
 - Childrens Research Centre, Ireland
 - Irish Lung Foundation
 - FSA, UK
 - Danone, Netherlands
- **Stockholding / directorships**
 - None
- **Gifts**
 - None
- **Consultancies**
 - None
- **Societies**
 - IAAI, EAACI, AAAAI, BSACI
- **Patent (applied for)**
 - Challenge outcome predictor
- **Speaker bureaux**
 - MSD
 - ALK Abello
 - Phadia
 - Nutricia
 - Mead Johnson
 - Pfizer
 - Allergy Therapeutics
 - Stallergenes

Take home message?



it's not just what you eat,

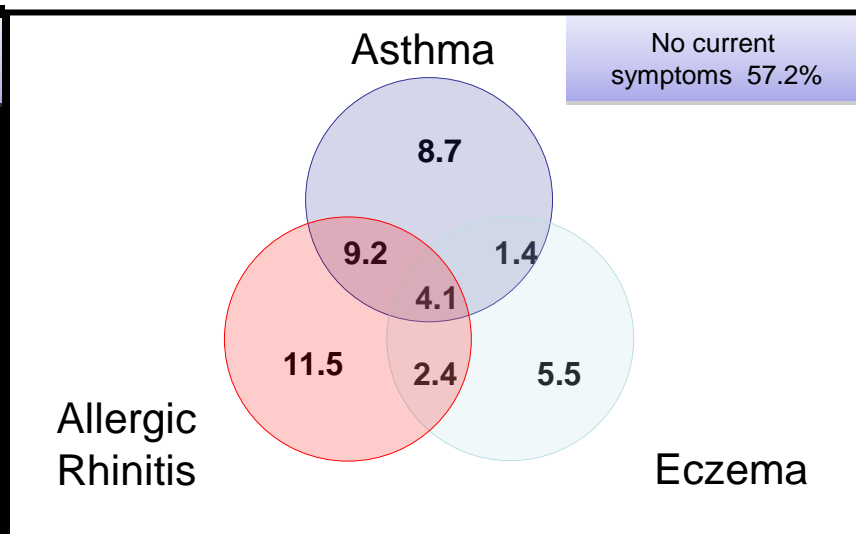
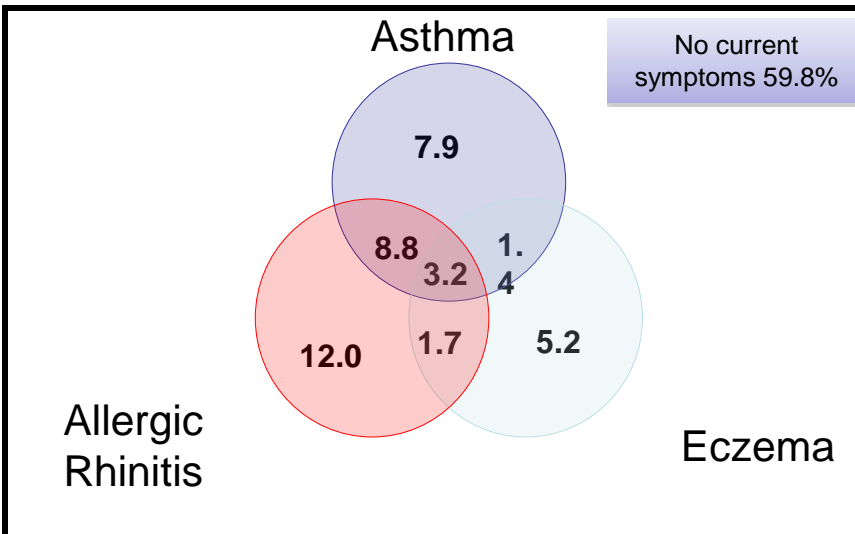
it's lots of other factors too

Co-morbidity of atopic conditions in Irish Schoolchildren 6-9 years

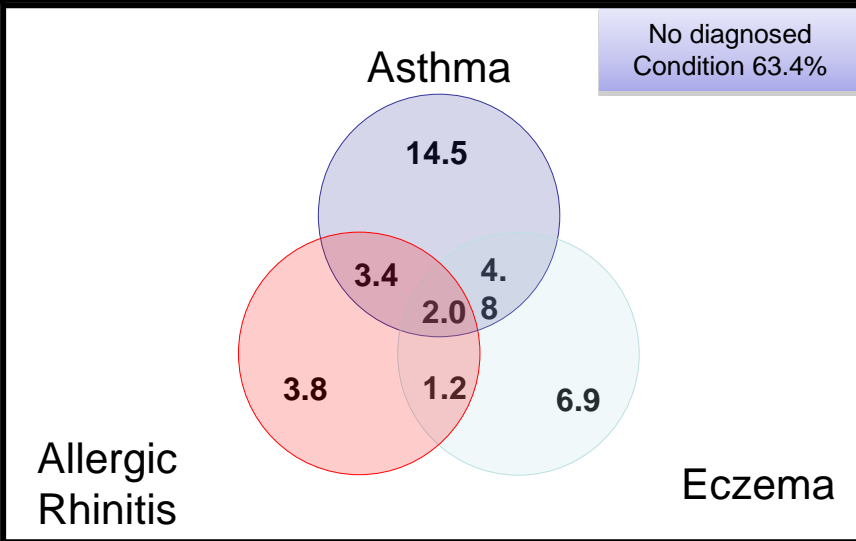
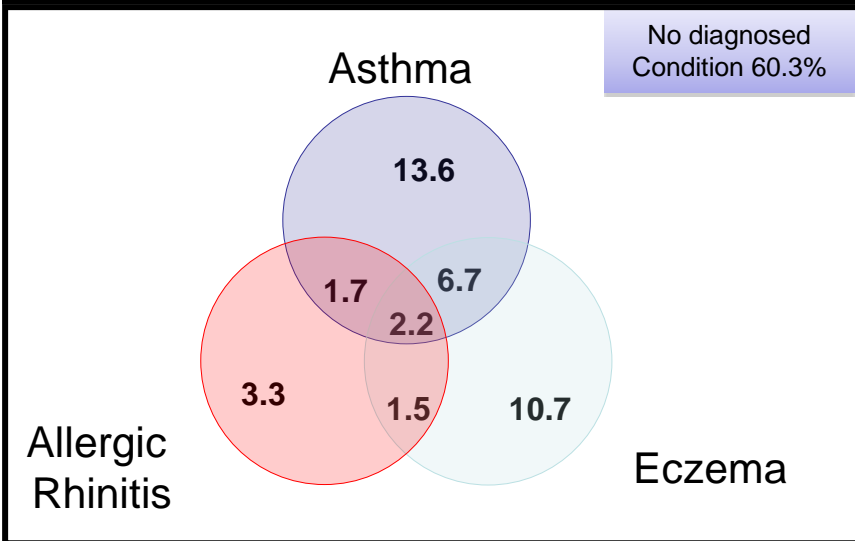
2002

2007

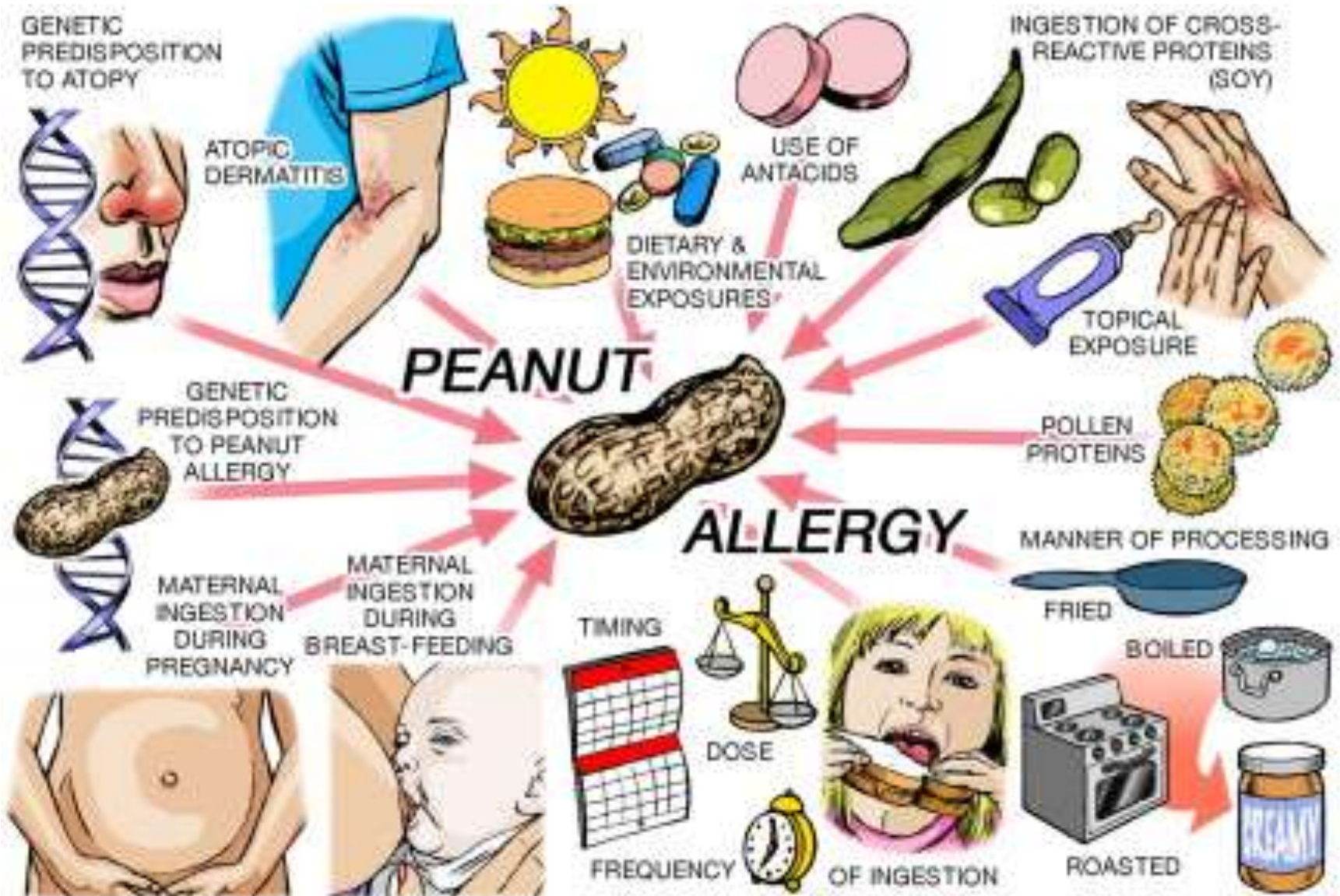
Current (%)



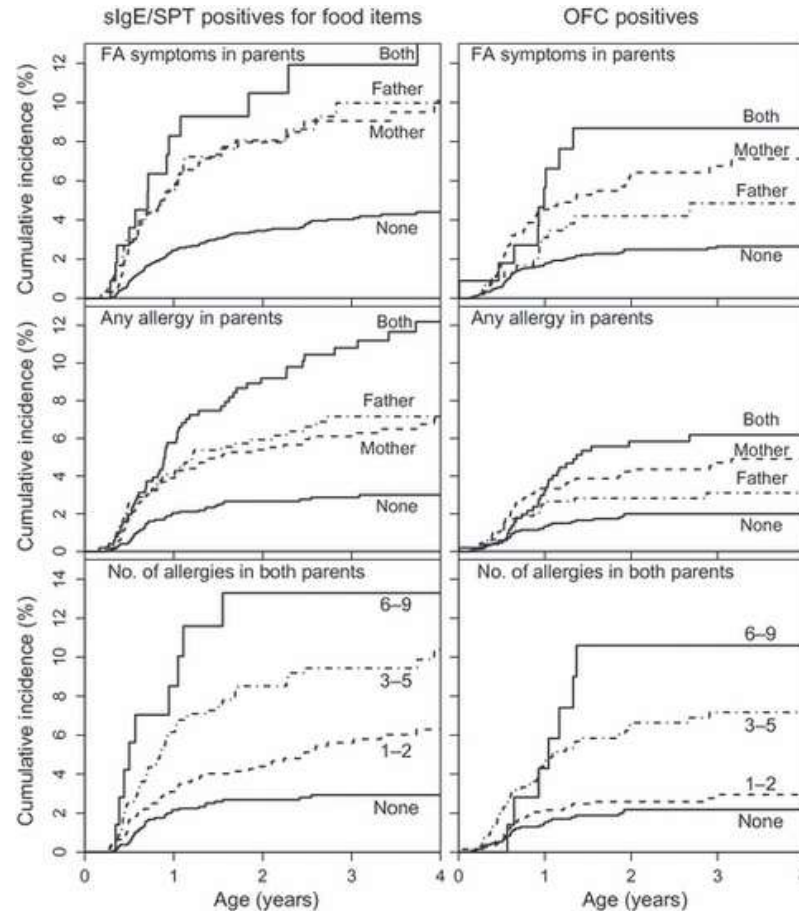
Lifetime (%)



Peanut allergy



Heredity of food allergies in an unselected child population: An epidemiological survey from Finland



GINI study, Germany

- High risk mothers
 - given 1 of 4 formulae if not exc BF to 6 mo
 - CMF, pHF-W, eHF-W, eHF-C

By 12 months of age

- Allergic manifestations
 - 0.51 with eHF-C vs cows milk (9% vs 16%)
- Atopic dermatitis
 - 0.42 with eHF-C vs cows milk
 - 0.56 with pHF-W vs cows milk

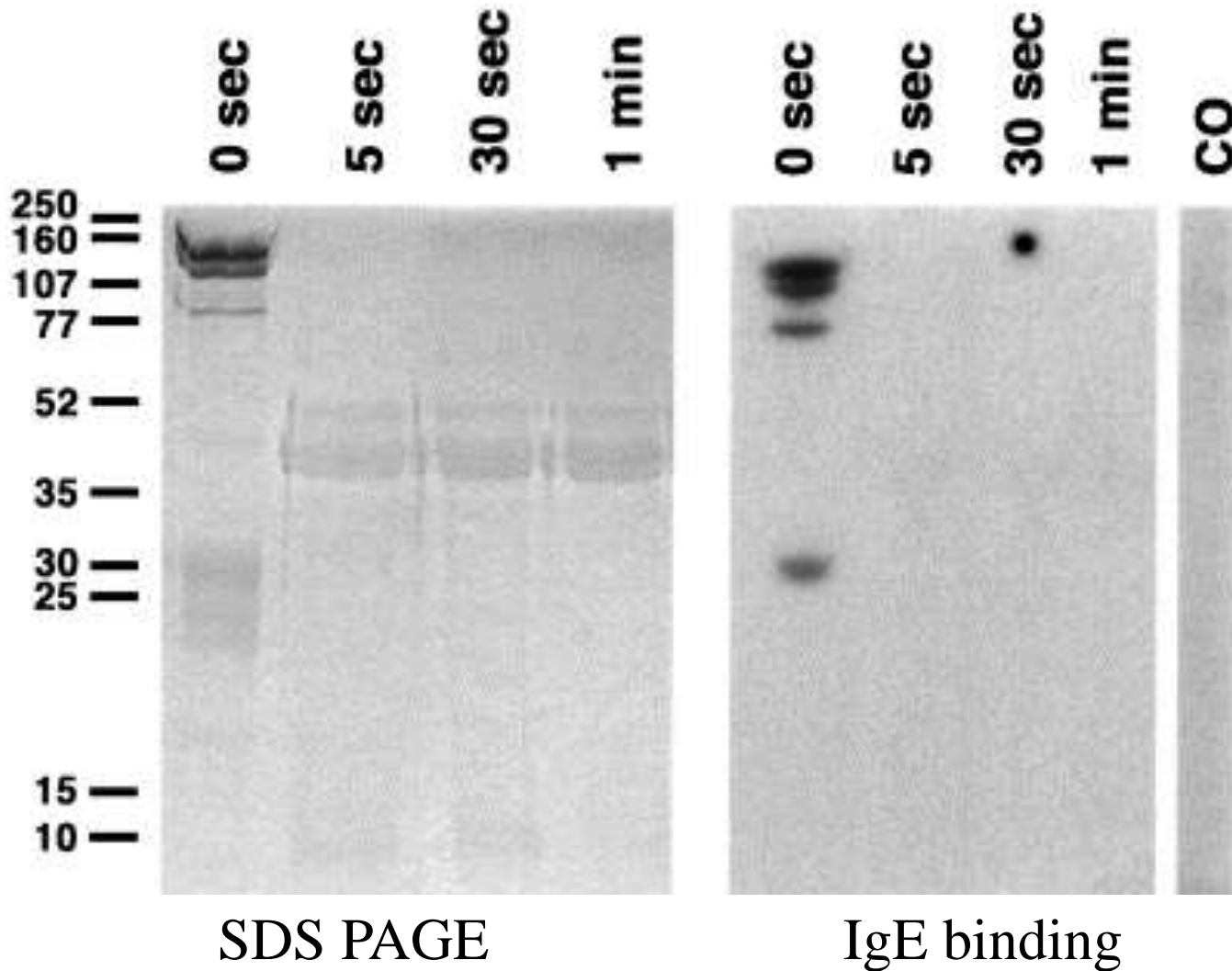
Do not offer formula to babies that mothers are trying to breast feed

	Cows milk allergic	Cows milk tolerant	Total
Given formula	39	200	239
Not given formula	0	1500	1500
Total	39	1700	1739

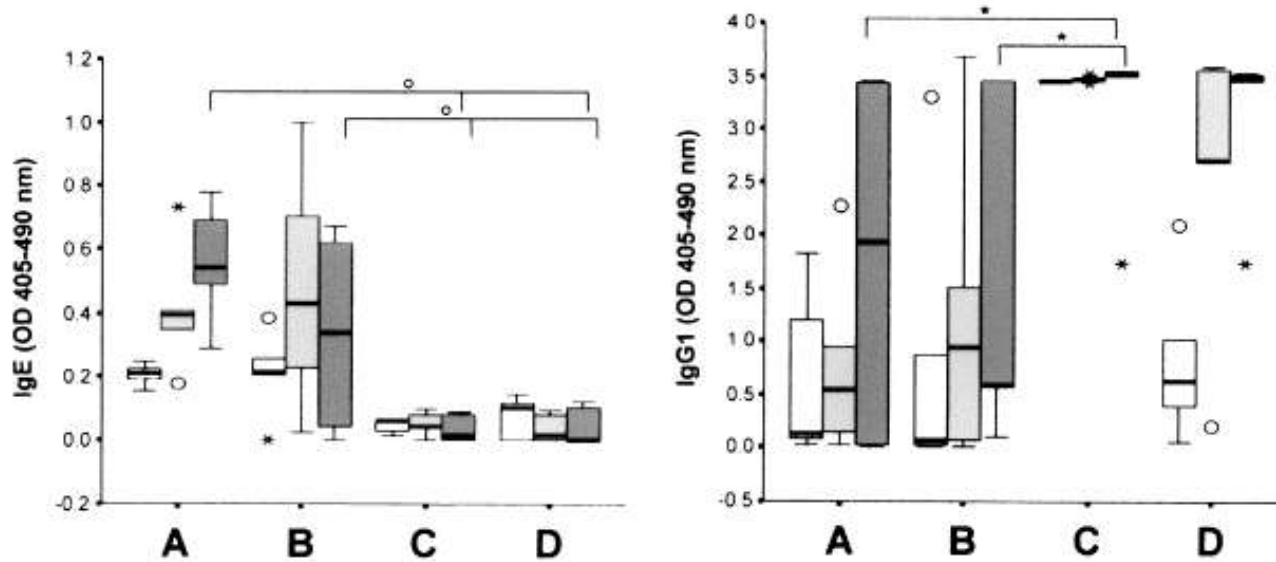
- 20% of breast fed infants given formula in first 24 hours developed cows milk allergy.
- No child exclusively breastfed in first 24 hours developed cows milk allergy.
- Consultant approval required to formula feed babies that are not yet established on breast caused a 50% reduction in incidence of CMA

Gastric digestion decreases allergenicity

(Untersmayr, 2003)

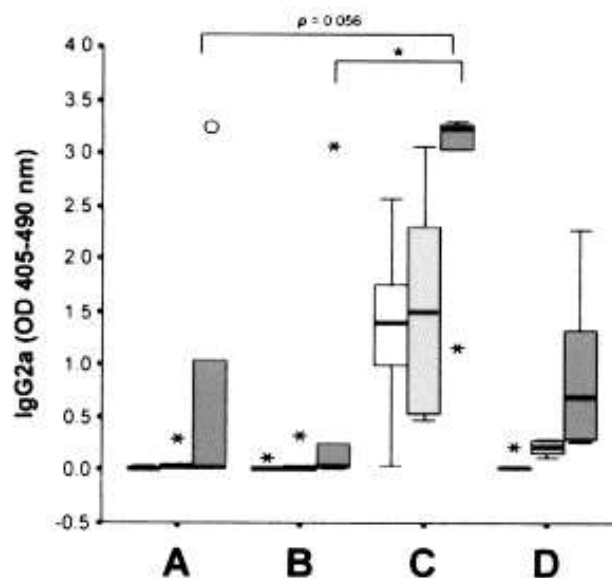


Antacid treatment increases allergenicity



A ranitidine

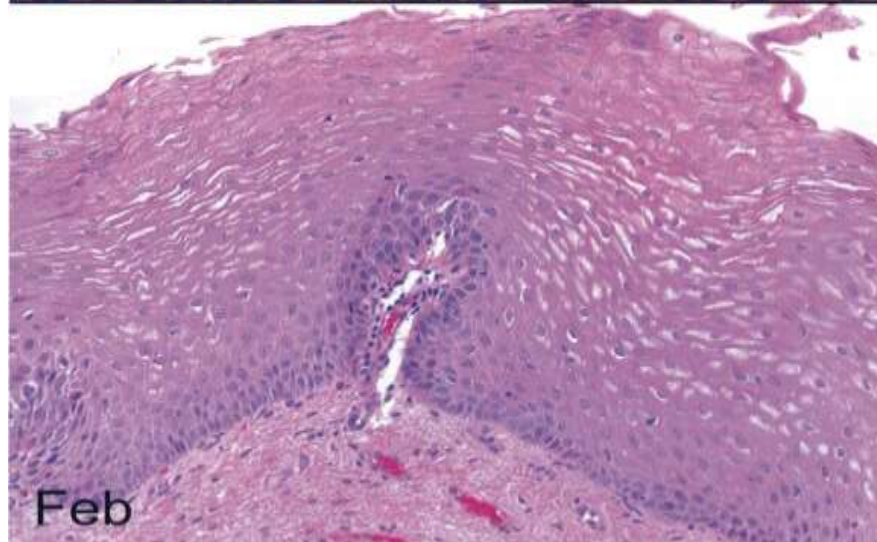
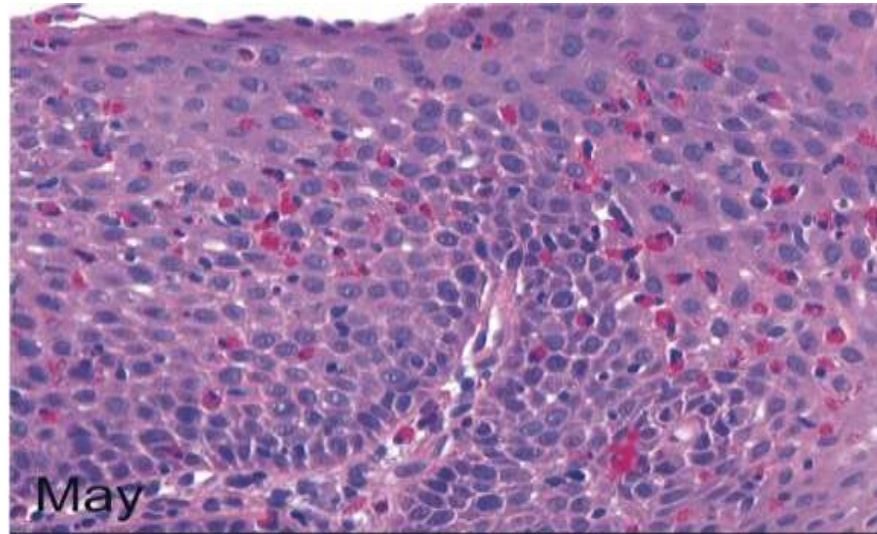
B Sucralfate



C caviar +
adjuvant

D just caviar!

Eosinophilic oesophagitis

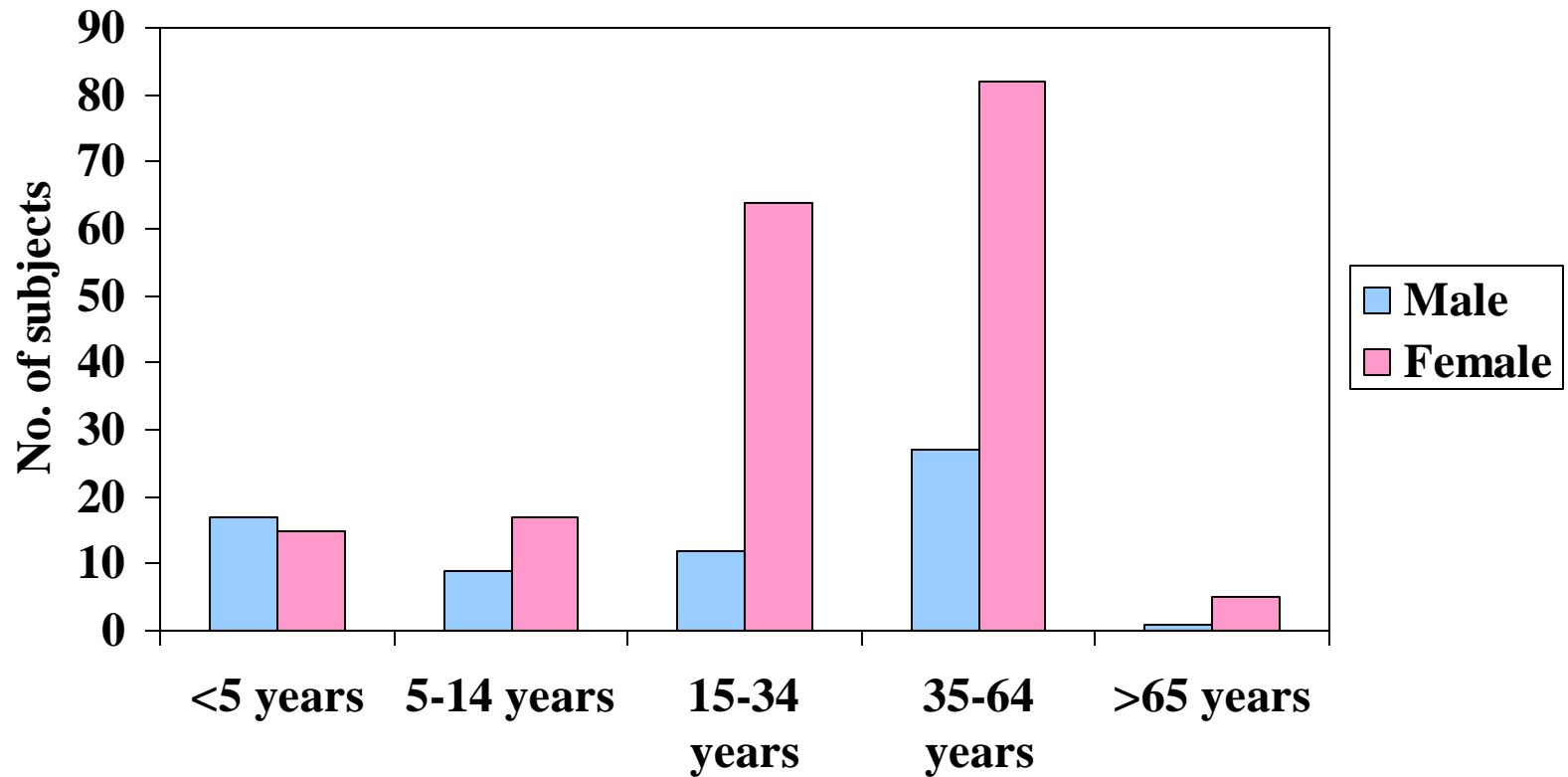


Cashew allergy has a much later age of onset than peanut allergy

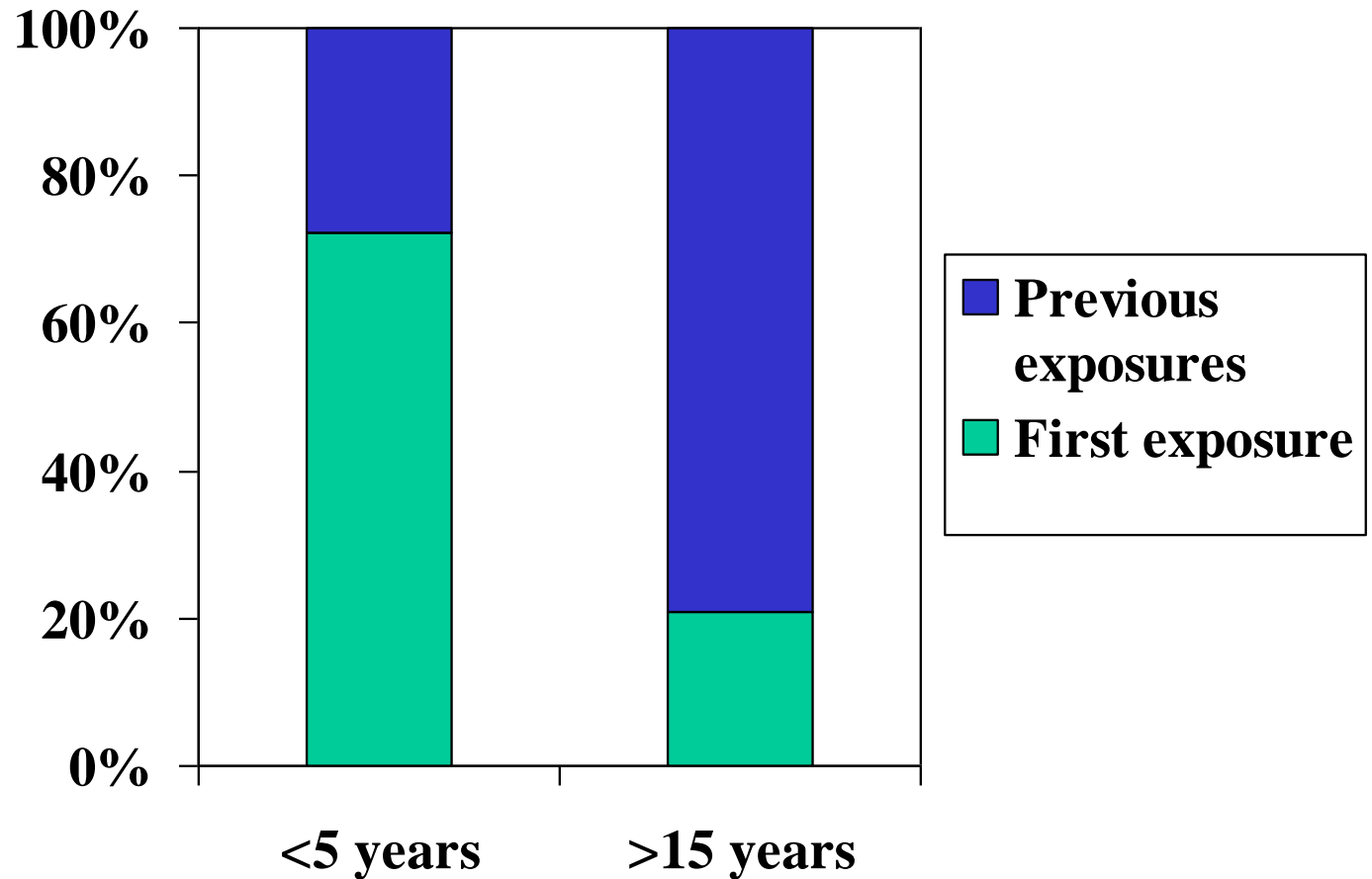
	Cashew allergic UK#	Peanut allergic US*	Tree nut allergic US*
Median age of onset	49 m (2m-27 y)	24 m (6-108)	62 m (10-204)

* Sicherer, 1998, # Hourihane 2001

Age at first reaction to kiwi

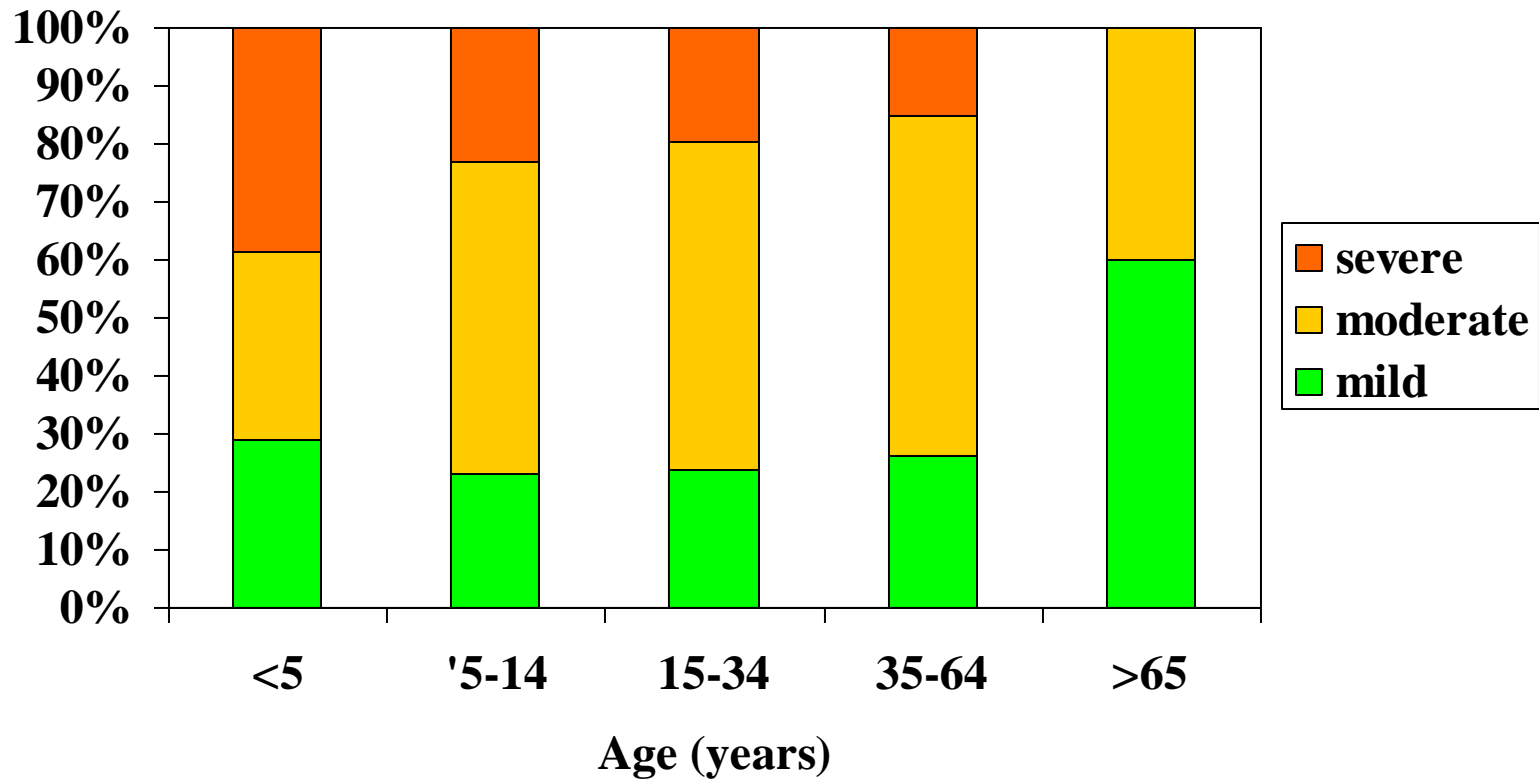


Previous exposures

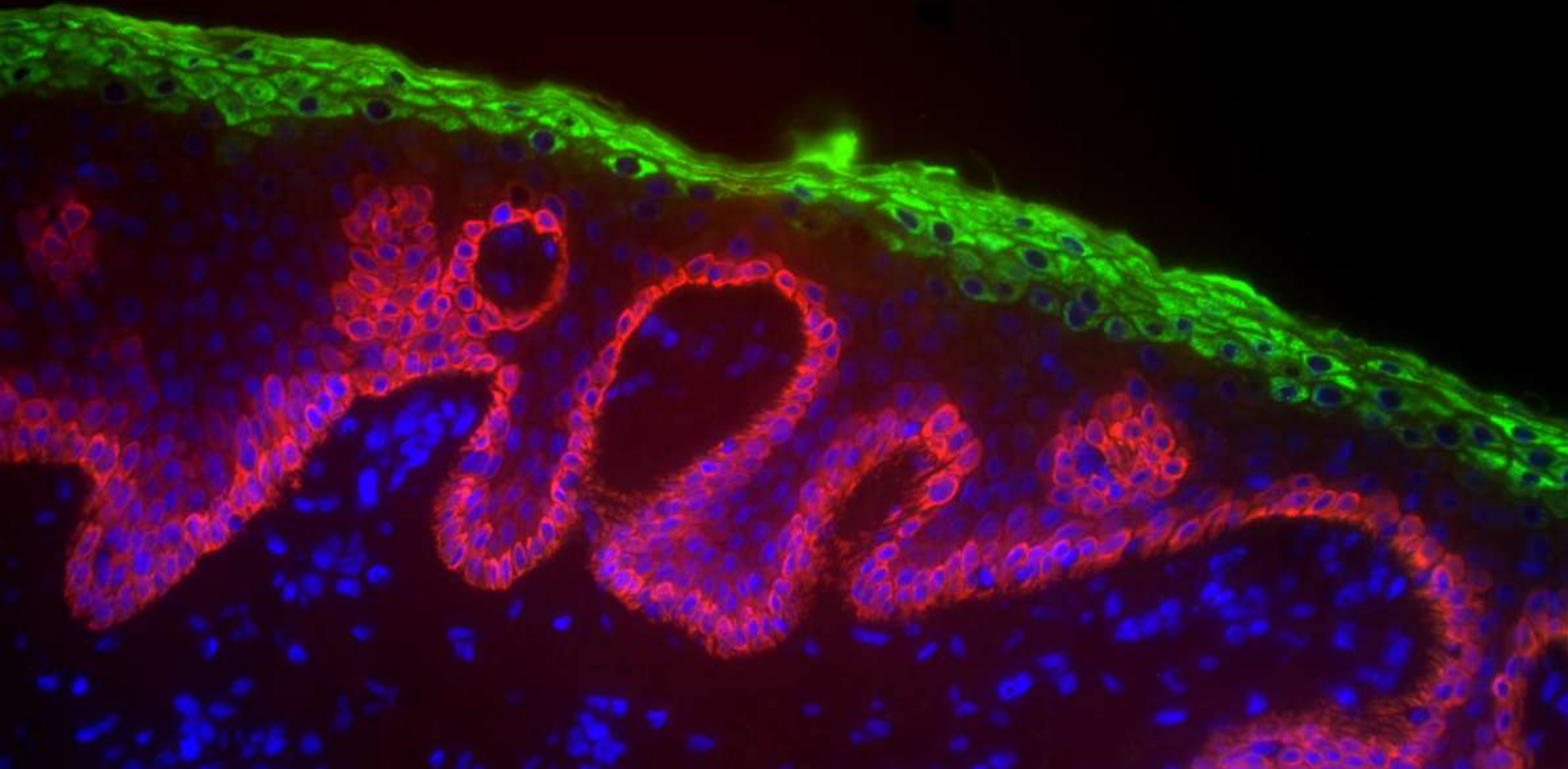


$P < 0.001$

Severity of first reactions



The skin barrier



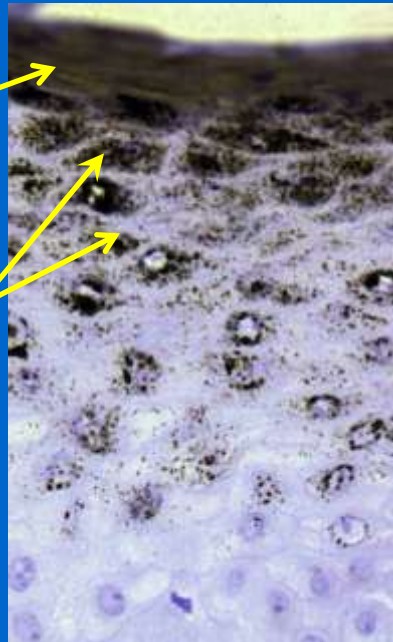
Consequences of Filaggrin Mutation

Normal Skin

Filaggrin Mutation

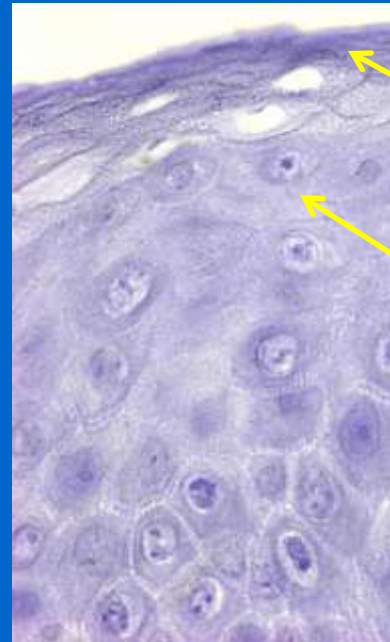
Normal skin barrier

Filaggrin granules



Defective skin barrier

No filaggrin granules



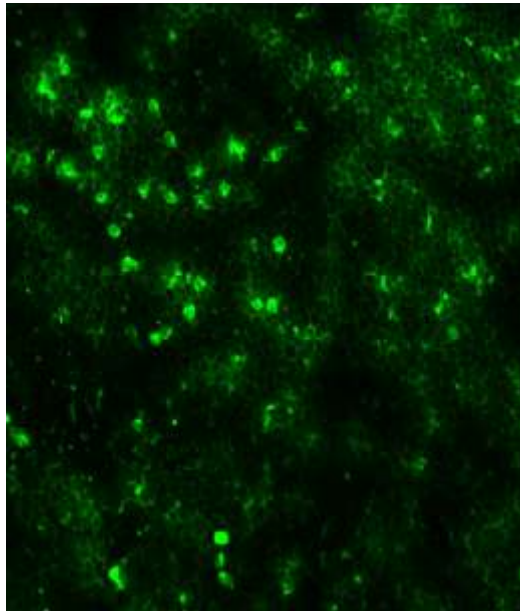
The murine model

Jessica Strid, ICH, London



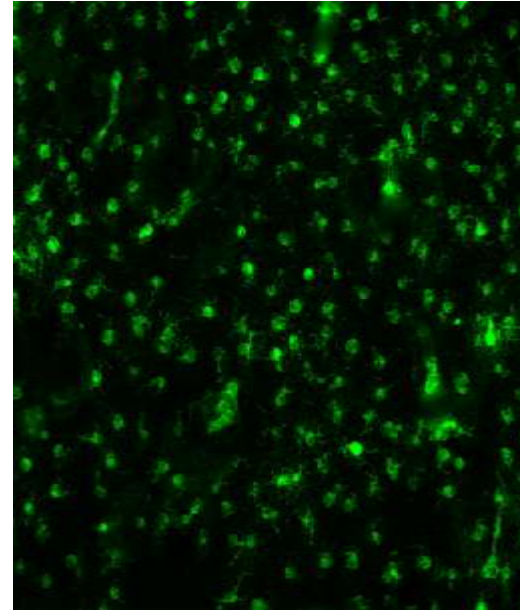
- BALB/c mice, 6-8 weeks, bred and maintained on peanut, soy, milk and chicken egg ovalbumin (OVA)-free diet
- Feeds of 0.01, 0.1, 1 and 5 mg peanut or OVA/g bodyweight

Langerhans cells only migrate from abraded skin on Ag encounter



Peanut paint

40 LC/mm²



Saline paint

293 LC/mm²

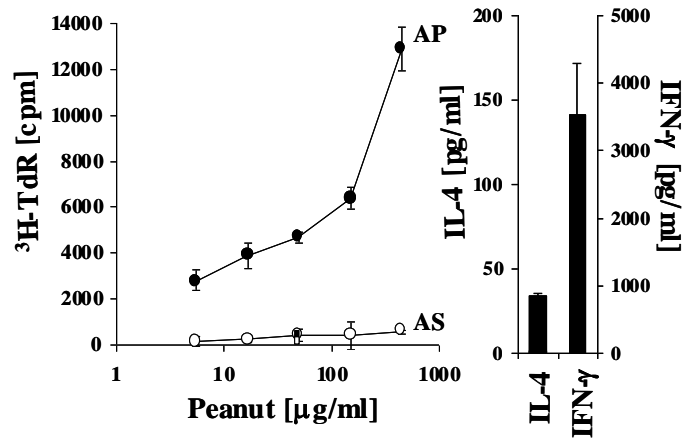
Exposure via abraded skin is sensitising

Days following epicutaneous peanut exposure

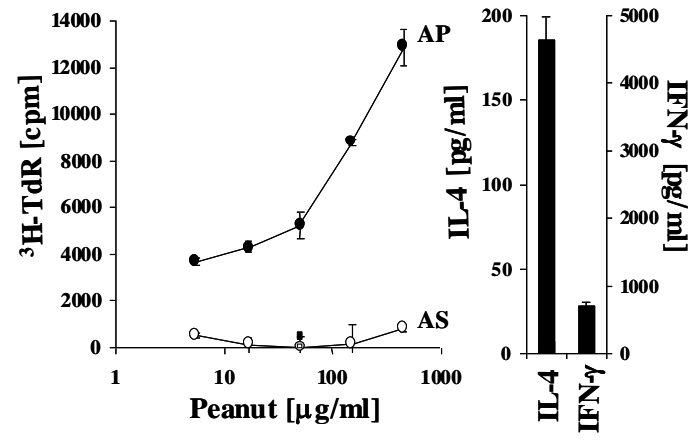
6 days

20 days

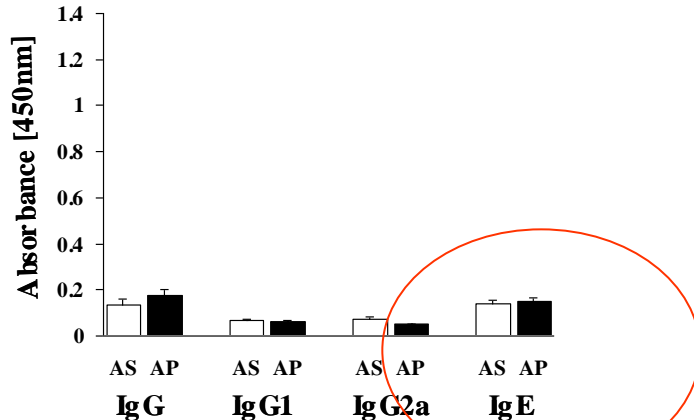
A



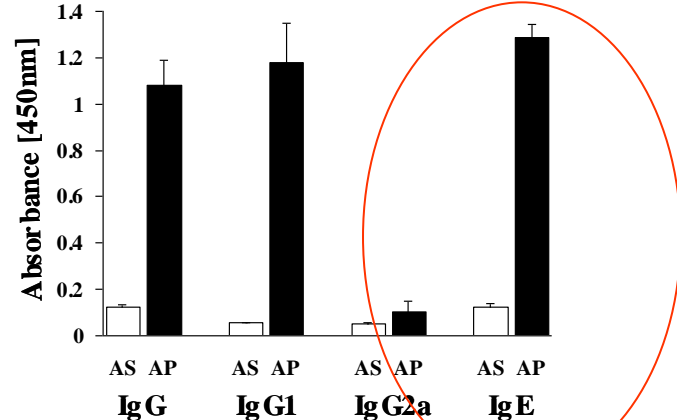
C



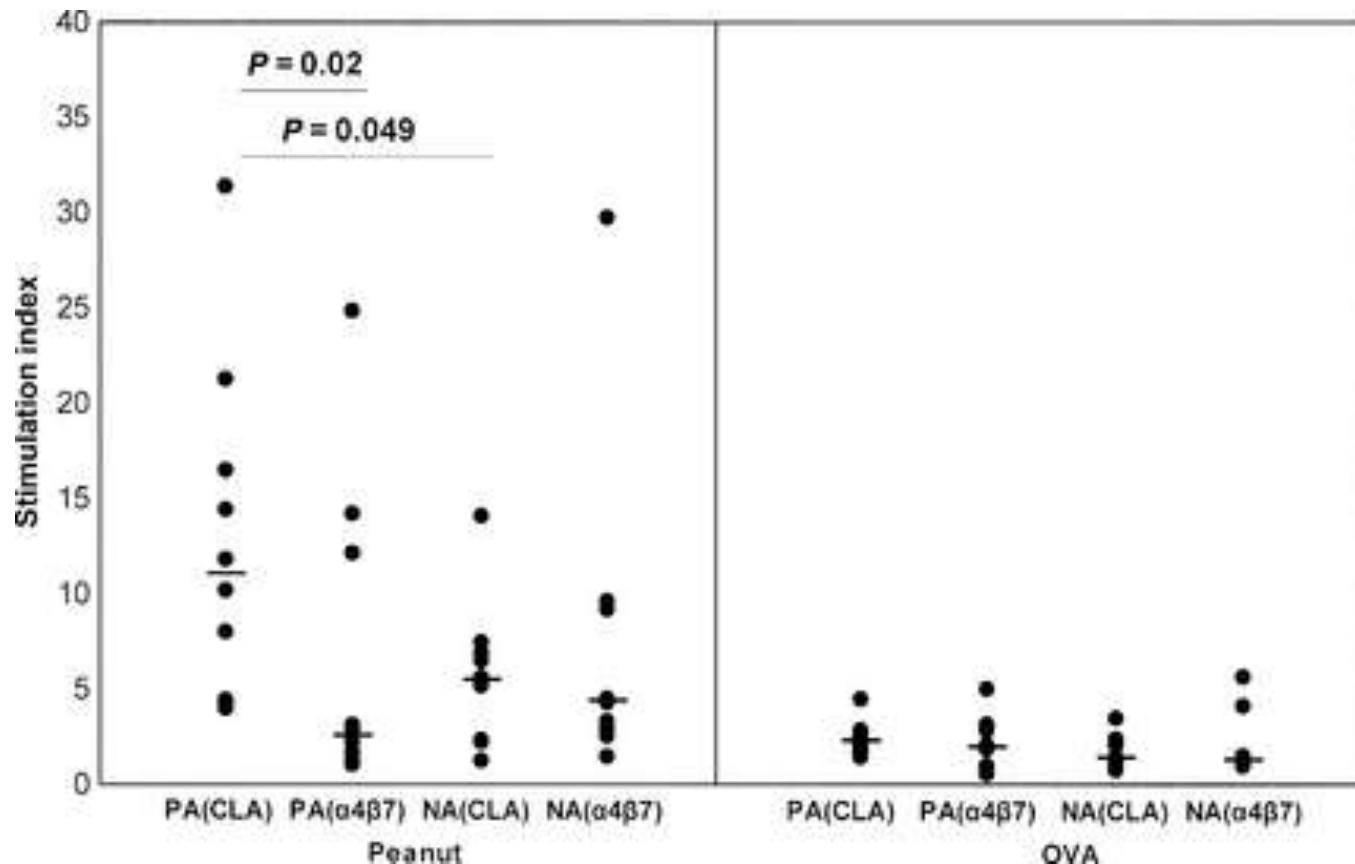
B



D



Cutaneous lymphocyte antigen and $\alpha 4\beta 7$ T-lymphocyte responses are associated with peanut allergy and tolerance in children



Allergy

Volume 67, Issue 3, pages 336-342, 16 JAN 2012 DOI: 10.1111/j.1398-9995.2011.02765.x
<http://onlinelibrary.wiley.com/doi/10.1111/j.1398-9995.2011.02765.x/full#all2765-fig-0003>

Loss-of-function variants in the filaggrin gene are a significant risk factor for peanut allergy

Results: FLG mutations showed a strong and significant association with peanut allergy in the food challenge–positive patients (OR 5.3;95% CI, 2.8-10.2), which remains significant ($P = 0.0008$) after controlling for coexistent atopic dermatitis.

Conclusion: Filaggrin mutations represent a significant risk factor for IgE-mediated peanut allergy, indicating a role for epithelial barrier dysfunction in the pathogenesis of this disease.

(S Brown et al J Allergy Clin Immunol 2011;127:661-7.)

Atopic Dermatitis

Atopic dermatitis is an itchy inflammatory skin disease that affects approximately 11% of children in the United States⁴⁶ and up to 25% in the United Kingdom,^{47,48} making it the most common chronic

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Slide

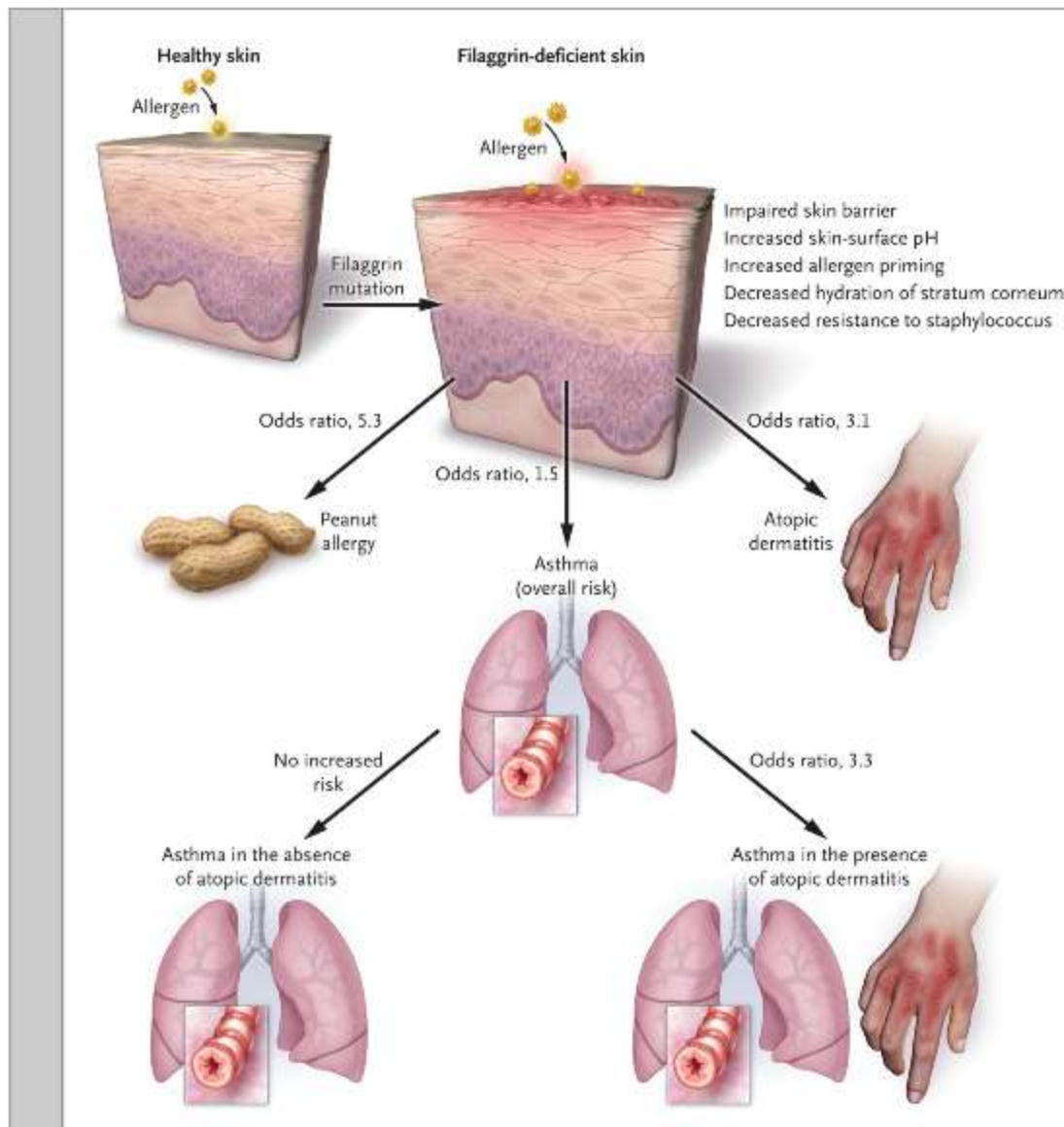


Figure 4. Filaggrin Haploinsufficiency and Increased Risk of Several Complex Traits.

Filaggrin haploinsufficiency is defined as a 50% reduction in the expression of the filaggrin protein. The odds ratios are for the risk of peanut allergy, asthma, or atopic dermatitis as compared with the risk in the absence of filaggrin mutation. The odds ratios listed for atopic dermatitis and asthma are from meta-analyses involving several thousand patients. *FLG* mutations confer an overall risk of asthma of 1.5, but this risk is restricted to patients with atopic dermatitis. The odds ratio for the complex phenotype of asthma plus atopic dermatitis is 3.3. The odds ratio for peanut allergy is based on the only available data, from a single study.

Irvine, McClean, Leung,
NEJM 2011

Latitude

= sunlight/Vit D??

or cultural eating habits?

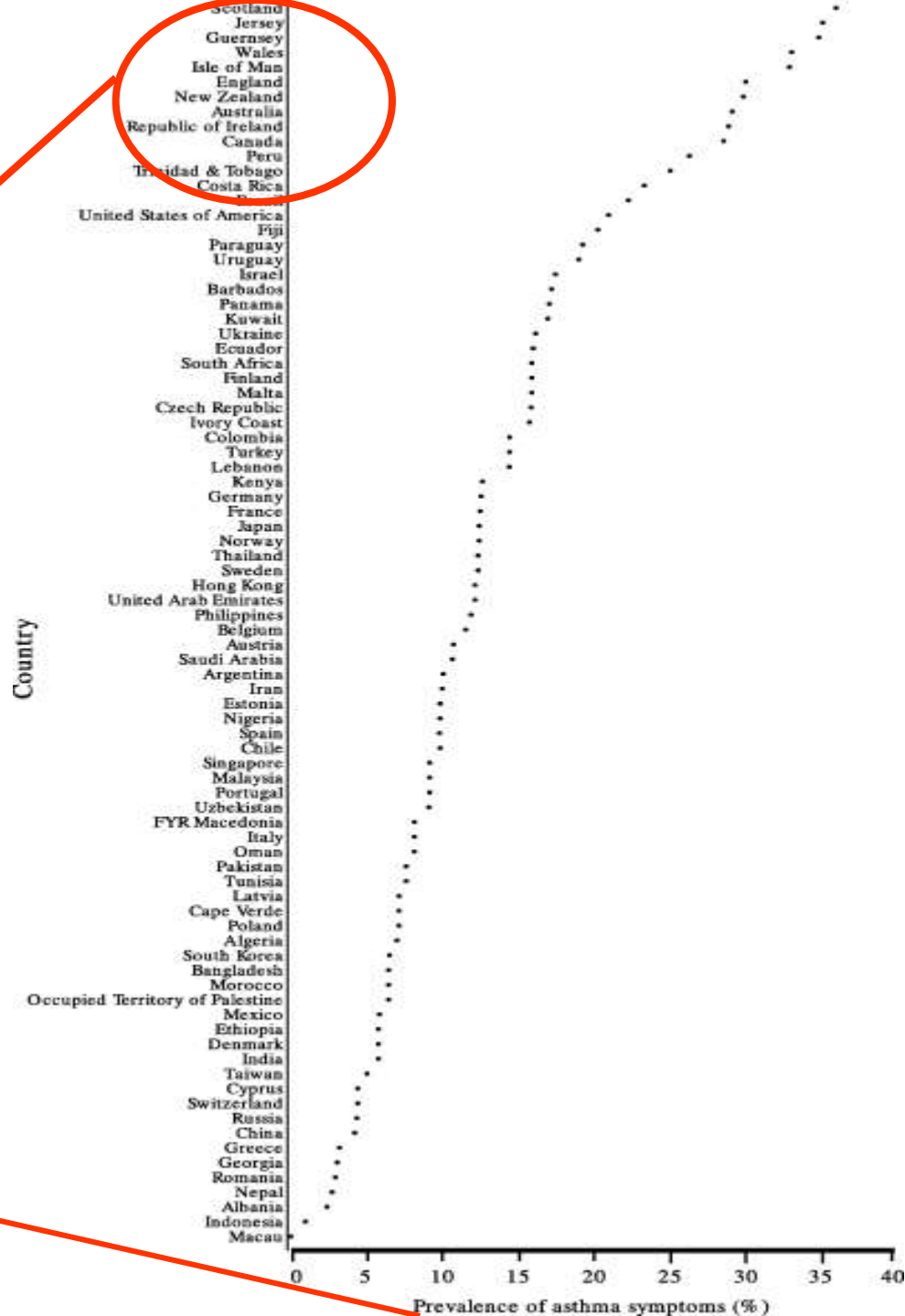
or health care access?

ISAAC
Studies
International
Study of
Asthma and
Allergies in
Childhood

1st Scotland

9th Ireland

% asthmatic





Darwin to Perth	4396km
Perth to Adelaide	3766km
Adelaide to Melbourne	316km
Melbourne to Sydney	887km
Sydney to Brisbane	913km
Brisbane to Cairns	1748km



Fraser Island
Noosa
Brisbane



Area size comparison of Australia and Europe

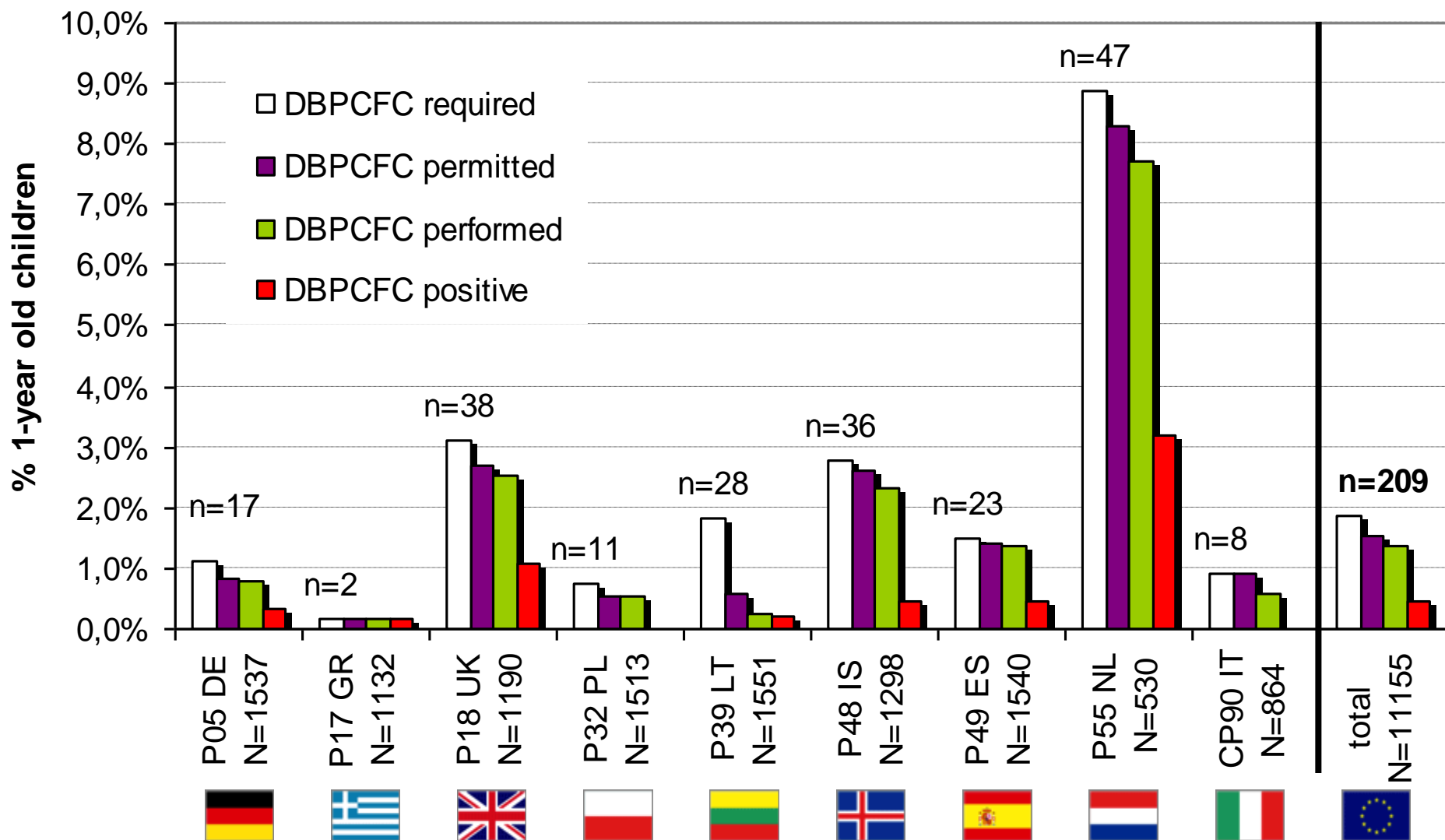
Australia's area = 7,708,168 sq km
 Europe's area as shown = 3,483,066 sq km

LSAC

Allergic Condition		Prevalence %	Adj OR
Peanut	North	0.3	1
	Central	1.2	3.98 (0.89—17)
	South	1.7	6.1 (1.42-24.3)
Egg			No diff
Eczema	North	7.7	1
	Central	11.7	1.6 (1.14-2.26)
	South	13.1	1.9 (1.36-2.67)
Asthma			No diff

(Osborne JACI 2012)

Cow's milk allergy in the first year of life



Take home messages?



It's not just what you eat,

Take home messages?



it's who your parents are,

where you live,

what medical conditions you have
and

How and when you eat what you eat

Thanks to

- Eileen Duggan, PhD student, UCC
Ivan Perry, Tony Fitzgerald UCC
- BASELINE Team, UCC
- Allergy Team, CUH
- Alan Irvine, TCD
- Jane Lucas, Southampton, UK
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