Allergic Disease in the 21st Century – a modern epidemic

Dr Robert Boyle

MBChB, MRCP

Clinical Lecturer in Paediatric Allergy

Imperial College/St. Mary's Hospital

Epidemiology

The science of occurrence of diseases in human populations

Derived from the Greek *epi* among

demos the people

Aim

- To introduce the allergy epidemic, and discuss the epidemiology of allergic diseases

Learning Objectives

- Knowledge: To understand the patterns of allergic disease prevalence
- Skills: To formulate a hypothesis to explain the recent epidemic of allergic disease
- Attitudes: To value the importance of research into the causes of allergic disease

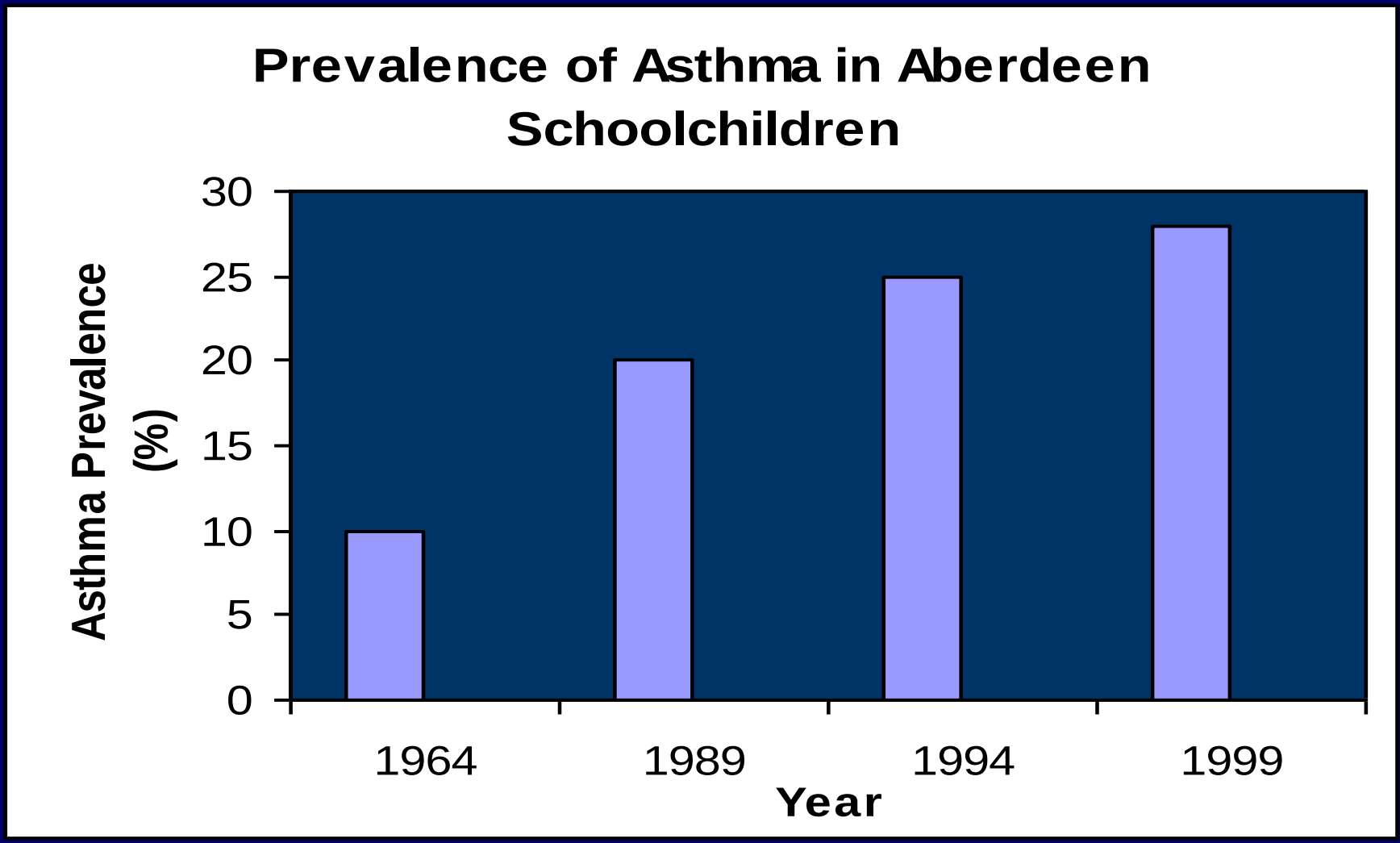
Overview – 3 core questions

- What is the allergy epidemic?
- What are the possible causes?
- How might we intervene to halt the epidemic?

Overview – 3 core questions

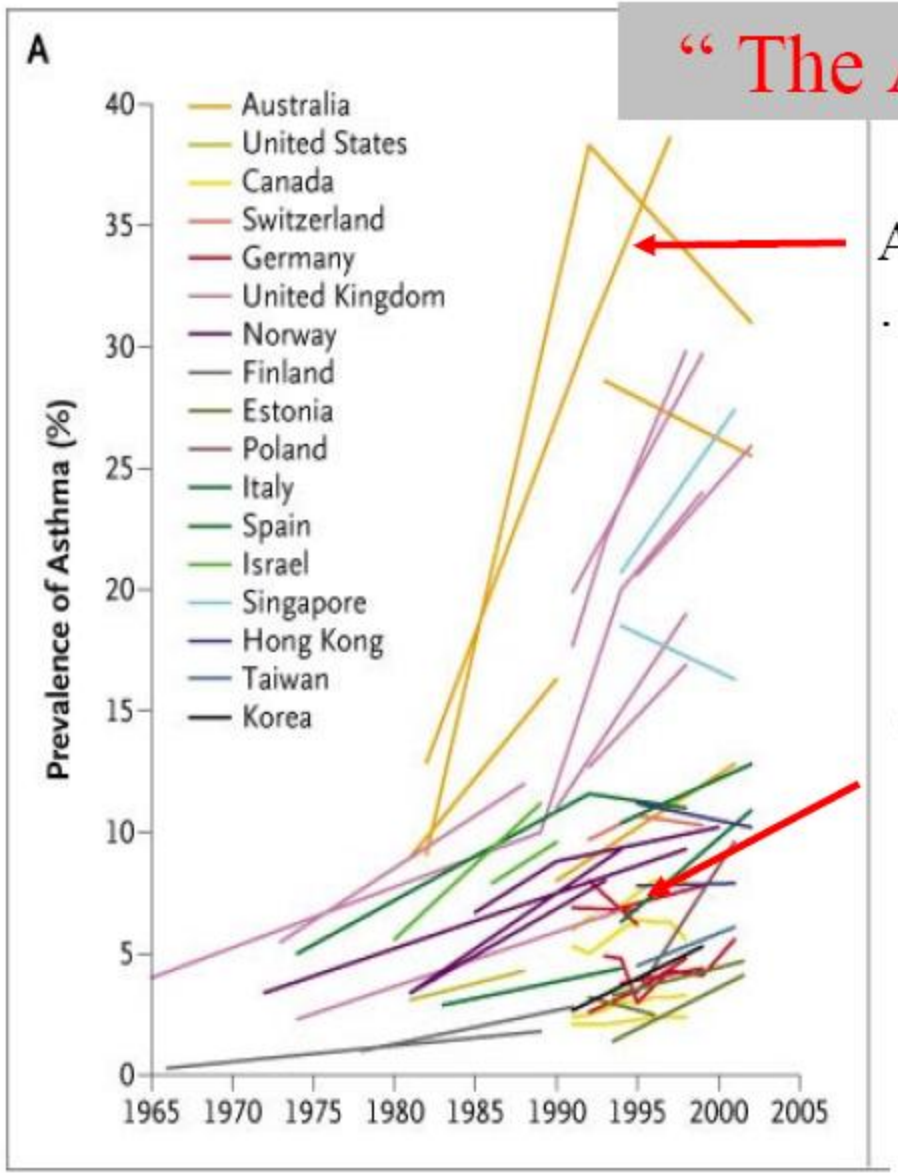
- What is the allergy epidemic?
- What are the possible causes?
- How might we intervene to halt the epidemic?

The Allergy Epidemic



BMJ 2004;329(7464):489-90

" The Asthma Epidemic"

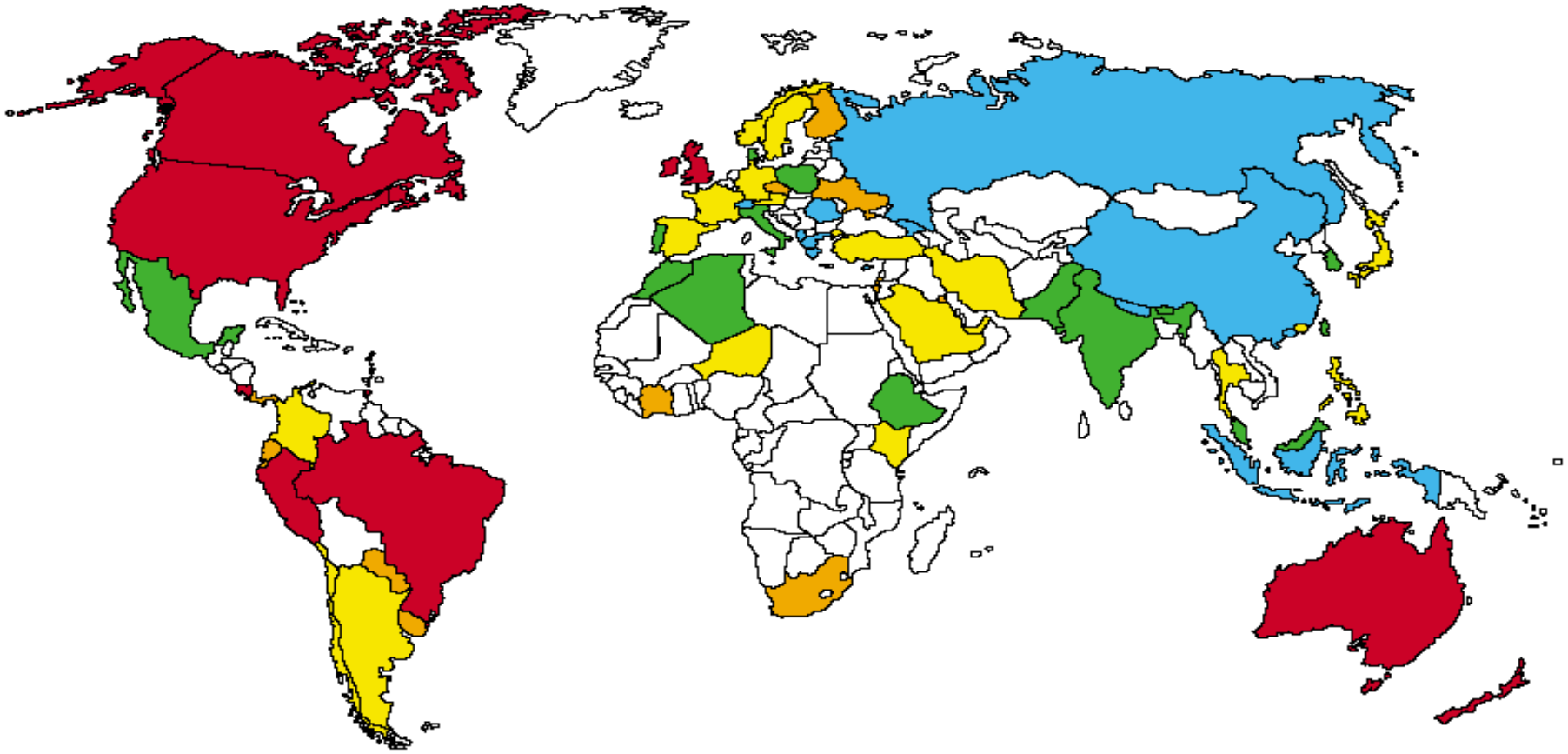


Australia, NZ, UK.
….>20% (and Harlem NYC)

Germany, Sweden, Spain…
…<10%

Prevalence of Asthma: from Eder, Ege and Von Mutius: *..N E J Med 355;21 2006*

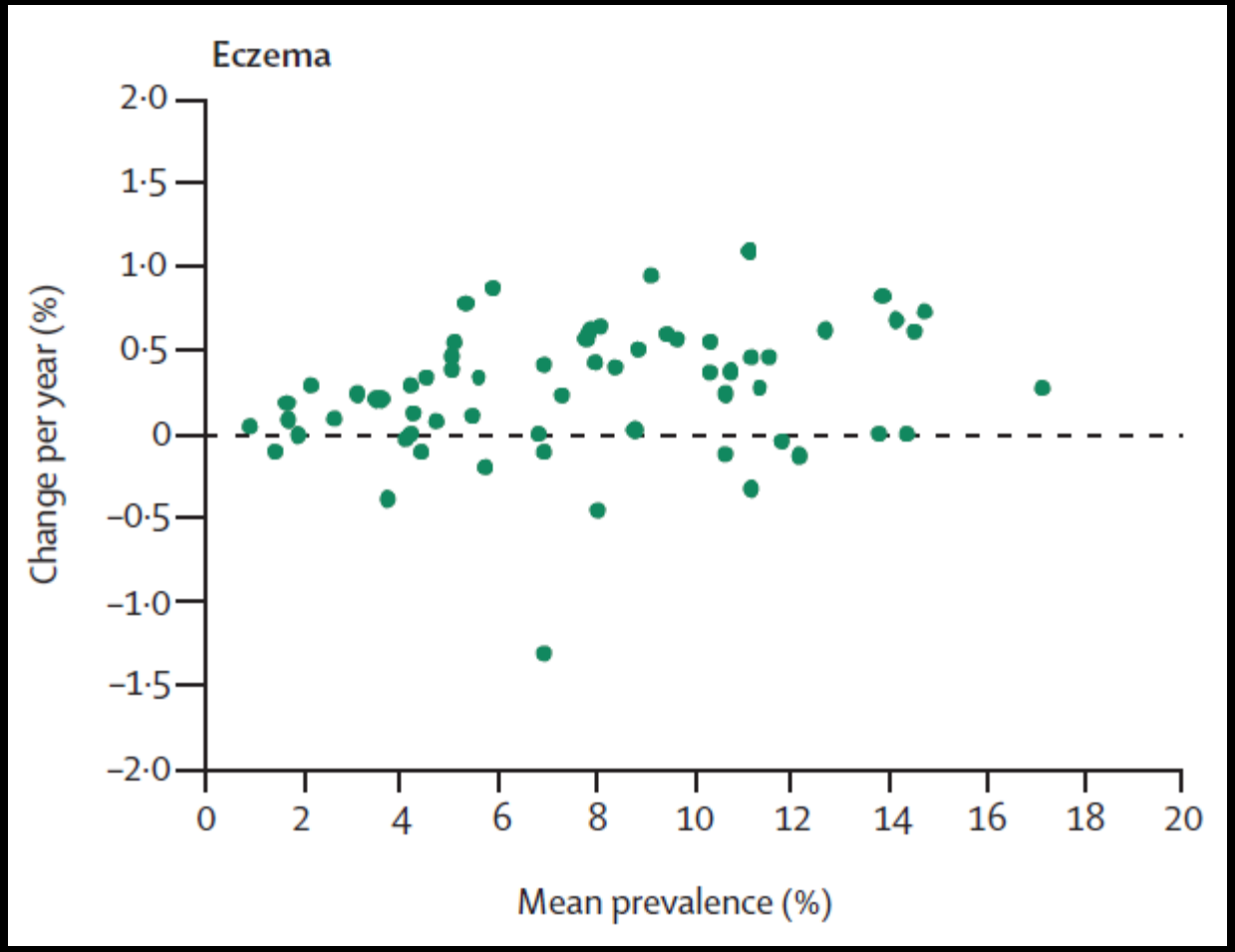
World Map of the Prevalence of Clinical Asthma



Proportion of population (%)*

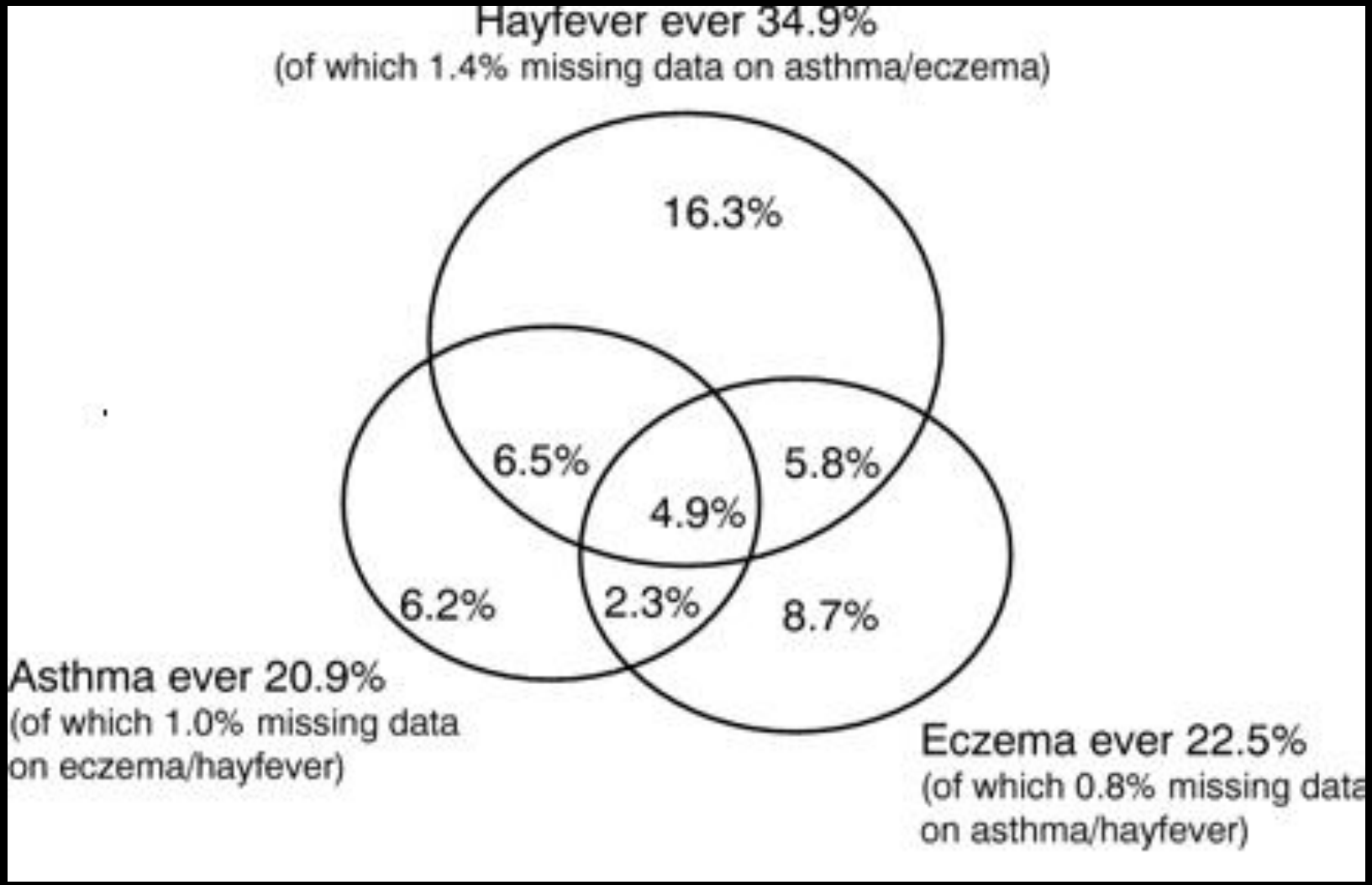
- ≥10.1
- 7.6-10.0
- 5.1-7.5
- 2.5-5.0
- 0-2.5
- No standardised data available

Eczema in 6-7 year old children – ISAAC III

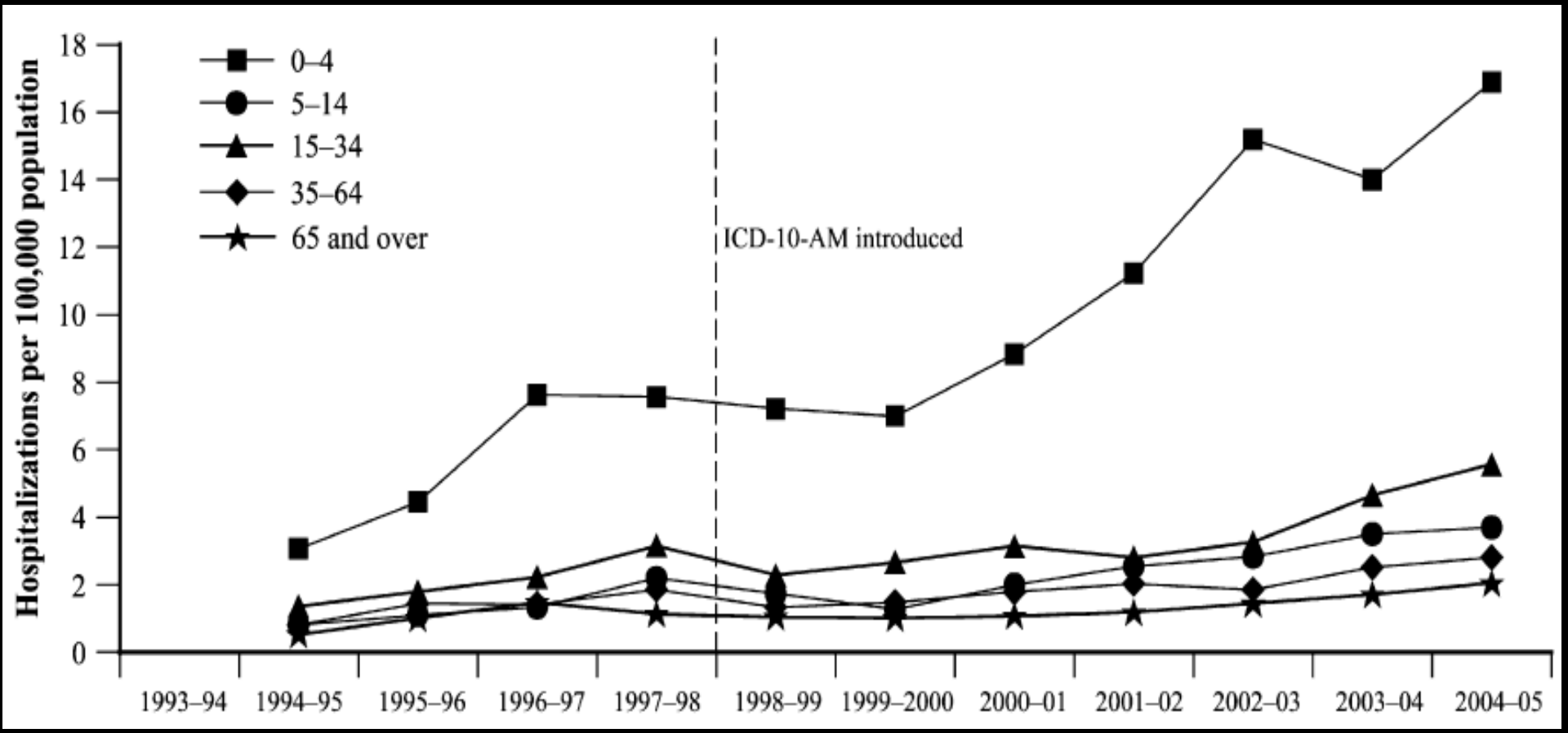


Lancet 2006;368:733-43

Overlap of Atopic diseases



The Allergy Epidemic – Anaphylaxis



J Allergy Clin Immunol 2007;120:878-84

Prevalence of food allergy in 1 year old infants: 2007-10

	Positive SPT	Positive oral food challenge
Raw egg	11.7	8.9
Peanut	6.4	3.0
Sesame	1.6	0.8

	Parent reported reaction	Immediate type reaction
Cow's milk	6.7	2.7

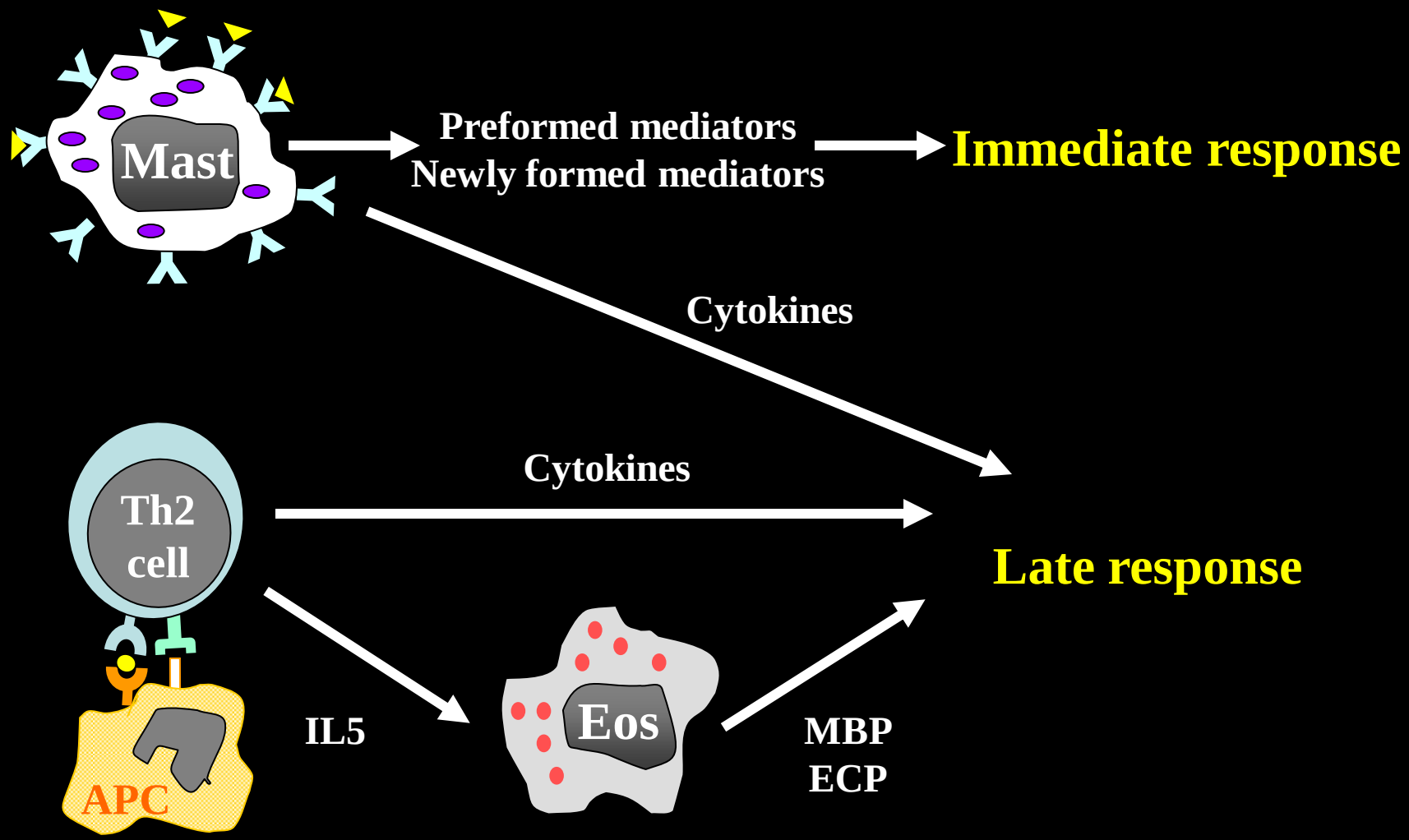
J Allergy Clin Immunol 2011;127:668-76

National Health and Nutritional Examination Surveys II and III

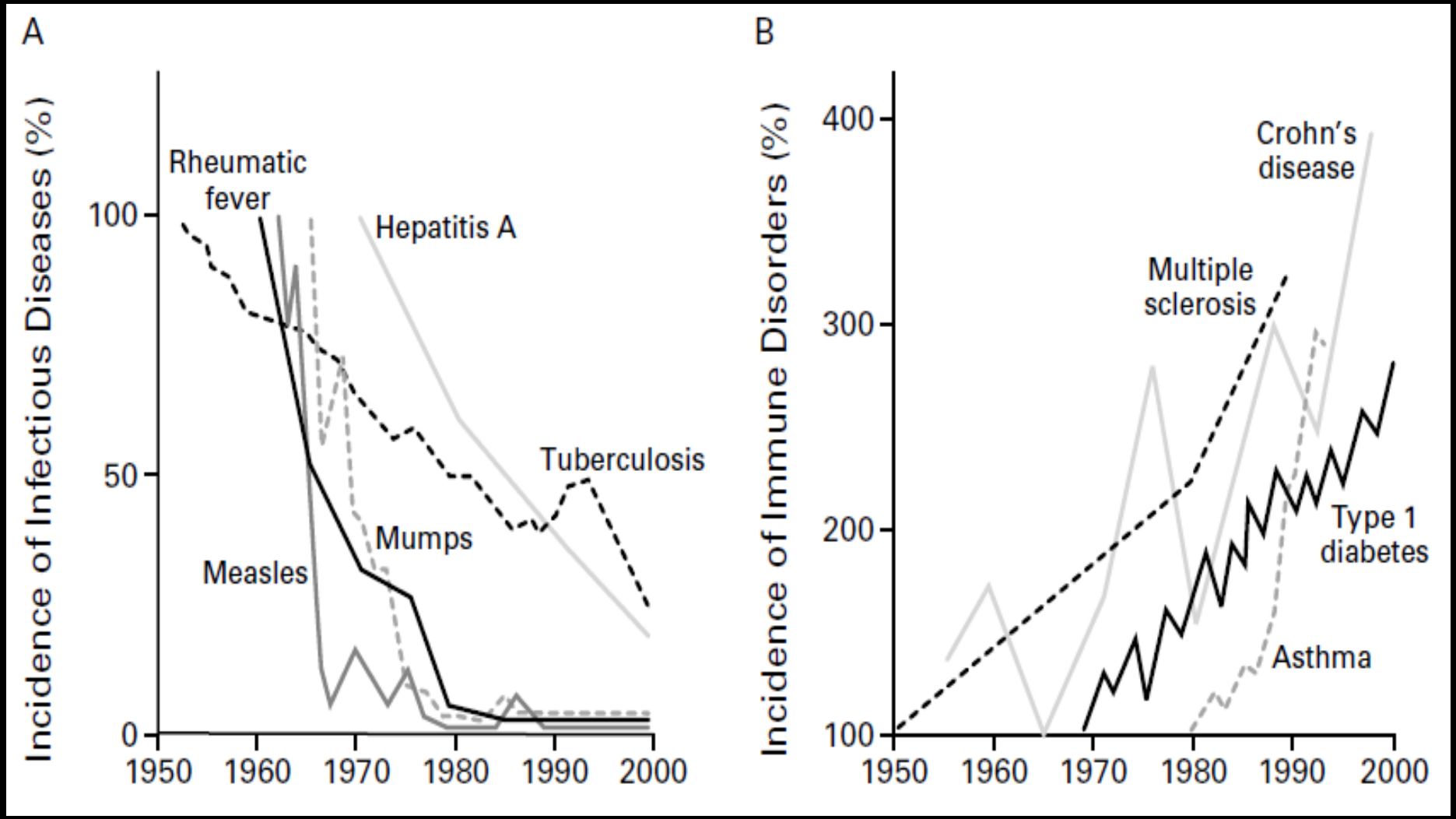
Allergen	NHANES II 1976-1980	NHANES III 1988-1994
Ragweed	12.5	26.2
Ryegrass	5.8	26.9
Oak	5.2	13.2
Bermuda grass	4.5	18.1
Cat	3.1	17.0
A.alternata	4.5	12.9
At least 1 allergen	21.8	41.9

J Allergy Clin Immunol 2005;116:377-83

Early and Late Phase IgE responses



The Immunopathology Epidemic



Overview – 3 core questions

- What is the allergy epidemic?
- What are the possible causes?
- How might allergy be prevented?

Genetic Predisposition

- Twin studies
- Asthma risk – estimated 73% inherited[1]
- Concordance for eczema risk:
  - 0.23 dizygotic twins
  - 0.72 monozygotic twins[2]

[1]Eur Resp J 1999;13:8-14 [2]J Am Acad Dermatol 1993;28:719-23

Defective Skin Barrier

Common loss-of-function variants of the epidermal barrier protein filaggrin are a major predisposing factor for atopic dermatitis

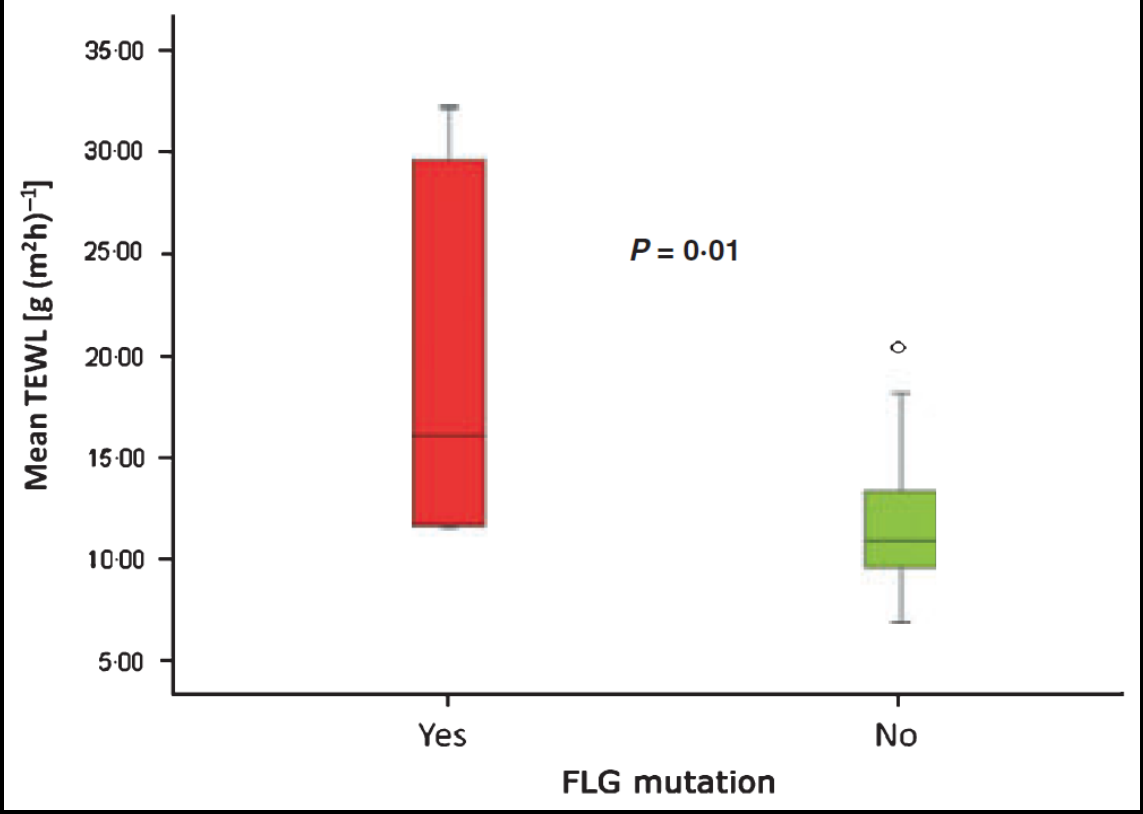
Nat Genet 2006;38:441-6

Defective Skin Barrier

- Filaggrin gene defects present in ~ 10% of European population
- Associated with:
  OR of eczema 1.99
  OR of allergic sensitisation 1.91
- Increased risk for allergic rhinitis (in those with or without eczema)
- Increased risk for asthma (only in those with eczema)

BMJ 2009;339:b2433; J Allergy Clin Immunol 2009;123:911-916

Skin barrier function



Br J Dermatol 2010:163(6):1333-6

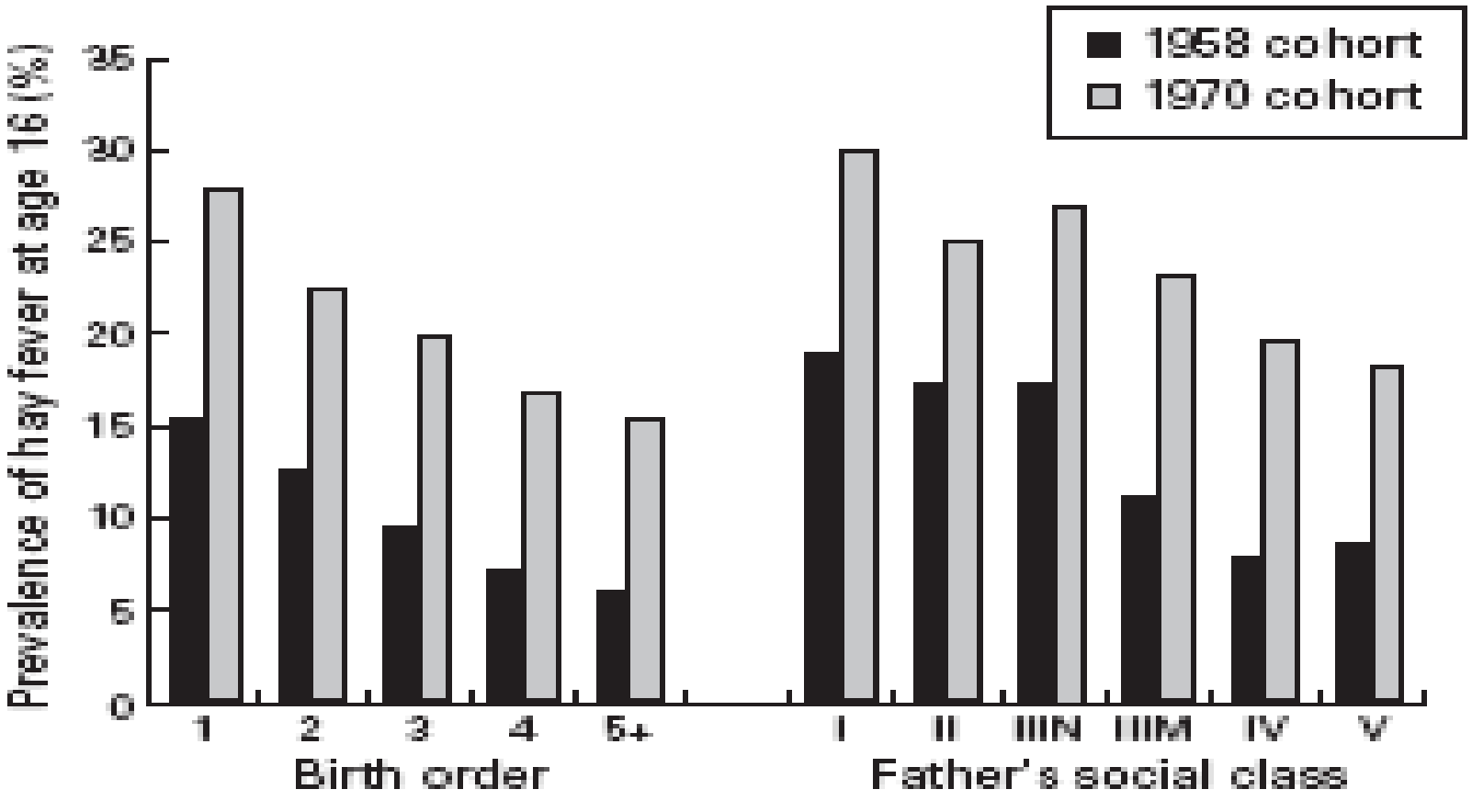


Figure 1 Prevalence of hay fever at the age of 16 in two national British birth cohorts born in 1958 and 1970, by birth order and father's social class.

BMJ 1989;299:1259-60

	Urban *n* (%)	Rural *n* (%)
Doctors' diagnosed current allergy		
Allergic rhinitis	78 (39)	22 (11)
Conjunctivitis	24 (12)	0
Asthma	33 (16)	4 (2)
Food allergy	5 (2.5)	0
Atopic eczema	5 (2.5)	1 (0.5)
Allergic sensitization (SPT)		
HDM	79 (39)	31 (15)
Cat	42 (21)	7 (3.5)
Dog	37 (18.5)	3 (1.5)
Pig	16 (7.96%)	0
Rabbit	20 (9.95%)	2 (0.99%)
Birch	42 (21)	5 (2.5)
Grasses	63 (31)	11 (5.5)
Plantain	33 (16.4)	3 (1.5)
Mugwort	51 (25)	7 (3)
Hamster	20 (10)	1 (0.5)
Alternaria	31 (15)	3 (1.5)
At least one positive SPT	128 (63.7)	46 (22.7)

Allergy 2007;62:1044-50

	Urban (no of cases 201) *n* (%)	Rural (no of cases 203) *n* (%
Mothers' history		
Number of pregnancies		
Mean (range)	1.73(0–7)	2.36(1–12)
Premature labor (miscarriage)	40 (20)	21 (10)
Treatment with progesterone	27 (13)	0
Treatment with antibiotics	10 (5)	0
Contact with animals during pregnancy		
Cat or dog	63 (31)	190 (94)
Livestock	17(8)	175(86)
Caesarian labor	41 (20)	10 (5)
Children's history		
Breast feeding for at least 3 month	28 (14)	54 (27)
Daily contact with livestock	30 (15)	177 (87)
Daily contact with dog/cat	115 (57)	197 (97)
Frequent URT infections	90 (45)	8 (4)
Kindergarten attendance	156 (78)	55 (27)
History of bronchitis	89 (44)	45 (22)
Frequent course of antibiotic therapy	31 (15)	12 (6)
Tonsillectomy/adenoidectomy	31 (15)	8 (4)
Food consumption		
Home-made food	49 (24)	168 (83)
Nonpasteurized milk	46 (23)	116 (57)
Nonboiled water	64 (32)	132 (65)
Sauer milk	50 (25)	146 (72)
Living conditions		
Individual house	20 (10)	7 (3)
Apartment house	173 (86)	0
Farm	0	196 (97)
Central heating	109 (54)	0

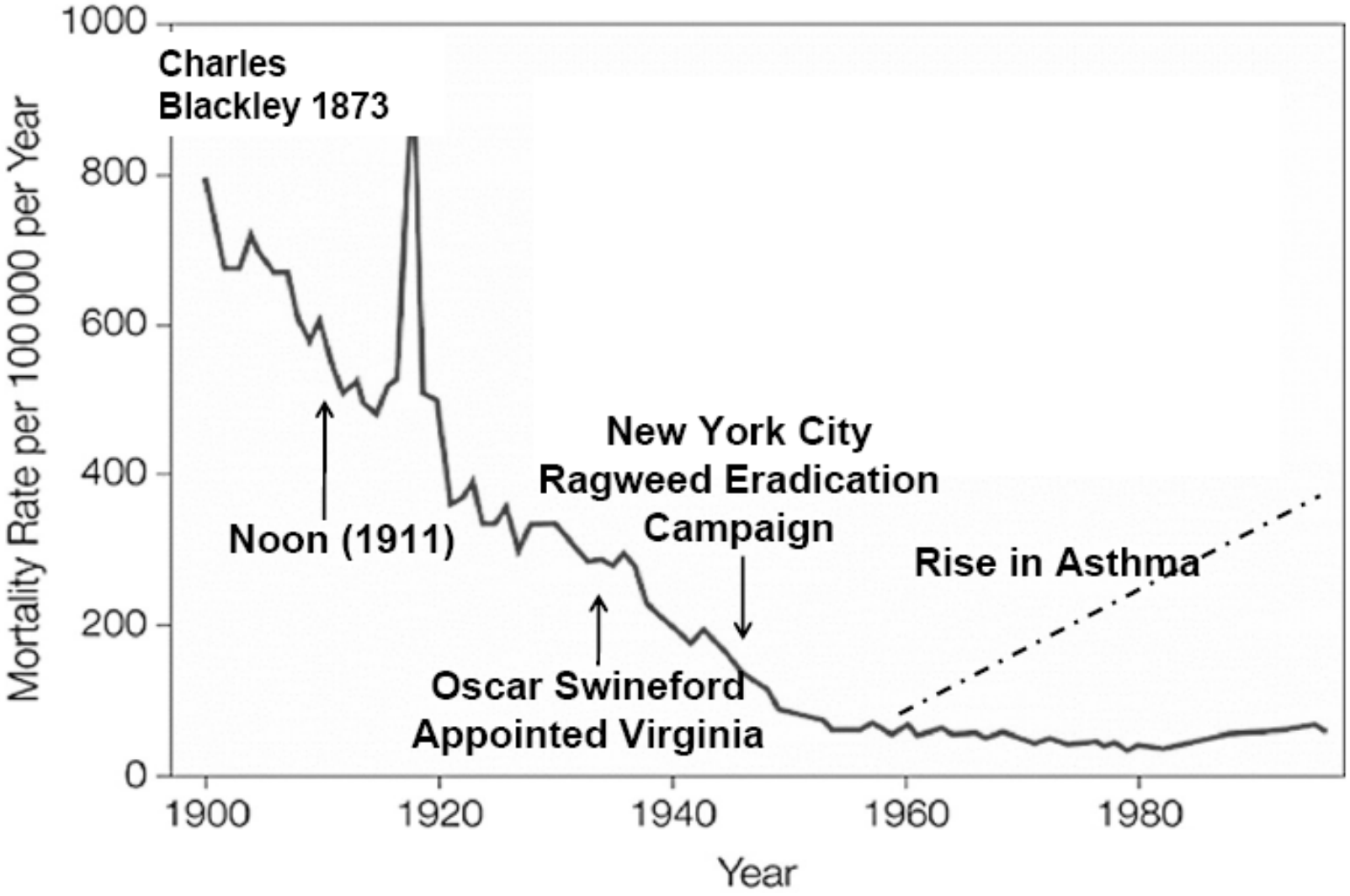
Allergy 2007;62:1044-50

Urban Developed vs Urban Underdeveloped

	West Germany	East Germany
Asthma/Hayfever	5.9	3.9
Atopy	36.7	18.2
BHR	8.3	5.5
Bronchitis	3.7	16.7

Am J Resp Crit Care Med 1994;149:358-64

Infectious Disease Mortality and the rise of Allergic disease in Europe and the States 1900-1996

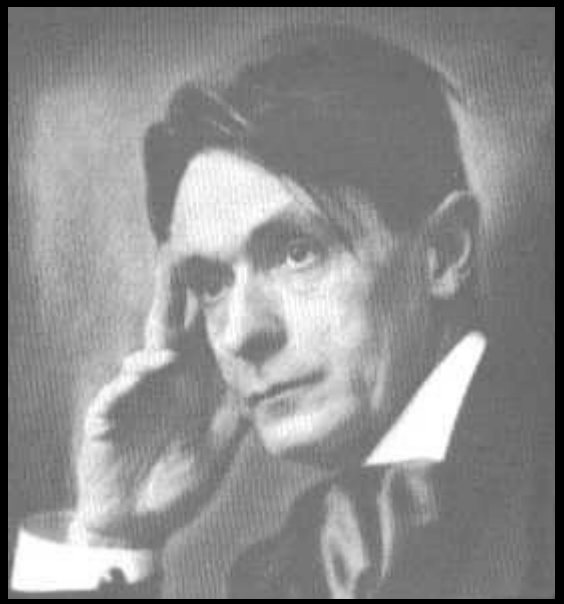


Armstrong, G. L. et al. JAMA 1999;281:61-66.

The anthroposophic life-style

PARSIFAL study
Prevention of Allergy - Risk factors for Sensitisation
in children related to Farming and Anthroposophic Life style

"Allergic Disease and Sensitization in Steiner School Children"
Journal of Allergy & Clinical Immunology
January 2006

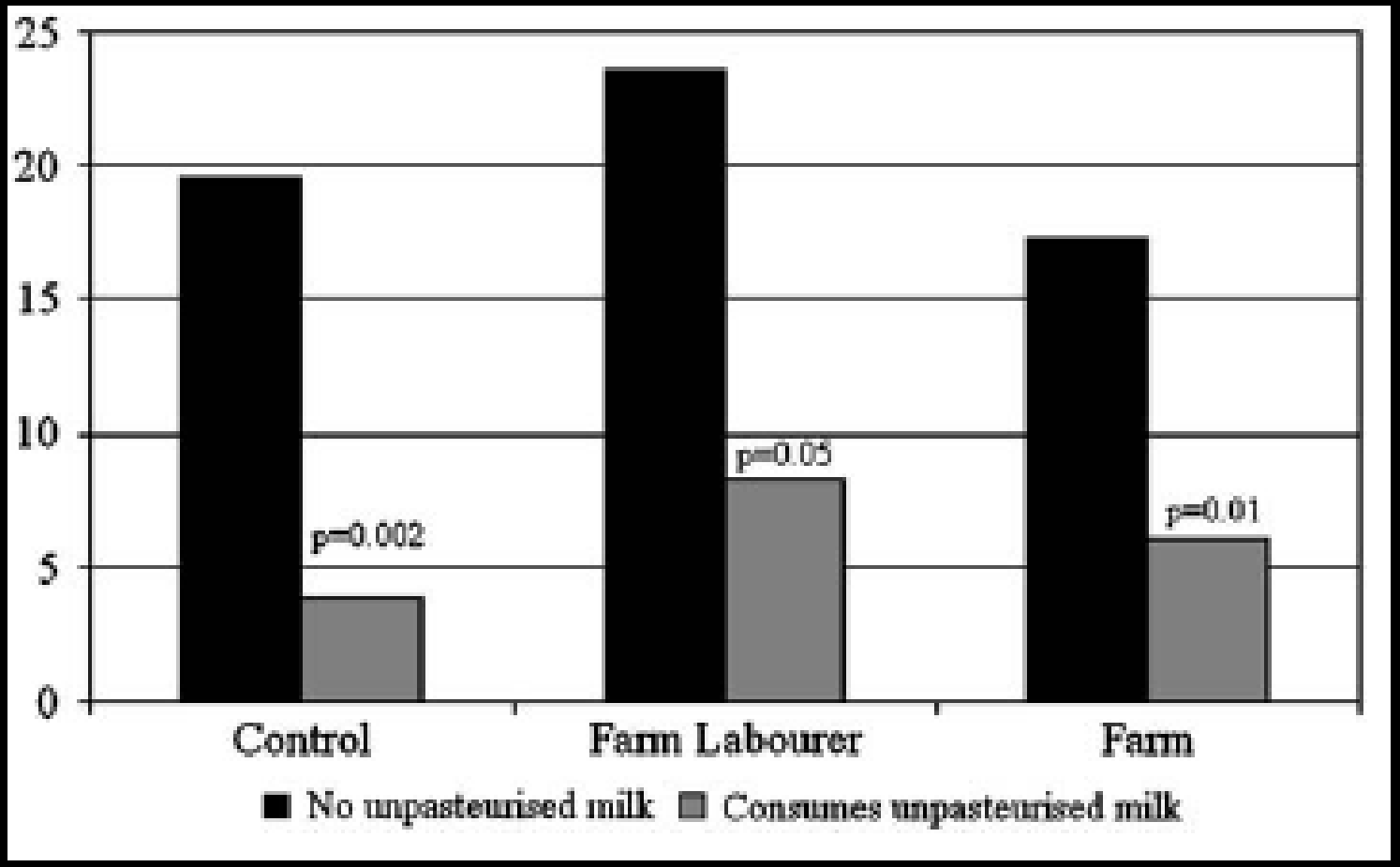


Rudolf Steiner

- 6,600 from five European countries ages 5 to 13 yr
- Restrictive use of antibiotics and fever antipyretics
- No combined measles, mumps, rubella vaccination.
- Organic or biodynamic food and spontaneously fermented vegetables
- Significant reduced risks for rhinoconjunctivitis, atopic eczema, and atopic sensitization

Farming environments confer protection against the development of allergy

Effect of Unpasteurised Milk



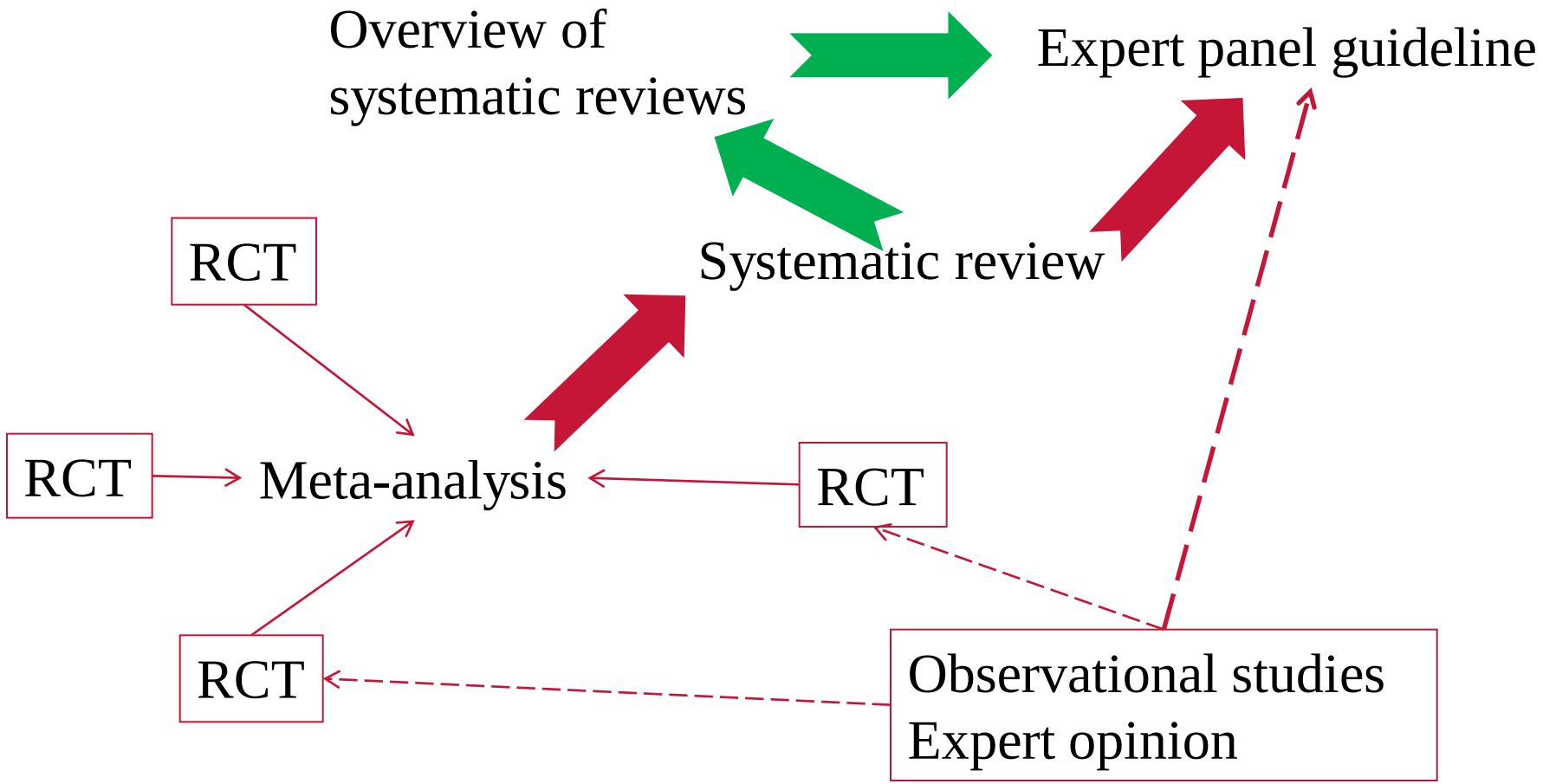
J Allergy Clin Immunol 2006;117:1374-81

Overview – 3 core questions

- What is the allergy epidemic?
- What are the possible causes?
- How might we intervene to halt the epidemic?

Imperial College London

Hierarchy of evidence...



BMJ 2001;323:334-6

Imperial College London

Primary prevention of eczema - overview of systematic reviews

All systematic reviews of interventions for preventing eczema, up to August 2010

7 reviews identified – 39 RCTs; 11,897 participants

Interventions with relevant systematic review(s) were:

- Exclusive breastfeeding
- Hydrolysed protein formula
- Soy formula
- Maternal antigen avoidance
- Omega 3/6 oil supplementation
- Prebiotics
- Probiotics

Evid.-Based Child Health 2011;6:1322-39

Imperial College London

Skin barrier function

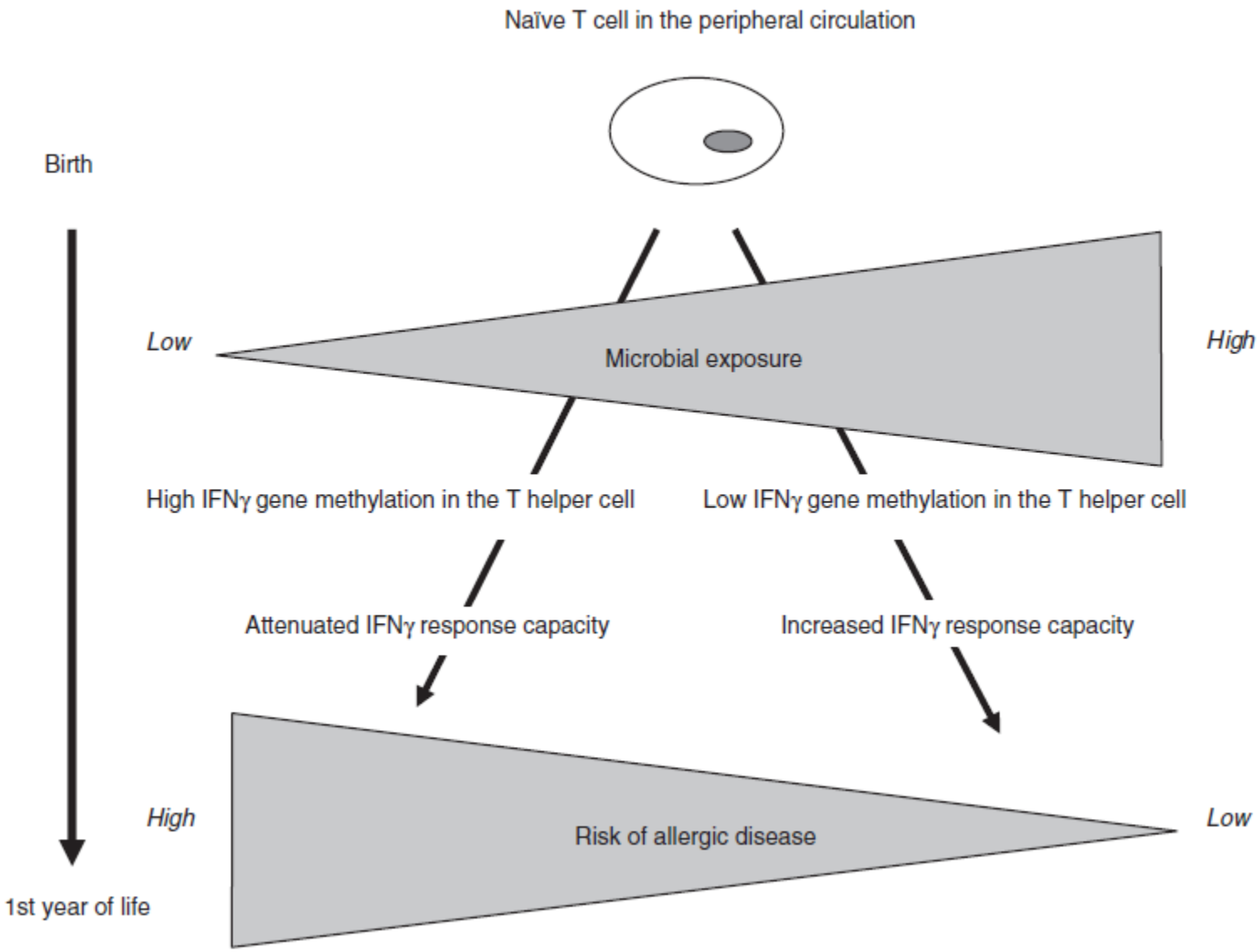
	Eczema	No Eczema	OR	P
[1]Vaseline use	30/49 (61%)	52/63 (84%)	0.33 (0.14, 0.80)	0.02

3 of 20 (15%) infants with high familial risk of eczema developed the disease, when treated from birth with Cetaphil emollient daily[2]

Pilot RCTs of emollient for eczema prevention:
UK - ISRCTN84854178
Japan - UMIN000004544

[1]Trop Doct 1991: 21(3): 104-6.
[2]J Am Acad Dermatol 2010: 63(4): 587-93

Promotion of immune development



Allergy 2009;64:348-53

Interventions (no trials; no participants)	RR (95%CI)	Heterogeneity (%)
Exclusive breastfeeding ≥6 vs 3-6 months (2;3731)	0.75 [0.42, 1.32]	61
Hydrolysed formula vs cow's milk formula (8;1478)	0.87 [0.70, 1.08]	0
eHF vs cow's milk formula (3;912)	0.84 [0.58, 1.23]	19
pHF vs cow's milk formula (7;823)	0.92 [0.72, 1.17]	0
Soy formula vs cow's milk formula (3;744)	1.23 [0.99, 1.53]	0
Maternal antigen avoidance vs standard diet (3;360)	0.95 [0.63, 1.44]	21
Omega-3 vs placebo (2;664)	1.10 [0.78, 1.54]	45
Omega-6 vs placebo (2;259)	0.80 [0.56, 1.16]	0
Prebiotic vs no prebiotic (2;432)	0.79 [0.21, 2.94]	80
Prebiotic vs other prebiotic (1;150)	**0.22 [0.07, 0.76]**	**-**
Probiotic vs no probiotic (6;1492)	0.85 [0.66, 1.08]	46