Food allergy.
What's new.

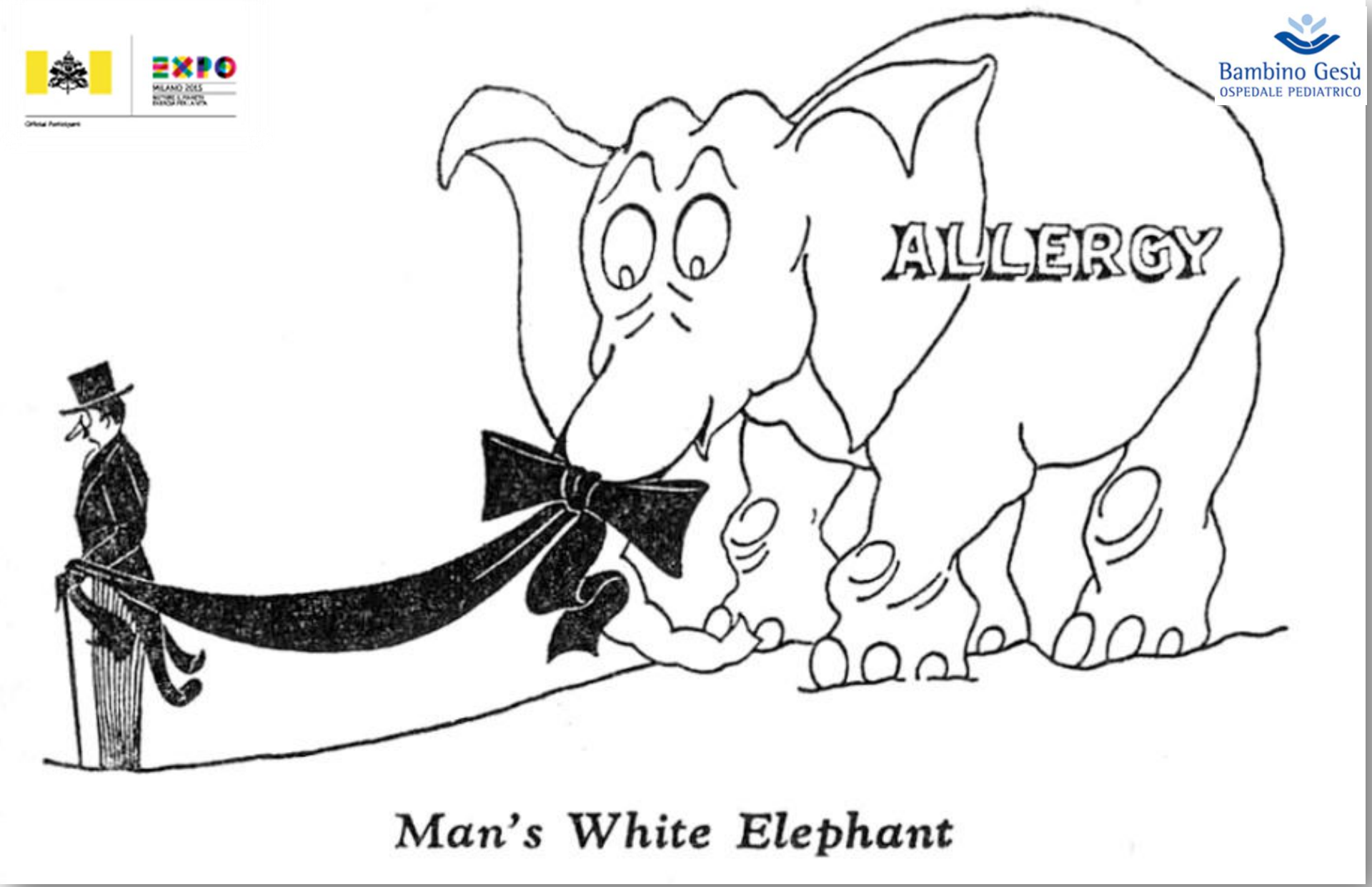
Alessandro Fiocchi

Milano, July 10°, 2015

Editor-in-chief,
the WAO Journal

1. Una malattia in aumento
2. Una malattia legata ai fattori sociali
3. Miti in allergia alimentare
4. Si può prevenire con I probiotici
5. Si può prevenire con l'alimentazione?
6. Conclusioni


CARTE DE LA NAVIGATION
DES ARGONAUTES
DU MONDE PRIMITIF
suivant les Periples
DE TIMÉE, D'HECATÉE,
D'APOLLONIUS ET D'ORPHÉE
Pour servir à l'Histoire de la Grèce.
PLATEAU DE LA TARTARIE
INDE EN DEÇA DU GANGE
ARABIE DESERTE
ARABIE HEUREUSE
LYBIE
EGYPTE
ETHYOPIE
ETHYOPIE INTERIEURE
ABISSINIE
MER ERYTHRÉE, ou MER DES INDES
OCEAN ATLANTIQUE
Tropique du Cancer
Ligne Equinoctiale



Vaughan VT. Primer of allergy. Mosby, St Louis MO, 1939

There has been a rise in asthma & allergy

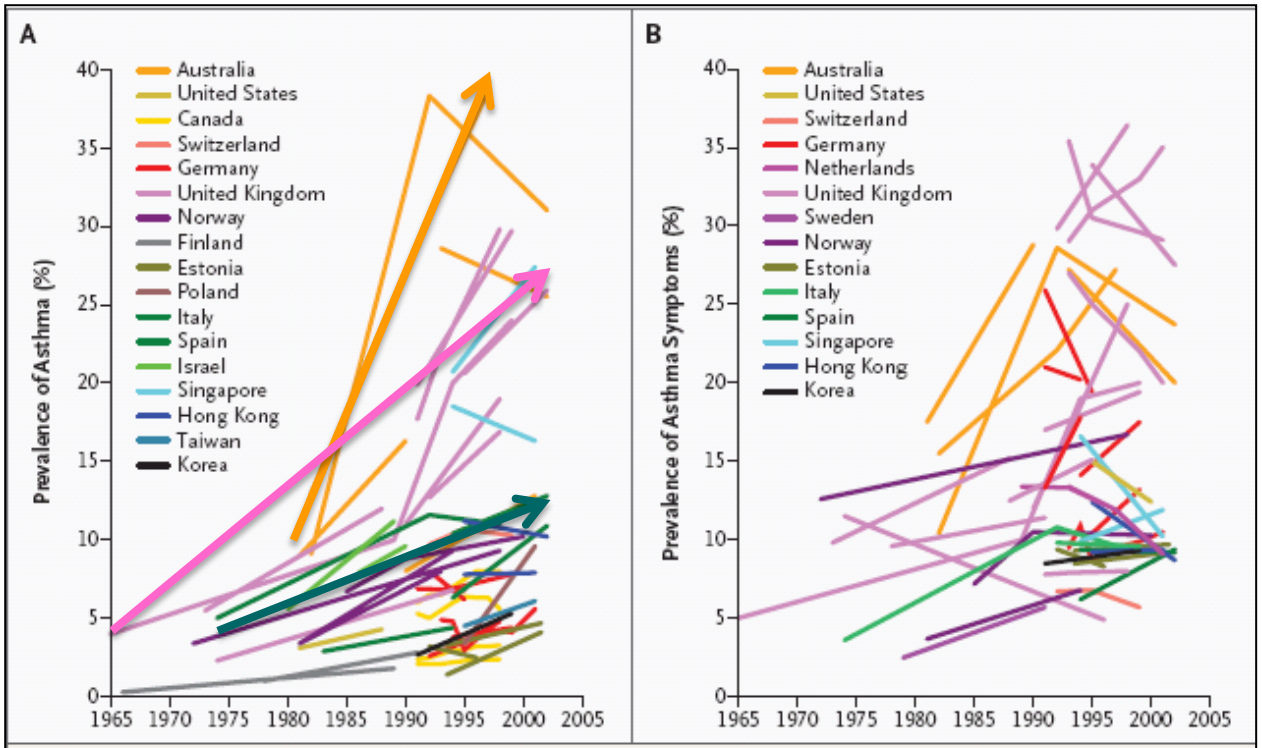
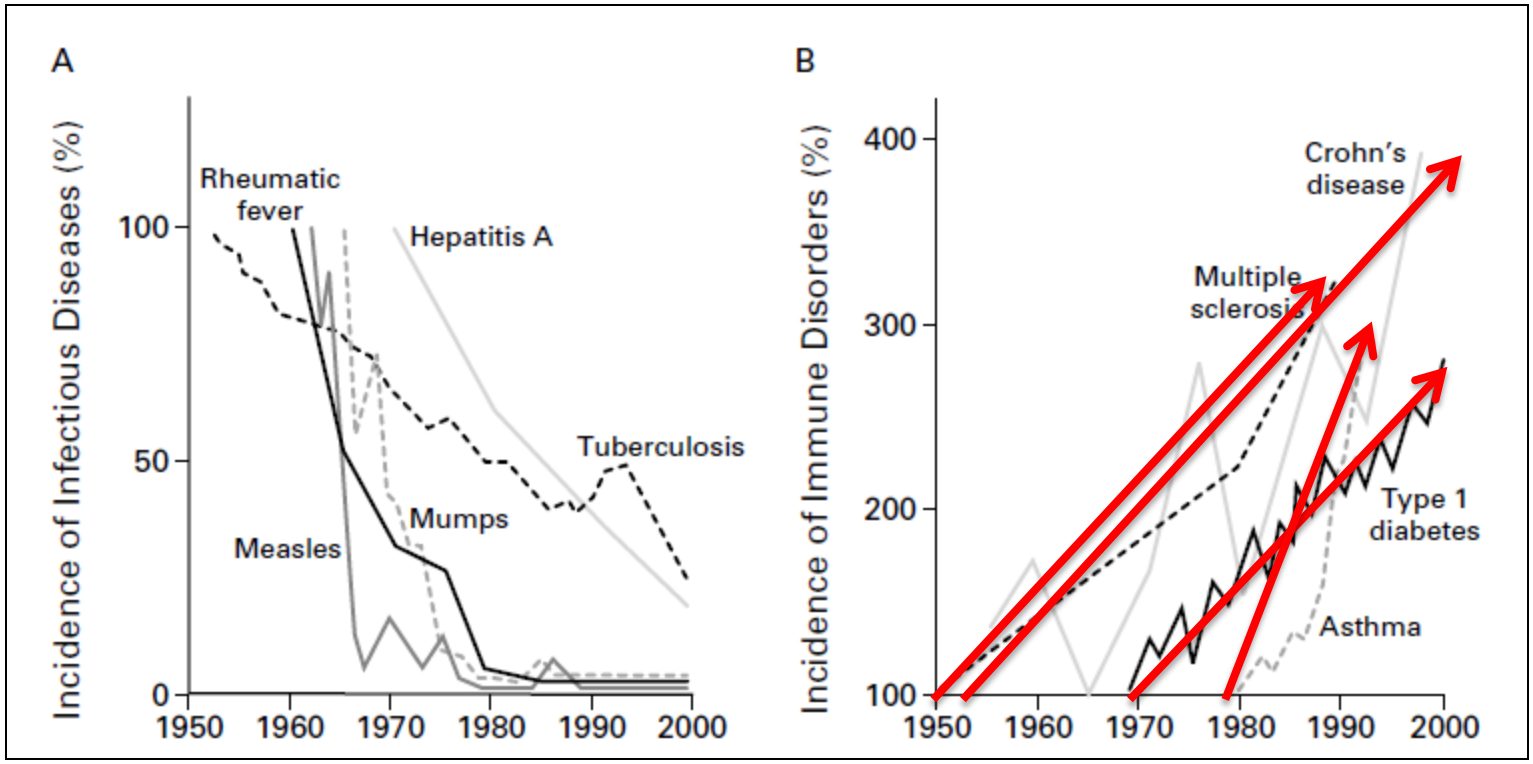


Figure 1. Changes in the Prevalence of Diagnosed Asthma and Asthma Symptoms over Time in Children and Young Adults.

Data in Panel A are from Australia,[2-6] the United States,[7] Canada,[8,9] Switzerland,[10] Germany,[11-15] the United Kingdom,[16-23] Norway,[24-27] Finland,[28,29] Estonia,[30,31] Poland,[32] Italy,[33,34] Spain,[35] Israel,[36,37] Singapore,[38] Hong Kong,[39,40] Taiwan,[41] and Korea.[42] Data in Panel B are from Australia,[2-5] the United States,[43] Switzerland,[10] Germany,[11,13,15,44] the Netherlands,[45] the United Kingdom,[16-23,46-49] Sweden,[50] Norway,[25-27] Estonia,[30,31] Italy,[33,51] Spain,[35] Singapore,[38] Hong Kong,[39,40] and Korea.[42]

Eder W. The asthma epidemic. N Engl J Med. 2006;355:2226-35

There has been a rise in many immune diseases

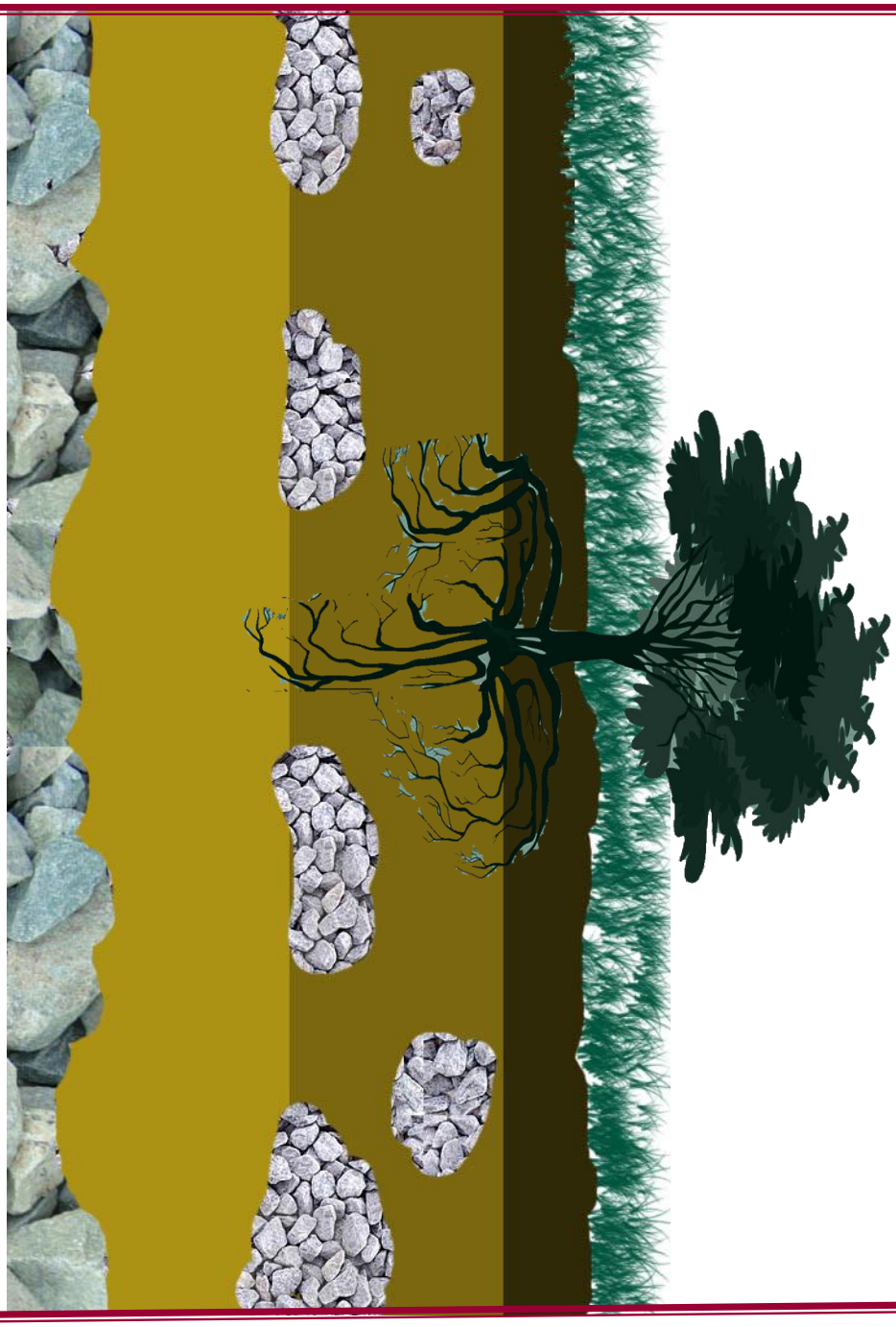


Bach JF. The effect of infections on susceptibility to autoimmune and allergic diseases. N Engl J Med. 2002;347:911-20

Prescott S, Fiocchi A. Avoidance or exposure to foods in prevention and treatment of food allergy? Curr Opin Allergy Clin Immunol 2010,10:258–66

Trends in hospital admission rates of food allergy by age (1990-2003)

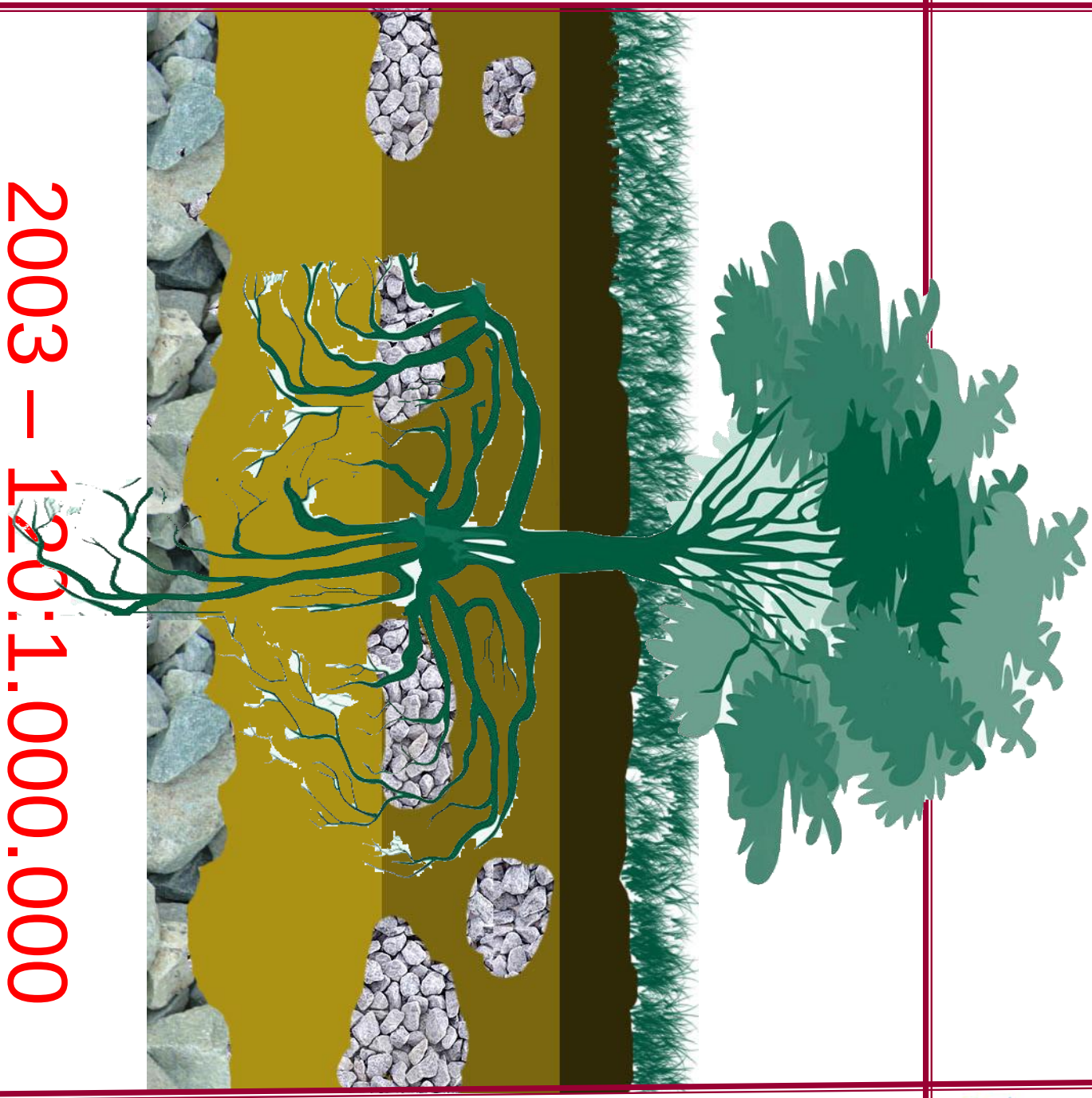
1990 – 20:1.000.000



Gupta R. Time trends in allergic disorders in the UK. Thorax 2007; 62:91-6

Bambino Gesù
OSPEDALE PEDIATRICO

Trends in hospital admission rates of food allergy by age (1990-2003)



Gupta R. Time trends in allergic disorders in the UK. Thorax 2007; 62:91-6

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Over 10% with challenge-proven food allergy!

Reactions on challenge:

- egg: 9%
- peanut: 3%
- other: 2%
-

More than 1 in 10 of all 1 year olds
in Australia have clinical food allergy

Osborne NJ. Prevalence of challenge-proven IgE-mediated food allergy using population-based sampling and predetermined chal-lenge criteria in infants. J Allergy Clin Immunol 2011;127:668-76

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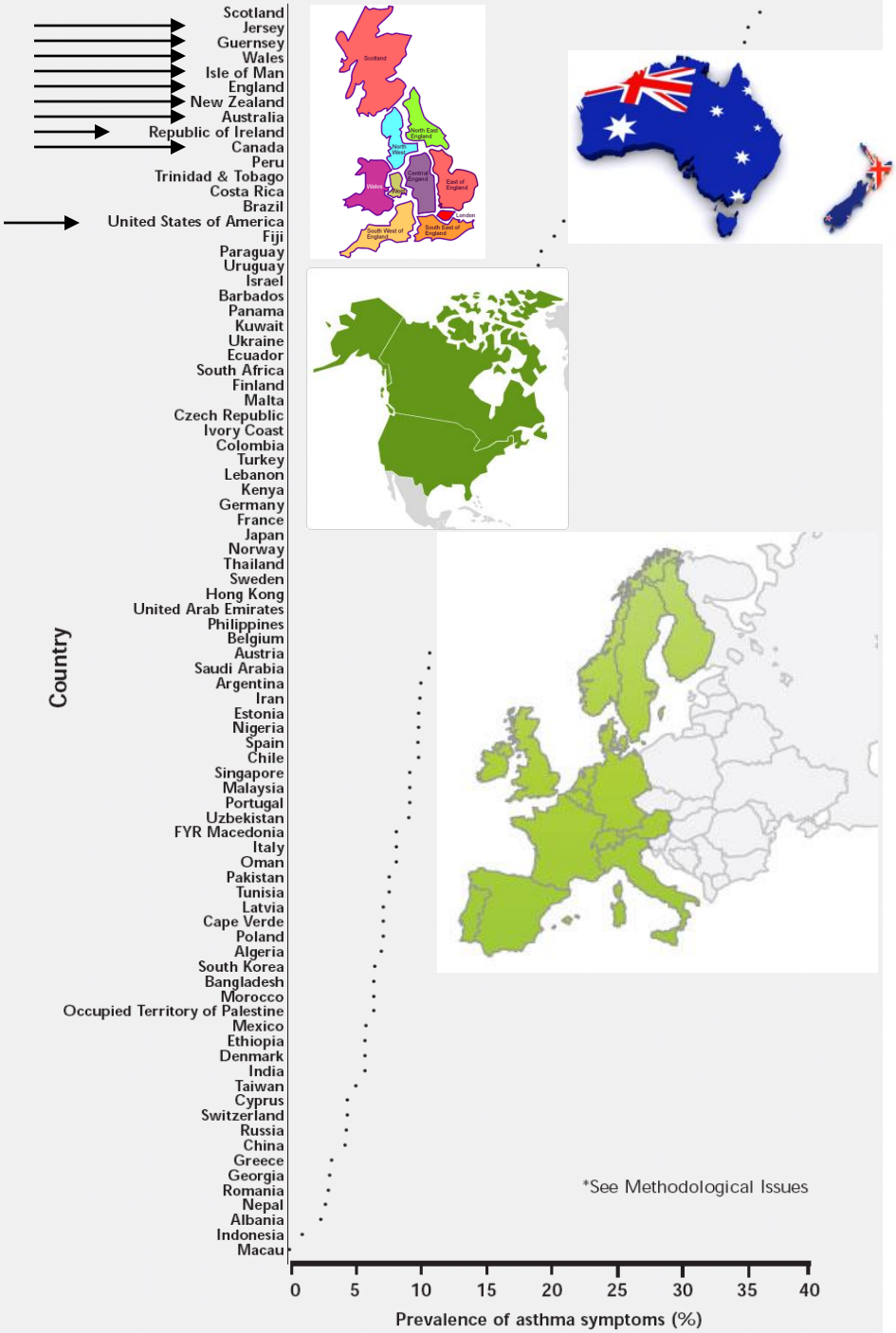
High asthma prevalence



In anglophone countries:

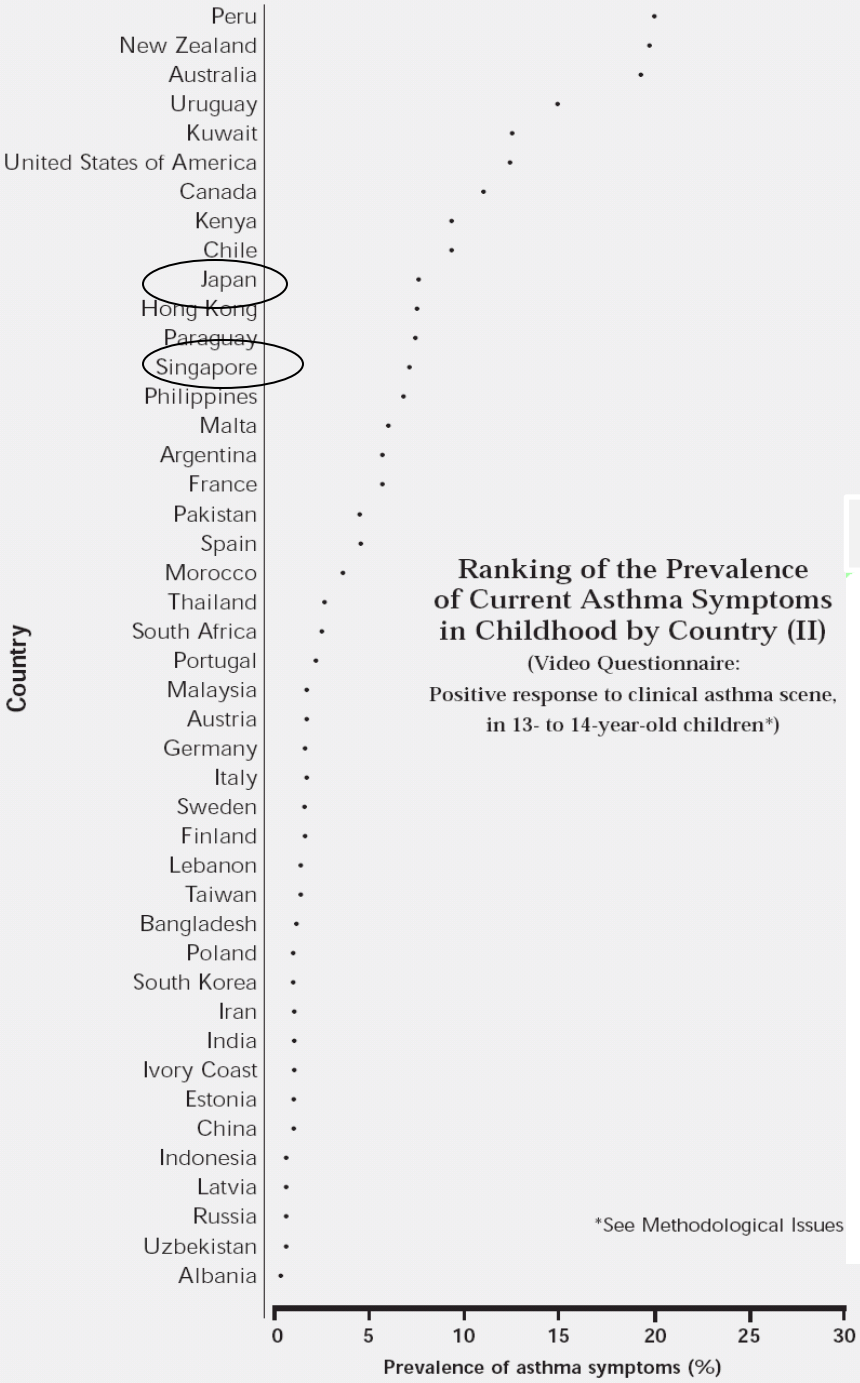
- UK
- NZ
- Australia
- Canada
- USA

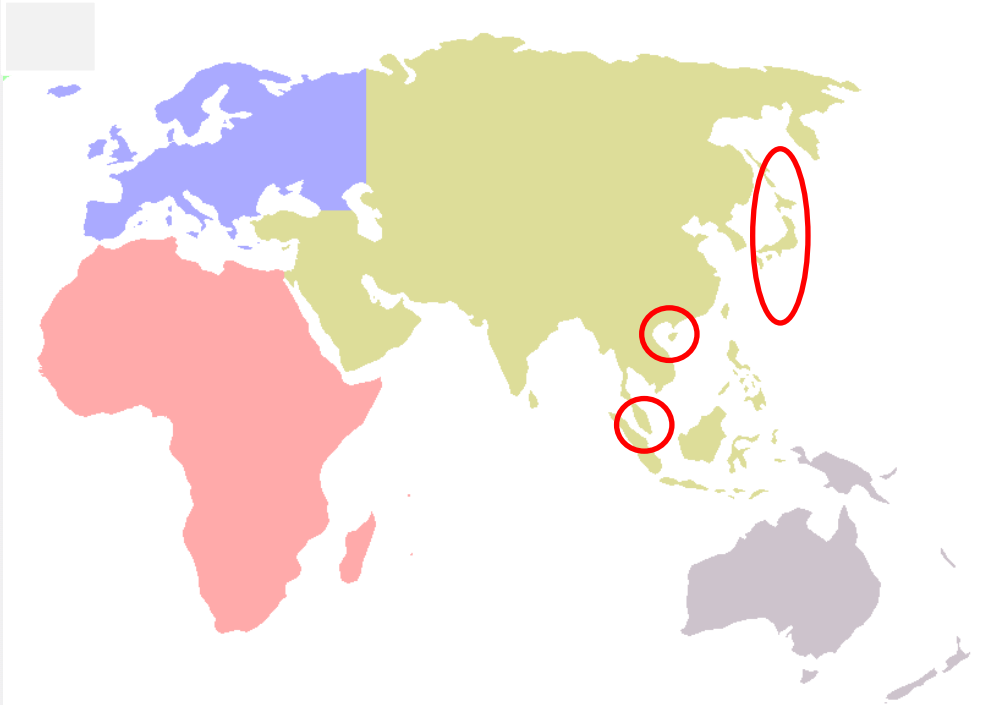
In Western Europe

http://www.worldallergy.org/UserFiles/file/WAO-White-Book-on-Allergy_web.pdf

Lower prevalence

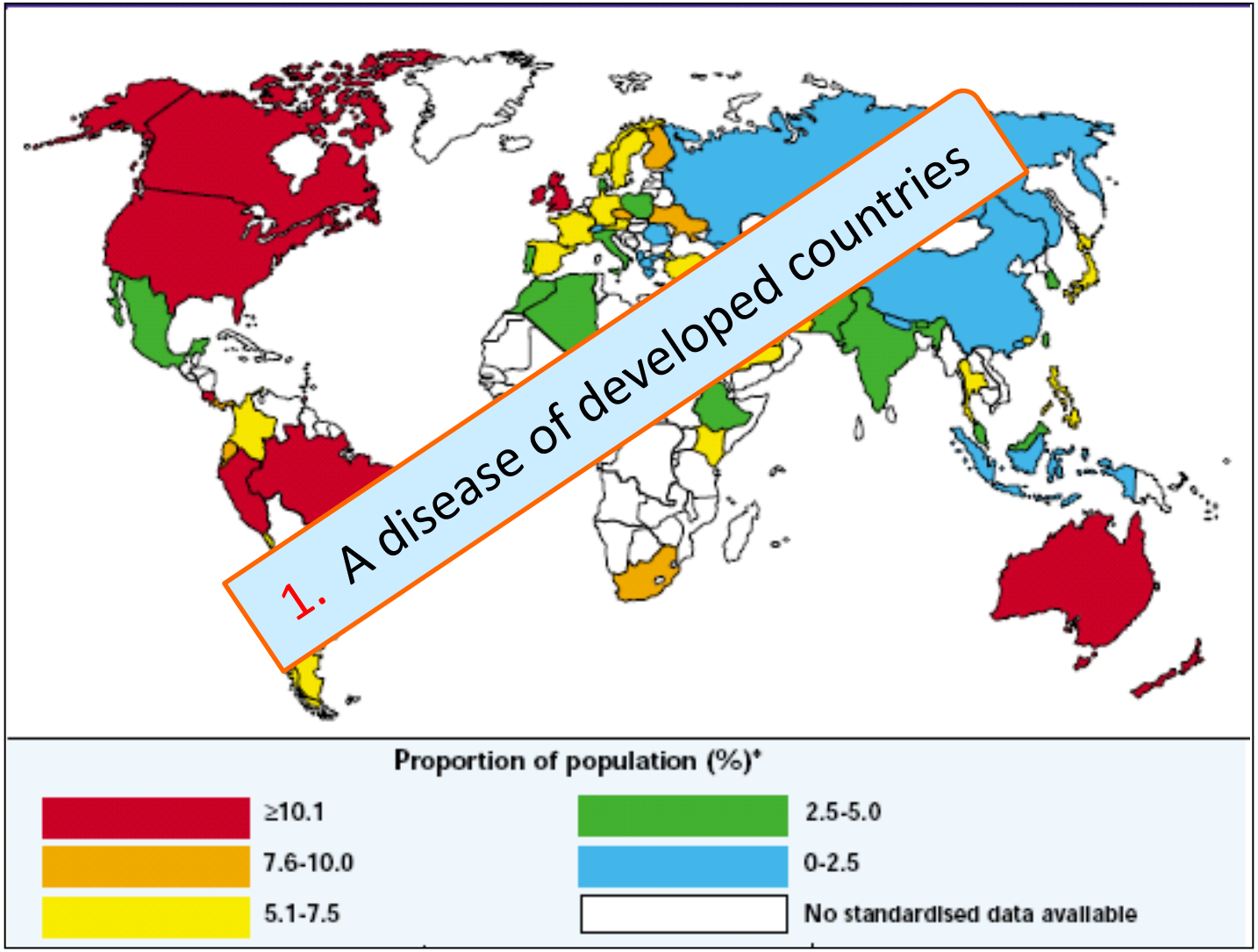
- In Asia
- In Africa





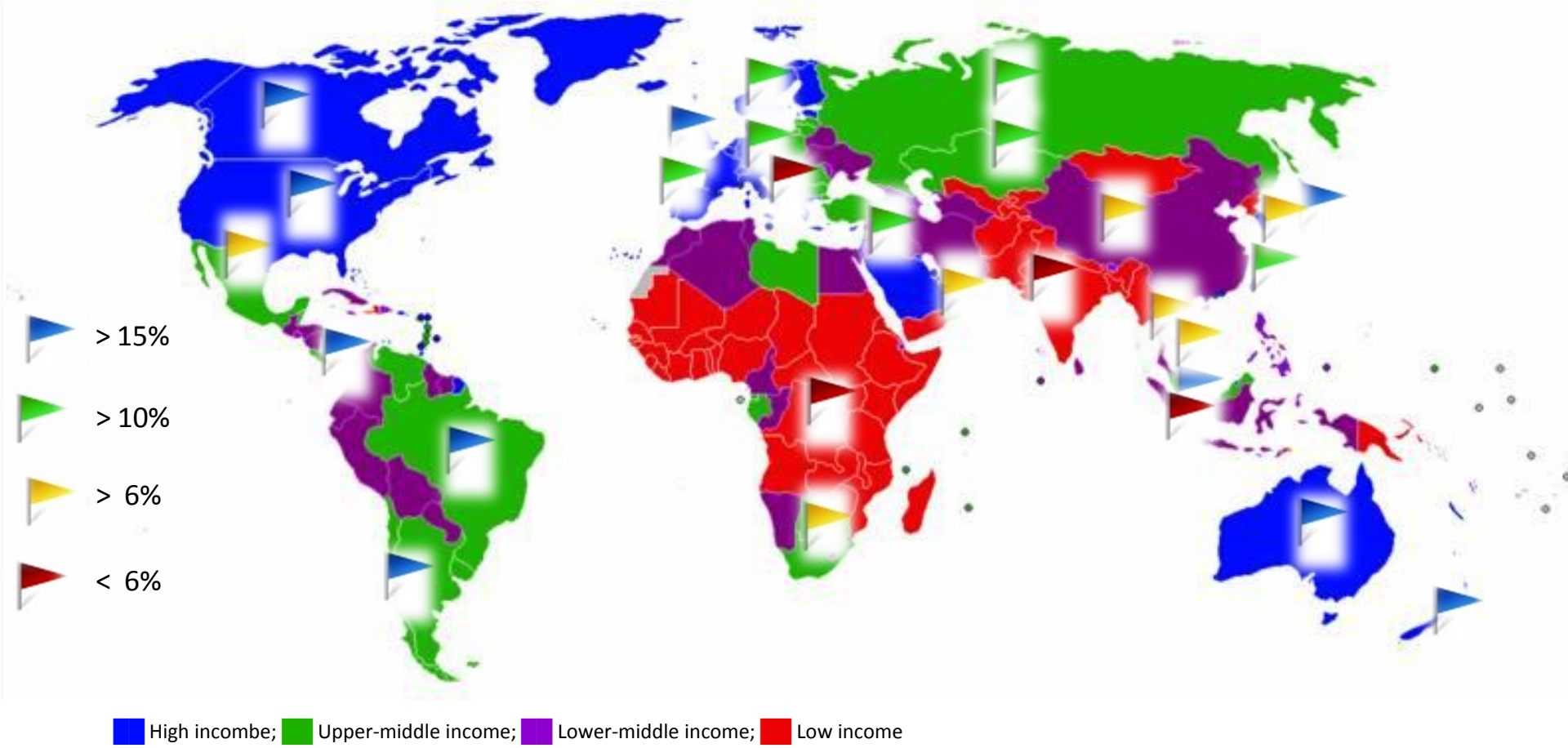
http://www.worldallergy.org/UserFiles/file/WAO-White-Book-on-Allergy_web.pdf

The world asthma map



Global Burden of Asthma, GINA 2004

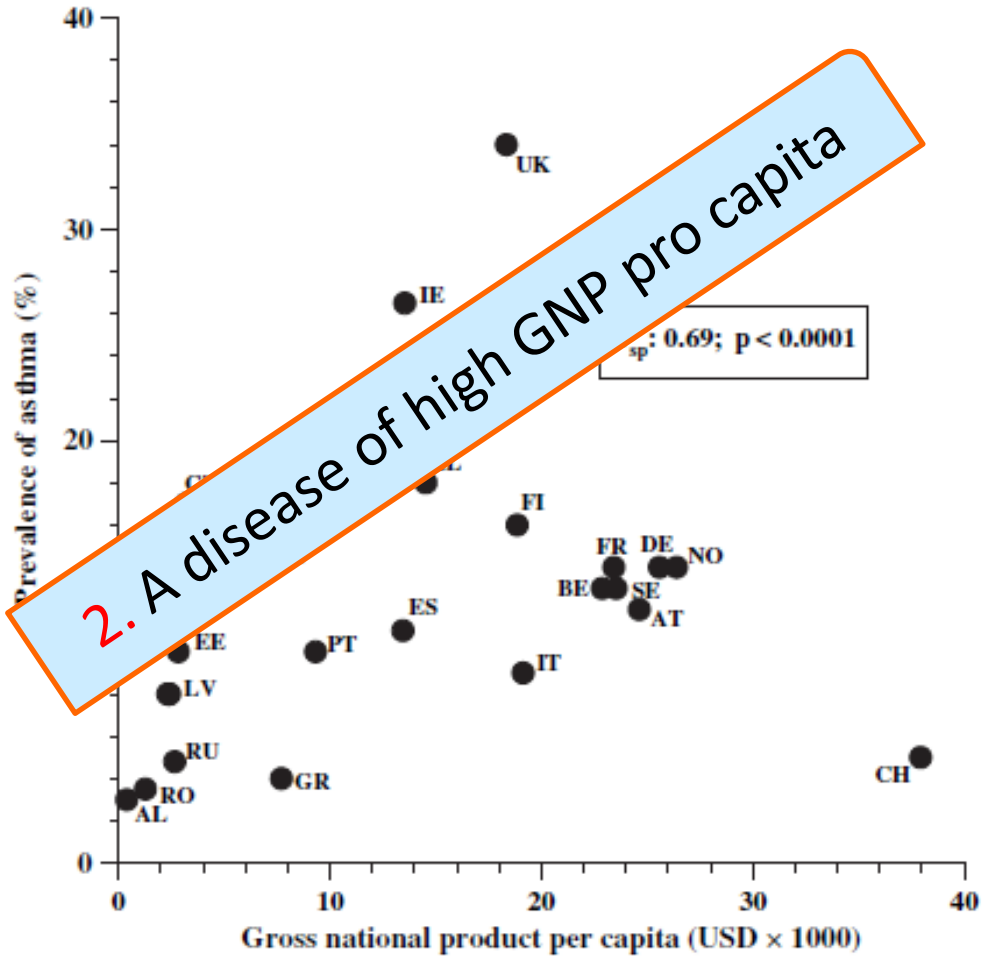
GNI pro capita and asthma in 6-7 years olds



http://data.worldbank.org/about/country-classifications/country-and-lending-groups, accessed May 24°, 2013

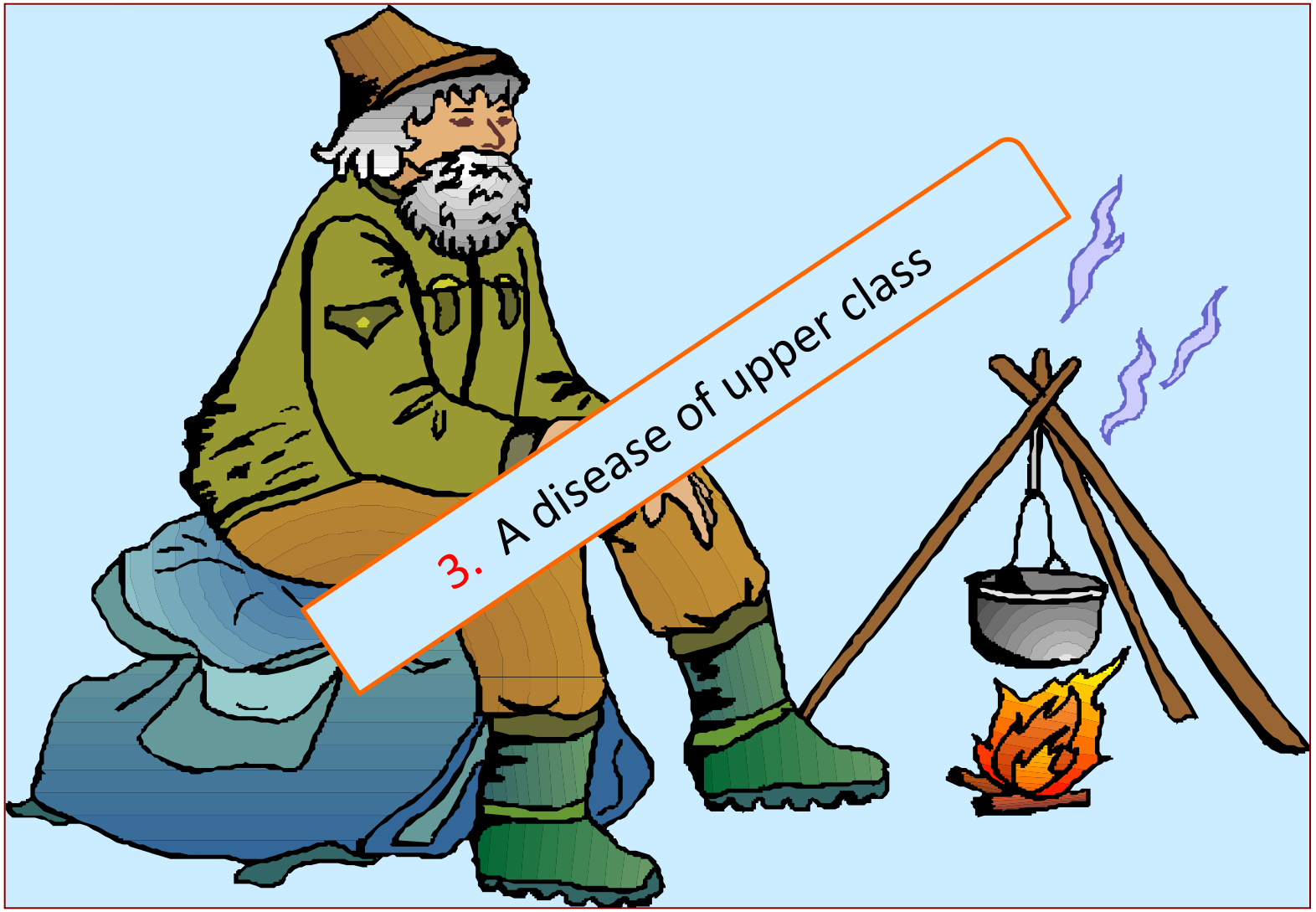
Asher MJ. Worldwide time trends in the prevalence of symptoms of asthma, allergic rhinoconjunctivitis, and eczema in childhood: ISAAC Phases One and Three repeat multicountry cross-sectional surveys. Lancet 2006; 368; 733-43

GNP & asthma



Tedeschi A. Is affluence a risk factor for bronchial asthma and type 1 diabetes? Pediatr Allergy Immunol. 2006;17:533-7

Paternal education and atopy in Italy

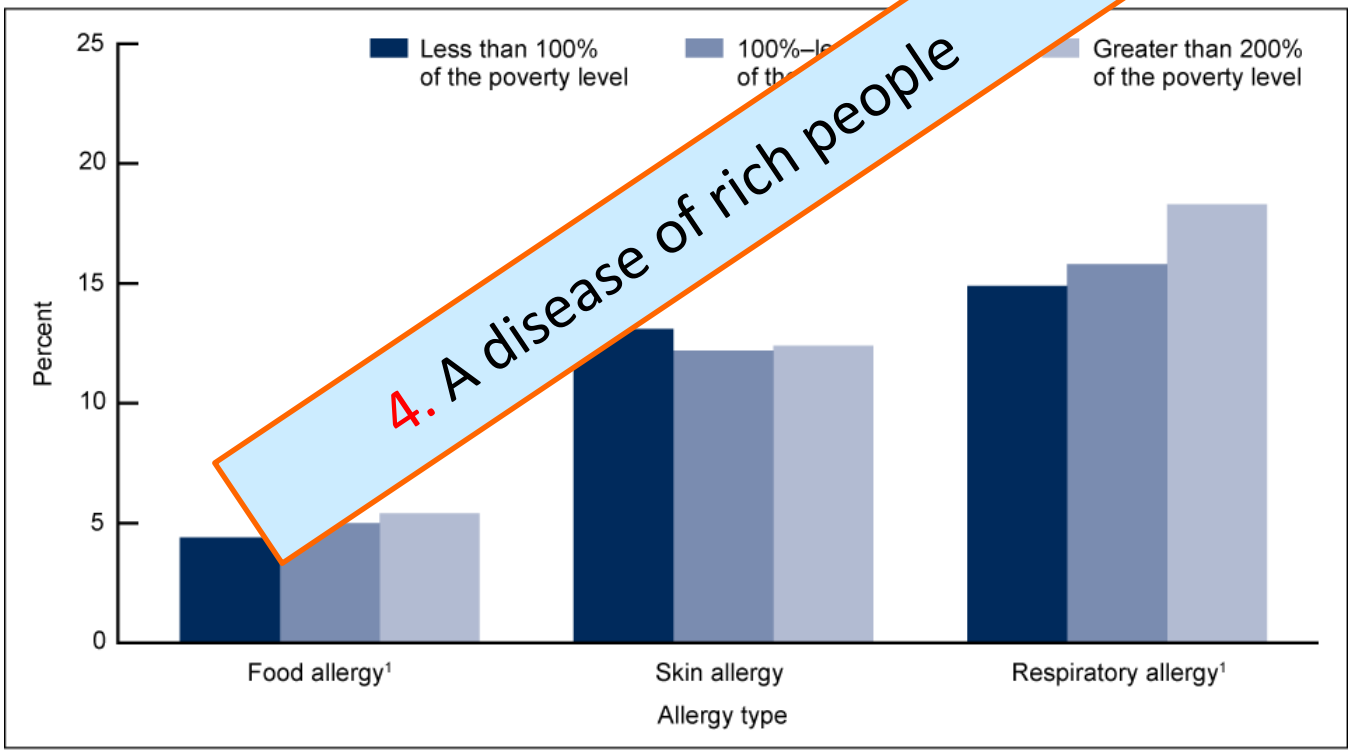


None: 15,6%

Matricardi PM. Sibship size, birth order, and atopy in 11,371 Italian young men. J Allergy Clin Immunol 1998;101:439–44

Allergy by poverty: USA

Figure 4. Percentage of children aged 0–17 years with a reported allergic condition in th nths, by poverty status: United States, average annual 2009–2011

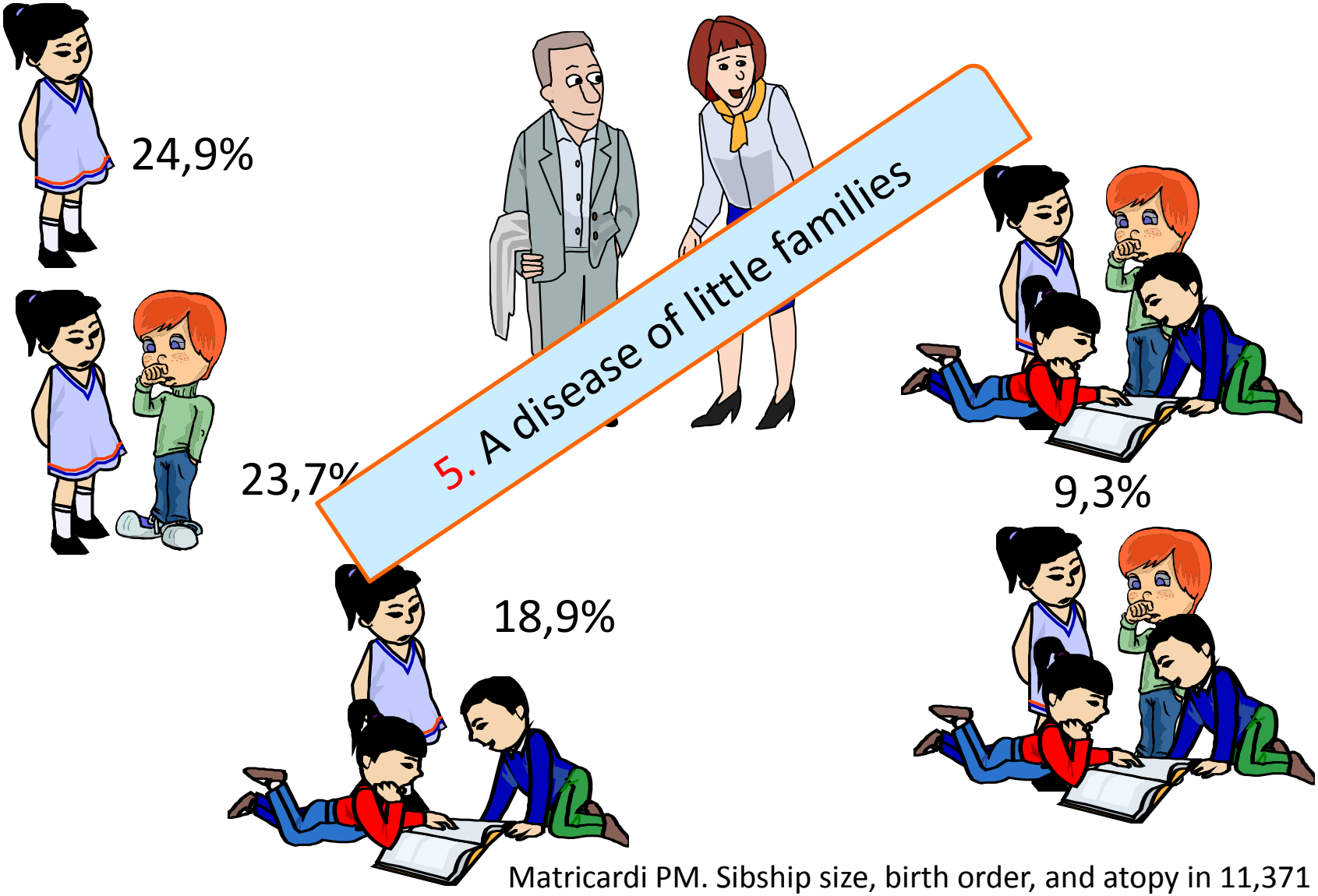


4. A disease of rich people

1Significant trend by poverty status.
SOURCE: CDC/NCHS, Health Data Interactive, National Health Interview Survey.

http://www.cdc.gov/nchs/data/databriefs/db121.htm
Accessed May 2015

Sibship size, birth order, and atopy in Italy



Matricardi PM. Sibship size, birth order, and atopy in 11,371 Italian young men. J Allergy Clin Immunol 1998;101:439–44

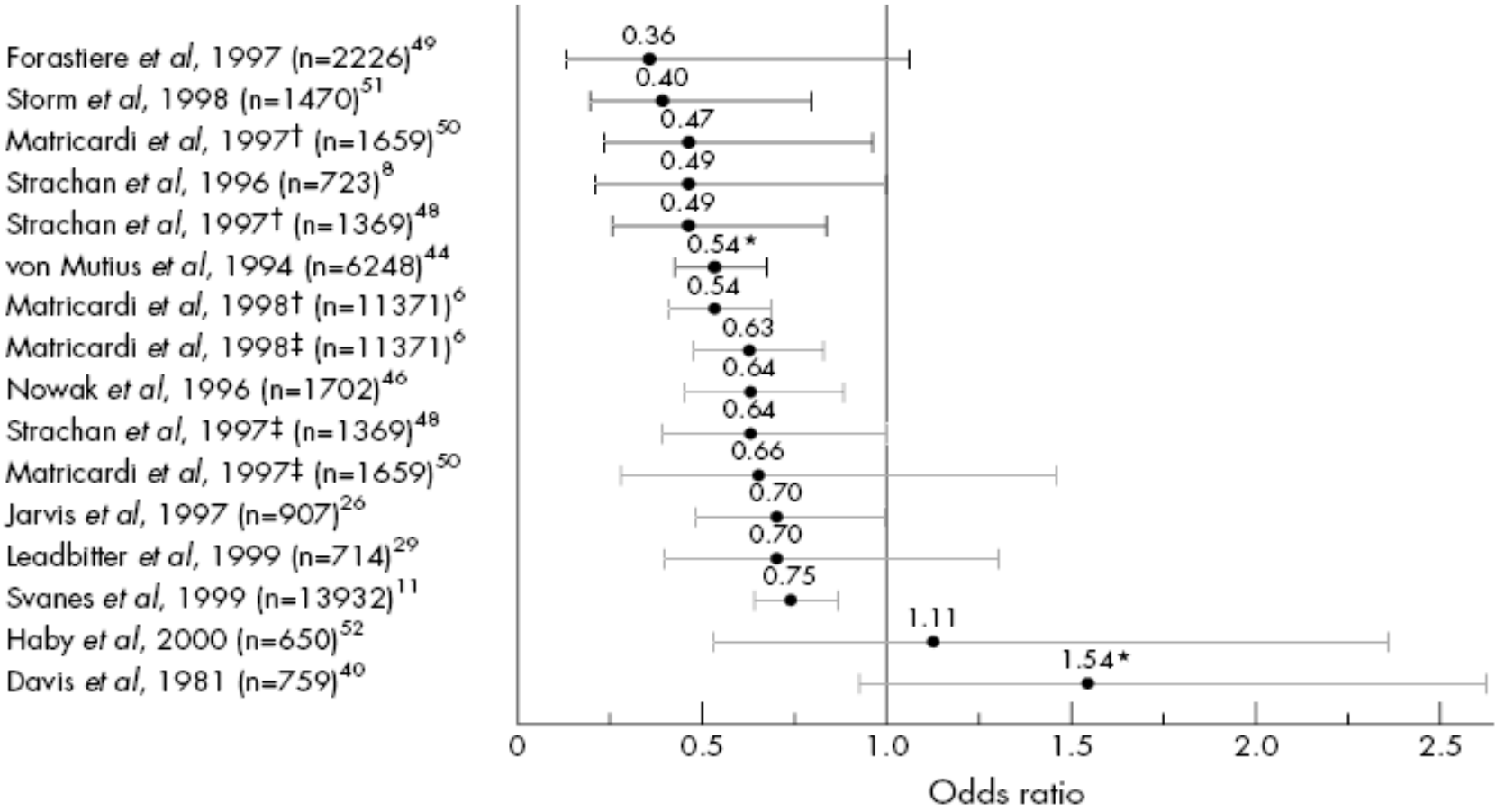
Birth order and asthma in Italy

OR 1

OR 1.86

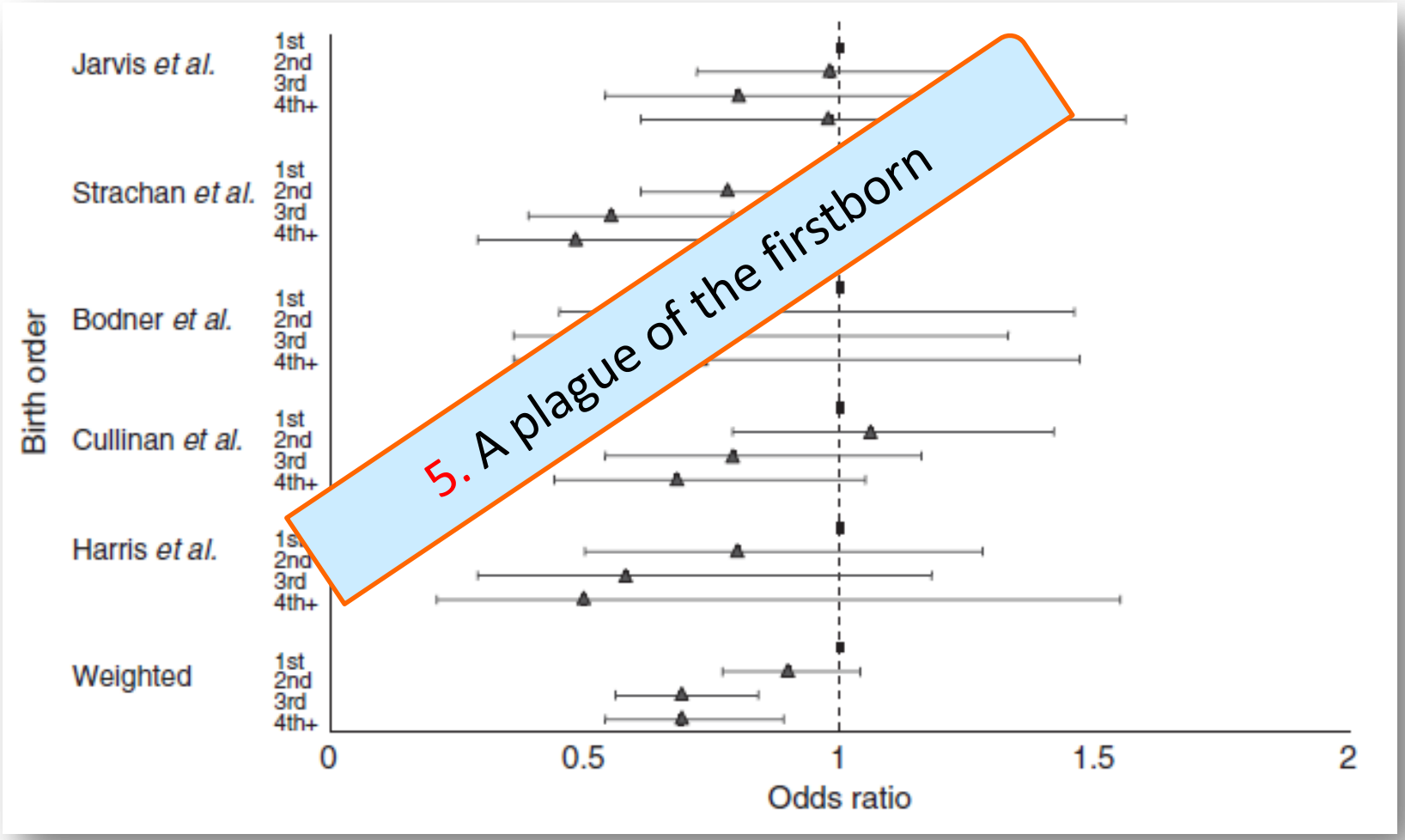
Attena F,. Prevalence of asthma among young men in a military recruitment office of South Italy. Eur J Epidemiol 1999;15:569–72.

SPT+ and number of siblings: 3+ vs. none



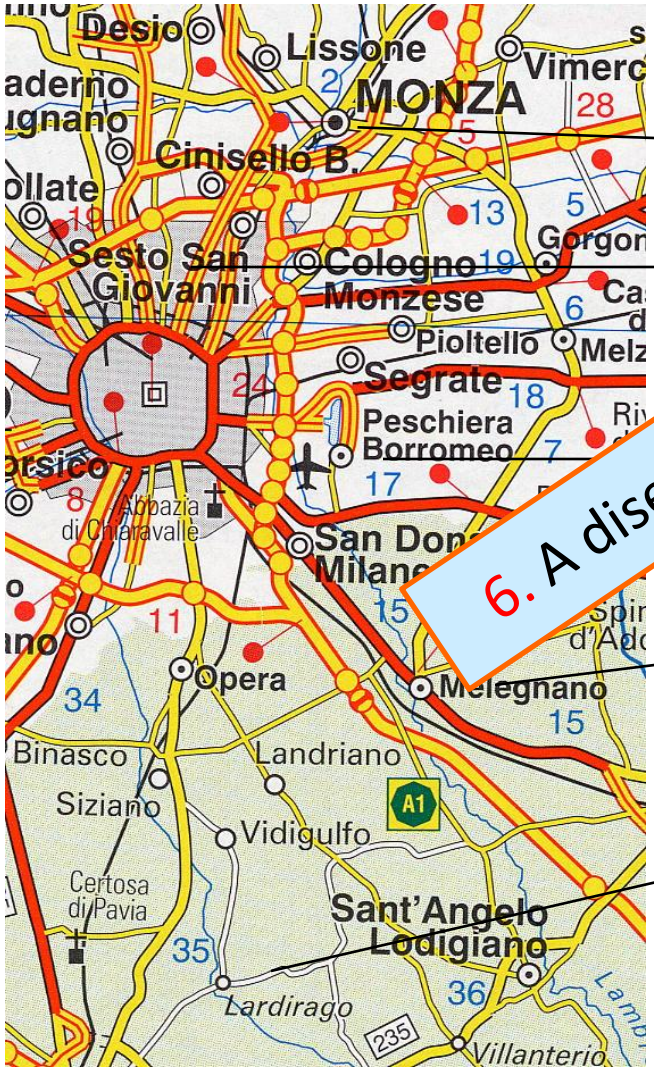
Karmaus W. Does an higher number of siblings protect against the development of allergy and asthma? J. Epidemiol. Community Health 2002;56;209-217

Atopy by order of birth



Upchurch S. . Temporal changes in UK birth order and the prevalence of atopy. Allergy 2010; 65: 1039–1041.

Allergy and Urbanisation

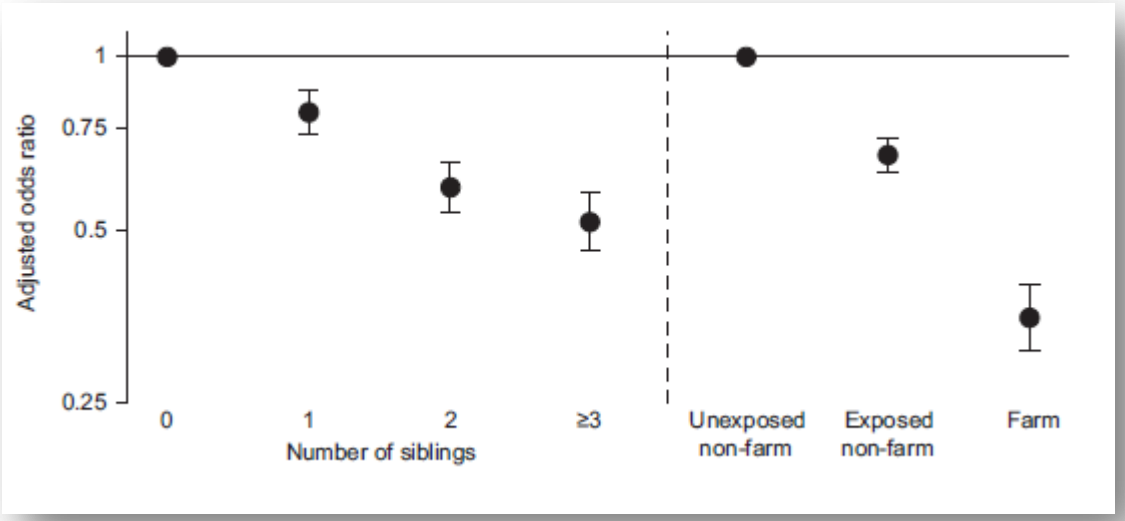


6. A disease of urban environment

64	23.3%
36.000	27.7%
16-64.000	20.0%
4-16.000	18.4%
< 4000	17.8%

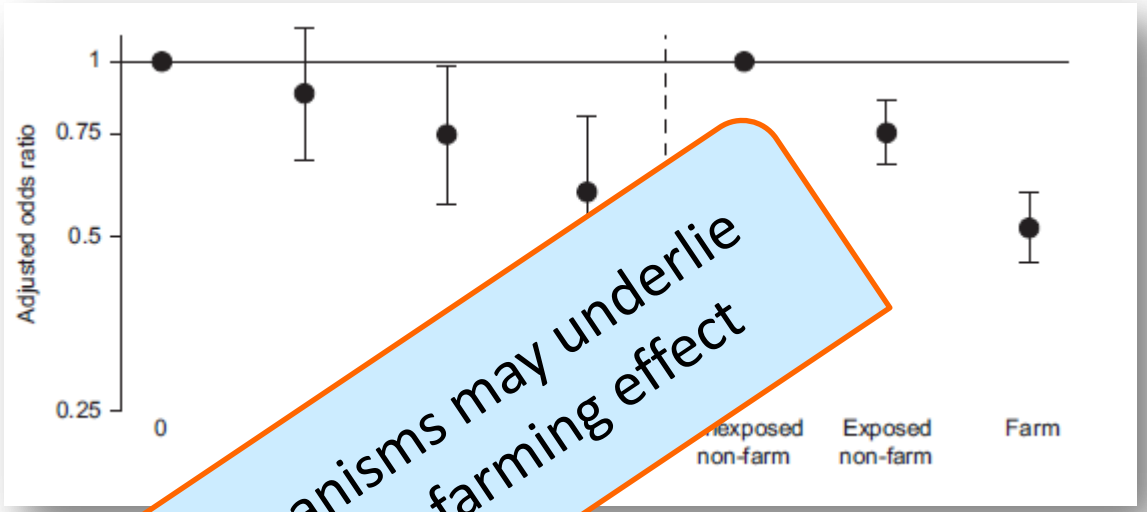
Matricardi PM. Sibship size, birth order and atopy in 11,371 italian young men. *J ACI* 1998 ; 101: 439-44

Hayfever, number of siblings and exposure to farming environments



Genuneit J; GABRIELA study group. The combined effects of family size and farm exposure on childhood hay fever and atopy. Pediatr Allergy Immunol. 2013;24:293-8

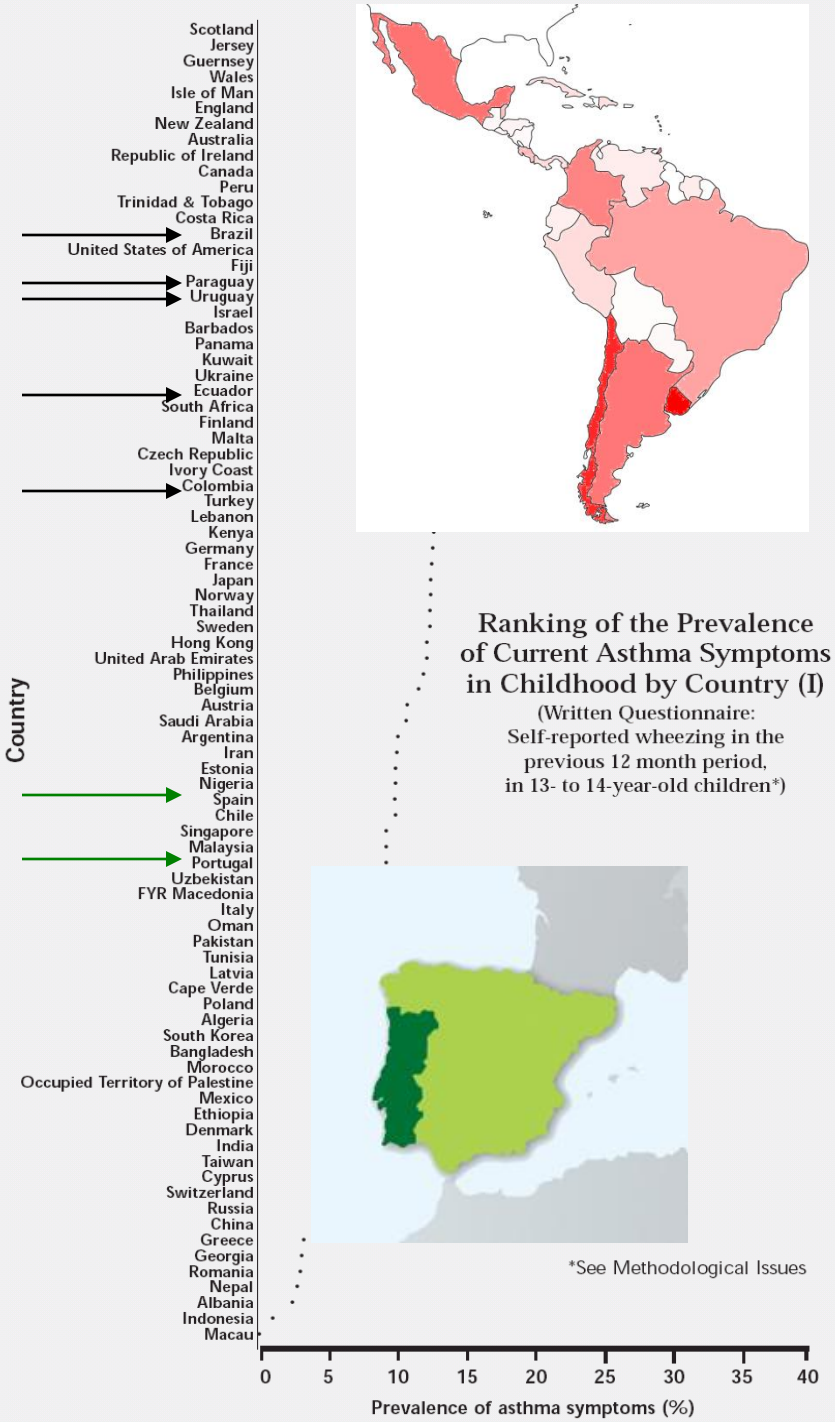
Atopy, number of siblings and exposure to farming environments



7- different biological mechanisms may underlie the cibship size effect and the farming effect

Genuneit J; GABRIELA study group. The combined effects of family size and farm exposure on childhood hay fever and atopy. Pediatr Allergy Immunol. 2013;24:293-8

High asthma prevalence



- High in Latin America:

Brazil

Uruguay

Chile

Argentina

Colombia

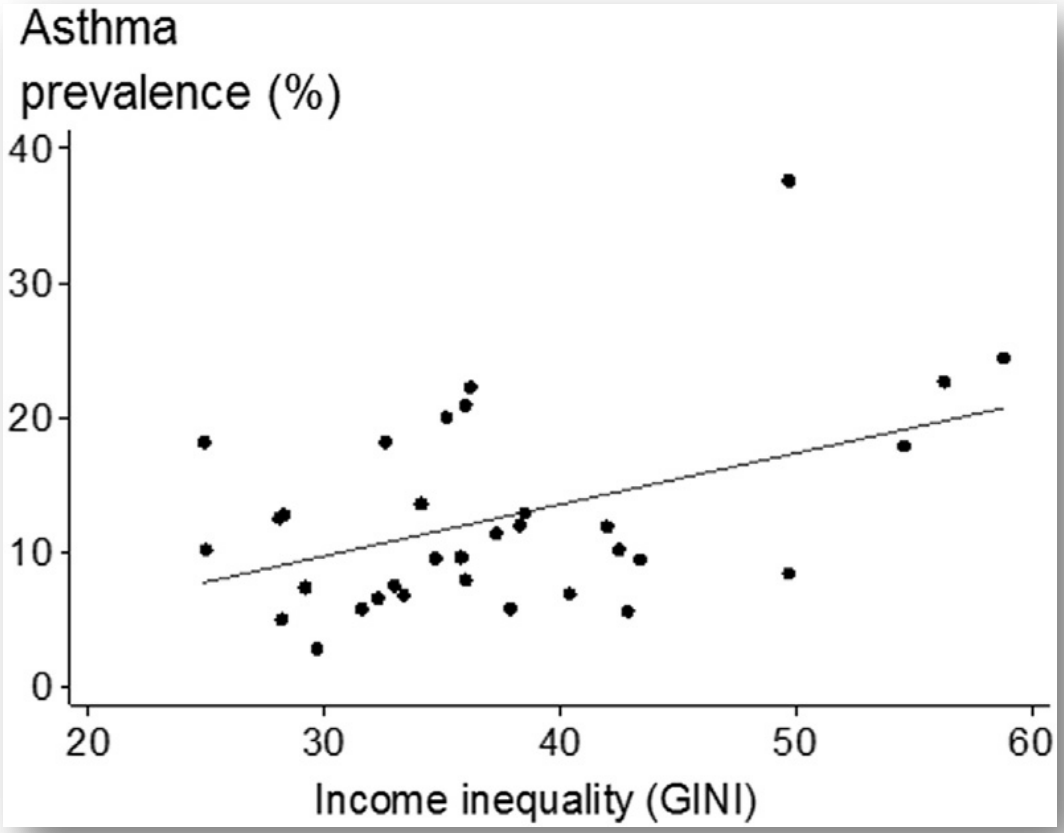
- Lower in

Spain

Portugal

http://www.worldallergy.org/UserFiles/file/WAO-White-Book-on-Allergy_web.pdf - accessed May 2015

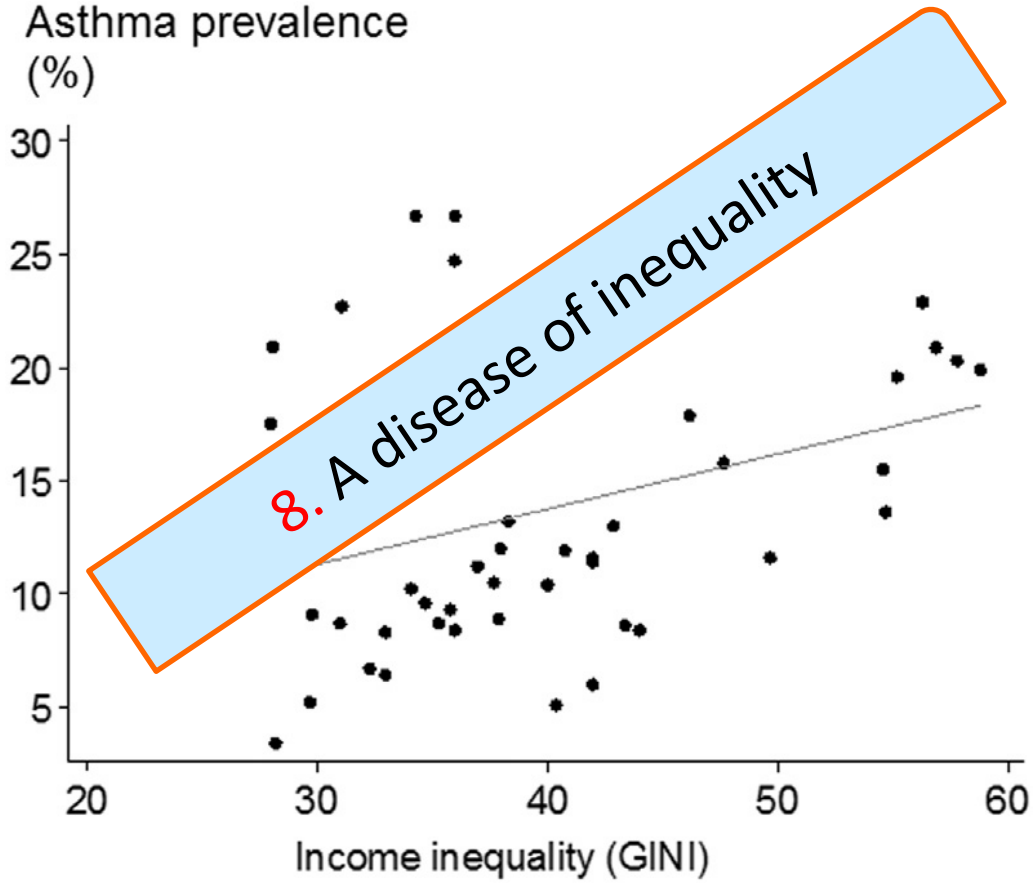
Asthma prevalence rates by income inequality [6- 7-year]



(β= 0.17; r = 0.39; P=.029)

Uphoff EP. International prevalence rates of asthma and allergy are associated with income inequality. J Allergy Clin Immunol. 2015 Mar 17, *e-pub ahead of print*

Asthma prevalence rates by income inequality [13-14 year]



(β= 0.31; r = 0.42; P=.003)

Uphoff EP. International prevalence rates of asthma and allergy are associated with income inequality. J Allergy Clin Immunol. 2015 Mar 17, *e-pub ahead of print*

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Bambino Gesù
OSPEDALE PEDIATRICO

Food hypersensitivity

- Food allergy
  - IgE-mediated food allergy
  - Non-IgE-mediated food allergy
- Nonallergic food hypersensitivity

Johansson SGO. Revised nomenclature for allergy for global use: Report of the Nomenclature of WAO
J Allergy Clin Immunol 2004; 113; 832-6

Symptom-based Clinical Score (Cow's Milk Protein Intolerance Score)

Symptom	Score	
Crying*	0	<1 hour/day
	1	1-1.5 hours/day
	2	1.5-2 hours/day
	3	2 to 3 hours/day
	4	3 to 4 hours/day
	5	
	6	
Regurgitation†	0	
	1	
	2	
	3	
	4	
	5	
	6	
Stools (Bristol scale)†	4	
	0	
	2	
	4	
	6	
Skin symptoms	0 t	
		Severe 3 3
	0 or 6	Urticaria (no 0/yes 6)
Respiratory symptoms	0	No respiratory symptoms
	1	Slight symptoms
	2	Mild symptoms
	3	Severe symptoms

*Crying was only considered if the child was crying for 1 week or more, assessed by the parents, without any other obvious cause.
†Vandenplas Y, Hachimi-Idrissi S, Casteels A, Mahler T, Loeb H. A clinical trial with an "anti-regurgitation" formula. Eur J Pediatr 1994;153:419-23.
†Lewis SJ, Heaton KW. Stool form scale as a useful guide to intestinal transit time. Scand J Gastroenterol 1997;32:920-4.

10. Vandenplas Y, Steenhout P, Planoudis Y, Grathwohl D; Althera Study Group Treating cow's milk protein allergy: a double-blind randomized trial comparing two extensively hydrolysed formulas with probiotics. Acta Paediatr 2013;102:990-8.
11. Vandenplas Y, Althera Study Group, Steenhout P, Grathwohl D. A pilot study on the application of a symptom-based score for the diagnosis of cow's milk protein allergy. SAGE Open Med 2014;2:2050312114523423.

Vandenplas Y. Treatment of Cow's Milk Protein Allergy. Pediatr Gastroenterol Hepatol Nutr. 2014;17:1-5

Cronache

Barletta La vittima aveva 29 anni. Due donne salvate dall'antidoto

Test anti allergie da eBay Muore nel centro clinico

Medicina forse contaminata, controlli in tutta Europa

Il commento

QUEI FARMACI IN RETE SENZA CONTROLLI

di ADRIANA BAZZI

La vicenda di Barletta (una donna morta dopo un esame per le intolleranze alimentari e altre due ricoverate in osservazione) è complicata e pone almeno tre tipi di problemi. Primo: l'utilizzo di medicinali comperati su eBay (in questo caso il sorbitolo che, usato per il test, doveva dimostrare l'incapacità dell'intestino di assorbire certi cibi e spiegare certi sintomi del paziente, come il gonfiore intestinale, il sovrappeso, la cefalea e via dicendo). Il commercio di medicine via Internet è senza controllo: al top della classifica ci sono i farmaci Viagra-simile, contro l'impotenza sessuale, che di solito sono acquistati da cittadini comuni, ma, a quanto pare, anche i medici privati (per risparmiare?) comprano prodotti farmaceutici (il sorbitolo) da utilizzare nei loro ambulatori, senza prove di sicurezza. Secondo: i centri privati dovrebbero garantire la qualità delle loro prestazioni (il

Risparmi
Per risparmiare i

DAL NOSTRO INVIATO

BARLETTA — Cinque grammi. Solo cinque. Di una sostanza innocua. Ma acquistata via internet su eBay da una partita probabilmente contaminata da un veleno potentissimo. Che ora si cerca, in tutta Europa, di fermare prima che possa uccidere ancora. Sperando che, come si sospetta, non lo abbia già fatto. Teresa Sunno, ventinovenne di Andria, residente a Trani, è morta così. In dieci minuti. Dopo aver bevuto quella sostanza, somministratale dal suo gastroenterologo privato alla ricerca di intolleranze alimentari. Non ha avuto il tempo nemmeno di arrivare al pronto soccorso, Teresa. Dove invece sono state salvate per un soffio Anna Abrascia di 40 anni e Addolorata Piazzolla, di 62, che avevano ingerito la stessa sostanza e in pochi minuti hanno avuto un collasso. Vive grazie a una fiala blu che Cosimo Sannito, responsabile del Pronto soccorso mostra orgoglioso: sono riusciti tempestivamente a individuare l'antidoto e a som-

Giovane La vittima di ieri a Barletta: Teresa Sunno, 29 anni, originaria di Andria. Salve per un soffio altre due donne

La sostanza

Sorbitolo

Il sorbitolo è uno zucchero semplice, contenuto in frutti come mele, pere, susine, ciliegie e in quelli del sorbo (da cui deriva proprio il nome sorbitolo). Secondo alcune approfondite ricerche scientifiche la sostanza può essere responsabile di malassorbimento intestinale, con la comparsa di sintomi diversissimi che vanno dal gonfiore di pancia, ai dolori addominali, alla stanchezza, fino al mal di testa. Il test al sorbitolo viene utilizzato per diagnosticare questi disturbi. Il suo uso è, bambini di età inferiore a un anno di vita

lo, vi siano nitrati fortemente tossici. A Rovigo si indaga su un altro laboratorio che commercializzava la stessa sostanza. Un'operazione capillare seguita passo passo dal ministro della Salute, Renato Balduzzi. Che ieri ha portato ad un primo risultato: ci sono altre situazioni sospette.

Il capo della Procura di Trani, competente delle indagini, Carlo Maria Capristo, raccomanda cautela: «Non dobbiamo spargere il panico. Sono in corso test specialistici sulla tossicità del farmaco. Sono analisi approfondite. Occorre un po' di tempo e un po' di prudenza». Forse ne doveva avere di più il medico ad acquistare il farmaco online. Dove sicuramente si può risparmiare. Ma si trovano, sempre più Spesso provenienti dalla Cina. Il test letale, si sospetta che possa essere stato originariamente prodotto lì. Ora il medico, Ruggero Spinazzola, rischia un'accusa di omicidio colposo, lesioni gravi e avvelenamento colposo di sostanze alimentari. Ma si approfondisce anche la posizione del dottor Pappagallo, medico associato in quello studio clinico, cui si era rivolta la ragazza.

«Aveva un po' di acidità di stomaco» racconta Giovanni, l'amico che l'aveva accompagnata agli accertamenti e ora non si dà pace. «Teresa è stata sottoposta prima a una gastroscopia e poi a una colonscopia su consiglio del dottor Pappagallo, che la mandava però allo studio Spinazzola a Barletta». E non era sempre andata bene. Lo racconta il ragazzo: «Dopo alcune analisi, ha ritenuto di farla sottoporre a test per le intolleranze alimentari. Il primo lo ha fatto due settimane fa per verificare l'intolleranza al lattosio: è stata male tutto il giorno dopo averlo fatto. Il secondo era oggi (ieri, *ndr*). Si è sentita male, ma non è stata l'unica. Solo che lei poi è morta». Non consola, ma grazie all'allerta lanciato la morte di Teresa potrebbe non essere stata inutile.

Virginia Piccolillo

Dalla Gran Bretagna
La sostanza prodotta in Gran Bretagna. Sotto sequestro il centro che cura le intolleranze

Sympt ed to food

Haemorroids

Psoriasis

Refractive changes

Bedwetting

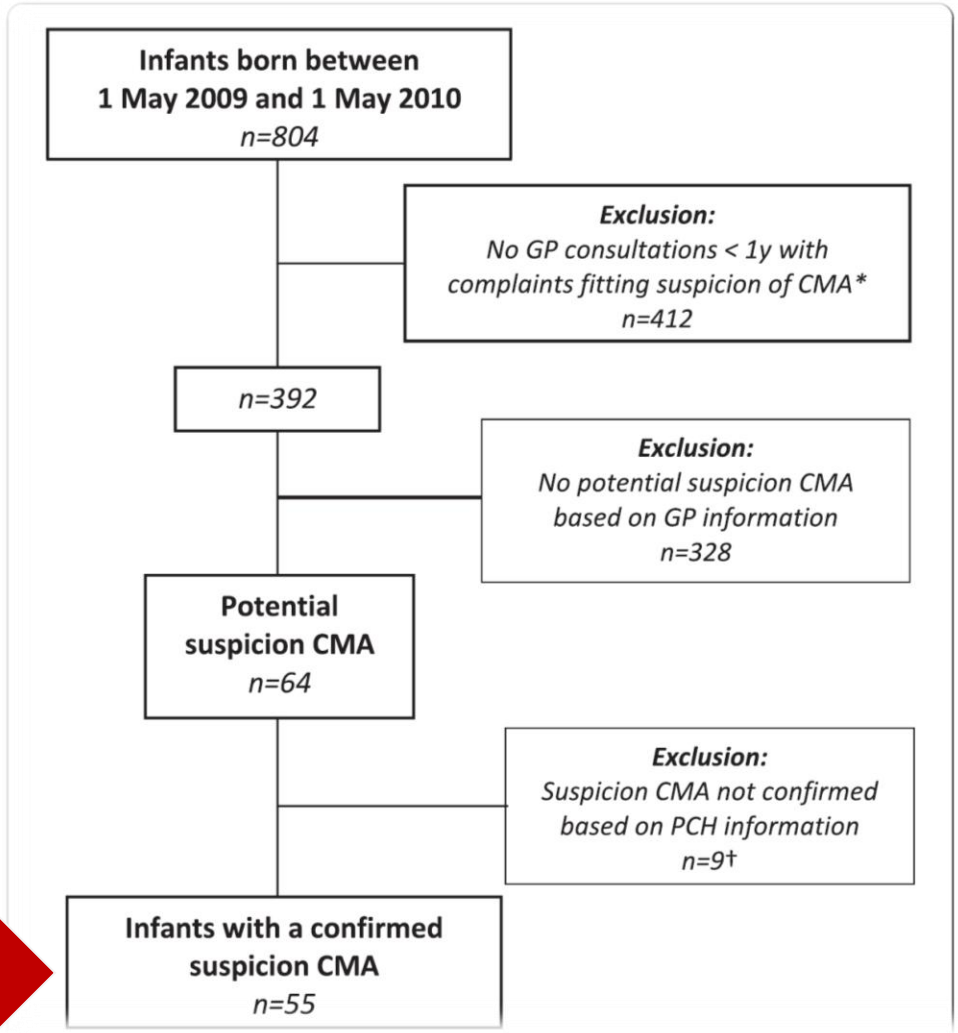
Body odour

Overweight

SKIN: Acne, dermatitis, e .
HEADACHES: various kind .
EYE CONDITIONS: conjunctiviti , periods of blurred visi ring, temporary refractive changes.
earing loss, fections, inflammations, Meniere s , repeated
gina, high blood pressure, irregular heartbeat, low blood pressure, rapid pulse.
constipation, diarrhoea, gall bladder pains, wind, gastric ulcer, gastro-intestinal
n, haemorrhoids, indigestion, mucous colitis, nausea, pains or cramps, spastic
ng.
RESPIRATORY sthma, c ing, frequent "colds", hay fever, mouth breathing, nosebleeds, p nasal d fy nose, wheezing.
UROLOGICAL: bedwe tion, frequent urination, painful or difficult urination.
MUSCULO-SKELETAL: a cle cramps, muscle a cle spasms, muscle weakness.
MENTAL-BEHAVIOURAL: a sions, depression (includin drowsiness, epilepsy, floating sensations, general fatigue, hallucinations, hype bility, learning disorders, minimal b n dysfunction, nervousness, peri bias, poor concentration, poor memory, poor muscle coord tion, restlessnes mia, sleeps at inappropriate times, sleeps too little, sleeps too much, tension-fatigue syndrome, unsteadiness.
OTHER: Abnormal body odour, excessive sweating, general weakness, hypoglycaemia, night-sweating, overweight, underweight, virus infections

http://www.foodallergycure.com/

Unnecessary milk elimination diets in children with uncorrected diagnosis of CMA.

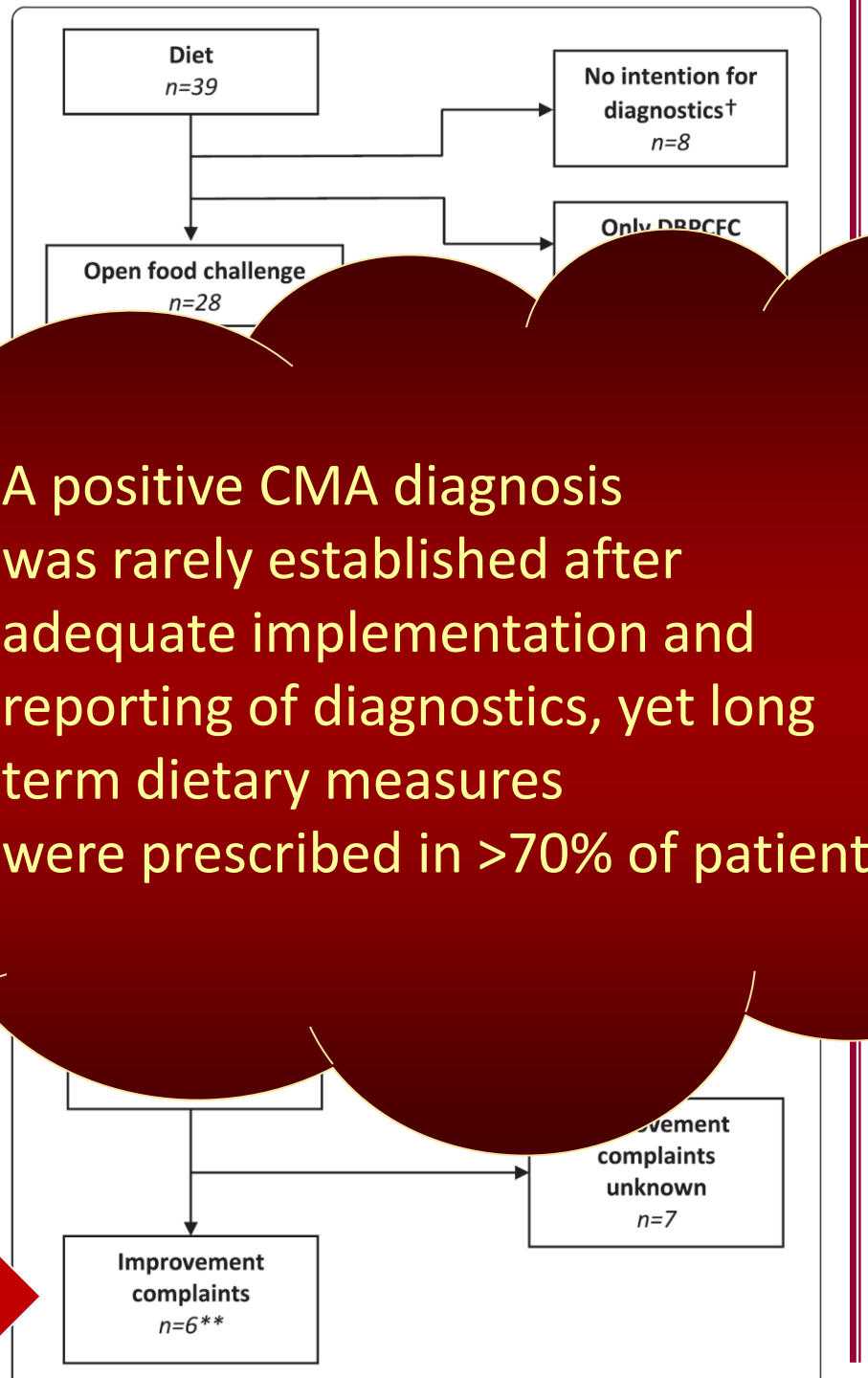


7%

van den Hoogen S.: Suspected cow's milk allergy in everyday general practice: a retrospective cohort study on health care burden and guideline adherence. BMC Research Notes 2014 7:507.

Bambino Gesù
OSPEDALE PEDIATRICO

Unnecessary milk elimination diets in children with atopic dermatitis.



A positive CMA diagnosis was rarely established after adequate implementation and reporting of diagnostics, yet long term dietary measures were prescribed in >70% of patients.

0.8%

n den Hoogen S
pected cow's milk allergy in everyday general practice: a retrospective cohort study on health care burden and guideline adherence. BMC Research Notes 2014 7:507

NIAID guidelines: avoidance

- Guideline 19: The EP recommends that individuals with documented IgE-mediated FA should avoid ingesting their specific allergen.

- Guideline 20: The EP recommends that individuals with documented non-IgE-mediated FA should avoid ingesting their specific allergen.

NIAID. Guidelines for the diagnosis and management of food allergy
J Allergy Clin Immunol 2010;126:S1-S58

Avoiding milk, dairy products, and egg












Bambino Gesù
OSPEDALE PEDIATRICO

RICE MILK

Just add water!

- Dairy Free Alternative to Milk
- Soy Free
- Gluten Free
- Lactose Free
- Fortified
- Calcium Enriched

(Makes 4 Litre) 450g

Rice milk is a perfect substitute for people with a lactose, dairy or soy intolerance or allergy. It is lactose free, dairy free, soy free and kosher. Our rice milk powder is made from milling sound broken long grain white rice, and blended with the remaining ingredients to produce the final product. Used as a substitute for milk and milk powder.

Ingredients: Rice Flour, Maltodextrin, Vegetable fat, Fructose, Xanthan Gum, Salt, Vitamin & mineral supplement, Nature Identical flavour .

Carvalho NF. Severe nutritional deficiencies in toddlers resulting from health food milk alternatives. Pediatrics. 2001;107(4):E46

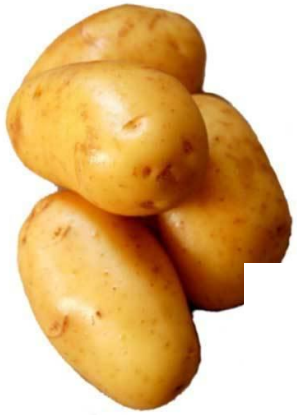
Generalized edema more evident (A) in the face and (B) in the legs (fovea sign)

Novembre E. Severe hypoproteinemia in infant with AD. Allergy. 2003;58:88-9

Bambino Gesù
OSPEDALE PEDIATRICO

Nickel allergy.
a diet regimen for diagnosis

- Chocolate
- Potatoes
- Salmon
- Nuts and Legumes (beans, lentils)
- Any canned food or canned fruit
- Hot water from the tap
- Anything acidic (like tomatoes) cooked in a stainless steel pan
- Leafy green vegetables





Braga M. Systemic nickel allergy syndrome: nosologic framework and usefulness of diet regimen for diagnosis. Int J Immunopathol Pharmacol. 2013; 26:707-16

Bambino Gesù
OSPEDALE PEDIATRICO
DE MARSEILLE

MALADIE DE LA PEAU, DES ONGLES
ET DU CUIR CHEVELU
ALLERGOLOGIE ESTHÉTIQUE MÉDICALE

SUR RENDEZ-VOUS

9, AVENUE GERY
3ème ETAGE
13600 LA CIOTAT
TÉL : 04 42 83 41 19

LA CIOTAT, LE

REGIME SANS COBALT

SUPPRIMER LES ALIMENTS SUIVANT

haricots, betteraves, choux,

abricots, noix,

foie,

pain complet,

clous de girofle,

café, thé, cacao, chocolats,

bière,

Dieta senza latte vaccino, uovo e loro derivati

EVITARE:

Latte, Yogurt, Burro, Formaggi,

Uovo, Pasta all'uovo,

Prosciutto cotto,Insaccati (salame, salsiccia, wurstel, mortadella…) se contengono latte,

Carne vaccina (vitello, vitellone e manzo), pollo, tacchino,

Omogeneizzati di carne vaccina (vitello, vitellone e manzo), di pollo e tacchino,

Dolci e prodotti commerciali con latte e uovo, mela

PUO' ASSUMERE:

Latte di riso, Latte di soia, Thè, Camomilla, Orzo

Biscotti senza latte e senza uovo, Fette Biscottate senza latte e senza uovo

Cereali: pasta di grano duro, riso, polenta, pane di grano duro, crackers, altri cereali

Prosciutto crudo, Cotto al vapore, Lonza, Bresaola di cavallo

Carne di agnello, coniglio, cavallo, maiale, struzzo

Pesce a piacere (eccetto crostacei e molluschi)

Verdura: carote, patate, finocchi, lattuga, bieta, spinaci, pomodoro

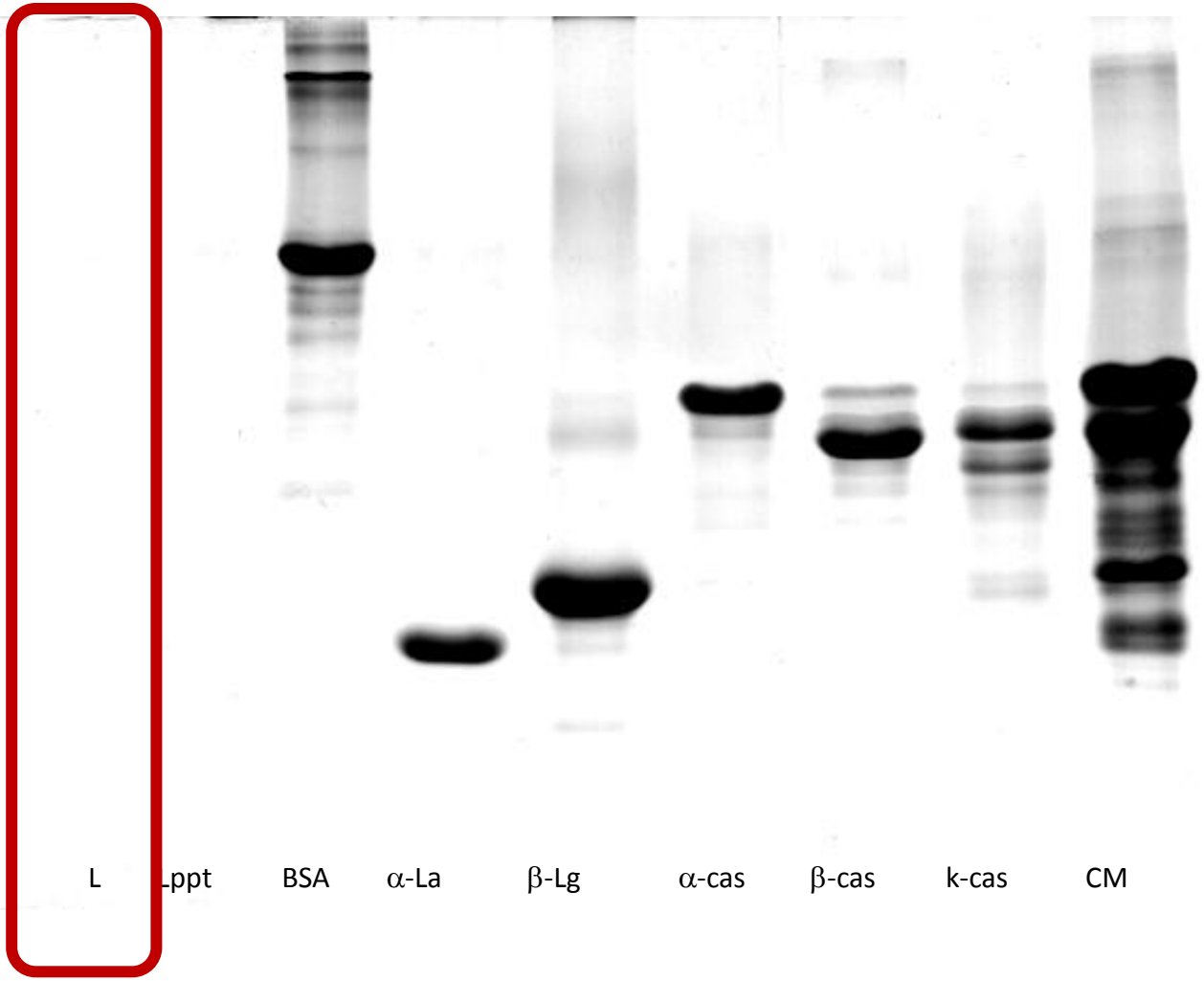
Legumi: fagioli, ceci, piselli, lenticchie

Frutta: a piacere (eccetto mela)

Dolci non contenenti latte e uovo.

Bambino Gesù
OSPEDALE PEDIATRICO

SDS-PAGE of commercially available lactose and cow's milk proteins



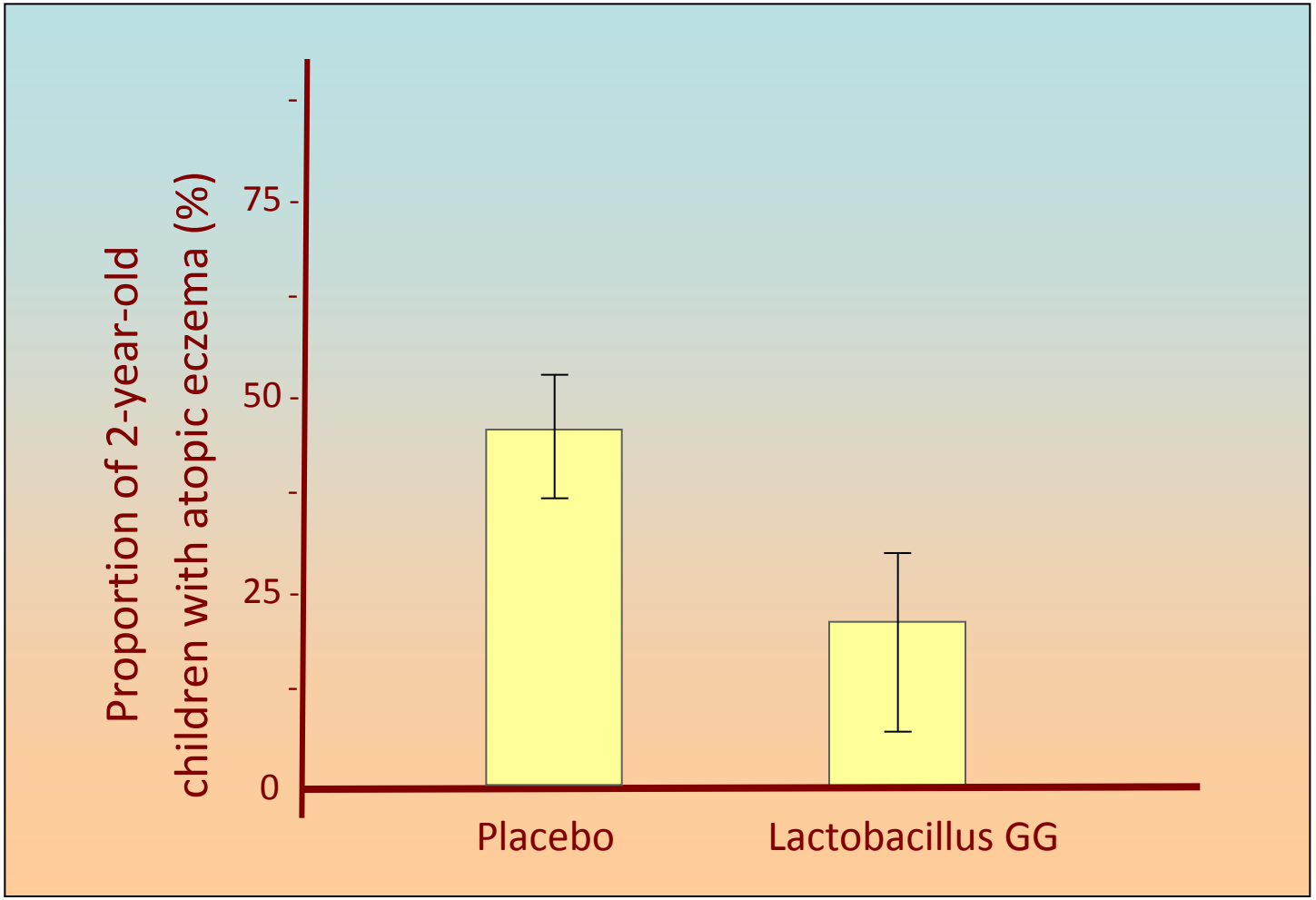
Fiocchi A. Clinical tolerance to lactose in children with cow's milk allergy. Pediatrics. 2003; 112:359-6

1. Una malattia in aumento
2. Una malattia legata ai fattori sociali
3. Miti in allergia alimentare
4. Si può prevenire con I probiotici
5. Si può prevenire con l'alimentazione?
6. Conclusioni

Bambino Gesù
OSPEDALE PEDIATRICO

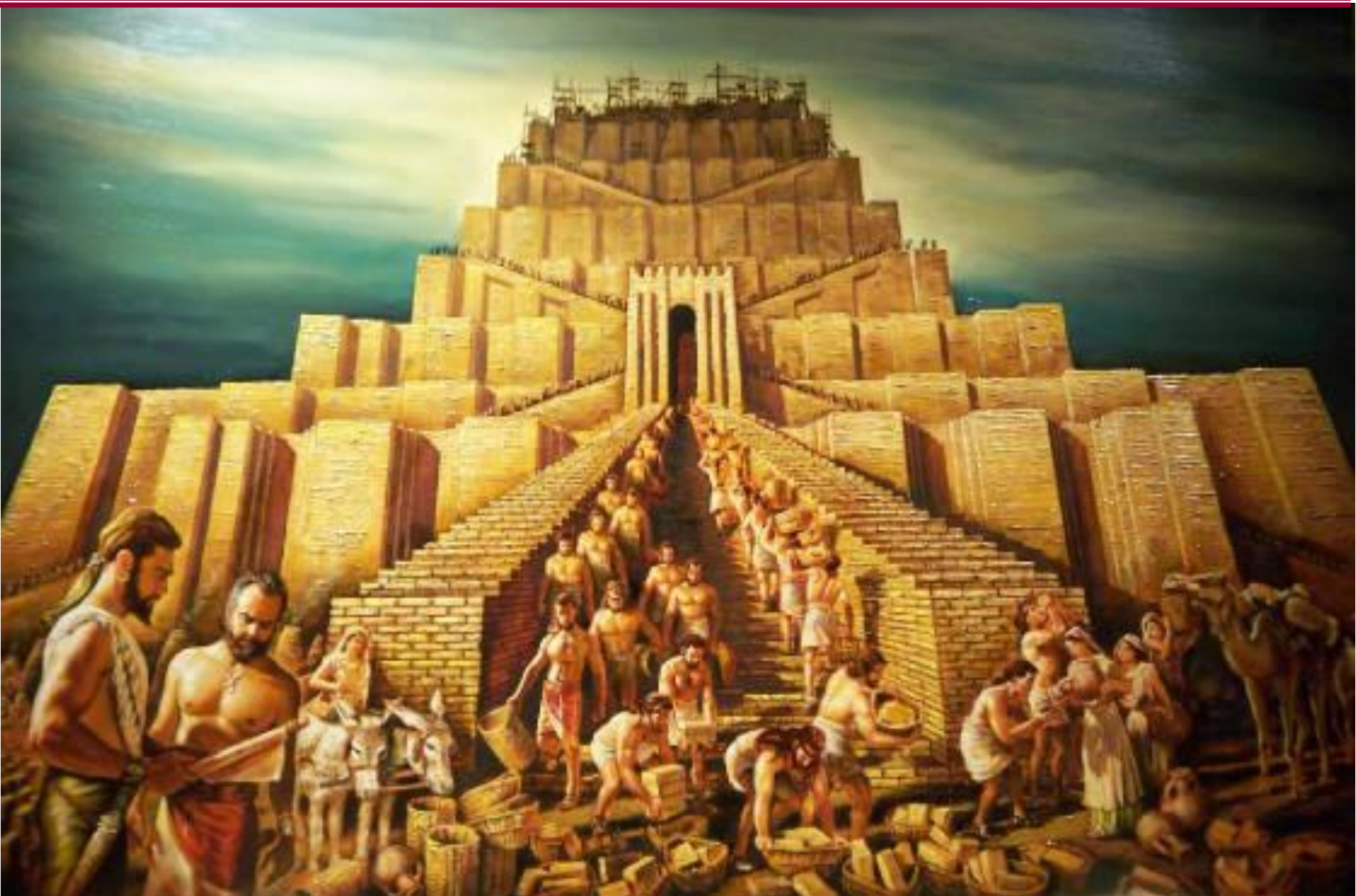
Reduction of AD by 50%

Kalliomaki M. Probiotics and prevention of atopic disease: a randomised placebo controlled trial. Lancet 2001; 357:1076-79

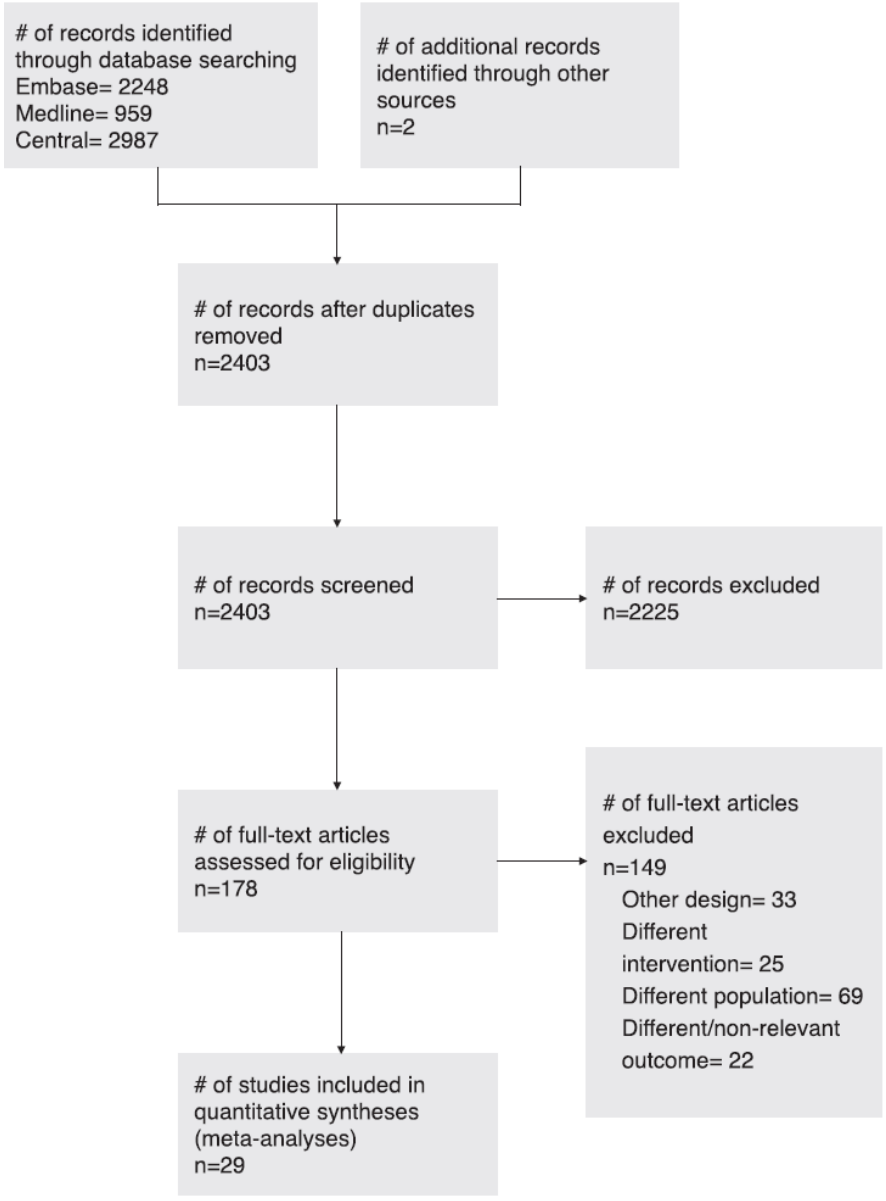


Probiotic & prevention of allergic disease

Bambino Gesù
OSPEDALE PEDIATRICO

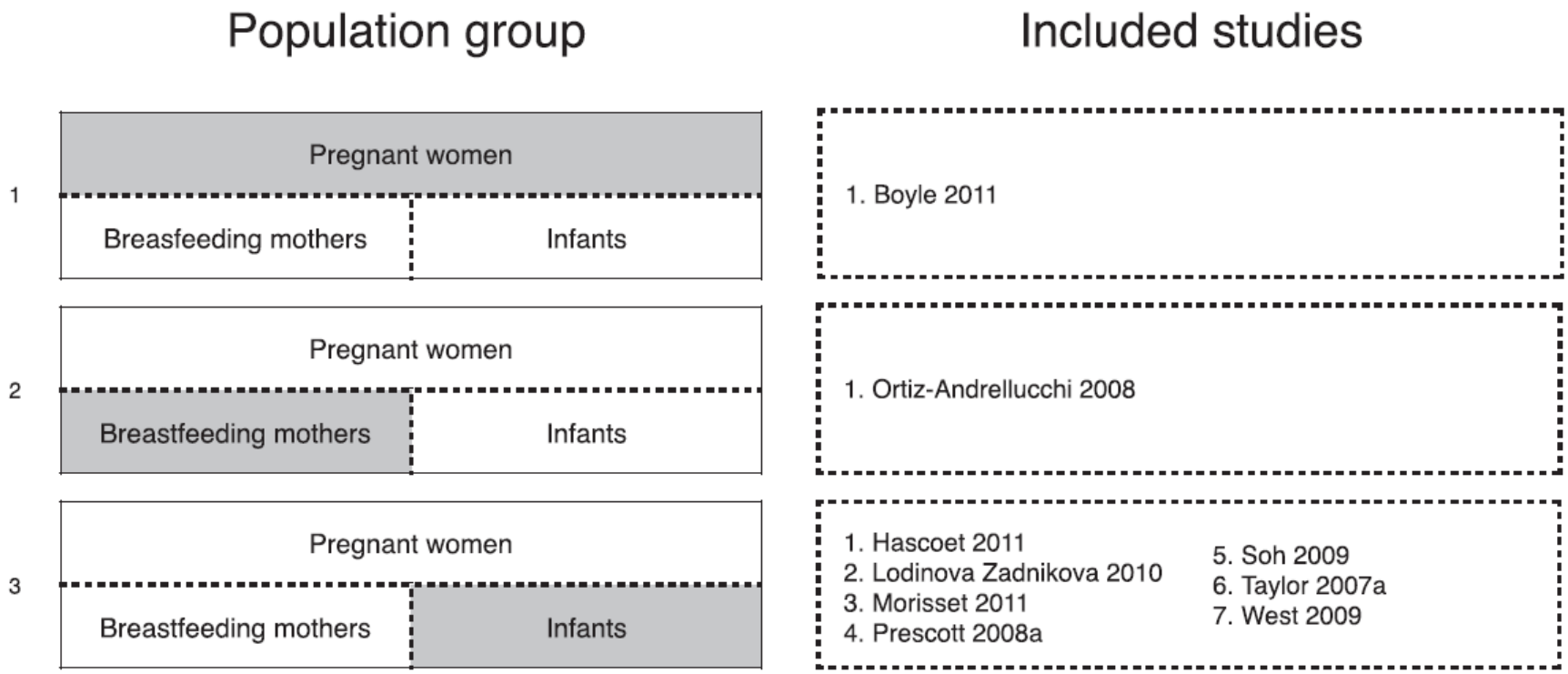


Study flow diagram



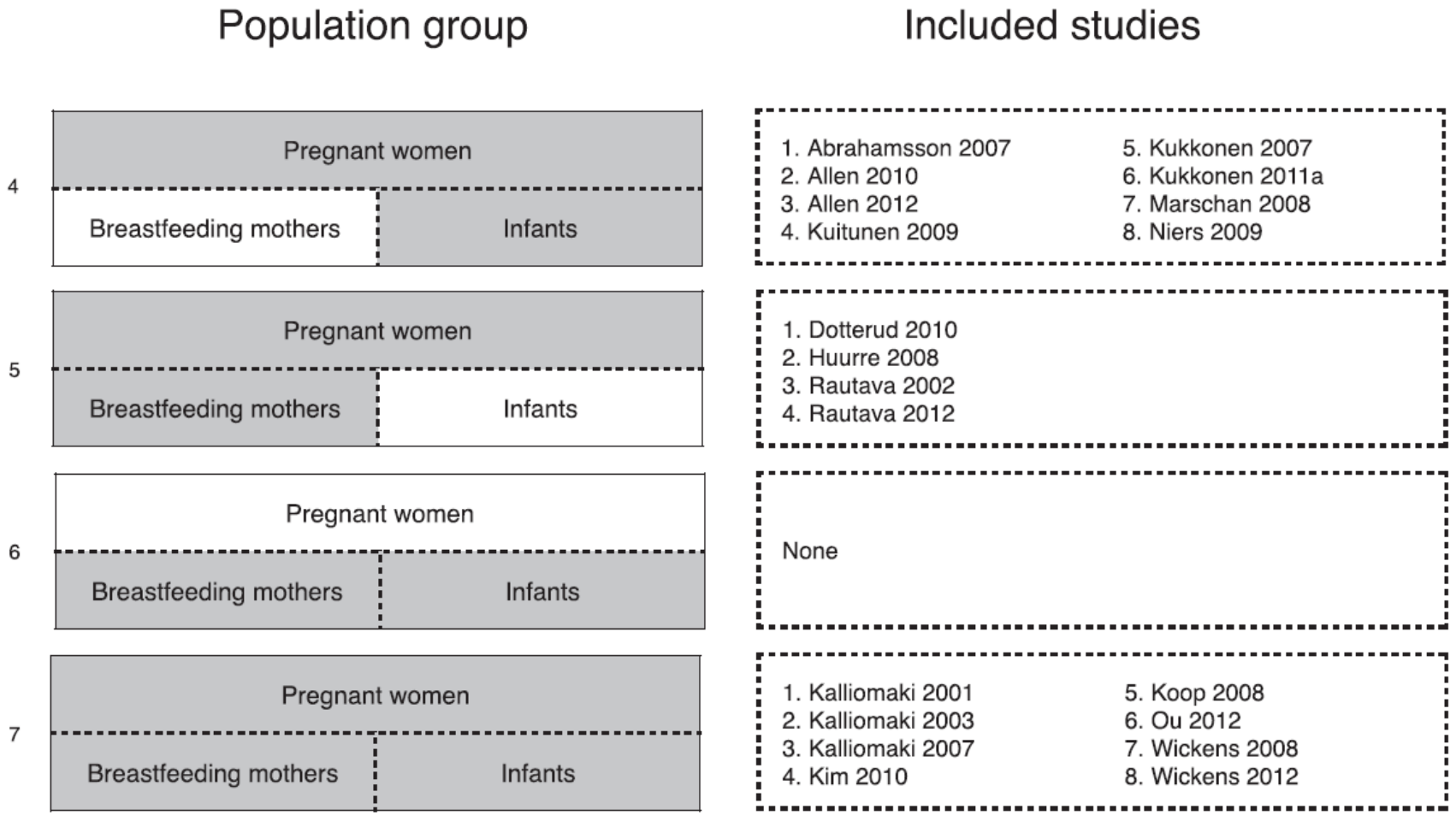
Cuello-Garcia CA. Probiotics for the prevention of allergy: A systematic review and meta-analysis of randomized controlled trials. J Allergy Clin Immunol. 2015 Jun 1 [Epub ahead of print]

Studies included: direct evidence



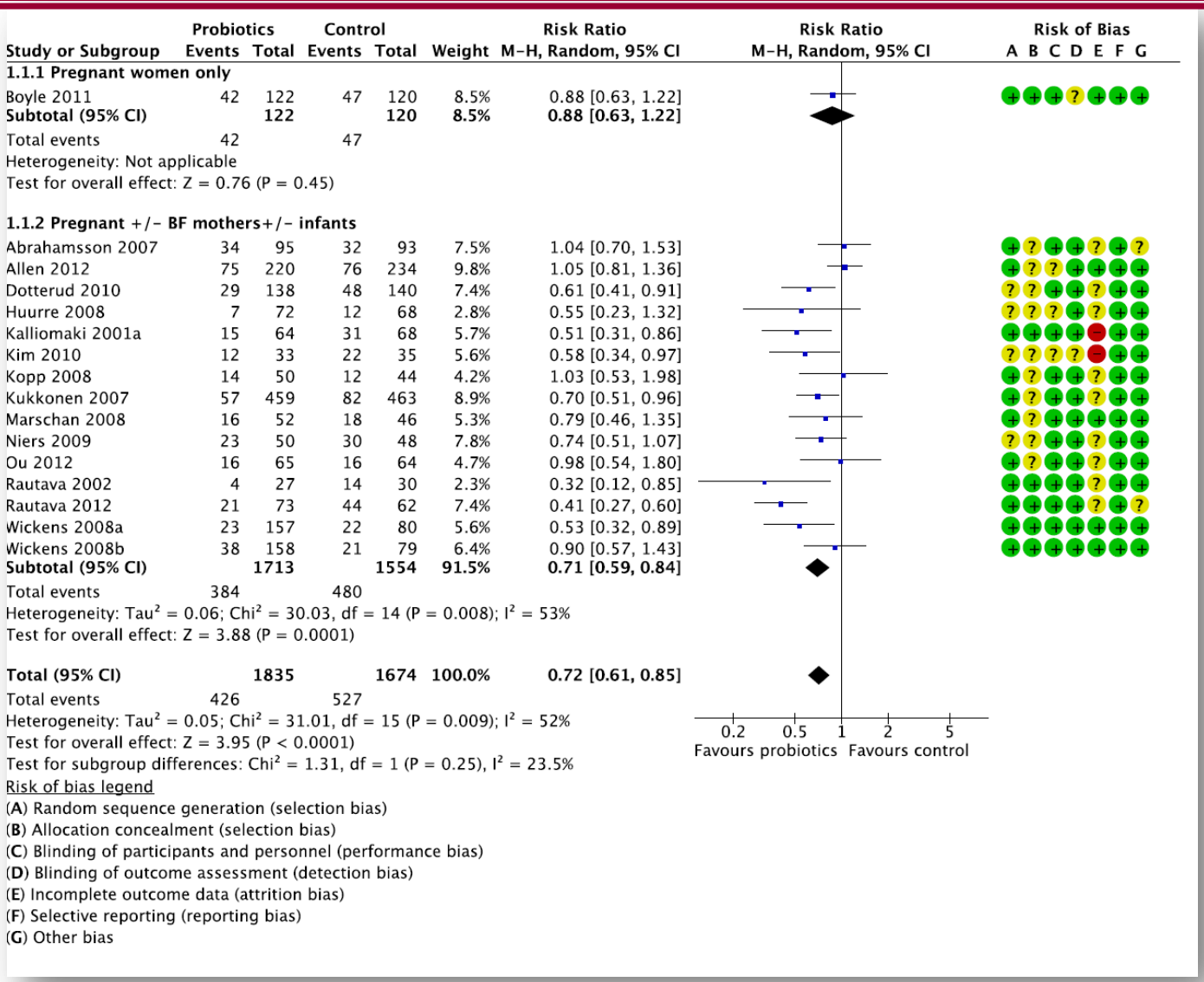
Cuello-Garcia CA. Probiotics for the prevention of allergy: A systematic review and meta-analysis of randomized controlled trials. J Allergy Clin Immunol. 2015 Jun 1 [Epub ahead of print]

Studies included: indirect evidence



Cuello-Garcia CA. Probiotics for the prevention of allergy: A systematic review and meta-analysis of randomized controlled trials. J Allergy Clin Immunol. 2015 Jun 1 [Epub ahead of print]

Probiotics in pregnancy & eczema

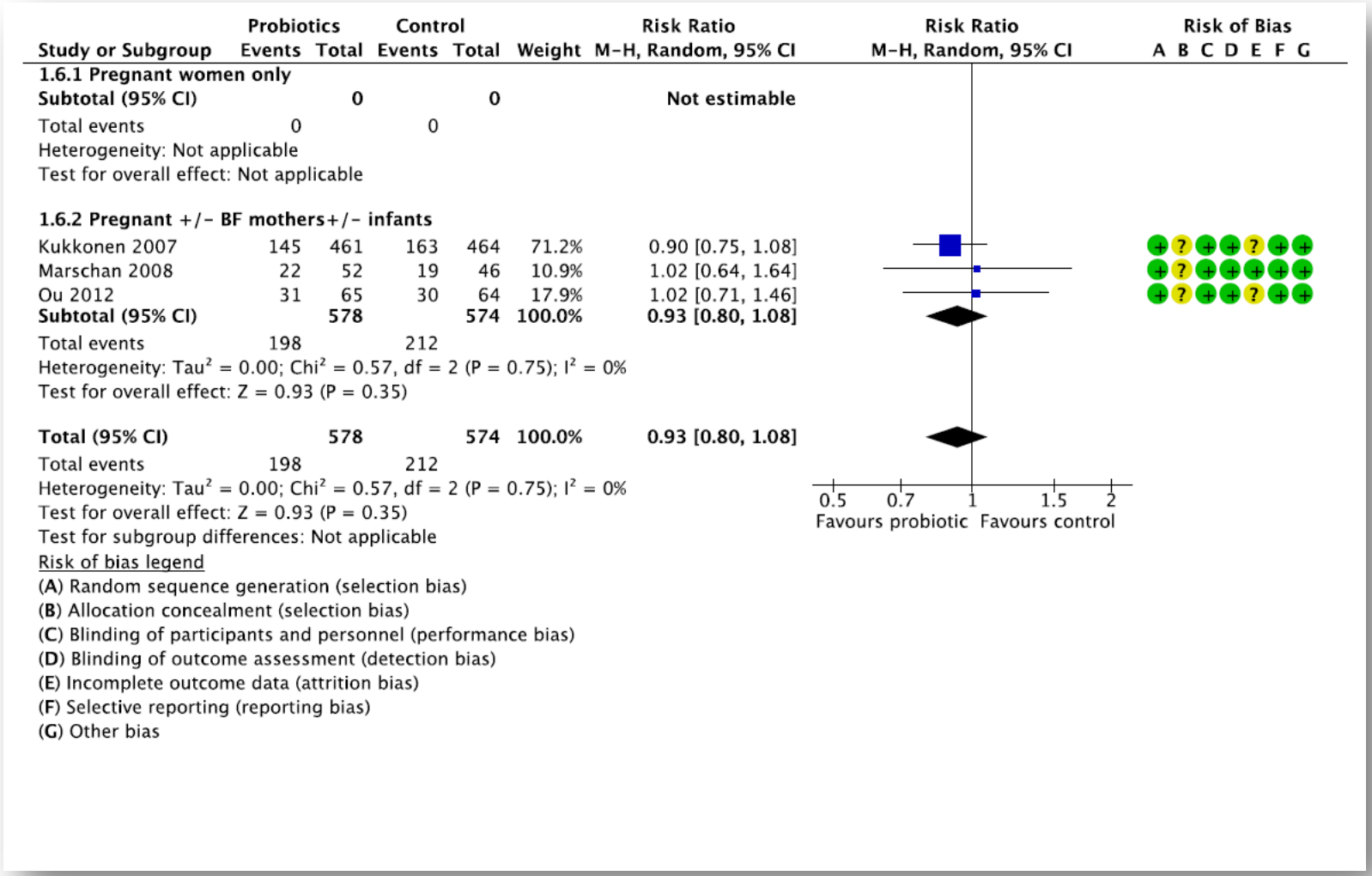


Study or Subgroup	Probiotics Events	Total	Control Events	Total	Weight	Risk Ratio M-H, Random, 95% CI
1.1.1 Pregnant women only						
Boyle 2011	42	122	47	120	8.5%	0.88 [0.63, 1.22]
Subtotal (95% CI)		**122**		**120**	**8.5%**	**0.88 [0.63, 1.22]**
Total events	42		47			
Heterogeneity: Not applicable						
Test for overall effect: Z = 0.76 (P = 0.45)						
1.1.2 Pregnant +/- BF mothers+/- infants						
Abrahamsson 2007	34	95	32	93	7.5%	1.04 [0.70, 1.53]
Allen 2012	75	220	76	234	9.8%	1.05 [0.81, 1.36]
Dotterud 2010	29	138	48	140	7.4%	0.61 [0.41, 0.91]
Huurre 2008	7	72	12	68	2.8%	0.55 [0.23, 1.32]
Kalliomaki 2001a	15	64	31	68	5.7%	0.51 [0.31, 0.86]
Kim 2010	12	33	22	35	5.6%	0.58 [0.34, 0.97]
Kopp 2008	14	50	12	44	4.2%	1.03 [0.53, 1.98]
Kukkonen 2007	57	459	82	463	8.9%	0.70 [0.51, 0.96]
Marschan 2008	16	52	18	46	5.3%	0.79 [0.46, 1.35]
Niers 2009	23	50	30	48	7.8%	0.74 [0.51, 1.07]
Ou 2012	16	65	16	64	4.7%	0.98 [0.54, 1.80]
Rautava 2002	4	27	14	30	2.3%	0.32 [0.12, 0.85]
Rautava 2012	21	73	44	62	7.4%	0.41 [0.27, 0.60]
Wickens 2008a	23	157	22	80	5.6%	0.53 [0.32, 0.89]
Wickens 2008b	38	158	21	79	6.4%	0.90 [0.57, 1.43]
Subtotal (95% CI)		**1713**		**1554**	**91.5%**	**0.71 [0.59, 0.84]**
Total events	384		480			
Heterogeneity: $Tau^2 = 0.06$; $Chi^2 = 30.03$, df = 14 (P = 0.008); $I^2 = 53\%$						
Test for overall effect: Z = 3.88 (P = 0.0001)						
Total (95% CI)		**1835**		**1674**	**100.0%**	**0.72 [0.61, 0.85]**
Total events	426		527			
Heterogeneity: $Tau^2 = 0.05$; $Chi^2 = 31.01$, df = 15 (P = 0.009); $I^2 = 52\%$						
Test for overall effect: Z = 3.95 (P < 0.0001)						
Test for subgroup differences: $Chi^2 = 1.31$, df = 1 (P = 0.25), $I^2 = 23.5\%$						

Risk of bias legend
(**A**) Random sequence generation (selection bias)
(**B**) Allocation concealment (selection bias)
(**C**) Blinding of participants and personnel (performance bias)
(**D**) Blinding of outcome assessment (detection bias)
(**E**) Incomplete outcome data (attrition bias)
(**F**) Selective reporting (reporting bias)
(**G**) Other bias

Cuello-Garcia CA. Probiotics for the prevention of allergy: A systematic review and meta-analysis of randomized controlled trials. J Allergy Clin Immunol. 2015 Jun 1 [Epub ahead of print]

Probiotics in pregnancy & any allergy



Study or Subgroup	Probiotics Events	Total	Control Events	Total	Weight	Risk Ratio M-H, Random, 95% CI
1.6.1 Pregnant women only						
Subtotal (95% CI)		**0**		**0**		**Not estimable**
Total events	0		0			
Heterogeneity: Not applicable						
Test for overall effect: Not applicable						
1.6.2 Pregnant +/- BF mothers+/- infants						
Kukkonen 2007	145	461	163	464	71.2%	0.90 [0.75, 1.08]
Marschan 2008	22	52	19	46	10.9%	1.02 [0.64, 1.64]
Ou 2012	31	65	30	64	17.9%	1.02 [0.71, 1.46]
Subtotal (95% CI)		**578**		**574**	**100.0%**	**0.93 [0.80, 1.08]**
Total events	198		212			
Heterogeneity: $Tau^2 = 0.00$; $Chi^2 = 0.57$, df = 2 (P = 0.75); $I^2 = 0\%$						
Test for overall effect: Z = 0.93 (P = 0.35)						
Total (95% CI)		**578**		**574**	**100.0%**	**0.93 [0.80, 1.08]**
Total events	198		212			
Heterogeneity: $Tau^2 = 0.00$; $Chi^2 = 0.57$, df = 2 (P = 0.75); $I^2 = 0\%$						
Test for overall effect: Z = 0.93 (P = 0.35)						
Test for subgroup differences: Not applicable						

Risk of bias legend
(A) Random sequence generation (selection bias)
(B) Allocation concealment (selection bias)
(C) Blinding of participants and personnel (performance bias)
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(G) Other bias

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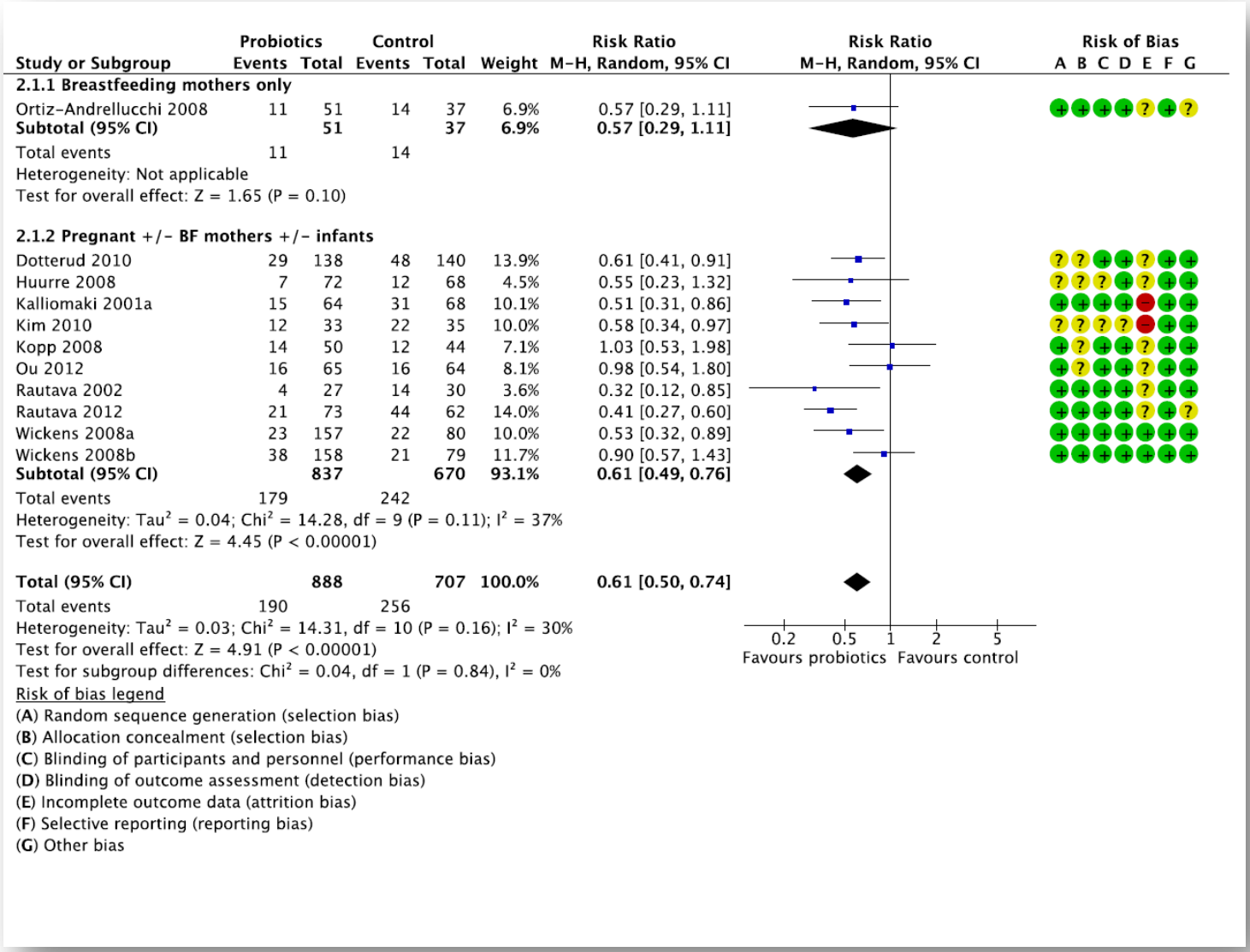
Probiotics in breastfeeding & eczema



Study or Subgroup	Probiotics Events	Total	Control Events	Total	Weight	Risk Ratio M-H, Random, 95% CI
2.1.1 Breastfeeding mothers only						
Ortiz-Andrellucchi 2008	11	51	14	37	6.9%	0.57 [0.29, 1.11]
Subtotal (95% CI)		**51**		**37**	**6.9%**	**0.57 [0.29, 1.11]**
Total events	11		14			
Heterogeneity: Not applicable						
Test for overall effect: Z = 1.65 (P = 0.10)						
2.1.2 Pregnant +/- BF mothers +/- infants						
Dotterud 2010	29	138	48	140	13.9%	0.61 [0.41, 0.91]
Huurre 2008	7	72	12	68	4.5%	0.55 [0.23, 1.32]
Kalliomaki 2001a	15	64	31	68	10.1%	0.51 [0.31, 0.86]
Kim 2010	12	33	22	35	10.0%	0.58 [0.34, 0.97]
Kopp 2008	14	50	12	44	7.1%	1.03 [0.53, 1.98]
Ou 2012	16	65	16	64	8.1%	0.98 [0.54, 1.80]
Rautava 2002	4	27	14	30	3.6%	0.32 [0.12, 0.85]
Rautava 2012	21	73	44	62	14.0%	0.41 [0.27, 0.60]
Wickens 2008a	23	157	22	80	10.0%	0.53 [0.32, 0.89]
Wickens 2008b	38	158	21	79	11.7%	0.90 [0.57, 1.43]
Subtotal (95% CI)		**837**		**670**	**93.1%**	**0.61 [0.49, 0.76]**
Total events	179		242			
Heterogeneity: $Tau^2 = 0.04$; $Chi^2 = 14.28$, df = 9 (P = 0.11); $I^2 = 37\%$						
Test for overall effect: Z = 4.45 (P < 0.00001)						
Total (95% CI)		**888**		**707**	**100.0%**	**0.61 [0.50, 0.74]**
Total events	190		256			
Heterogeneity: $Tau^2 = 0.03$; $Chi^2 = 14.31$, df = 10 (P = 0.16); $I^2 = 30\%$						
Test for overall effect: Z = 4.91 (P < 0.00001)						
Test for subgroup differences: $Chi^2 = 0.04$, df = 1 (P = 0.84), $I^2 = 0\%$						

Risk of bias legend
(A) Random sequence generation (selection bias)
(B) Allocation concealment (selection bias)
(C) Blinding of participants and personnel (performance bias)
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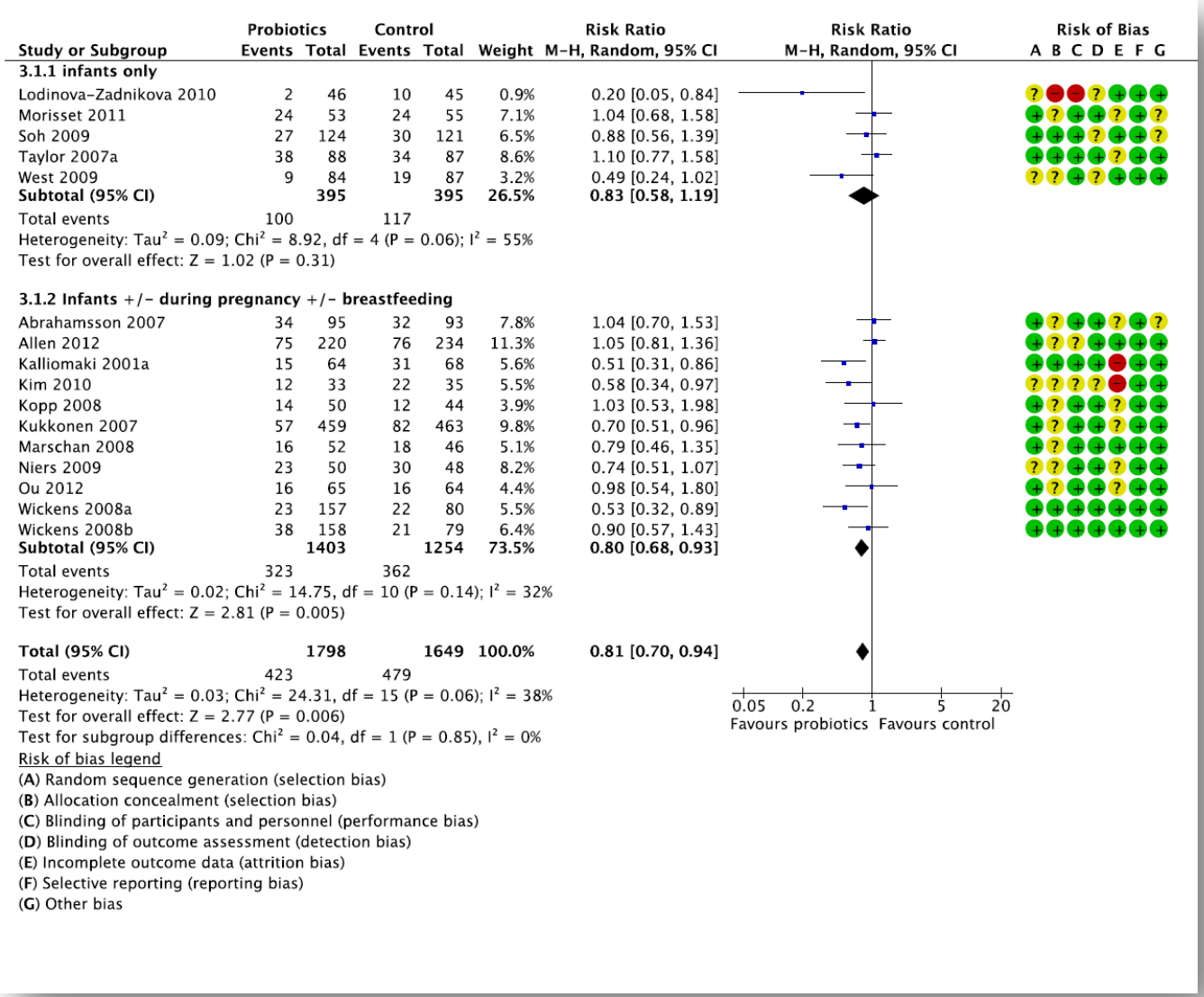
Probiotics in infancy & eczema



Study or Subgroup	Probiotics Events	Total	Control Events	Total	Weight	Risk Ratio M-H, Random, 95% CI	Risk of Bias A B C D E F G
3.1.1 infants only							
Lodinova-Zadnikova 2010	2	46	10	45	0.9%	0.20 [0.05, 0.84]	? - - ? + + +
Morisset 2011	24	53	24	55	7.1%	1.04 [0.68, 1.58]	+ ? + + ? + ?
Soh 2009	27	124	30	121	6.5%	0.88 [0.56, 1.39]	+ + + ? + + ?
Taylor 2007a	38	88	34	87	8.6%	1.10 [0.77, 1.58]	+ + + + ? + +
West 2009	9	84	19	87	3.2%	0.49 [0.24, 1.02]	? ? + ? + + +
Subtotal (95% CI)		**395**		**395**	**26.5%**	**0.83 [0.58, 1.19]**	
Total events	100		117				
Heterogeneity: $Tau^2 = 0.09$; $Chi^2 = 8.92$, df = 4 (P = 0.06); $I^2 = 55\%$							
Test for overall effect: Z = 1.02 (P = 0.31)							
3.1.2 Infants +/- during pregnancy +/- breastfeeding							
Abrahamsson 2007	34	95	32	93	7.8%	1.04 [0.70, 1.53]	+ ? + + ? + ?
Allen 2012	75	220	76	234	11.3%	1.05 [0.81, 1.36]	+ ? ? + + + +
Kalliomaki 2001a	15	64	31	68	5.6%	0.51 [0.31, 0.86]	+ + + + - + +
Kim 2010	12	33	22	35	5.5%	0.58 [0.34, 0.97]	? ? ? ? - + +
Kopp 2008	14	50	12	44	3.9%	1.03 [0.53, 1.98]	+ ? + + ? + +
Kukkonen 2007	57	459	82	463	9.8%	0.70 [0.51, 0.96]	+ ? + + ? + +
Marschan 2008	16	52	18	46	5.1%	0.79 [0.46, 1.35]	+ ? + + + + +
Niers 2009	23	50	30	48	8.2%	0.74 [0.51, 1.07]	? ? + + ? + +
Ou 2012	16	65	16	64	4.4%	0.98 [0.54, 1.80]	+ ? + + ? + +
Wickens 2008a	23	157	22	80	5.5%	0.53 [0.32, 0.89]	+ + + + + + +
Wickens 2008b	38	158	21	79	6.4%	0.90 [0.57, 1.43]	+ + + + + + +
Subtotal (95% CI)		**1403**		**1254**	**73.5%**	**0.80 [0.68, 0.93]**	
Total events	323		362				
Heterogeneity: $Tau^2 = 0.02$; $Chi^2 = 14.75$, df = 10 (P = 0.14); $I^2 = 32\%$							
Test for overall effect: Z = 2.81 (P = 0.005)							
Total (95% CI)		**1798**		**1649**	**100.0%**	**0.81 [0.70, 0.94]**	
Total events	423		479				
Heterogeneity: $Tau^2 = 0.03$; $Chi^2 = 24.31$, df = 15 (P = 0.06); $I^2 = 38\%$							
Test for overall effect: Z = 2.77 (P = 0.006)							
Test for subgroup differences: $Chi^2 = 0.04$, df = 1 (P = 0.85), $I^2 = 0\%$							

Risk of bias legend
(**A**) Random sequence generation (selection bias)
(**B**) Allocation concealment (selection bias)
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Fiocchi *et al. World Allergy Organization Journal* _####################_
DOI 10.1186/s40413-015-0055-2

WAO journal
WORLD ALLERGY ORGANIZATION

POSITION ARTICLE AND GUIDELINES Open Access

World Allergy Organization-McMaster University Guidelines for Allergic Disease Prevention (GLAD-P): Probiotics

Alessandro Fiocchi[1†], Ruby Pawankar[2†], Carlos Cuello-Garcia[3,4], Kangmo Ahn[5], Suleiman Al-Hammadi[6], Arnav Agarwal[3,7], Kirsten Beyer[8], Wesley Burks[9], Giorgio W Canonica[10], Motohiro Ebisawa[11], Shreyas Gandhi[3,7], Rose Kamenwa[12], Bee Wah Lee[13], Haiqi Li[14], Susan Prescott[15], John J Riva[16], Lanny Rosenwasser[17], Hugh Sampson[18], Michael Spigler[19], Luigi Terracciano[20], Andrea Vereda-Ortiz[22], Susan Waserman[21], Juan José Yepes-Nuñez[3], Jan L Brożek[3,21*] and Holger J Schünemann[3,21]

Abstract

Background: Prevalence of allergic diseases in infants, whose parents and siblings do not have allergy, is approximately 10% and reaches 20–30% in those with an allergic first-degree relative. Intestinal microbiota may modulate immunologic and inflammatory systemic responses and, thus, influence development of sensitization and allergy. Probiotics have been reported to modulate immune responses and their supplementation has been proposed as a preventive intervention.

Objective: The World Allergy Organization (WAO) convened a guideline panel to develop evidence-based recommendations about the use of probiotics in the prevention of allergy.

Methods: We identified the most relevant clinical questions and performed a systematic review of randomized controlled trials of probiotics for the prevention of allergy. We followed the Grading of Recommendations Assessment, Development and Evaluation (GRADE) approach to develop recommendations. We searched for and reviewed the evidence about health effects, patient values and preferences, and resource use (up to November 2014). We followed the GRADE evidence-to-decision framework to develop recommendations.

Results: Currently available evidence does not indicate that probiotic supplementation reduces the risk of developing allergy in children. However, considering all critical outcomes in this context, the WAO guideline panel determined that there is a likely net benefit from using probiotics resulting primarily from prevention of eczema. The WAO guideline panel suggests: a) using probiotics in pregnant women at high risk for having an allergic child; b) using probiotics in women who breastfeed infants at high risk of developing allergy; and c) using probiotics in infants at high risk of developing allergy. All recommendations are conditional and supported by very low quality evidence.

Conclusions: WAO recommendations about probiotic supplementation for prevention of allergy are intended to support parents, clinicians and other health care professionals in their decisions whether to use probiotics in pregnancy and during breastfeeding, and whether to give them to infants.

Keywords: Allergy, Prevention, Probiotics, Practice guidelines, GRADE

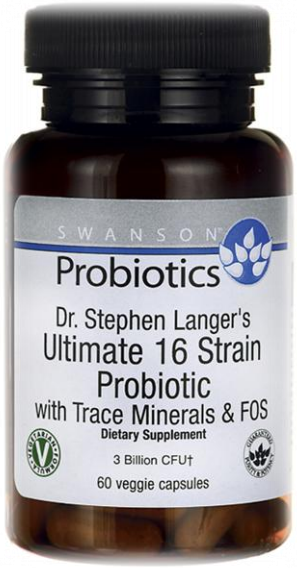
* Correspondence: brozekj@mcmaster.ca

Strains and species.

It is hard to define a role for probiotics on allergen sensitization or on other manifestations of allergic disease including food allergy, wheezing and/or asthma or allergic rhinitis.

It is hypothesized that probiotics may play a role in modifying and regulating immune responses in early life.

The strain of probiotic may be an important factor in preventive efficacy.



Campbell DE. Probiotics and primary prevention of atopic disease: Are we closer to a firm evidence base for clinical use? Clinical & Experimental Allergy 2013:43, 978-80

Probiotics in everyday food (e.g. yoghurt or fermented milk)

We suggest not asking separate questions but rather treat them as selected specific sources of probiotics.

This does not mean we should forget them

Yoghurts & fermented milks should be treated as special cases of the more general questions about probiotics.

WAO / McMaster working group. GuideLines for Allergic Disease Prevention. WAO Journal, 2015; 8:3, 28 January 2015

Who are the high-risk children?

High risk for allergy in a child =

- a biological parent or sibling with existing or history of
  - allergic rhinitis,
  - asthma,
  - eczema,
  - food allergy.

WAO / McMaster working group. GuideLines for Allergic Disease Prevention. WAO Journal, 2015; 8:3, 28 January 2015

Should probiotics vs. no probiotics be used in pregnant women? How substantial are the anticipated effects?

Outcome	With	Without	Difference (per 100) (95%CI)	Relative effect (RR) (95%CI)	Certainty of the evidence (GRADE)
Eczema (follow-up 1 to 5 years)	365/1520 (24%)	484/1515 (31.9%)	9 fewer per 100	RR 0.72 (0.6 to 0.86)	⨁⊖⊖⊖ VERY LOW
Asthma/wheezing (follow-up 2 to 7 years)	143/992 (14.4%)	139/982 (14.2%)	0 fewer per 100	RR 0.97 (0.77 to 1.22)	⨁⨁⊖⊖ LOW
Food allergy (follow-up 1 to 2 years)	36/279 (12.9%)	41/284 (14.4%)	1 more per 100	RR 1.08 (0.73 to 1.59)	⨁⊖⊖⊖ VERY LOW
Adverse effects	101/394 (25.6%)	88/397 (22.2%)	3 more per 100	RR 1.13 (0.82 to 1.52)	⨁⊖⊖⊖ VERY LOW

WAO / McMaster working group. GuideLines for Allergic Disease Prevention. WAO Journal, 2015; 8:3, 28 January 2015

Pregnancy

The WAO guideline panel suggests using probiotics in pregnant women at high risk for allergy in their children

Considering all critical outcomes → net benefit resulting primarily from prevention of eczema

WAO / McMaster working group.
GuideLines for Allergic Disease Prevention.
WAO Journal, 2015; 8:3, 28 January 2015

Should probiotics vs. no probiotics be used in breastfeeding women?

Outcome	With	Without	Difference (per 100) (95%CI)	Relative effect (RR) (95%CI)	Certainty of the evidence (GRADE)
Eczema (follow-up 6 months)	129/573 (22.5%)	213/548 (38.9%)	16 fewer per 100	RR 0.58 (0.47 to 0.72)	⨁⊖⊖⊖ VERY LOW
Asthma/wheezing (follow-up 1 to 4 years)	31/256 (12.1%)	26/266 (9.8%)	3 more per 100	RR 1.29 (0.58 to 2.86)	⨁⊖⊖⊖ VERY LOW
Food allergy (follow-up 2 to 4 years)	8/82 (9.8%)	5/85 (5.9%)	4 more per 100	RR 1.7 (0.58 to 4.96)	⨁⊖⊖⊖ VERY LOW
Adverse effects (follow-up 2 years)	35/79 (44.3%)	24/70 (34.3%)	10 more per 100	RR 1.29 (0.85 to 1.77)	⨁⊖⊖⊖ VERY LOW

WAO / McMaster working group. GuideLines for Allergic Disease Prevention. WAO Journal, 2015; 8:3, 28 January 2015 – Report

Breastfeeding

The WAO guideline panel suggests using probiotics in women who breastfeed infants at high risk of developing allergy

Considering all critical outcomes → net benefit resulting primarily from prevention of eczema

WAO / McMaster working group. GuideLines for Allergic Disease Prevention. WAO Journal, 2015; 8:3, 28 January 2015

Should probiotics vs. no probiotics be used in breastfed infants?

Outcome	With	Without	Difference (per 100) (95%CI)	Relative effect (RR) (95%CI)	Certainty of the evidence (GRADE)
Eczema (follow-up 0.5 to 6 years)	373/1607 (23.2%)	457/1614 (28.3%)	5 fewer per 100	RR 0.82 (0.7 to 0.96)	⨁⨁⨁⨀ MODERATE
Asthma/wheezing (follow-up to 9 months)	153/1117 (13.7%)	171/1136 (15.1%)	15 fewer per 1000	RR 0.9 (0.68 to 1.2)	⨁⨁⨀⨀ LOW
Food allergy (follow-up 1 to 6 years)	29/323 (9%)	33/321 (10.3%)	1 fewer per 100	RR 0.9 (0.57 to 1.41)	⨁⨀⨀⨀ VERY LOW
Adverse effects (follow-up 4 to 24 months)	118/408 (28.9%)	114/421 (27.1%)	2 more per 100	RR 1.07 (0.71 to 1.53)	⨁⨀⨀⨀ VERY LOW

WAO / McMaster working group. GuideLines for Allergic Disease Prevention. WAO Journal, 2015; 8:3, 28 January 2015 – Report [Epub ahead of print], Jan 29, 2014

Infants

The WAO guideline panel suggests using probiotics in infants at high risk of developing allergies

Considering all critical outcomes → net benefit resulting primarily from prevention of eczema

WAO / McMaster working group. GuideLines for Allergic Disease Prevention. WAO Journal, 2015; 8:3, 28 January 2015

How large are the net benefit?

The intervention might be cost-effective:

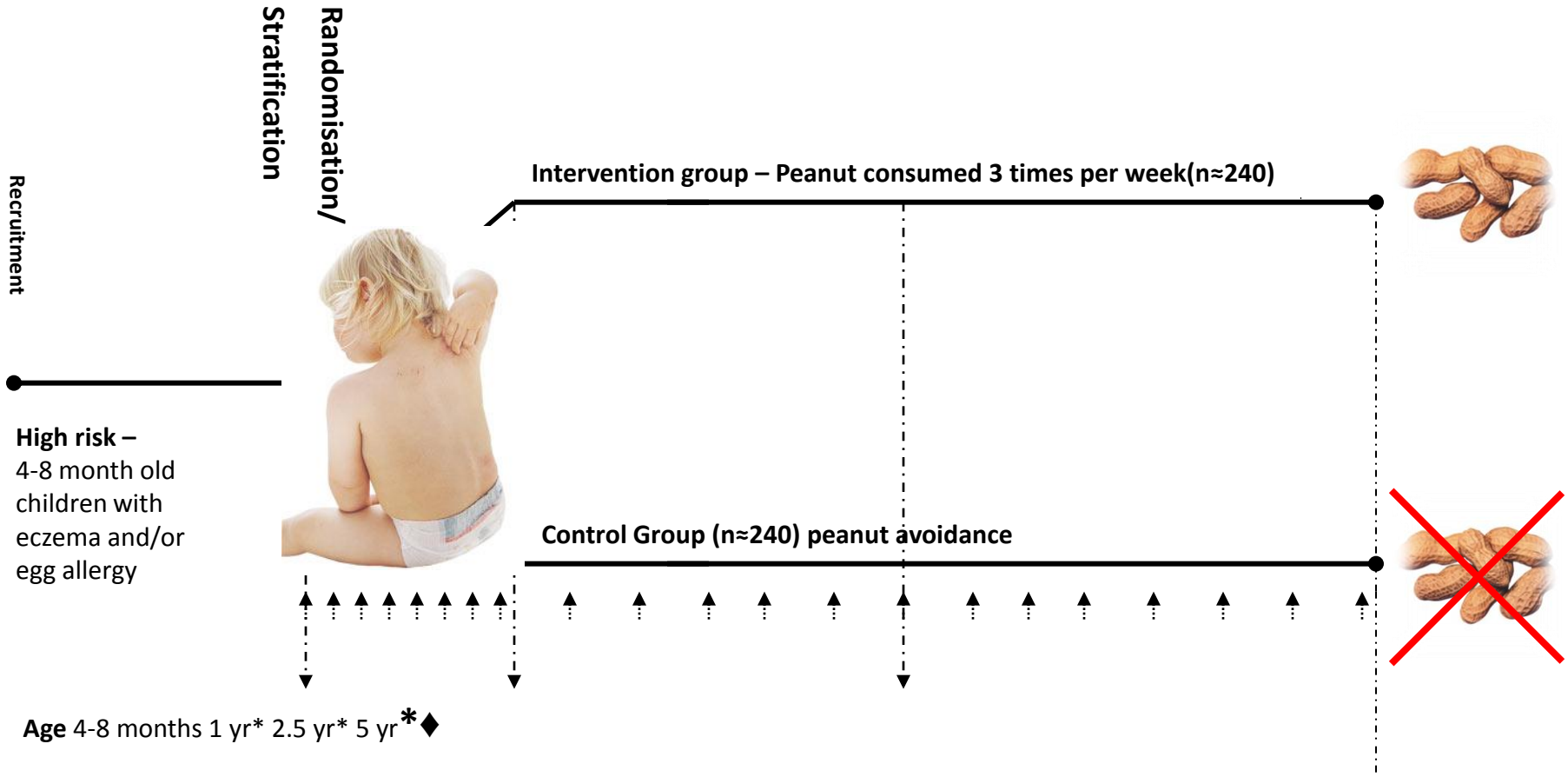
- fewer office visits ($17,400 to $34,100 /100 / year)

- Balance point for preventing 9 cases of eczema: $162 to 306/year

WAO / McMaster working group. GuideLines for Allergic Disease Prevention. WAO Journal, 2015; 8:3, 28 January 2015

1. Una malattia in aumento
2. Una malattia legata ai fattori sociali
3. Miti in allergia alimentare
4. Si può prevenire con I probiotici
5. Si può prevenire con l'alimentazione?
6. Conclusioni

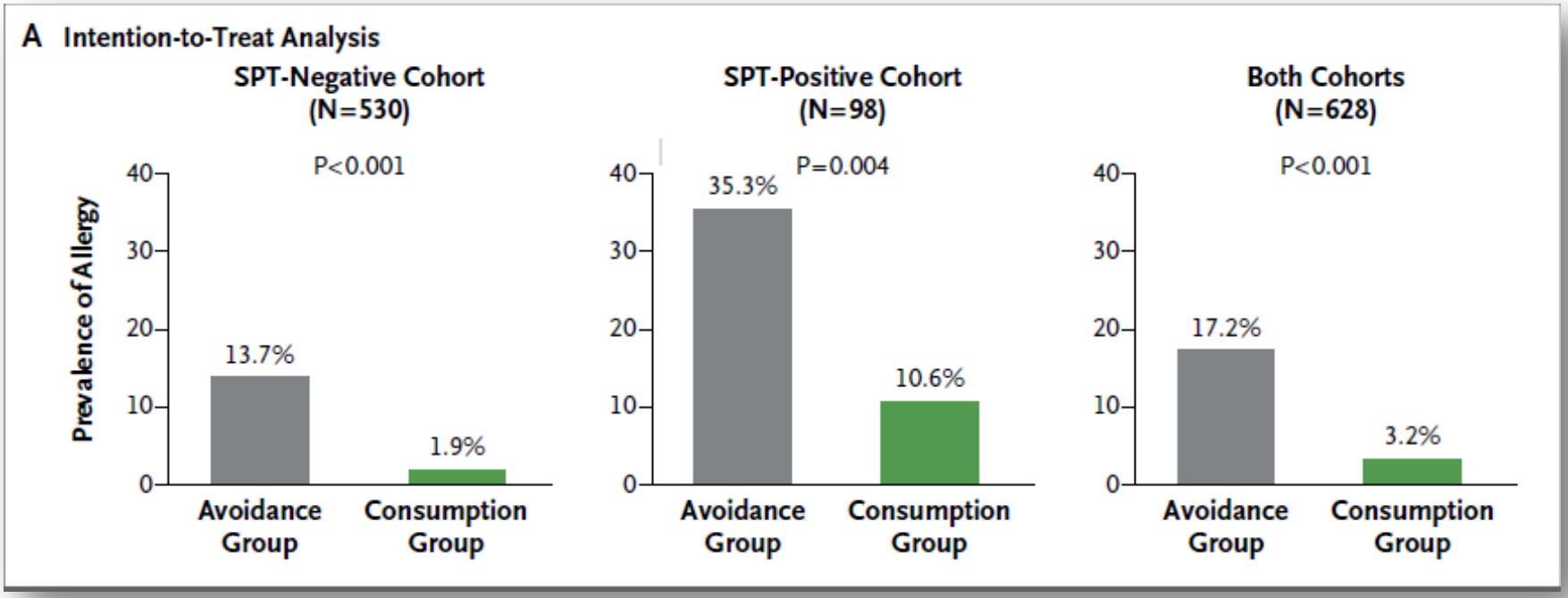
LEAP Study – Immune Tolerance Network – London, UK



Outcome: Prevalence of clinically-defined peanut allergy at 5 years of age.

NCT00329784 - Date of trial registration 23/05/2006 – contact person Gideon Lack

LEAP study: primary outcome



Du Toit G; LEAP Study Team. Randomized trial of peanut consumption in infants at risk for peanut allergy. N Engl J Med. 2015;372:803-13


Bambino Gesù
OSPEDALE PEDIATRICO


Bambino Gesù
OSPEDALE PEDIATRICO

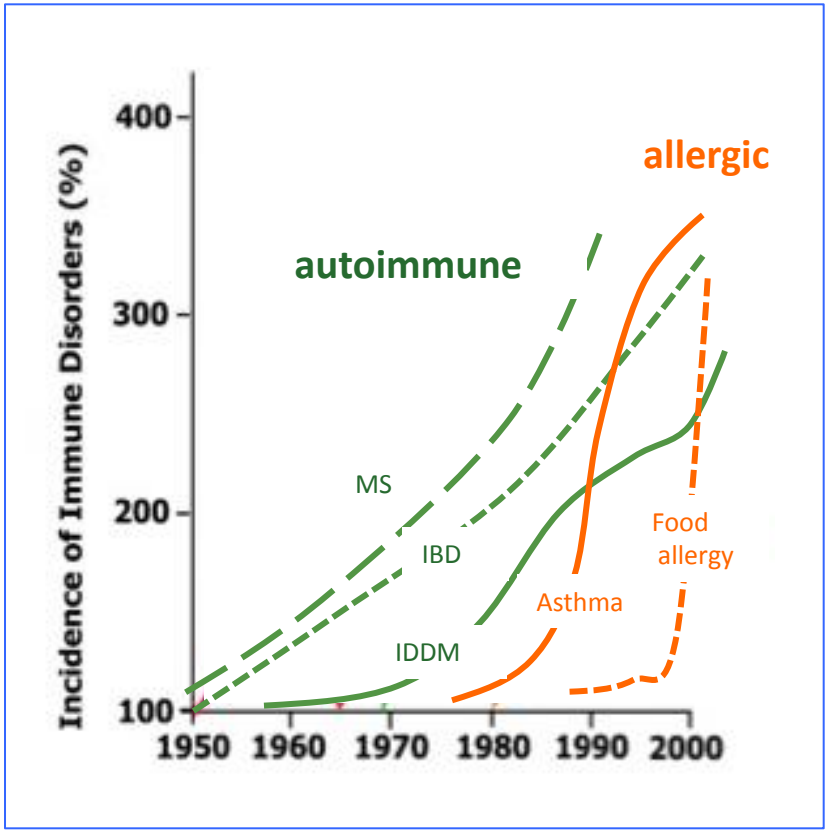

Bambino Gesù
OSPEDALE PEDIATRICO
NORMAL
PEANUT
BUTTER

There has been a rise in many immune diseases

Epidemic of allergic and autoimmune diseases suggests common mechanisms

Surely: changes in allergen exposure did not cause this !?

Surely: we cannot hope to solve this by early feeding with allergenic foods !?



Prescott S, Fiocchi A. Avoidance or exposure to foods in prevention and treatment of food allergy? Curr Opin Allergy Clin Immunol 2010,10:258–66

1. The waves of allergic disease
2. Epidemiological facts
3. Not only hygiene?
4. Prevention at weaning

5. Conclusions

1. Allergy is a disease of inequality
2. Epidemiological facts indicate hygiene as a driving factor
3. Early peanut may prevet peanut allergy
4. Weaning may have only marginal role in preventing allergy
5. Probiotics may prevent allergy

Allergy Prevention
can be achieved
without giving up
the benefits of civilization