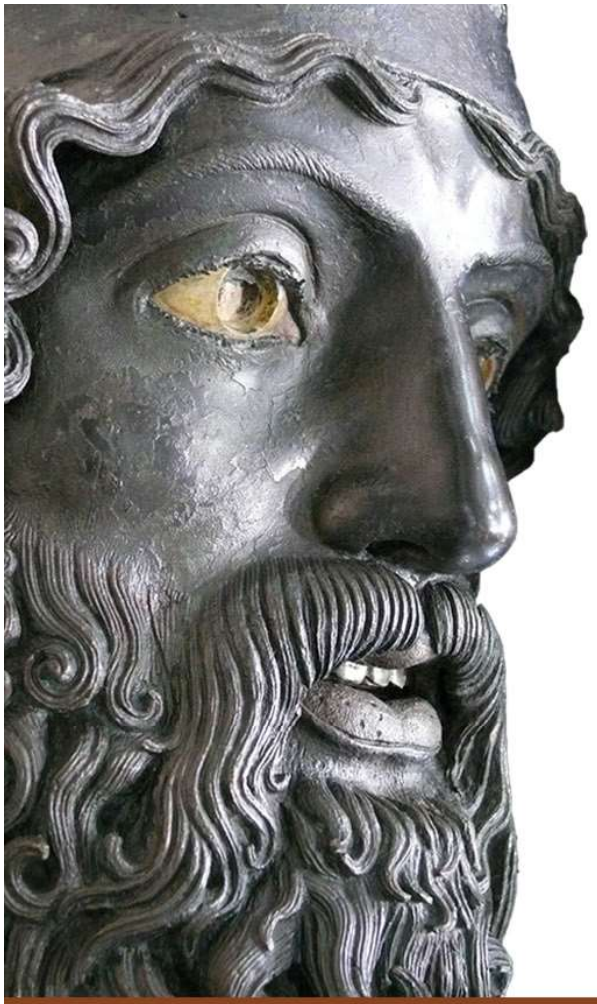


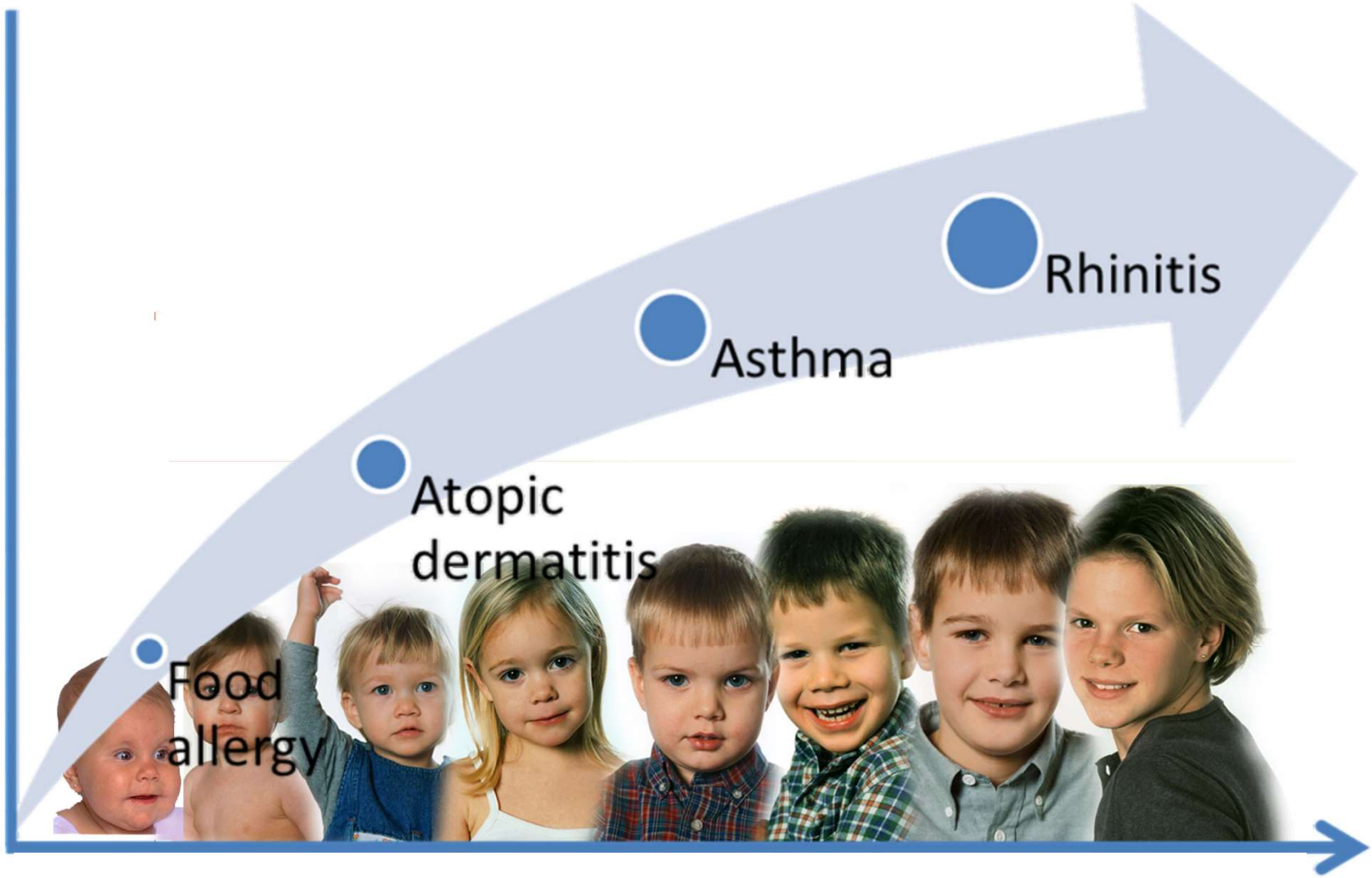
REGGIO CALABRIA 19-22 ottobre 2016

Associazione Allergologi Immunologi Italiani Territoriali e Ospedalieri
AAIITO

L'impatto della dieta sulla marcia allergica

Giuseppe Pingitore, Roma

VI CONGRESSO NAZIONALE AAIITO



La marcia allergica

Rinite allergica

European Community Respiratory Health Survey I

Table 1. Standardized (age and sex) prevalence of nasal allergy and atopy in subjects with nasal allergy

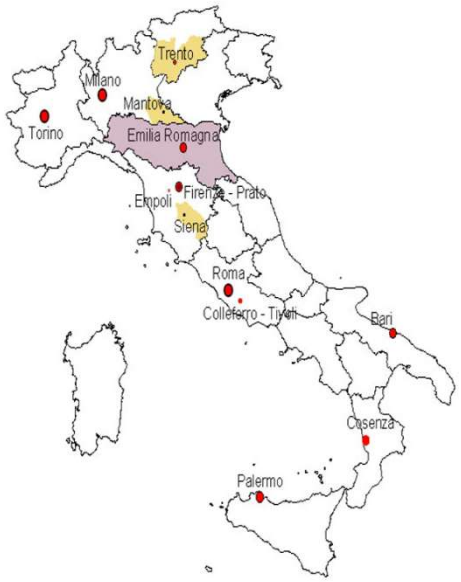
	Prevalence of 'nasal allergy'	Prevalence of atopic 'nasal allergy'	Prevalence of 'nasal allergy'		Prevalence of atopy in 'nasal allergy'	Prevalence of indoor–outdoor 'nasal symptoms on exposure'
			In atopic	In nonatopic		
Australia						
Melbourne (549)	46 (41.7–50.4)	31.8 (27.8–35.9)	84.7 (58.8–70.6)	27.9 (22.4–33.5)	69 (63–74.9)	64.1 (0–42.6)
Belgium						
Antwerp-City (322)	28.2 (23.2–33.3)	19.8 (15.3–24.3)	49.2 (40.3–58)	14.3 (9.1–19.5)	69.3 (60–78.6)	52.3 (42.6–24.3)
South-Antwerp (357)	25.5 (21–29.9)	14.3 (10.7–18)	49.1 (39.9–58.2)	15.3 (10.9–19.6)	57.4 (48.1–66.7)	48.7 (52.3–42.6)
Overall	26.3 (23–29.6)	16.4 (13.6–19.2)	49.1 (42.6–55.6)	14.7 (11.4–17.9)	62.4 (55.3–69.5)	49.9 (46.2–53.7)
France						
Bordeaux (543)	41.6 (37.4–45.8)	25.4 (21.8–29)	51.6 (54.6–68.7)	25.6 (20.9–30.3)	61.9 (56–67.7)	53.7 (51.6–43.9)
Grenoble (466)	29.1 (24.4–33.8)	20.9 (16.7–25.1)	51.6 (43.7–59.4)	13.7 (8.9–18.5)	71.5 (63.3–79.7)	51.6 (43.9–47.4)
Montpellier (434)	40.1 (35.1–45.2)	24.8 (20.2–29.3)	75.9 (68.3–83.4)	22.7 (17.3–28.2)	61.1 (53.7–68.5)	43.9 (47.4–45.5)
Paris (609)	32.9 (28.4–37.3)	18.2 (14.4–21.9)	50.3 (42.8–57.8)	23.5 (17.8–29.1)	56.1 (47.3–64.8)	47.4 (45.5–26.9)
Overall	36 (33.8–38.2)	22.7 (20.8–24.7)	59.3 (55.8–62.9)	21 (18.7–23.4)	62.9 (59.5–66.3)	49.6 (47.4–51.9)
Germany						
Erfurt (729)	12.1 (9.7–14.5)					24.3 (12.9–12.8)
Hamburg (1252)	24.7 (22.3–27.2)					42.6 (24.3–12.9)
Overall	20 (18.2–21.8)					35.7 (33.6–37.9)
Iceland						
Reykjavik (513)	23.6 (19.9–27.4)	11.2 (8.4–14)	51.2 (41.5–60.8)	15.7 (12.1–19.3)	46.9 (38.3–55.5)	28.5 (32.7–39.2)
Italy						
Pavia (281)	14.6 (10.1–19.1)	9.2 (5.5–13)	43.7 (31.2–56.1)	6.8 (3.4–10.2)	61.3 (49–73.6)	26.9 (42.1–45.6)
Turin (202)	21 (15.1–26.9)	17 (11.7–22.4)	49.4 (37.3–61.4)	6.1 (1.6–10.6)	80.6 (68–93.1)	42.1 (45.6–35)
Verona (337)	20.7 (16.4–25.1)	17.2 (13.1–21.2)	53.3 (43.8–62.7)	5.1 (2.3–7.9)	81.8 (72.8–90.8)	45.6 (35–31.1)
Overall	18.6 (15.9–21.3)	14.4 (12–16.9)	49.4 (43–55.9)	5.8 (3.9–7.8)	76.3 (69.4–83.3)	38.4 (35–41.8)
Ireland						
Dublin (303)	23.6 (18.8–28.3)	14.3 (10.3–18.3)	35.3 (26.8–43.7)	15.5 (10.4–20.6)	61.6 (51.1–72.1)	45.5 (26.9–42.1)
New Zealand						
Christchurch (340)	34.8 (29.7–39.9)	24.3 (19.8–28.9)	53.1 (45.2–60.9)	18.6 (13.1–24.1)	70.3 (62.3–78.2)	56.7 (64.5–67)
Hawkes-Bay (195)	35.1 (28.2–42)	24 (17.6–30.5)	53 (42.6–63.4)	18.9 (12.4–25.4)	71.6 (62.5–80.8)	64.5 (67–64.1)
Wellington (338)	43.9 (38.3–49.4)	28.7 (23.5–33.8)	60.8 (53–68.6)	30 (22.7–37.2)	66.1 (58–74.2)	67.7 (56.7–64.5)
Overall	38.2 (34.9–41.5)	25.8 (22.8–28.8)	55.8 (50.8–60.8)	23 (19.1–26.9)	68.3 (63.2–73.4)	62.5 (59.2–65.8)
Norway						
Bergen (781)	16.8 (14.2–19.5)	11.6 (9.3–13.9)	39.6 (33.2–46.1)	7.4 (5.2–9.5)	69.5 (62.2–76.9)	32.7 (39.2–39.8)

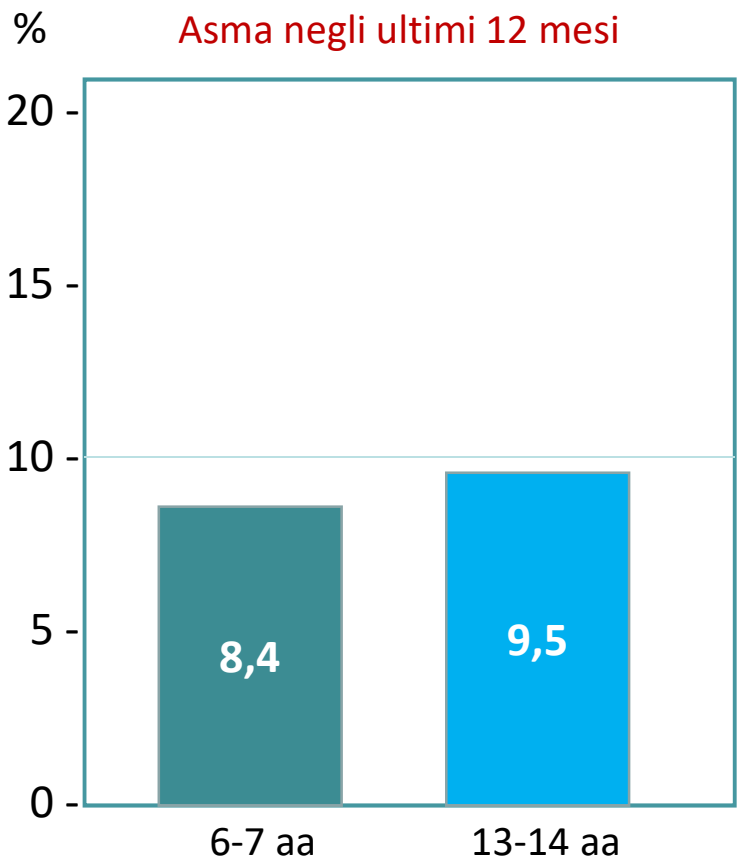
PJ Bousquet et al. Allergy 2008: 63: 1301–1309

Asma bronchiale

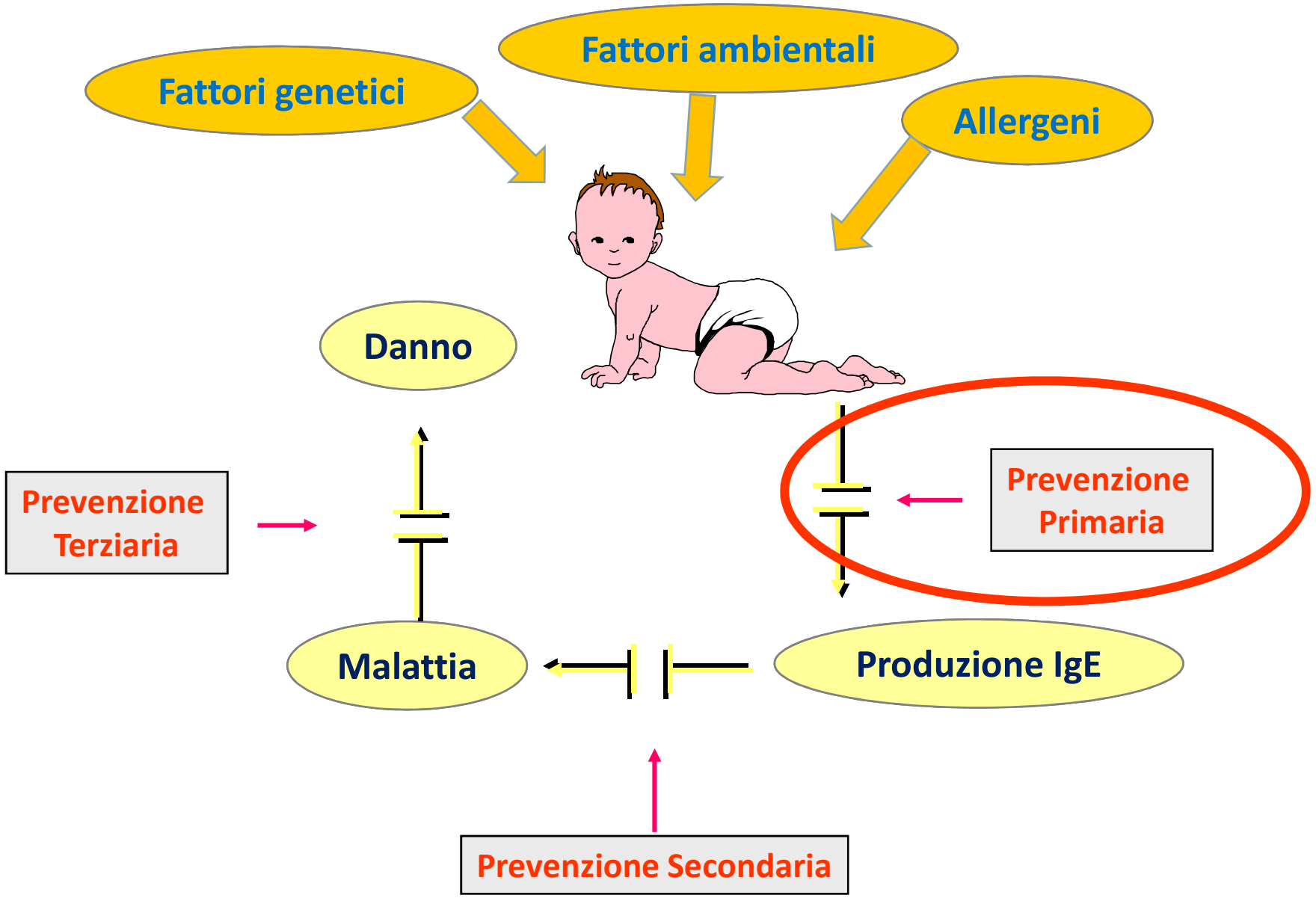
SIDRIA-2 2002

20016 bambini 6-7 anni
16175 adolescenti 13 anni





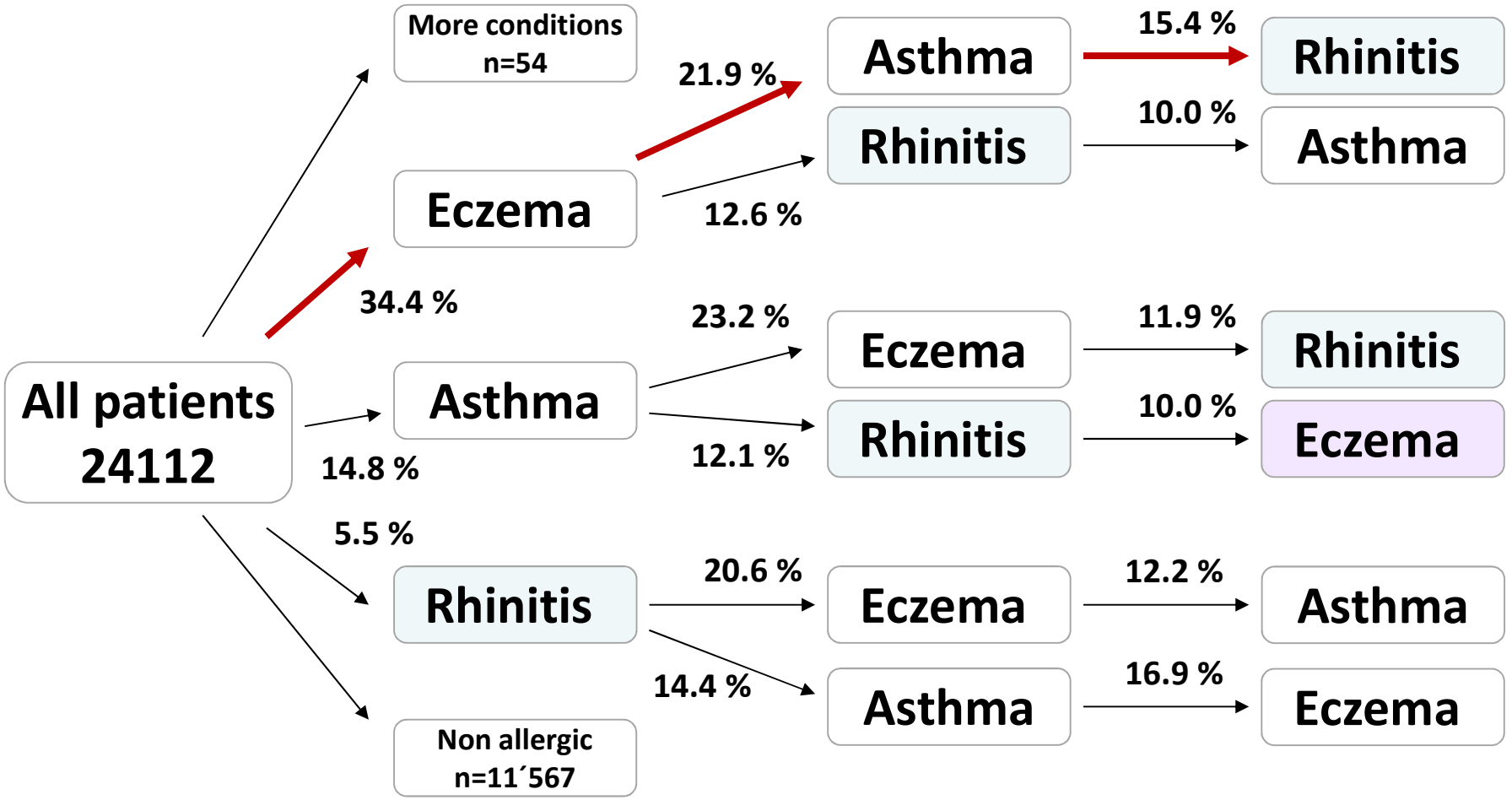
Sestini P et al. Epidemiol Prev 2005;29(2), Suppl:1-96.


Fattori genetici
Fattori ambientali
Allergeni
Danno
Prevenzione Terziaria
Prevenzione Primaria
Malattia
Produzione IgE
Prevenzione Secondaria

Bambino «a rischio»

lattante che presenta almeno un parente di 1° grado (padre, madre, fratello o sorella) affetto da patologia atopica documentata

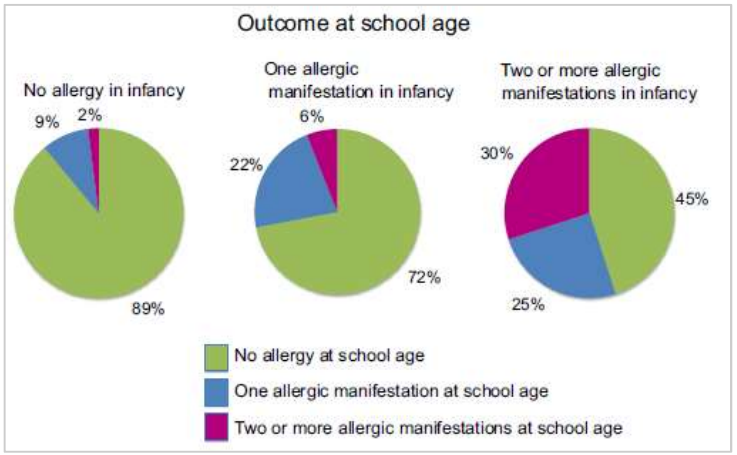
Sequential progression of diagnoses of multiple allergic conditions: variants of “the allergic march”

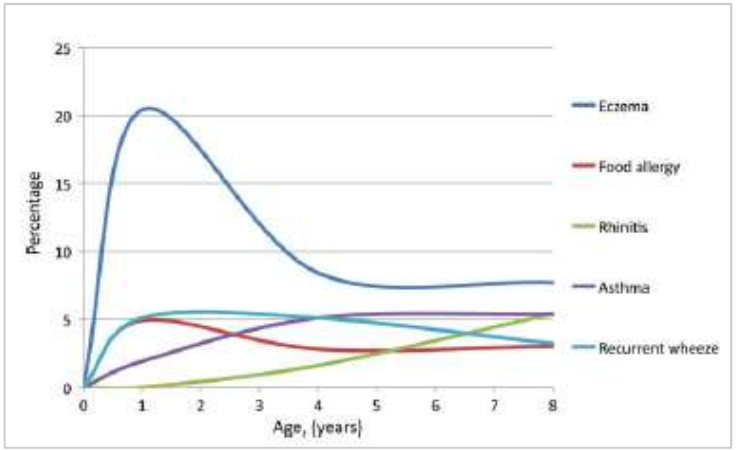


Punekar YS, Sheikh A. Clin exp Allergy 2009

The allergic march comprises the coexistence of related patterns of allergic disease not just the progressive development of one disease

- Inclusi 5654 bb nati in Svezia nel 2003
- Studio longitudinale per stabilire la relazione esistente tra le manifestazioni allergiche presenti nella prima infanzia e all'età di 8 anni
- **Conclusioni**: le malattie allergiche a 8 anni sono correlate al numero di manifestazioni allergiche presenti nella prima infanzia.
- Le manifestazioni sono simili in entrambe le età, ciò suggerisce una coesistenza di "*disease patterns*" più che uno sviluppo progressivo





Goksor E et al. Acta Paediatrica. Jul 2016

Dieta materna in gravidanza e durante l'allattamento

Sono utili le restrizioni dietetiche in gravidanza e durante l'allattamento?

- Non ci sono evidenze a favore della dieta di esclusione (incluso latte vaccino, uova, arachidi) durante la gravidanza, per la prevenzione delle malattie allergiche nel lattante a rischio

- La dieta di esclusione alla mamma durante l'allattamento non riduce nel bambino il rischio di malattie allergiche, come eczema ed asma

Netting MJ et al. Does maternal diet during pregnancy and lactation affect outcomes in offspring? A systematic review of food-based approaches. Nutrition. 2014 Nov-Dec;30(11-12):1225-41

Sono utili le restrizioni dietetiche in gravidanza e durante l'allattamento?

NESSUNA RESTRIZIONE

- Non ci sono evidenze a favore della dieta di esclusione (incluso latte vaccino, uova, arachidi) durante la gravidanza, per la prevenzione delle malattie allergiche nel lattante a rischio
- La dieta di esclusione alla mamma durante l'allattamento non riduce nel bambino il rischio di malattie allergiche, come eczema ed asma

Netting MJ et al. Does maternal diet during pregnancy and lactation affect outcomes in offspring? A systematic review of food-based approaches. Nutrition. 2014 Nov-Dec;30(11-12):1225-41

Latte materno

Ruolo preventivo del latte materno

- **Effetti benefici** del latte materno:
  - ridotta esposizione ad antigeni esogeni
  - protezione nei confronti di infezioni
  - promozione della maturazione della mucosa gastrointestinale
  - sviluppo di un microbiota intestinale “benefico”
  - presenza di sostanze ad azione immunomodulatoria e antinfiammatoria (immunoglobuline, citochine, cellule immunocompetenti)

Ruolo preventivo del latte materno

- Dati di letteratura controversi
- Non dimostrato in maniera univoca un effetto protettivo dell'allattamento al seno nei confronti della malattia allergica
- Tuttavia, per i riconosciuti effetti benefici nutrizionali, immunologici e psicologici, l'allattamento al seno esclusivo, **possibilmente per 6 mesi**, dovrebbe essere promosso in tutti i neonati

Szajewska H. IMAJ 2012;14:57-61; Fleischer DM et al. 2013;1:29-36; de Silva D et al. Allergy 2014;69:581-9; Gdalevich M et al. J Am Acad Dermatol 2001;45:520-7; Yang YW et al. Br J Dermatol 2009;161:373-83.

Quando il latte materno manca?

- *“If breastfeeding is not possible, a hydrolysed formula (usually a partially hydrolysed formula) is recommended for infants at high risk of allergic disease”*

Prescott S. Strategies to Prevent or Reduce Allergic Disease. Ann Nutr Metab 2011;59(suppl 1):28–42

Quando il latte materno manca?

- Le linee guida europee, americane ed australiane supportano l'uso delle formule idrolisate per la prevenzione primaria delle malattie allergiche, in bambini ad alto rischio che non sono allattati al seno.

Australasian Society of Clinical Immunology and Allergy. ASCIA Infant feeding advice. ASCIA, 2010. http://www.allergy.org.au/health professionals/papers/ascia-infant-feedingadvice

Fleischer DM,et al. Primary prevention of allergic disease through nutritional interventions. J Allergy Clin Immunol Pract 2013;1:29-36. doi: 10.1016/j.jaip.2012.09.003. 24229819

Muraro A, et al. EAACI Food Allergy and Anaphylaxis Guidelines Group. EAACI food allergy and anaphylaxis guidelines. Primary prevention of food allergy. Allergy 2014;69:590-601. doi:10.1111/all.12398. 24697491.

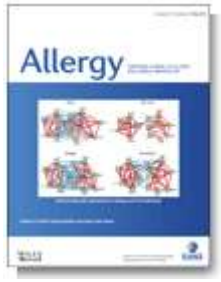
Sampson HA, et al. Food allergy: A practice parameter update—2014. JACI 2014 Nov;134(5):1016-25

Allergy EUROPEAN JOURNAL OF ALLERGY AND CLINICAL IMMUNOLOGY

POSITION PAPER

EAACI Food Allergy and Anaphylaxis Guidelines. Primary prevention of food allergy

A. Muraro[1,*], S. Halken[2,*], S. H. Arshad[3,4,5], K. Beyer[6], A. E. J. Dubois[7], G. Du Toit[8], P. A. Eigenmann[9], K. E. C. Grimshaw[3], A. Hoest[2], G. Lack[8], L. O'Mahony[10], N. G. Papadopoulos[11,12], S. Panesar[13], S. Prescott[14], G. Roberts[3,4,5], D. de Silva[13], C. Venter[4,15], V. Verhasselt[16], A. C. Akdis[17] & A. Sheikh[18,19] on behalf of EAACI Food Allergy and Anaphylaxis Guidelines Group



Allergy 2014; 69: 590–601

Box 6: Summary of recommendations for primary prevention of food allergy

Recommendations for all infants:

- No special diet during pregnancy or for the lactating mother.
- Exclusively breastfeeding for 4–6 months.

Further recommendations for high-risk infants:

- If supplement is needed during the first 4 months, a documented hypoallergenic formula is recommended.

Introduction of complementary foods after the age of 4 months according to normal standard weaning practices and nutrition recommendations, for all children irrespective of atopic heredity.

Level of evidence I, Grades of recommendation A-B

The German Infant Nutritional Intervention Study (GINI)

2003

- Between 1995 and 1998, **2252 infants** with a **hereditary risk for atopy** were enrolled in the German Infant Nutritional Intervention Study and randomly assigned at birth to one of 4 blinded formulas:
  - CMF
  - partially hydrolyzed whey formula (pHF-W)
  - extensively hydrolyzed whey formula (eHF-W)
  - extensively hydrolyzed casein formula (eHF-C)
- The primary end point **at 1 year of age** was the presence of **allergic manifestation** (atopic dermatitis, gastrointestinal manifestation of food allergy, allergic urticaria, or a combination of these factors)

A Von Berg et al. J Allergy Clin Immunol 2003;111:533-40

The German Infant Nutritional Intervention Study (GINI)

2003

TABLE IV. Results of the multivariable models: Adjusted OR for AM and AD dependent on the feeding regimen and stratified by AD in family history

			CMF	pHF-W	eHF-W	eHF-C
AM	All	Incidence, n/N (%)	40/256 (16)	26/241 (11)	34/238 (14)	19/210 (9)
		Adjusted OR* (95% CI)	1	0.65 (0.38-1.1)	0.86 (0.52-1.4)	0.51 (0.28-0.92)
		P value		.109	.544	.025
	No AD in FH	Incidence, n/N (%)	22/165 (13)	14/162 (9)	11/142 (8)	10/134 (7)
		Adjusted OR† (95% CI)	1	0.63 (0.31-1.3)	0.55 (0.26-1.2)	0.51 (0.23-1.1)
		P value		.210	.131	.101
	AD in FH	Incidence, n/N (%)	18/91 (20)	12/79 (15)	23/96 (24)	9/76 (12)
		Adjusted OR† (95% CI)	1	0.72 (0.32-1.6)	1.3 (0.63-2.5)	0.53 (0.22-1.3)
		P value		.426	.515	.148
AD	All	Incidence, n/N (%)	38/256 (15)	22/241 (9)	31/238 (13)	15/210 (7)
		Adjusted OR* (95% CI)	1	0.56 (0.32-0.99)	0.81 (0.48-1.4)	0.42 (0.22-0.79)
		P value		.048	.44	.007
	No AD in FH	Incidence, n/N (%)	21/165 (13)	10/162 (6)	11/142 (8)	8/134 (6)
		Adjusted OR† (95% CI)	1	0.46 (0.21-1.02)	0.58 (0.27-1.3)	0.42 (0.18-1.00)
		P value		.055	.173	.050
	AD in FH	Incidence, n/N (%)	17/91 (19)	12/79 (15)	20/96 (21)	7/76 (9)
		Adjusted OR† (95% CI)	1	0.75 (0.33-1.7)	1.1 (0.54-2.3)	0.43 (0.17-1.1)
		P value		.494	.757	.077

A Von Berg et al. J Allergy Clin Immunol 2003;111:533-40

Certain hydrolyzed formulas reduce the incidence of atopic dermatitis but not that of asthma: Three-year results of the German Infant Nutritional Intervention Study

2007

TABLE I. Results of the ITT analyses: PORs from marginal logistic models using GEE by study formula in comparison with cow's milk feeding

	CMF	pHF-W POR (95% CI)	eHF-W POR (95% CI)	eHF-C POR (95% CI)
All infants excluding exclusively breast-fed infants from the observational arm; completed 12-month follow-up, n = 1083; completed 3-year follow-up, n = 1017				
No. of followed children (N = 1363)	356	335	334	338
AM* period prevalence, first year (n = 144)	1	0.80 (0.51-1.24)	0.93 (0.62-1.41)	0.63 (0.40-1.01)
Period prevalence, third year (n = 192)	1	0.89 (0.57-1.37)	0.99 (0.65-1.51)	0.70 (0.44-1.11)
Cumulative incidence, birth to 3 years (n = 312)	1	0.87 (0.64-1.19)	1.03 (0.77-1.40)	0.80 (0.58-1.09)
AD period prevalence, first year (n = 130)	1	0.74 (0.46-1.18)	0.90 (0.59-1.39)	**0.54 (0.32-0.89)**
Period prevalence, third year (n = 86)	1	**0.52 (0.28-0.97)**	0.78 (0.45-1.38)	**0.53 (0.28-1.00)**
Cumulative incidence, birth to 3 years (n = 206)	1	0.76 (0.52-1.11)	0.99 (0.69-1.41)	**0.67 (0.45-0.99)**
Asthma period prevalence, third year (n = 111)	1	1.30 (0.75-2.27)	1.37 (0.79-2.36)	0.93 (0.51-1.69)

Follow-up età 3 anni: significativa riduzione dell'incidenza della DA nel gruppo con **eHF-C** (ITT) e nel gruppo **pHF-W** (PP) rispetto ai bambini che avevano assunto una formula di latte vaccino; nessuna riduzione dell'incidenza di asma.

A Von Berg et al. J Allergy Clin Immunol 2007;119: 718-25

Preventive effect of hydrolyzed infant formulas persists until age 6 years: Long-term results from the German Infant Nutritional Intervention Study (GINI)

2008

TABLE III. Prevalence of physician-diagnosed allergic diseases in the fourth to sixth years: relative risk and adjusted relative risk from marginal log-binomial models with generalized estimating equations by study formula in comparison with cow's milk feeding

	Prevalence (%)	CMF	pHF-W, RR (95% CI)	eHF-W, RR (95% CI)	eHF-C, RR (95% CI)
ITT AM*	21.6	1	0.82 (0.67-1.02)	0.85 (0.69-1.04)	0.82 (0.66-1.01)
AD	11.4	1	0.83 (0.61-1.12)	0.85 (0.63-1.15)	0.75 (0.55-1.03)
Rhinitis	6.6	1	0.87 (0.57-1.33)	0.66 (0.42-1.02)	0.82 (0.54-1.24)
Asthma	2.7	1	1.60 (0.74-3.45)	2.16 (1.02-4.58)	1.98 (0.92-4.29)
PP AM*†	20.0	1	0.71 (0.53-0.95)	0.61 (0.45-0.85)	0.62 (0.45-0.87)
AD‡	10.3	1	0.53 (0.34-0.84)	0.60 (0.39-0.93)	0.48 (0.29-0.78)
Rhinitis†	7.0	1	0.95 (0.55-1.63)	0.51 (0.26-1.02)	0.75 (0.40-1.41)
Asthma§‖	2.8	1	1.64 (0.59-4.53)	1.07 (0.34-3.38)	2.22 (0.77-6.41)

RR, Relative risk.
*Defined by any of physician-diagnosed AD, urticaria, food allergy/intolerance, asthma, and rhinitis.
†Adjusted for family history of AD, hay fever, and asthma, heredity of family allergy, sex, education, exposure to tobacco smoke, pets in the household, siblings, and study region.
‡Adjusted for family history of AD, sex, education, exposure to tobacco smoke, pets in the household, siblings, and study region.
§Adjusted for family history of asthma, heredity of family allergy, sex, education, exposure to tobacco smoke, pets in the household, siblings, and study region.
‖Estimated by using a logistic model because of low prevalences.

Follow-up età 6 anni: persiste effetto preventivo degli **eHF-C** e dei **pHF-W** sulle manifestazioni allergiche (riduzione significativa fino al 20%) e sulla DA.

A Von Berg et al. J Allergy Clin Immunol 2008;121:1442-7

Allergies in high-risk schoolchildren after early intervention with cow's milk protein hydrolysates: 10-year results from the German Infant Nutritional Intervention (GINI) study

2013

TABLE I. ITT analyses: cumulative incidence from 10-year follow-up and period prevalence at 7 to 10 years

	CMF	pHF-W	eHF-W	eHF-C
No. of followed children (n = 2252)	556	557	559	580
AM* cumulative incidence, birth to 10 y	63.1%	58.6%	59.9%	54.2%
RR (95% CI)	1	0.87 (0.77-0.99)	0.94 (0.83-1.07)	0.83 (0.72-0.95)
AM prevalence in 7th to 10th years (n = 1377)	34.3%	34.1%	35.0%	27.7%
RR (95% CI)	1	1.0 (0.81-1.23)	1.02 (0.83-1.26)	0.81 (0.64-1.01)
AD cumulative incidence, birth to 10 y	40.5%	35.3%	34.8%	29.3%
RR (95% CI)	1	0.82 (0.68-1.00)	0.91 (0.76-1.10)	0.72 (0.58-0.88)
AD prevalence in 7th to 10th years (n = 1389)	11.2%	13.2%	9.6%	8.2%
RR (95% CI)	1	1.18 (0.79-1.77)	0.86 (0.55-1.34)	0.74 (0.47-1.16)
Asthma cumulative incidence, 3-10 y	8.05%	11.4%	11.4%	8.9%
RR (95% CI)	1	1.56 (0.97-2.49)	1.58 (0.99-2.52)	1.08 (0.66-1.79)
Asthma prevalence in 7th to 10th years (n = 1407)	7.4%	9.3%	11.3%	6.3%
RR (95% CI)	1	1.26 (0.76-2.07)	1.53 (0.95-2.48)	0.85 (0.49-1.47)
Rhinitis cumulative incidence, 4-10 y	20.4%	18.9%	21.0%	18.7%
RR (95% CI)	1	0.95 (0.69-1.30)	0.93 (0.69-1.26)	0.92 (0.67-1.25)
Rhinitis prevalence in 7th to 10th years (n = 1393)	17.2%	14.7%	19.4%	14.0%
RR (95% CI)	1	0.85 (0.60-1.21)	1.13 (0.82-1.55)	0.82 (0.58-1.15)

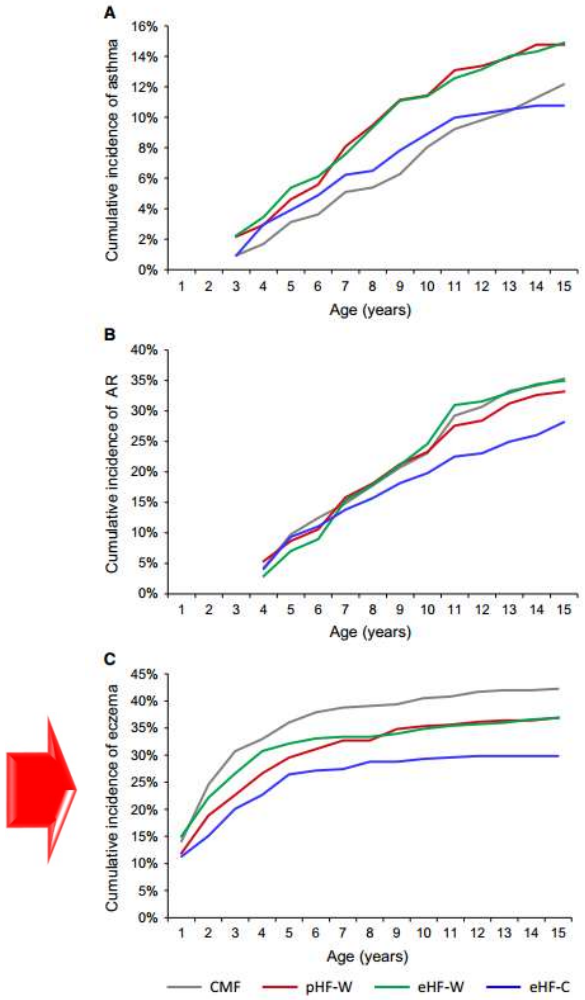
RRs are from log-binomial models using the 3 different hydrolysate formulas in comparison with CMF.
*Defined as any of the following: physician-diagnosed AD, urticaria and food allergy/intolerance, asthma (start at third year), and rhinitis (start at fourth year).

Follow-up età 10 anni: persiste effetto preventivo sull' incidenza cumulativa delle malattie allergiche, soprattutto DA, con **eHF-C** e **pHF-W**. Nessun effetto preventivo sull'asma e sulla rinite allergica.

A Von Berg et al. J Allergy Clin Immunol 2013;131:1565-73

Allergic manifestation 15 years after early intervention with hydrolyzed formulas – the GINI Study

2016



- **Incidenza cumulativa delle manifestazioni allergiche: asma, rinite allergica ed eczema fino ai 15 anni di età nei tre gruppi con le differenti formule idrolisate e nel gruppo con il latte vaccino**

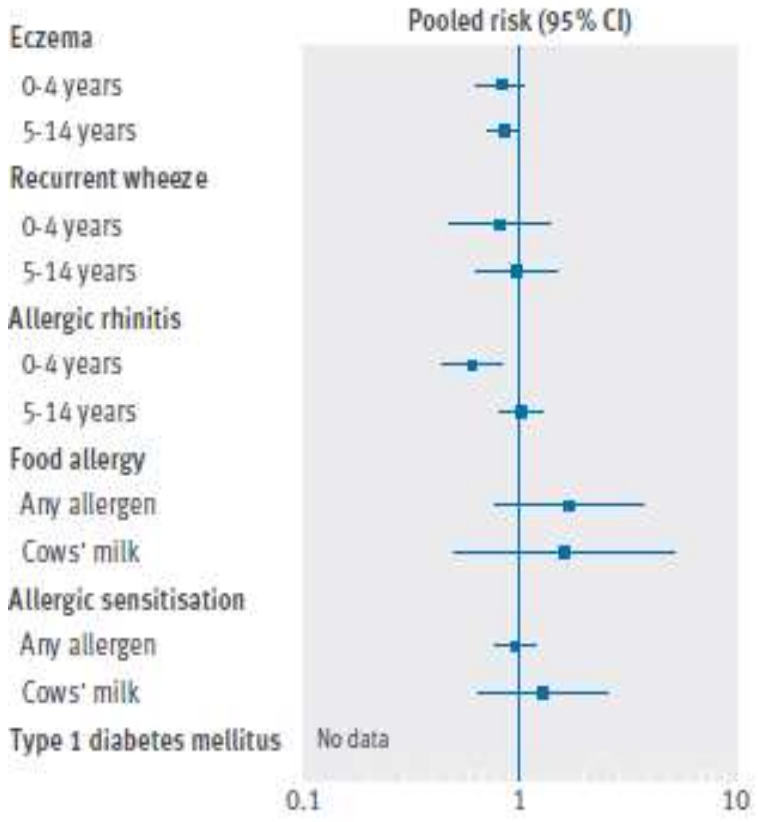
Conclusioni

- I risultati dei 15 anni di follow-up confermano l'effetto preventivo delle formule eHF-C e pHF-W **sull'eczema**, dalla nascita fino all'adolescenza.
- Durante gli anni 11-15 riduzione dell'incidenza della rinite allergica e dell' asma con l'uso della formula eHF-C.
- Questi risultati sulle allergie respiratorie vanno interpretati con **cautela** e confermati con ulteriori studi.

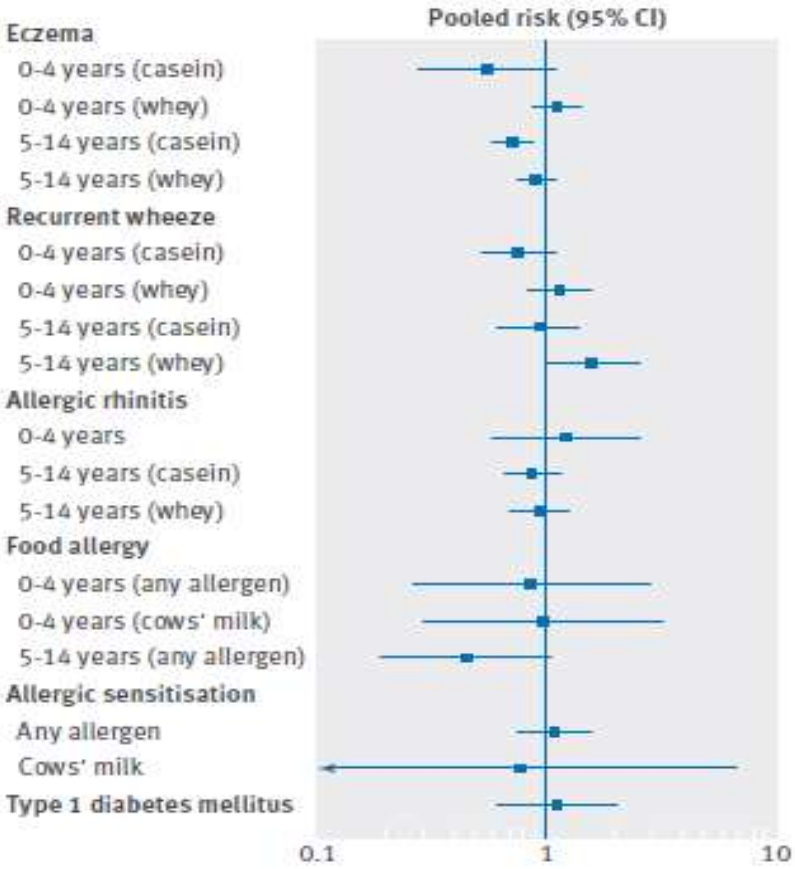
A Von Berg et al. Allergy 2016; 71: 210–219

Hydrolysed formula and risk of allergic or autoimmune disease: systematic review and meta-analysis

Formule parzialmente idrolisate *vs* latte vaccino



Formule estesamente idrolisate *vs* latte vaccino

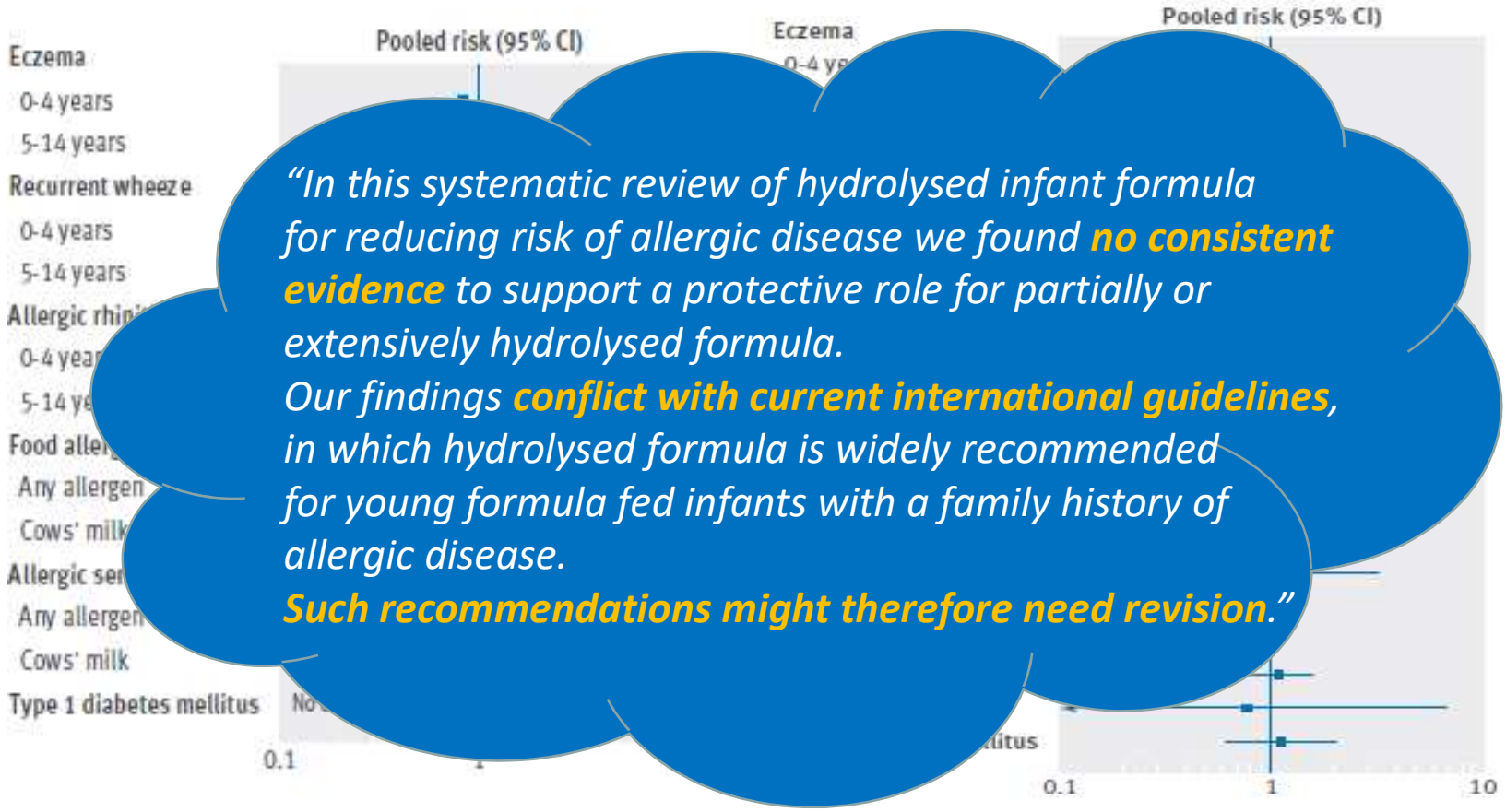


RJ Boyle et al. BMJ. 2016; 352: i974

Hydrolysed formula and risk of allergic or autoimmune disease: systematic review and meta-analysis

Formule parzialmente idrolisate *vs* latte vaccino

Formule estesamente idrolisate *vs* latte vaccino

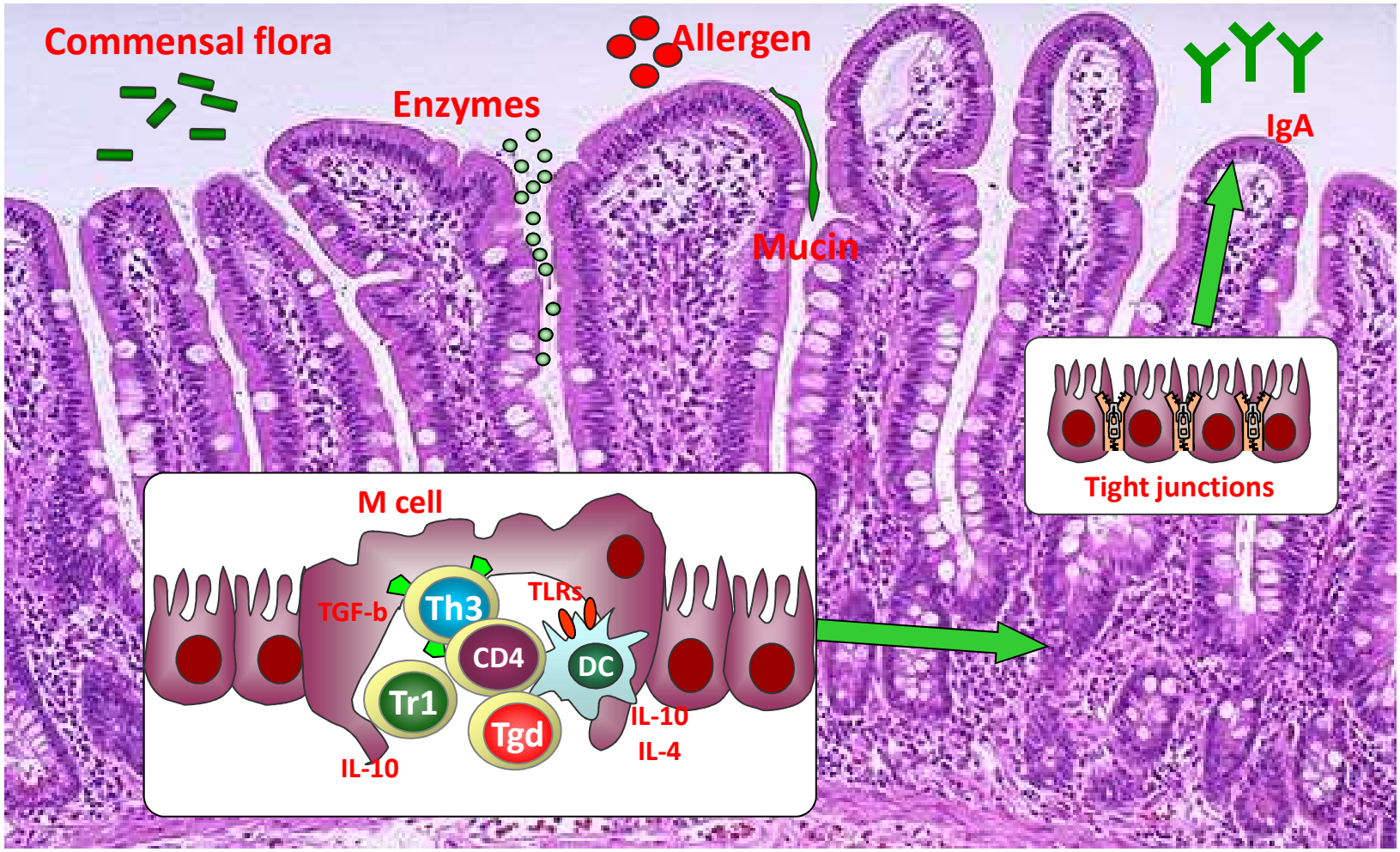


*"In this systematic review of hydrolysed infant formula for reducing risk of allergic disease we found **no consistent evidence** to support a protective role for partially or extensively hydrolysed formula.*
*Our findings **conflict with current international guidelines**, in which hydrolysed formula is widely recommended for young formula fed infants with a family history of allergic disease.*
***Such recommendations might therefore need revision**."*

RJ Boyle et al. BMJ. 2016; 352: i974

Svezzamento

Livelli di protezione nel tratto GE



Anni 90: avevamo capito tutto...

ESPOSIZIONE AGLI ALLERGENI

SENSIBILIZZAZIONI ALLERGICHE

AUMENTO DELLE ALLERGIE

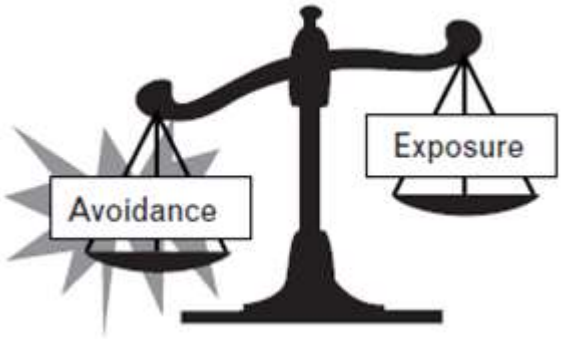
AVOIDANCE

RESTRIZIONI DIETETICHE

RIDOTTA ESPOSIZIONE AGLI ALLERGENI

RIDOTTE SENSIBILIZZAZIONI ALLERGICHE

DIMINUZIONE DELLE ALLERGIE



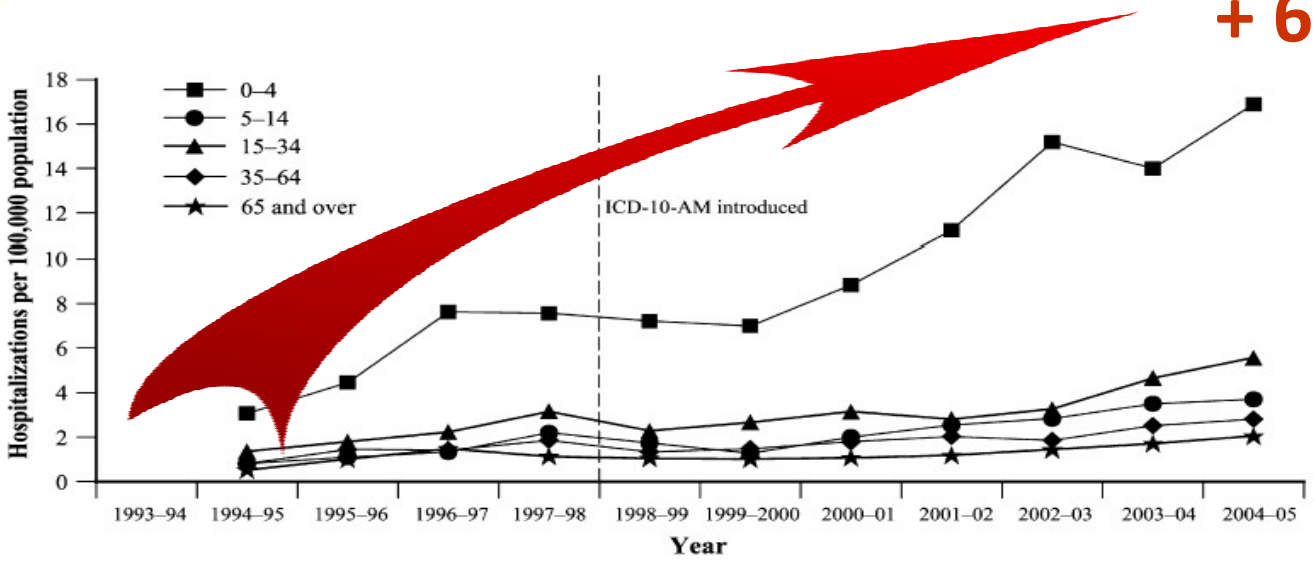
Trends in hospitalizations for anaphylaxis, angioedema, and urticaria in Australia, 1993-1994 to 2004-2005

Leanne M. Poulos, BMedSc (Hons),[a] Anne-Marie Waters, Grad Dip Pop Hlth,[a]
Patricia K. Correll, MPH,[a] Robert H. Loblay, PhD,[b] and Guy B. Marks, PhD[a]
Camperdown and Sydney, Australia

2007

da 0 a 4 anni

+ 6 x



Ricoveri per anafilassi da alimenti divisi per età dal 1994 al 2004

Ritardare lo svezzamento previene le allergie?

SI

1. Fergusson, JECH 1982
2. Kajosaari, Acta Paediatr Scand 1983
3. Zeiger, JACI 1989, JACI 1995
4. Fergusson, Pediatrics 1990
5. Lucas, BMJ 1990
6. Forsyth, BMJ 1993,
7. Kajosaari, PAI 1994
8. Armentia, Clin Exp Allergy 2001
9. Morgan, ADC 2004

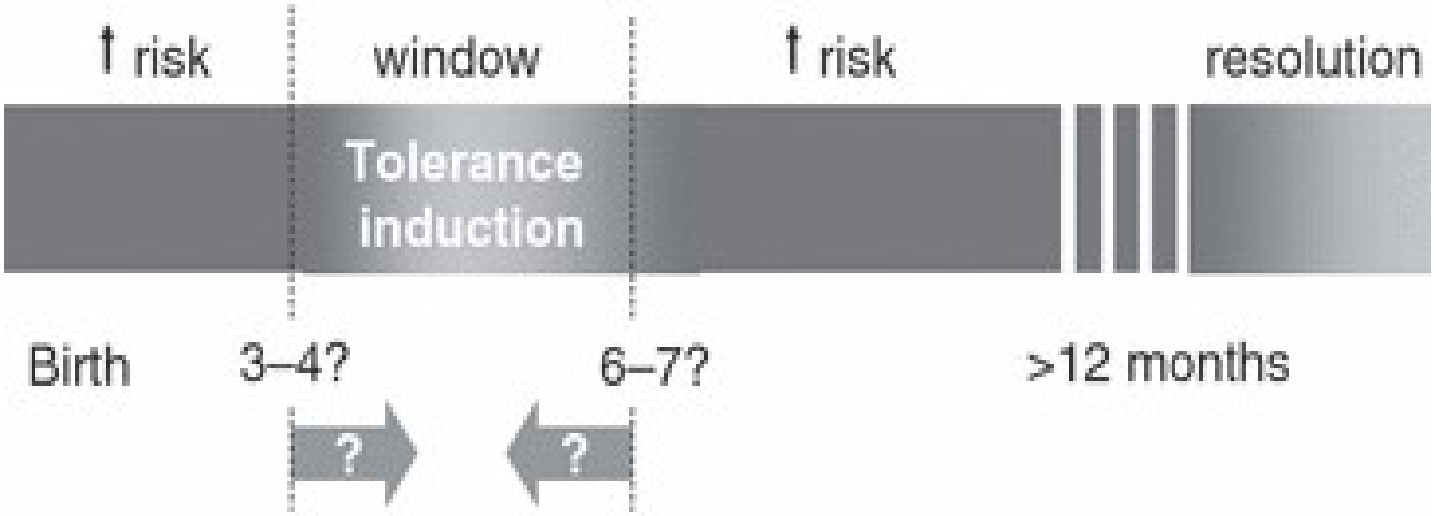
NO

1. Saarinen, Lancet 1980
2. Poysa, Allergy Proc 1991
3. Schoetzau, PAI 2002
4. Zutavern, ADC 2004
5. Pooole, Pediatrics 2006
6. Kull, Allergy 2006
7. Zutavern, Pediatrics 2006
8. Filipiak, J Pediatr 2007
9. Mihrshahi, Cl Exp All 2007
10. Zutavern, Pediatrics 2008
11. Snijders, Pediatrics 2008
12. Alm, Arch Dis Child 2009
13. Nwaru, Pediatrics 2010
14. Koplin, JACI 2010
15. Tromp, Arch Pediatr Adol Med 2011
16. Sausenthaler, Am J Clin Nutr 2011
17. Joseph, JACI 2011
18. Nwaru, JACI 2012

Ritardare lo svezzamento favorisce le allergie?

1. **Forsith, BMJ 1993** *(l'eczema aumenta nei bambini che introducono i solidi a 8-12 settimane)*
2. **Zutavern, ADC 2004** *(eczema aumenta se latte > 6 mesi e uovo > 8 mesi)*
3. **Pooole, Pediatrics 2006** *(introdurre i cereali > 6 mesi aumenta il rischio di allergia al grano)*
4. **Kull, Allergy 2006** *(il consumo di pesce > 8 mesi aumenta le malattie e sensibilizzazioni allergiche)*
5. **Snijders, Pediatrics 2008** *(latte e altri alimenti > 4 mesi aumentano eczema, wheezing e sensibilizzazioni)*
6. **Alm, Arch Dis Child 2009** *(la tardiva introduzione del pesce > 9 mesi aumenta l'eczema)*
7. **Nwaru, Pediatrics 2010** *(sensibilizzazioni sia ad alimenti che inalanti associate a tardiva introduzione di uovo (>8 mesi) grano e avena (> 6 mesi), pesci (> 8 mesi)*
8. **Koplin, JACI 2010** *(uovo > 6 mesi vs 4-6 mesi aumenta allergia uovo nei bambini con storia di familiarità o eczema)*
9. **Joseph, JACI 2011** *(epoca di introduzione non si associa a wheezing o eczema a 2-4, solo le arachidi < 4 mesi nel gruppo con familiarità allergica)*
10. **Nwaru, JACI 2012** *(grano e riso a 5½ mesi, pesce a 9 mesi, uovo a 11 mesi diminuisce il rischio di asma, rinite allergica e sensibilizzazioni)*

Finestra di tolleranza orale



Factors that influence the capacity for tolerance:

- optimal colonisation
- genetic pre-disposition
- allergen properties (dose, interval, timing, preparation)
- gut permeability/maturity/pH
- continued breast feeding?
- other immunomodulatory factors (fatty acids? stress? antioxidants?)

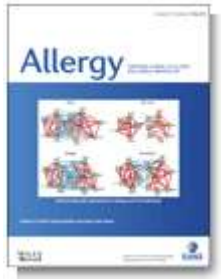
Allergy EUROPEAN JOURNAL OF ALLERGY AND CLINICAL IMMUNOLOGY

EAACI

POSITION PAPER

EAACI Food Allergy and Anaphylaxis Guidelines. Primary prevention of food allergy

A. Muraro[1,*], S. Halken[2,*], S. H. Arshad[3,4,5], K. Beyer[6], A. E. J. Dubois[7], G. Du Toit[8], P. A. Eigenmann[9], K. E. C. Grimshaw[3], A. Hoest[2], G. Lack[8], L. O'Mahony[10], N. G. Papadopoulos[11,12], S. Panesar[13], S. Prescott[14], G. Roberts[3,4,5], D. de Silva[13], C. Venter[4,15], V. Verhasselt[16], A. C. Akdis[17] & A. Sheikh[18,19] on behalf of EAACI Food Allergy and Anaphylaxis Guidelines Group



Allergy 2014; 69: 590–601

Box 3: Recommendations for primary prevention of food allergy

	Evidence level	Grade	Key ref
Exclusive breastfeeding is recommended for all infants for the first 4–6 months.	II–III	C	de Silva D, Systematic-Review 2013 (1); Muraro A, 2004, (60) Kull I, 2010 (33); Venter C, 2009 (37); Høst A, 1988 (36), Lucas A, 1990 (30)
Dietary restrictions are not recommended for all pregnant or lactating mothers.	I–II	B	de Silva D, Systematic-Review 2013 (1)
If breastfeeding is insufficient or not possible: High-risk infants should receive a hypoallergenic formula with documented preventive effect for the first 4 months. Other infants may receive a standard formula. After the age of 4 months, a standard cow's milk-based formula is recommended according to standard nutrition recommendations, irrespective of atopic heredity.	I	A–B	de Silva D, Systematic-Review 2013 (1); Muraro A, 2004 (60) Zeiger RS, 1989, 1992, 1995 (47–49); Odelram H, 1996 (50); Von Berg A, 2003, 2008 (45, 46)
Introduction of complementary foods after the age of 4 months according to normal standard weaning practices and nutrition recommendations, for all children irrespective of atopic heredity.	II–III	C	de Silva D, Systematic-Review 2013 (1)
No special dietary restrictions after the age of 4 months for infants with high risk for development of allergic disease No withholding or encouraging exposure to 'highly allergenic' foods such as cow's milk, hen's egg, and peanuts irrespective of atopic heredity, once weaning has commenced.	II–III	C	de Silva D, Systematic-Review 2013 (1)

2008: adesso abbiamo capito tutto!!

FROM AVOIDANCE TO TOLERANCE

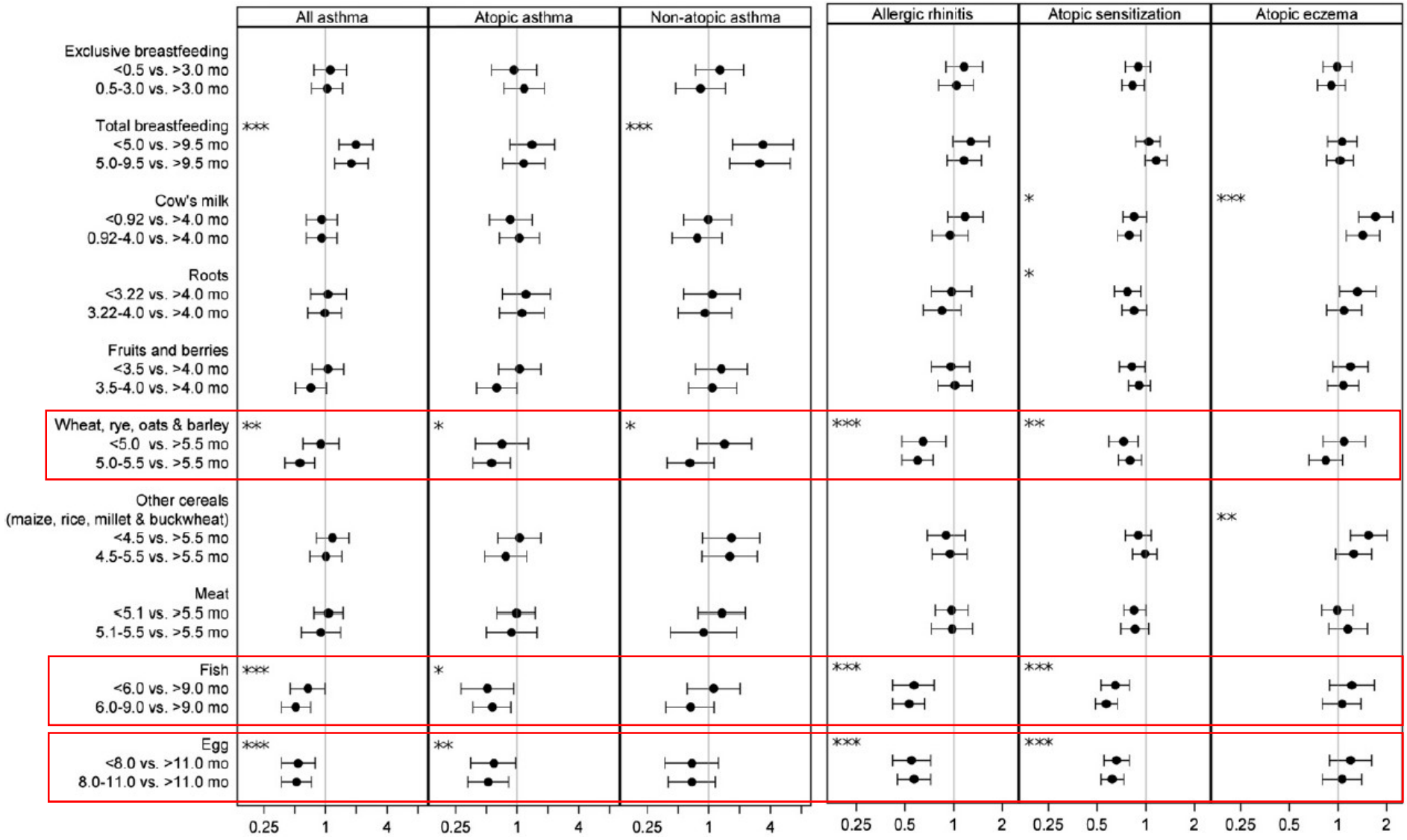
Prevenire mangiando

Timing of infant feeding in relation to childhood asthma and allergic diseases

- Associazione tra durata dell'allattamento al seno, epoca dello svezzamento e sviluppo di asma e allergie a 5 anni d'età
- 3781 neonati consecutivi
- Questionario ISAAC, IgE a 5 anni
- **Conclusioni**: la precoce introduzione di *grano, segale, avena, orzo, pesce e uovo* sembra ridurre il rischio di asma, rinite e sensibilizzazione allergica

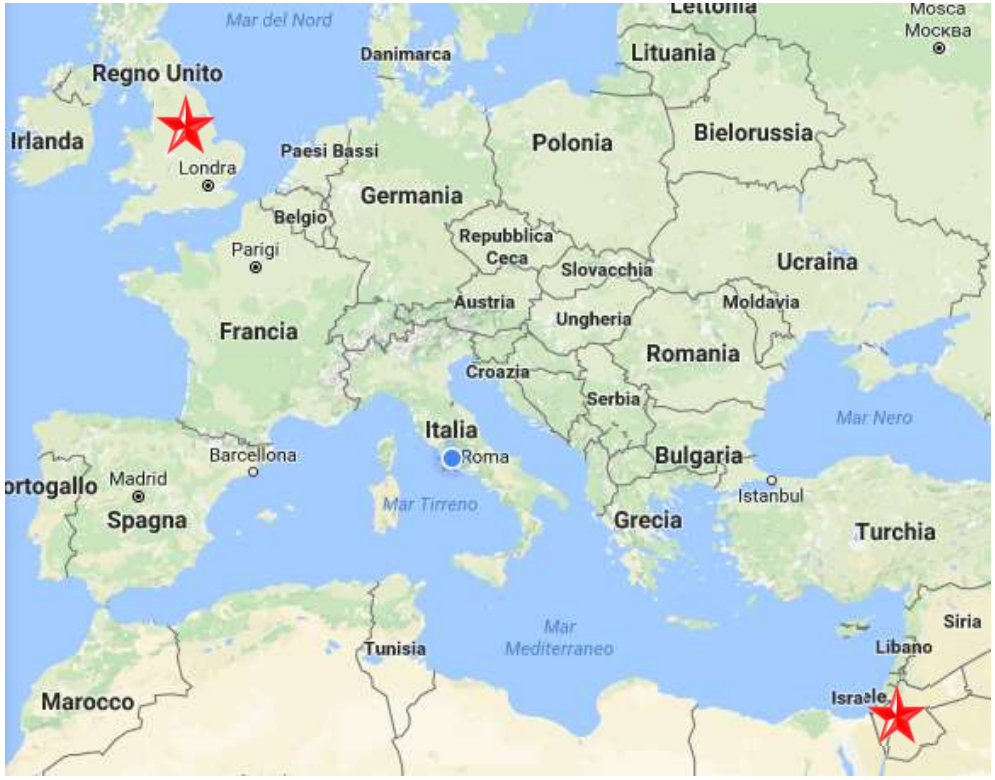
Bright I Nwaru et al. J Allergy Clin Immunol 2013;131:78-86

Timing of infant feeding in relation to childhood asthma and allergic diseases



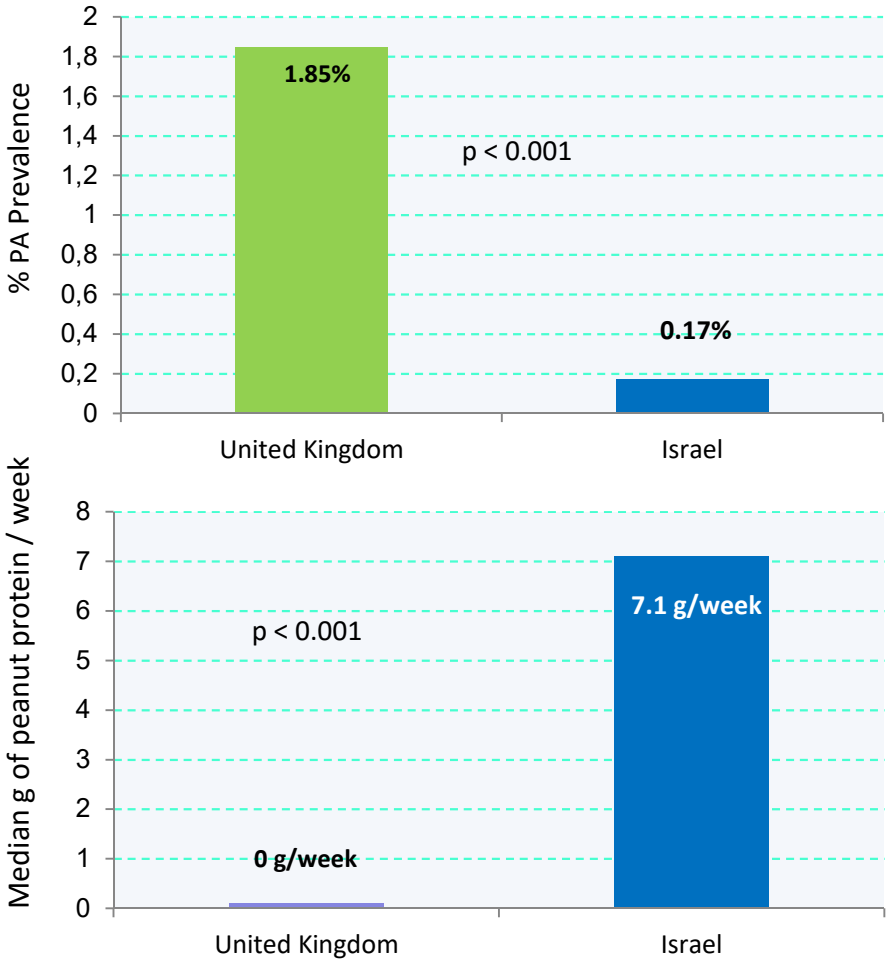
Early consumption of peanuts in infancy is associated with a low prevalence of peanut allergy

- 5171 Jewish school children in UK and 5615 Jewish school children in Israel were compared for food allergies and atopy.
- Questionnaire based assessment of peanut allergy validated by challenges.
- Infant weaning for peanut and other foods was determined in infants using a validated FFQ.



Du Toit G. J Allergy Clin Immunol. 2008;122:984-91

Early consumption of peanuts in infancy is associated with a low prevalence of peanut allergy



Prevalence of Peanut Allergy in Children 4 - 18yrs

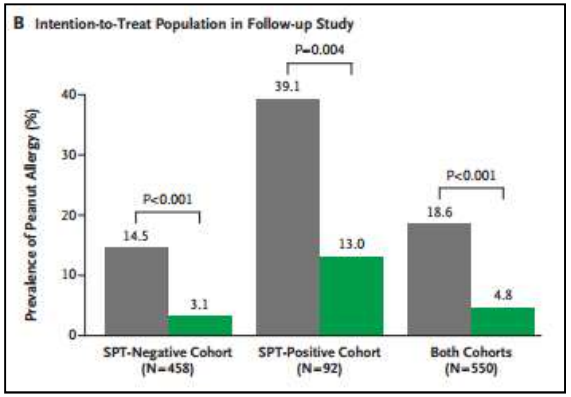
Peanut Protein Consumption 8 - 14 month

Du Toit G. J Allergy Clin Immunol. 2008;122:984-91

Randomized Trial of Peanut Consumption in Infants at Risk for Peanut Allergy

Learning Early About Peanut (LEAP)

- 640 infants (4-11 mm) with severe eczema, egg allergy, or both to consume or avoid peanuts until 60 months of age
- **peanut allergy prevalence at 60 months**
  - 530 SPT neg:
    - 13.7 % (avoidance group)
    - 1.9 % (consumption group) (p<0.001)
  - 98 SPT pos:
    - 35.3 % (avoidance group)
    - 10.6 % (consumption group) (p<0.004)



- ***Conclusions:*** *The early introduction of peanuts significantly decreased the frequency of the development of peanut allergy among children at high risk for this allergy [..]*

Du Toit G et al. N Engl J Med 2015;372:803-13 (LEAP study)

Randomized Trial of Introduction of Allergenic Foods in Breast-Fed Infants

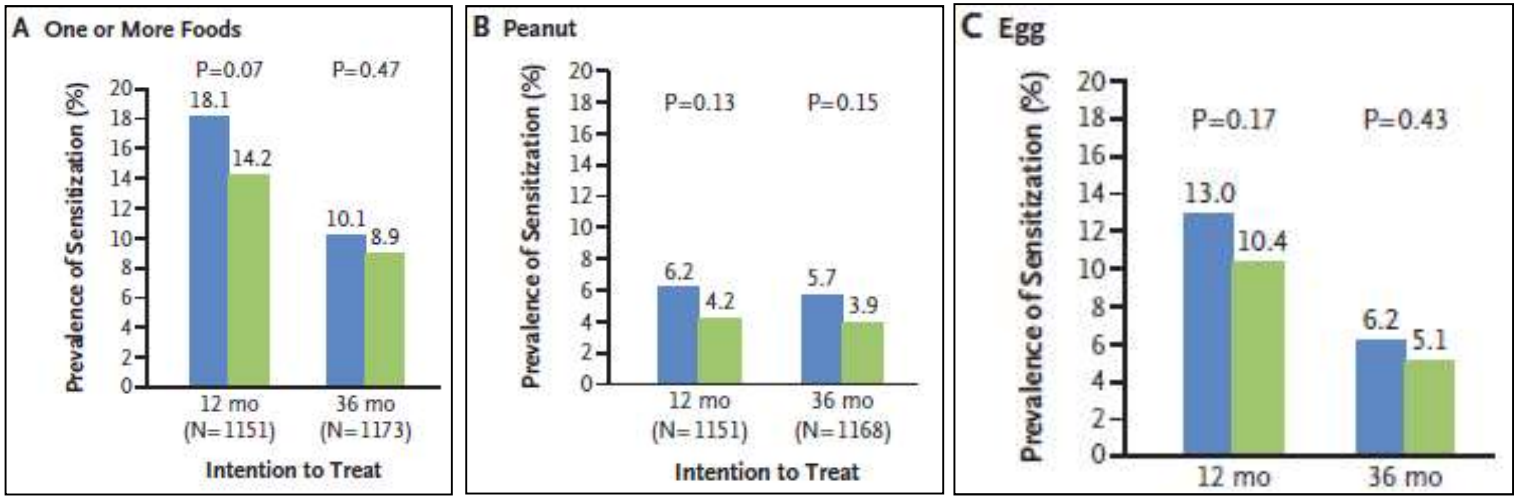
EAT
Enquiring About Tolerance

- 1303 exclusively breast-fed infants
- randomly assigned to
  - the ***early introduction*** of six allergenic foods (peanut, cooked egg, cow's milk, sesame, whitefish, and wheat)
  - to the ***current practice*** recommended in the United Kingdom of exclusive breast-feeding to approximately 6 months of age
- **Primary outcome**: food allergy to one or more of the six foods between 1 year and 3 years of age.
- **RESULTS**: food allergy to one or more of the six intervention foods developed in
  - **7.1%** of the participants in the standard-introduction group and in
  - **5.6%** of those in the early-introduction group **(p=0.32)**

MR Perkin et al. New England Journal Med 2016, March 4

Randomized Trial of Introduction of Allergenic Foods in Breast-Fed Infants

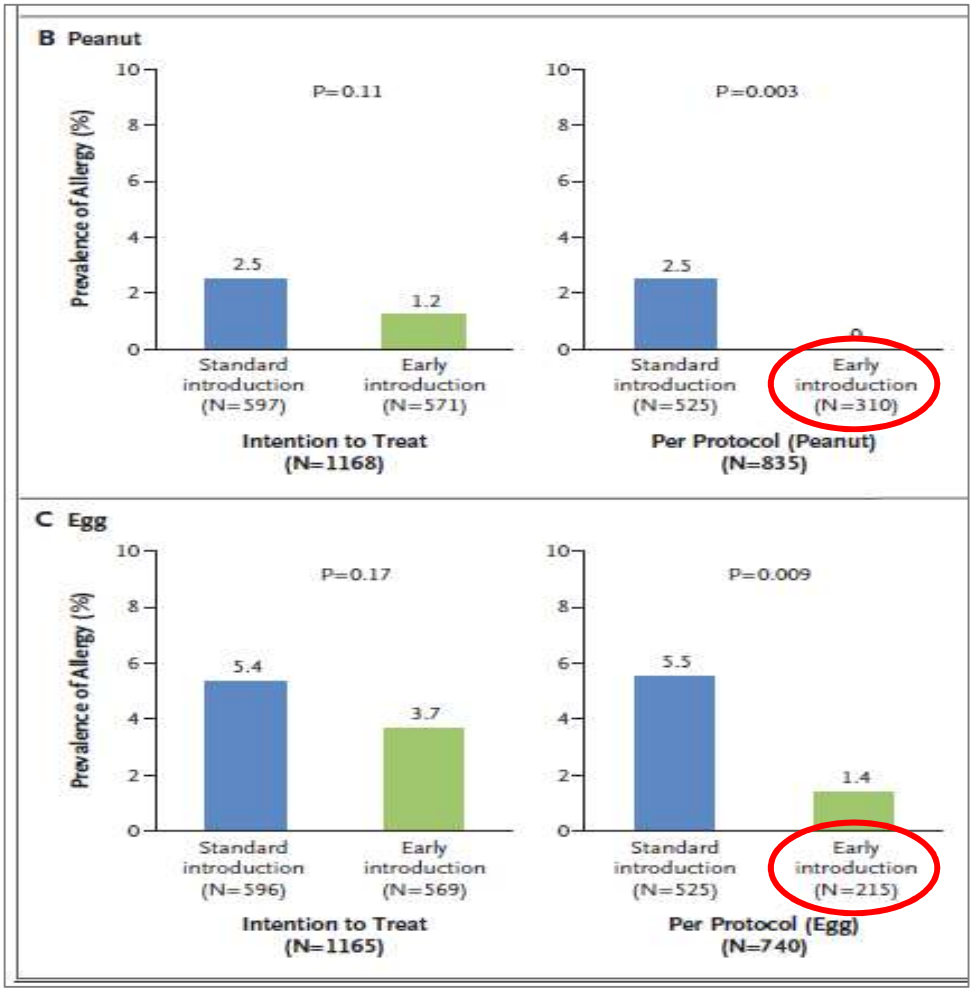
EAT
Enquiring About Tolerance



CONCLUSIONS: The trial did not show the efficacy of early introduction of allergenic foods in an intention-to-treat analysis

MR Perkin et al. New England Journal Med 2016, March 4

Randomized Trial of Introduction of Allergenic Foods in Breast-Fed Infants



EAT
Enquiring About Tolerance

Drop-out: 46%

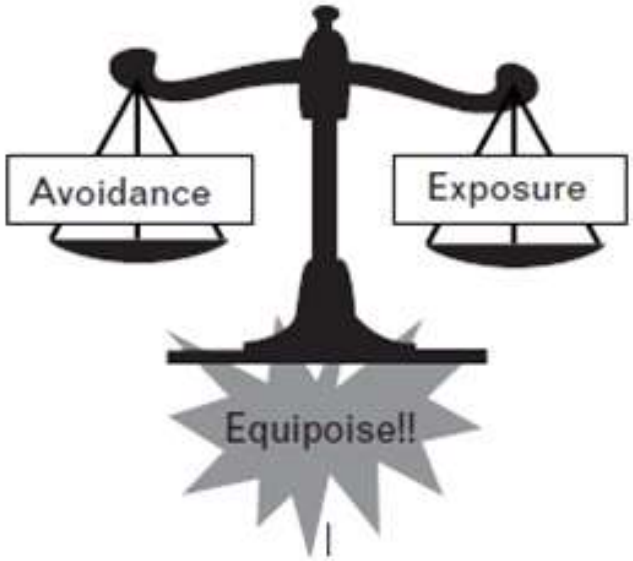
Drop-out: 62%

MR Perkin et al. New England Journal Med 2016, March 4

Studio EAT: conclusioni

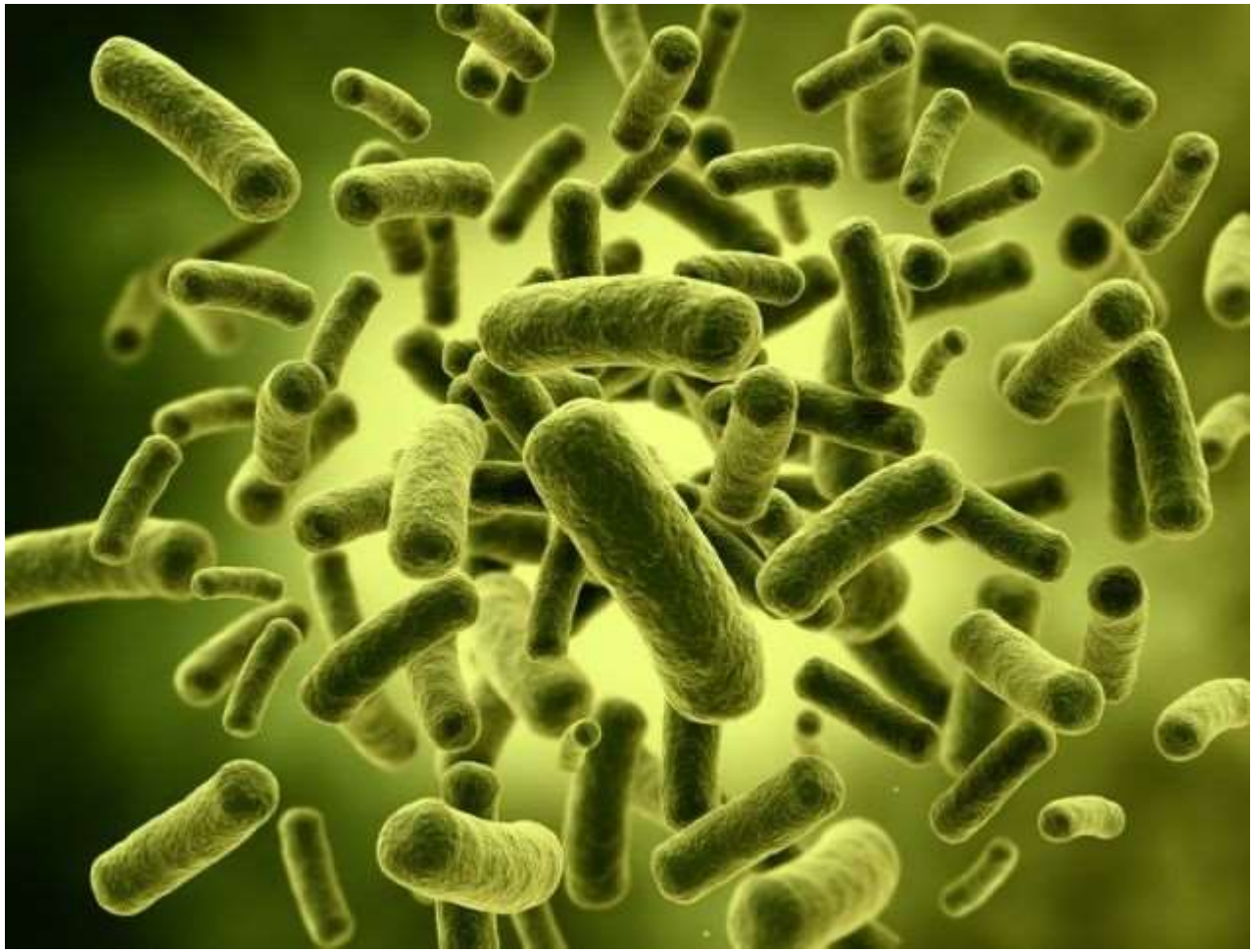
- Lo studio non ha dimostrato l'azione preventiva di una precoce introduzione di alimenti allergizzanti rispetto ad una introduzione standard, con l'analisi intention to treat.
- La possibilità di prevenire l'allergia alimentare attraverso l'introduzione precoce degli alimenti in lattanti al seno potrebbe dipendere dall'aderenza nell'assunzione di tali cibi e dalle dosi assunte.

Svezzamento: approccio attuale



- Una banale osservazione…contro la «early exposure»

Probiotici e prebiotici



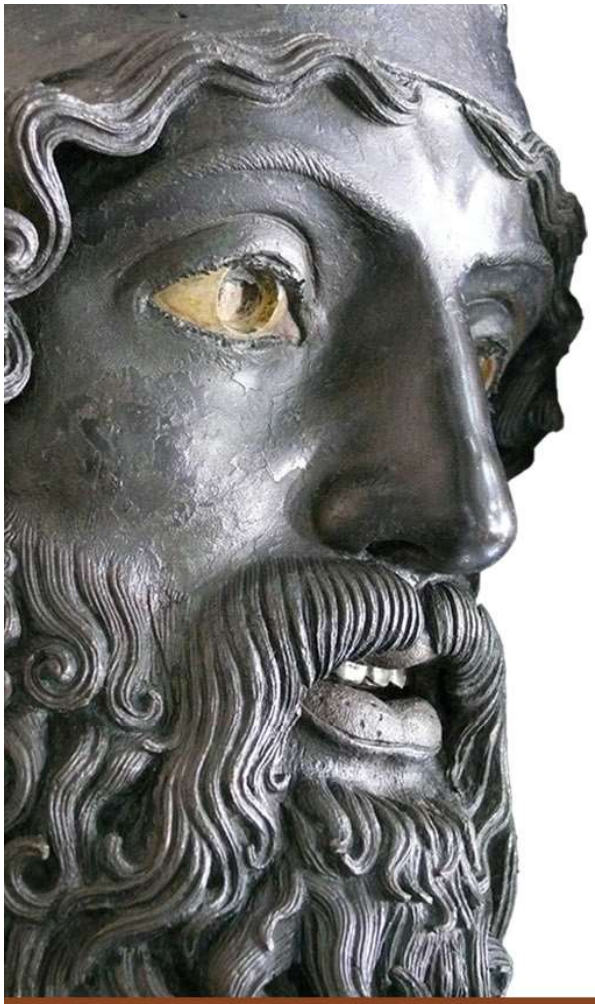
Probiotici e prebiotici

Non ci sono evidenze che raccomandino l'uso di probiotici o prebiotici per prevenire l'allergia alimentare (B)

Muraro A, et al. Allergy 2014; 69: 590–601

La somministrazione di probiotici nella madre in gravidanza e/o dopo la gravidanza, e al bambino nei primi 6 mesi di vita, può essere presa in considerazione come intervento per la **prevenzione dell'eczema** in bambini a rischio.
L'effetto è **modesto** e la qualità delle evidenze è **bassa**.

Fiocchi et al. World Allergy Organization Journal (2015) 8:4



REGGIO CALABRIA 19-22 ottobre 2016

Associazione Allergologi Immunologi Italiani Territoriali e Ospedalieri
AAIITO

thank you!

giuseppe.pingitore@gmail.com

VI CONGRESSO NAZIONALE AAIITO