Alimentazione e prevenzione

Tabarka, 7 Luglio 2006

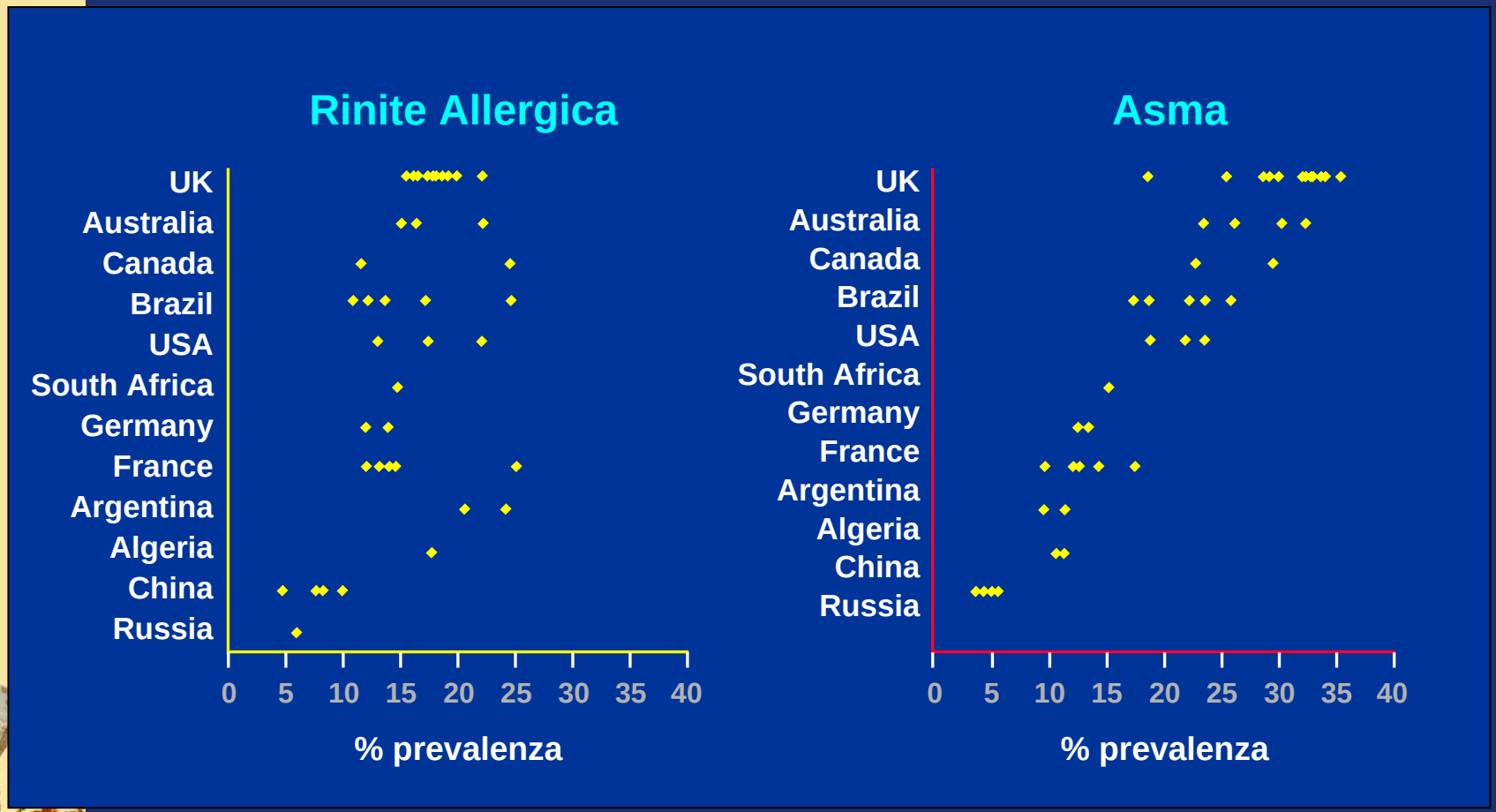
Luigi Terracciano
Melloni Pediatria, Milano

La prevenzione delle allergie

1. Vale la pena?

2. Si può?

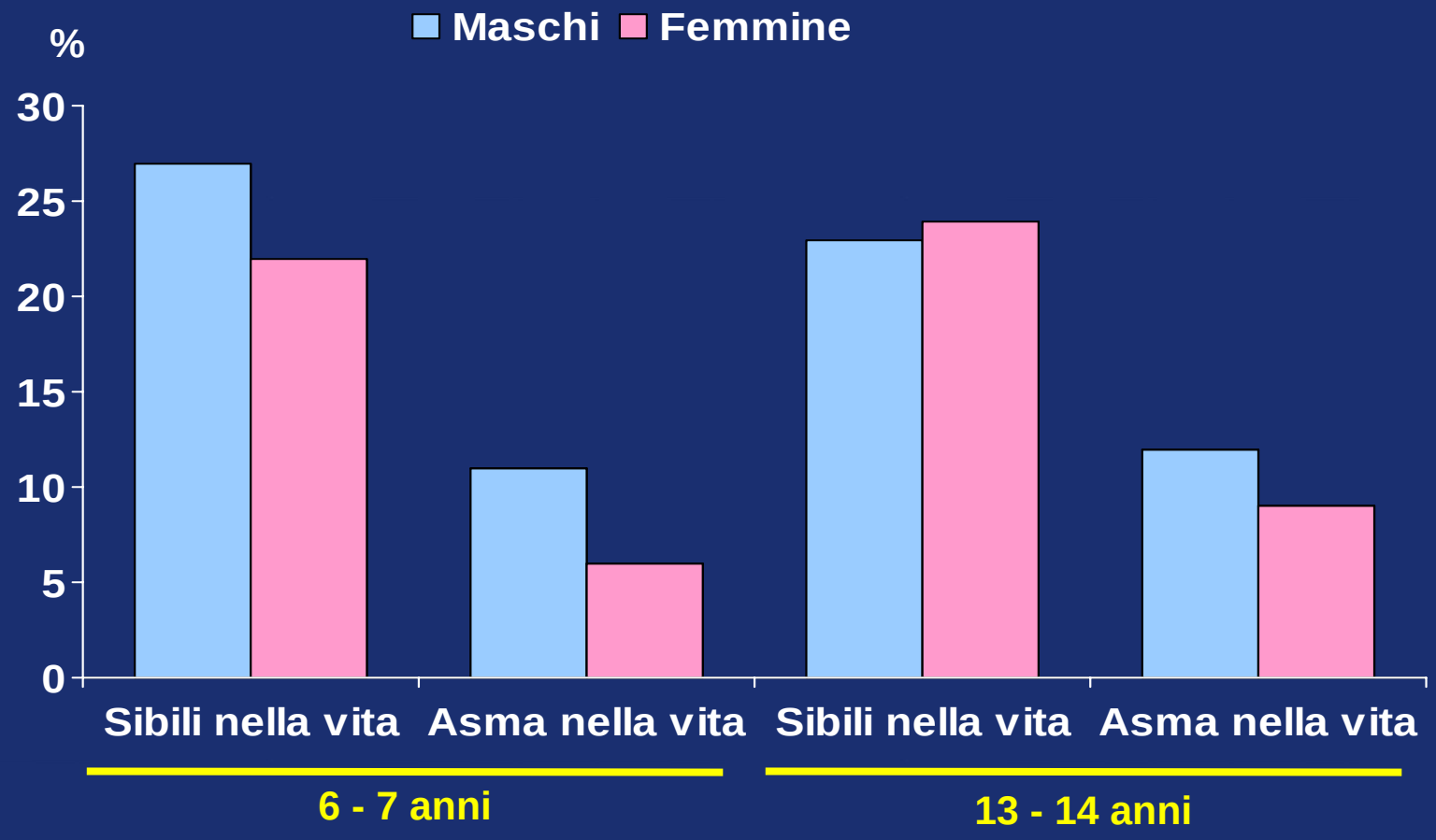
Rinite Allergica e Asma presentano quadri di prevalenza simili



International Study of Asthma and Allergies in Childhood (ISAAC) Steering Committee
Lancet 1998;351:1225–1232.

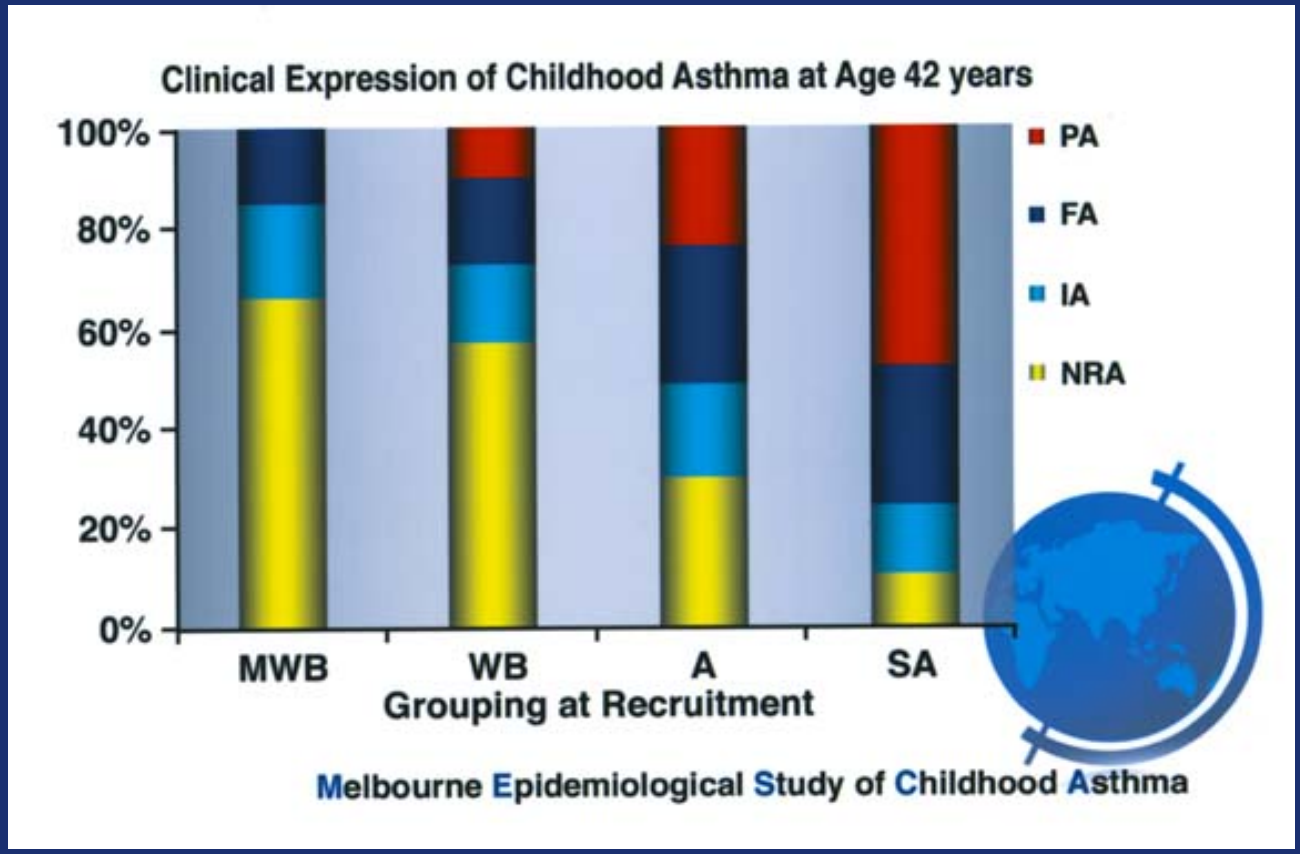
Prevalenza di sibili e asma in bambini ed adolescenti italiani

Studio SIDRIA (1994-95)



SIDRIA Collaborative Group - Eur Respir J 1997; Eur Respir J 1999

The Melbourne Asthma Study: 1964-1999



Phelan PD. The Melbourne Asthma Study: 1964-1999.
J Allergy Clin Immunol 2002;109:189-94

Epidemiologia e impatto socio-economico dell'asma

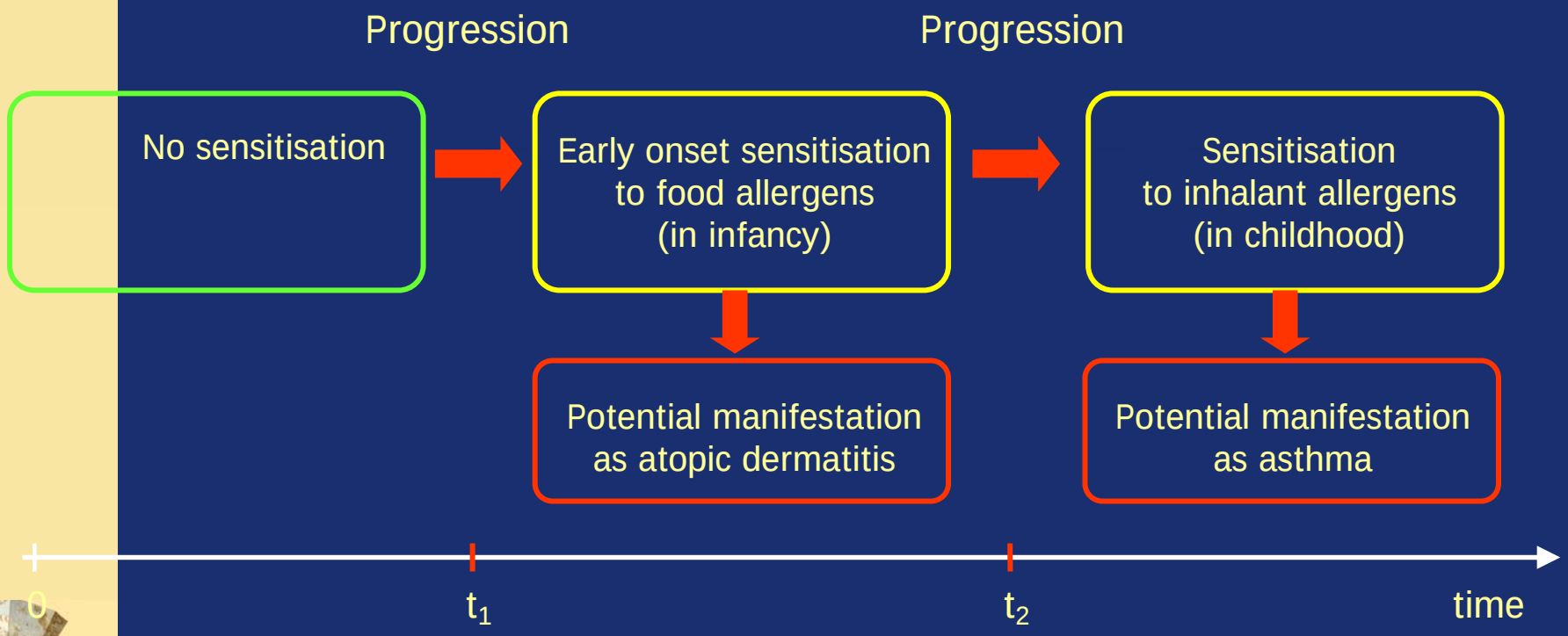
- **L'attuale prevalenza di asma in Italia, benché inferiore a quella di molte altre nazioni, rappresenta una notevole fonte di costi sia sociali sia umani**
- **Considerevole spesa sanitaria**
- **Costi diretti pari all'1-2% della spesa sanitaria totale**
- **Costi indiretti rappresentano oltre il 50% della spesa totale**
- **Costi simili a quelli degli altri Paesi industrializzati**
- **L'asma è una delle cause principali di assenza dal lavoro o da scuola**

CIPELLI S.R.L.
LAVANDERIA-INDUSTRIALE

- Il Papà di Riccardo faceva sempre il turno di notte ……..
” Dottore….quello a casa nostra non si dorme da 4 anni !”

Current understanding of atopy:

the atopic march



Fattori di rischio significativi per lo sviluppo di asma

- 100 bambini a rischio seguiti per 22 anni
- Nel 25% dei pazienti fu diagnosticata asma
- Il 28% dei bambini manifestò wheezing nei primi 2 anni di vita, senza correlazione con lo sviluppo di asma (OR 0,3)
- La positività dei test cutanei per latte vaccino , uovo o entrambi nel primo anno di vita era predittivo di asma (OR 10.7; 95% CI, 2.1-55.1; P = .001; sensitivity, 57%; specificity, 89%)

Rhodes HL Early life risk factors for adult asthma: a birth cohort study of subjects at risk. J Allergy Clin Immunol 2001; 108:720-5

Allergia Alimentare ed asma: prevalenza in categorie a rischio

Popolazione clinica	Prevalenza stimata
Popolazione generale di bambini con asma	5,7 %
Bambini con CMA	29 %
Broncospasmo durante reazioni acute da alimenti	2 % - 24 %
Pazienti con AEDS	17 %- 27 %

James JM. Pediatrics 2003;111:1625-1630

Allergia alimentare ed asma grave

• 19 pazienti (1-16 anni) sottoposti a procedure rianimatorie per asma grave, 38 controlli asmatici

•Fattori di rischio per la necessità di rianimazione:

- •Allergia alimentare (OR, 8.58; 95% CI, 1.85-39.71)
- •Ricoveri frequenti (OR, 14.2; 1.77-113.59).

Roberts G. J Allergy Clin Immunol 2003;112(1):168-74

Dietary treatment of childhood AEDS: lessons from the literature

minor AD → no food allergy
moderate AD → 33%
severe AD → 96%.

The younger the higher the frequency of food sensitization.

Guillet G, Guillet M. Natural history of sensitizations in atopic dermatitis. Arch Dermatol 1992;128:187-92

Conclusioni

Prevenire la sensibilizzazione ad alimenti è vantaggioso:

- per il paziente (minore severità dei quadri allergici associati)
- per il pediatra (minor carico di patologie associate alla sensibilizzazione)
- per il sistema sanitario (minore spesa per ricoveri e terapie)

La prevenzione delle allergie

1. Vale la pena?

1.Si può?

1. Prohibitionistic approach

2. Proactive approach

Rostrum

The role of breast-feeding in the development of allergies and asthma

Noah J. Friedman, MD, and Robert S. Zeiger, MD, PhD *San Diego, Calif*

The role of breast-feeding in the development of allergies and asthma

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J Allergy Clin Immunol 2005;115:1238-48

TABLE II. Recent prospective birth cohort studies on effect of breast-feeding on atopy

Study	Birth cohorts	Comparison	Outcome, OR (95% CI)
Kramer et al[36] (Belarus)	Unselected RC (n = 16,491)	BF support/promotion group vs controls (43% of intervention group was exclusively BF at 3 mo)	1-y AD: 0.54 (0.31-0.95)
Kull et al[37,38] (Sweden)	Observational (n = 773 vs 3013)	Sole BF ≥4 mo vs <4 mo	(a) 2-y AD: 0.85 (0.7-1) (b) 2-y Asthma cumulative prevalence, 0.7 (0.5-0.8) (c) 4-y Asthma period prevalence, 0.72 (0.53-0.97)
Oddy et al[42] (Australia)	Observational (n = 2602)	Predominant BF ≥4 mo vs <4 mo	1-y Wheeze and ≥2 acute visits: 0.6 (0.4-0.8)
Kerkhof et al[40] (Netherlands)	High-risk RC (n = 708)	Sole BF ≥3 mo vs <3 mo	1-y AD: 0.4 (0.2-1.0)
Laubereau et al[41] (Germany)	High-risk RC (n = 2030 vs 522)	Sole BF ≥4 mo vs cow's milk formula	AD in first 3 y: 0.64 (0.45-0.90)

AD, Atopic dermatitis; *BF*, breast-feeding; *RC*, randomized controlled study.

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TABLE III. Studies reporting an increase in atopy with breast-feeding

Study	Cohort	Finding	Comment
Taylor et al[48]	13,135 British 5-y-olds	Any BF: increased AD	Recall bias
Kaplan and Mascie-Taylor[49]	14,000 British 7-y-olds	Any BF: increased asthma at 7 y	Recall bias FH not controlled
Rusconi et al[50]	16,333 Italian 6-7-y-olds	BF ≥6 mo: increased transient asthma; decreased late-onset asthma; no change in persistent asthma	Recall bias No control FH atopy
Wright et al[51]	1246 Tucson birth cohort: birth-13-y-olds	BF ≥4 mo: increased recurrent wheeze at age ≥6 y	BF recall at 2 y Questionnaires
Bergmann et al[52]	1314 German children: birth-7-y-olds	> BF > AD to age 7 y: OR, 1.03 (1.02-1.06)	Parent AD > factor Nursery cow's milk common
Miyake et al[53]	5614 Japanese middle school children	BF first 3 mo: increased AD	Recall bias Only in high-risk
Sears et al[54]	1037 New Zealand birth cohort: 3-26-y-olds	BF 4 wk or longer: increased current asthma 9-26 y; + skin tests at 13 y	Recall bias (?) Lack of dose-response

AD, Atopic dermatitis; *BF*, breast-feeding; *FH*, family history.

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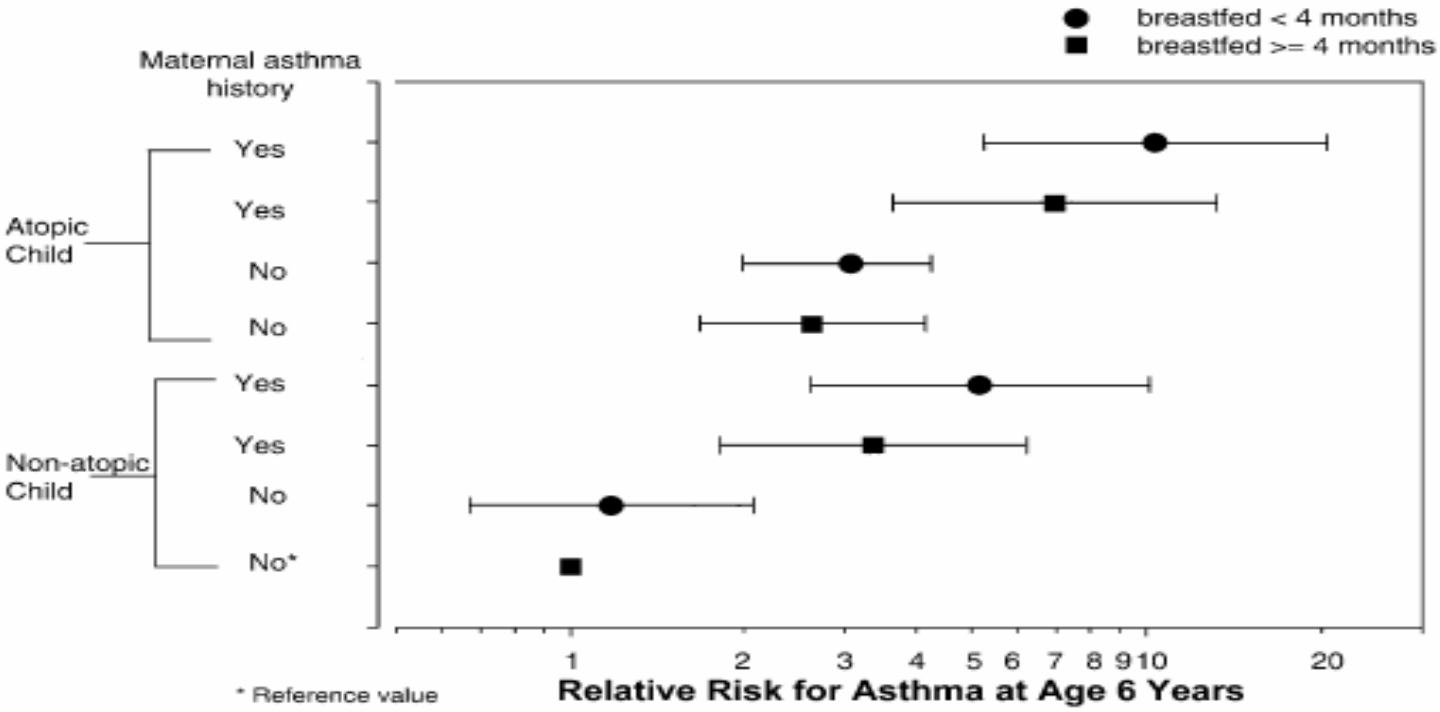

FIG 1. Data suggesting that maternal asthma does not affect the protective effect of breast-feeding on doctor diagnosis of asthma at 6 years in an Australian birth cohort of 2602 infants. Reprinted with permission.[39]

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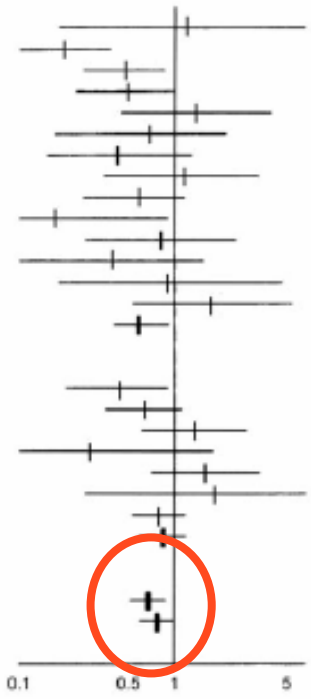
A. Atopic Dermatitis

	OR	95% CI	
Positive family history			
Businco[31,32]	1.20	0.18	6.62
Chandra[33]	0.15	0.06	0.39
Chandra[34]	0.48	0.26	0.86
Chandra[35-37]	0.49	0.23	1.00
Cogswell[27-29]	1.36	0.45	4.01
Gruskay[8]	0.68	0.17	2.06
Herrmann[16]	0.43	0.15	1.28
Hide[10,38,39]	1.16	0.35	3.35
Marini[20]	0.59	0.26	1.16
Matthew[9]	0.17	0.03	0.9
Poysa[12]	0.81	0.27	2.42
Pratt[11]	0.40	0.07	1.54
Ruiz[30]	0.90	0.18	4.72
van Asperen[42]	1.68	0.53	5.53
Subtotal	0.58	0.41	0.92
Negative family history			
Berth-Jones[10]	0.44	0.2	0.91
Fergusson[44,45]	0.65	0.36	1.11
Gordon[43]	1.32	0.62	2.81
Gruskay[8]	0.28	0.01	1.78
Hide[10,38,39]	1.59	0.71	3.42
Pratt[11]	1.80	0.27	9.01
Tariq[1,39-41]	0.79	0.53	1.18
Subtotal	0.84	0.59	1.19
Total	0.68	0.52	0.88
Total*	0.77	0.60	0.98



B. Asthma/wheezing

	OR	95% CI Lower	Upper
Positive family history			
Gruskay	0.85	0.21	2.62
Businco	0.26	0.03	1.28
Chandra	0.35	0.12	0.88
Hide	0.73	0.13	2.82
McConnochie	0.48	0.13	1.59
Fergusson	1.19	0.21	4.58
Marini	0.50	0.26	0.91
Subtotal	0.52	0.35	0.79
Negative family history or unstratified			
Wilson	0.47	0.18	1.07
Oddy	0.80	0.66	0.98
Tariq	0.55	0.37	0.82
Gordon	0.39	0.09	1.37
Wright	0.67	0.36	1.25
Gruskay	0.48	0.01	3.30
Hide	1.26	0.34	4.00
McConnochie	0.00	0.00	4.13
Fergusson	1.02	0.35	2.48
Subtotal	0.73	0.62	0.86
Children without a family history of atopy			
Gruskay	0.48	0.01	3.30
Hide	1.26	0.34	4.00
McConnochie	0.00	0.00	4.13
Fergusson	1.02	0.35	2.48
Subtotal	0.99	0.48	2.03
Total	0.70	0.60	0.81

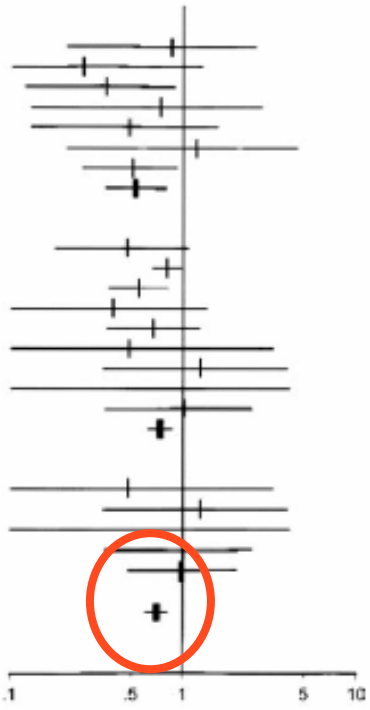


FIG 2. Meta-analyses of studies demonstrating a protective effect of exclusive breast-feeding compared with cow's milk feeding on the development of atopic dermatitis/eczema **(A)** (*analyses after exclusion of studies with unblinded outcomes; numbers next to authors refer to references in original article; reprinted with permission from the American Academy of Dermatology, Inc[58]) and asthma/wheezing **(B)** (reprinted with permission from Mosby, Inc[59]) in infants with allergic parents.

Kramer MS, Kakuma R. Maternal dieta igen avoidance during pregnancy and/or lactati or preve treating atopic disease the

chrane Da 3; CD 133.

- 4 (

American and European guidelines recommended a normal diet during pregnancy and lactation

dietary

ancy on

itis during

high-risk

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As such, consistent with the tenets of not interfering

with Mother Nature and at the same time attempting to do no harm with interventions, exclusive breast-feeding for 4 to 6 months should remain the keystone for promoting allergy health, as recommended by the AAP and ESPACI/ESPGHAN.

1. Prohibitionistic approach

2. Proactive approach

GINI (German Infant Nutritional Intervention Study Group)

2252 newborns enrolled (1995-98)
Randomised to four formulae: **pHF - W**
eHF – W
eHF – C
CMF

945 formula-fed vs. 865 breastfed:

CMF:	16% incidence of atopic manifestations	OR = 1
eHF – W:	14% incidence of atopic manifestations	OR = 0.86
pHF – W:	11% incidence of atopic manifestations	OR = 0.65
eHF – C:	9% incidence of atopic manifestations	OR = 0.51

Andrea Von Berg – Book of Abstracts,
EAACI Section on Paediatrics Annual Symposium – Prevention of food allergy – 2002; 31

Formulas containing hydrolysed protein for prevention of allergy and food intolerance in infants.

Cochrane Database Syst Rev. 2003;(4):CD003664

- There is no evidence to support feeding with a hydrolysed formula for the prevention of allergy in preference to exclusive breast feeding.
- In high risk infants who are unable to be completely breast fed, there is evidence that prolonged feeding with a hydrolysed compared to a cow's milk formula reduces infant and childhood allergy and infant CMA.
- Further trials are required to determine if significant clinical benefits persist beyond 5 years of age and if there is any additional benefit from use of an extensive compared to a partially hydrolysed formula.
- Incremental costs of formula and the effect on compliance should be measured.

Cow's milk protein avoidance and development of childhood wheeze in children with a family history of atopy.
Cochrane Database Syst Rev. 2002;(3):CD003795.

- Breast-milk should remain the feed of choice for all babies.
- In infants with at least one first degree relative with atopy, hydrolysed formula for a minimum of 4 months combined with dietary restrictions and environment measures may reduce the risk of developing asthma or wheeze in the first year of life.
- There is insufficient evidence to suggest that soya-based milk formula has any benefit.

Definition of weaning

To accustom an infant or other young mammal to food other than milk

Thompson D, Fowler HW, Fowler FG, editors.
The concise Oxford dictionary. 9th ed. London: BCA/Oxford University Press, 1996.

The process of accustoming an infant to a full adult diet (while maintaining breastfeeding)

Savage King F, Burgess A. Nutrition for developing countries.
2nd ed. Oxford, United Kingdom: Oxford University Press, 1996:123.

WHO recommandations on weaning (2001)

WHO Expert Consultation:

- exclusive breastfeeding for six months
- then introduction of complementary foods and continued breastfeeding thereafter
- breastfeeding continue until 12 months of age (thereafter as long as mutually desired).
- breastfeeding can continue beyond 12 months

WHO. Complementary feeding.
Report of the global consultation. Geneva, 10-13 December 2001
www.who.int/inf-pr-2001/en/note2001-07.html accessed February 6th, 2005

WHO recommandations on timing

Early introduction of solid foods

- Less time on the breast, → maternal milk production may decline
- The infant will reject the spoon (a hard object)
- Food allergies can develop
- Pathogens → diarrhoeal diseases

WHO. Complementary feeding.
Report of the global consultation. Geneva, 10-13 December 2001
www.who.int/inf-pr-2001/en/note2001-07.html accessed February 6th, 2005

Schema alternativo

1. n

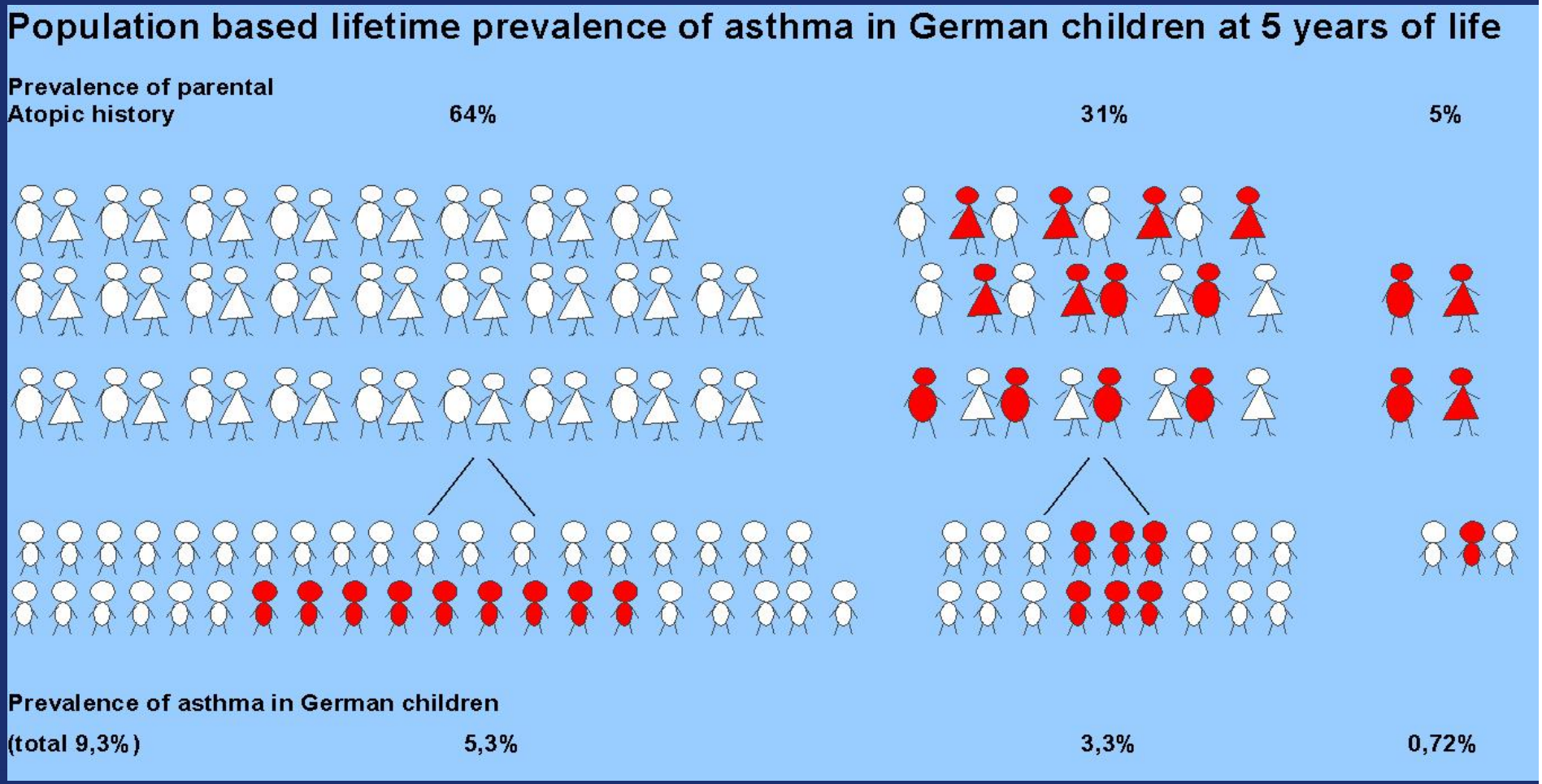
Tempi e modi del divezzamento dettati dal farmacista? Dal supermercato?

troduzione
degli a dettato dalla tradizione

Realtà in pediatria

Dobbiamo svezzare i bambini a rischio allergico diversamente dai normali?

Asthmatic children born to families without allergy risk are more numerous than asthmatic children born to families with mono- or bi-parental allergy risk



Wahn U. What drives the allergic march? 2000; 55: 591-9

Realtà in pediatria

Può l'introduzione di alimenti solidi modulare lo sviluppo di allergie?

A step-by-step introduction of solid foods: theorical framework

- can an early introduction of solid foods anticipate the development of food allergy?
- can their avoidance prevent the development of food allergy?
- are some foods more allergenic than other foods?
- are some food allergies more persistent than others?

L’introduzione precoce di alimenti solidi può influenzare lo sviluppo di allergia alimentare?

- 135 bambini con familiarità allergica, alimentati al seno fino a 6 mesi

- **gruppo a (70) -** a 6 mesi: verdure cotte, mela, pera, cereali
  a 8 mesi: carne, pesce
  a 10 mesi: uovo

- **gruppo b (65) -** a 3 mesi: patata, carota cotta, cereali, carne
  a 4 mesi: uovo, pesce
  a 5 mesi: frutti diversi, "commercial foods"
  a 6 mesi: dieta libera ed estesa

→ **sia eczema che allergia alimentare vennero riscontrati in misura maggiore nel gruppo b rispetto al gruppo a**

Saarinen UM, Kajosaari M Prophylaxis of atopic disease: role of infant feeding. Lancet i: 166-167, 1980
Kajosaari M, Saarinen UM Prophylaxis of atopic disease by six months' total solid foods elimination. Acta Paed Scand 72:411, 1983

L'introduzione precoce di alimenti solidi può influenzare lo sviluppo di allergia alimentare?

- 279 lattanti ad alto rischio atopico *vs.* 80 lattanti con lo stesso rischio (non-intervention group)
- Incidenza di sintomi allergici : 1 anno (11.5 *vs.* 54.4%,) a 2 anni (14.9 *vs.* 65.6%) a 3 anni (20.6 *vs.* 74.1%).
- Fattori più importanti nella patogenesi dei sintomi: (i) formula somministrata nella prima settimana di vita; (ii) divezzamento precoce (< 4 mesi); (iii) assunzione di manzo (< 6 mesi); (iv) introduzione precoce di latte vaccino (< 6 mesi); (v) fumo passivo e socializzazione precoce (< 2 anni di vita).

Marini A, Acta Paediatr Suppl 1996;; 14:1-21

Eczema and early solid feeding

Groups contrasted in adjusted odds ratio		Adjusted odds ratio	95% CI Lower limit	Upper limit
Four or more foods by 17 weeks post-term n=203	**Less than four foods** by 17 weeks post-term n=54	3,49	1,51	8,05

Morgan J. Eczema and early solid feeding in preterm infants.

Arch Dis Child. 2004;89:309-14

Timing of Solid Food Introduction in Relation to Atopic Dermatitis and Atopic Sensitization: Results From a Prospective Birth Cohort Study

Anne Zutavern, MD, MSca,j, Inken Brockow, MD, MPHa,b, Beate Schaaf, MDc,

RESULTS. Solid food introduction past the first 4 months of life decreased the odds of symptomatic AD but not for doctor-diagnosed AD, combined doctor-diagnosed and symptomatic AD, or atopic sensitization.

Postponing the introduction beyond the sixth month of life was not protective in relation to either definition of AD or atopic sensitization.

There was clear evidence for reverse causality between early skin or allergic symptoms and the introduction of solids.

PEDIATRICS Volume 117, Number 2, February 2006

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- can an early introduction of solid foods anticipate the development of food allergy?
- can their avoidance prevent the development of food allergy?
- are some foods more allergenic than other foods?
- are some food allergies more persistent than others?

GINI (German Infant Nutritional Intervention Study Group)

2252 newborns enrolled (1995-98)
945 formula-fed vs. 865 breastfed
Randomised to four formulae:

CMF:	16% incidence of atopic manifestations	OR = 1
eHF – W:	14% incidence of atopic manifestations	OR = 0.86
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Von Berg A, J Allergy Clin Immunol 2003; 111:533-40

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Directive 2000/13/EC
(amended by Directive 2003/89/EC)

1. Cereals containing gluten
2. Crustaceans
3. Eggs
4. Fish
5. Peanuts
6. Soybeans
7. Milk and products thereof (including lactose)
8. Nuts *i. e.* Almond, Hazelnut, Walnut, Cashew, Pecan nut, Brazil nut, Pistachio nut, Macadamia nut and Queensland nut
9. Celery
10. Mustard
11. Sesame seeds

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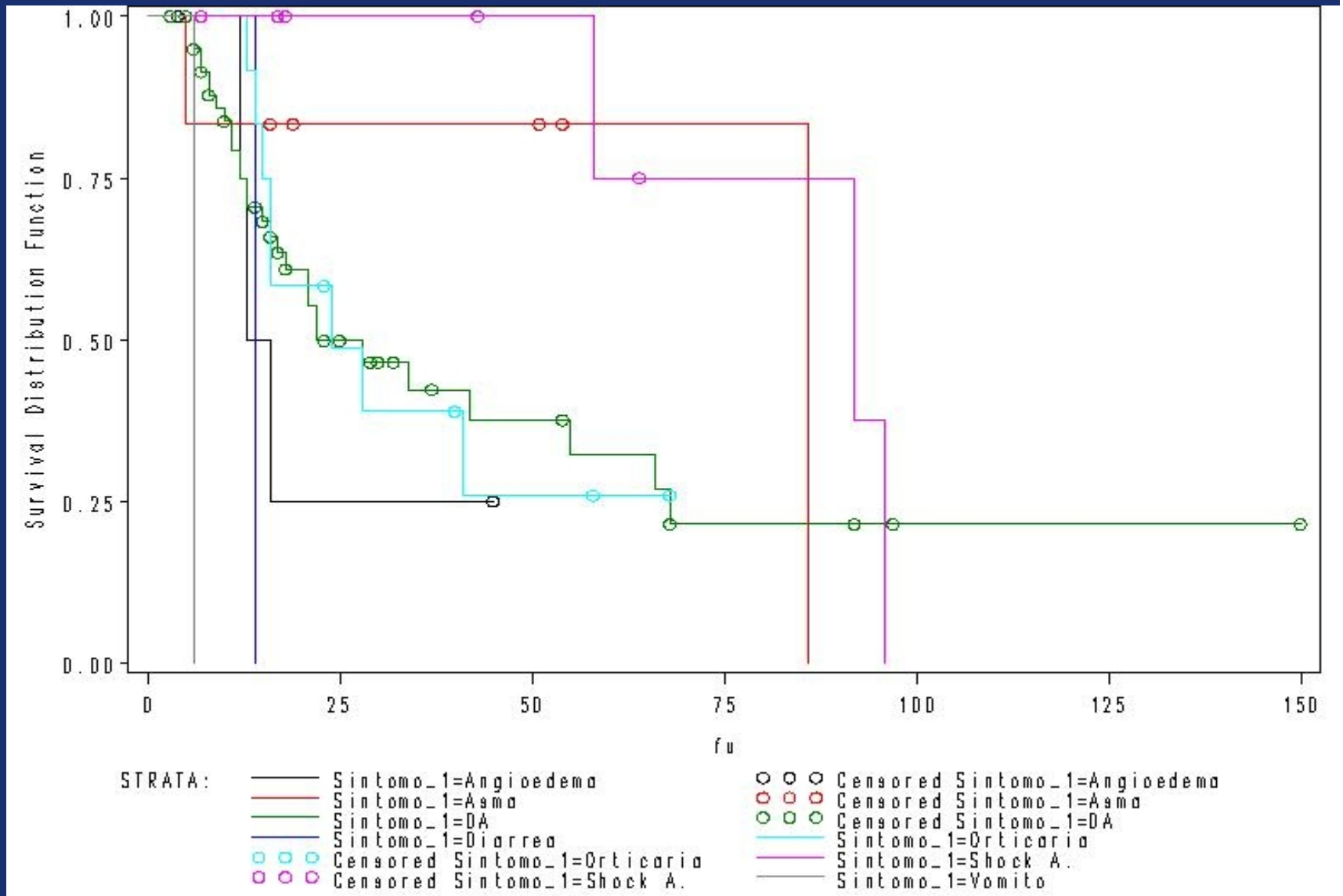
Melloni Pediatria (2005)



Prediction of tolerance on the basis of quantification of egg white-specific IgE antibodies in children with egg allergy.

Boyano-Martinez T, Garcia-Ara C, Diaz-Pena JM, Martin-Esteban M. J Allergy Clin Immunol. 2002;110:304-9.

Age (years)	Recovery
4	28 %
5	52 %
7	66 %

58 children allergic to egg, follow-up period of 7 - 86 months, (all the children were <2 years of age). The cumulative tolerance probability was 50% at 35 months of follow-up.

Tolleranza all'arachide

Autore	N.pazienti	% acquisizione di tolleranza
Tariq 1996	6	33
Hourihane 1998	120	18
Skolnick 2001	85	21,5

Skolnick HS, Conover-Walker MK, Koerner CB, Sampson HA, Burks W, Wood RA. The natural history of peanut allergy. J Allergy Clin Immunol 2001;107:367-374.

A step-by-step introduction of solid foods: theorical framework

- can an early introduction of solid foods anticipate the development of food allergy? yes
- can their avoidance prevent the development of food allergy? yes
- are some foods more allergenic than other foods? yes
- are some food allergies more persistent than others? yes

Alcune considerazioni

1. L’epidemiologia indica che l’esposizione precoce si associa ad allergia specifica
2. L’epidemiologia indica che ci sono nuove allergie anche in Italia
3. Non ci sono evidenze che un carico allergenico sia tollerogeno in epoca postnatale
4. Evitare gli alimenti ritarda o riduce la sensibilizzazione e l’allergia
5. Gli alimenti processati possono essere meno allergizzanti
6. In assenza di evidenze, vale il principio di precauzione.

Schema classico

1. la
2.
3.
4.

Il pediatra detta i tempi