



**La prevenzione
primaria dell'allergia:
Linee-guida & aspetti
pratici.**

Alessandro Fiocchi
Pula, 27 maggio 2012

**Giornate di Pediatria
Preventiva e Sociale
2012**



Presidente: Giuseppe Di Mauro

27 - 30 Maggio 2012

Centro Congressi Forte Village - Santa Margherita di Pula



Matteo. Andrea.

Al seno
Familiarità per allergie bilaterale
Criceto
Pastori maremmani
Fumo paterno

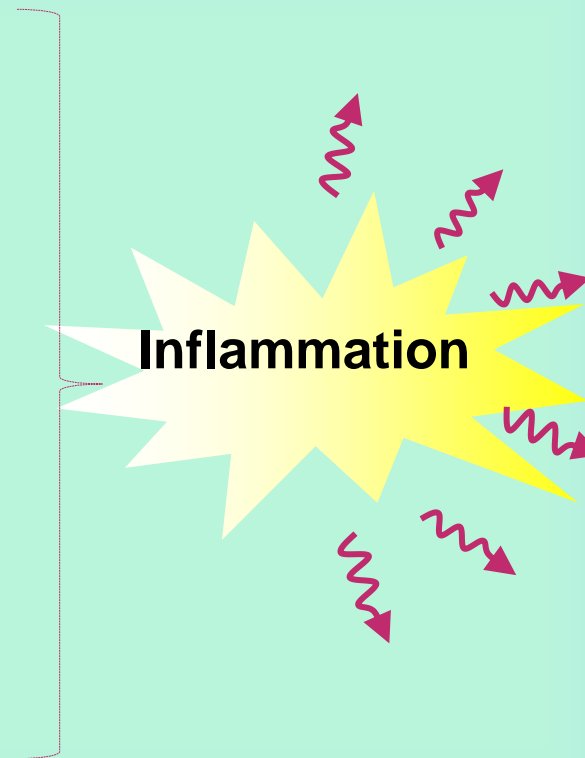
Ipogalattia.

Che tipo di latte consigliare?

Common risk factors

For many modern diseases

- Δ microbial balance
- Δ dietary profile
 - ☞ ↑ Saturated fat
 - ☞ ↓ Dietary fibre
 - ☞ ↓ n3/n-6 PUFA
 - ☞ ↓ Fresh foods
- Δ Sunlight (vitamin D)
- Δ Stress patterns
- Δ Exercise patterns
- Δ Pollutants
 - Smoking
 - Toxins & POPs
 - EM radiation?



- Allergy
- Autoimmunity
- Obesity
- Metabolic disease
- Diabetes
- Cardiovascular Disease
- Neurodegenerative Disease
- Inflammatory Bowel Disease
- Cancer

**= Common interventions
for prevention**



Food allergy prevention

1. **Fattori nutrizionali implicati nell'incremento delle allergie**
 2. L'approccio proibizionistico
 3. Quali sono le formule ipoallergeniche in commercio?
 4. Quali studi sono stati fatti sulla efficacia delle formule ipoallergeniche?
5. Cosa ci dicono le reviews sistematiche sulla efficacia preventiva delle formule ipoallergeniche?
 6. Possiamo contare sui probiotici?
 7. Fibre solubili e prebiotici
 8. Acidi grassi essenziali
 9. Ridurre lo stress
 10. Riequilibrare il metabolismo della vitamina D
 11. Conviene fare la prevenzione dell'allergia al latte?
12. Il ruolo dello svezzamento precoce nel bambino a rischio allergico?



Over 10% with challenge-proven food allergy

Reactions on challenge:

(hives, swelling, noisy breathing, choking, vomiting, pallor, floppiness)

- egg: 9%
- peanut



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 challenge criteria in infants. *J Allergy Clin Immunol* 2011;127:668-76

The first culprit

- Allergens: exposure is necessary for sensitisation.
- Allergens have been demonised and ostracized

A black and white cartoon illustration of a white, stitched figure with a human-like form, including a head with eyes and a torso with a small protrusion. The figure is confined within a dark, rectangular cage with vertical bars. The cage is surrounded by a circular border of barbed wire. The figure's hands are gripping the bars.

Did we imprison an innocent?



Now: significant rates of food allergy *prior* to starting foods at 4-6 months

DB-RCTs: early egg feeding



(n=1512)

- RCTs: start egg/placebo at 4-6 months
- **22% reaction rate** at randomization (*prior* to the intervention)
- **1.2% anaphylaxis** Rx adrenaline
- On 'first' known oral exposure to 'egg'

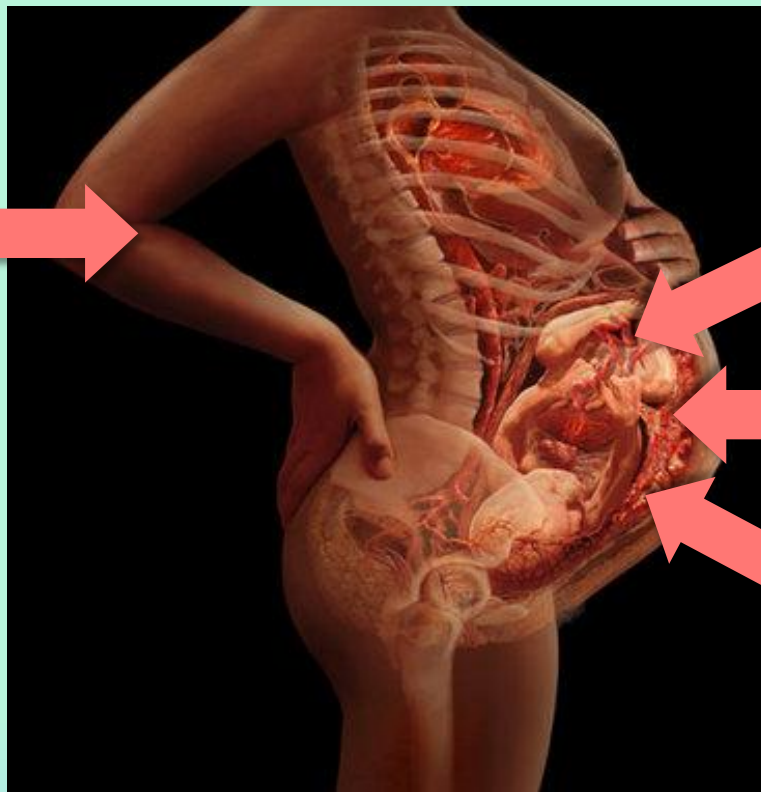
much earlier allergen exposure:
pregnancy, lactation,
transcutaneous....



Allergen detection in pregnancy

first encounter with allergen

Maternal
blood



Placental
tissues

Fetal
blood

Amniotic
Fluid

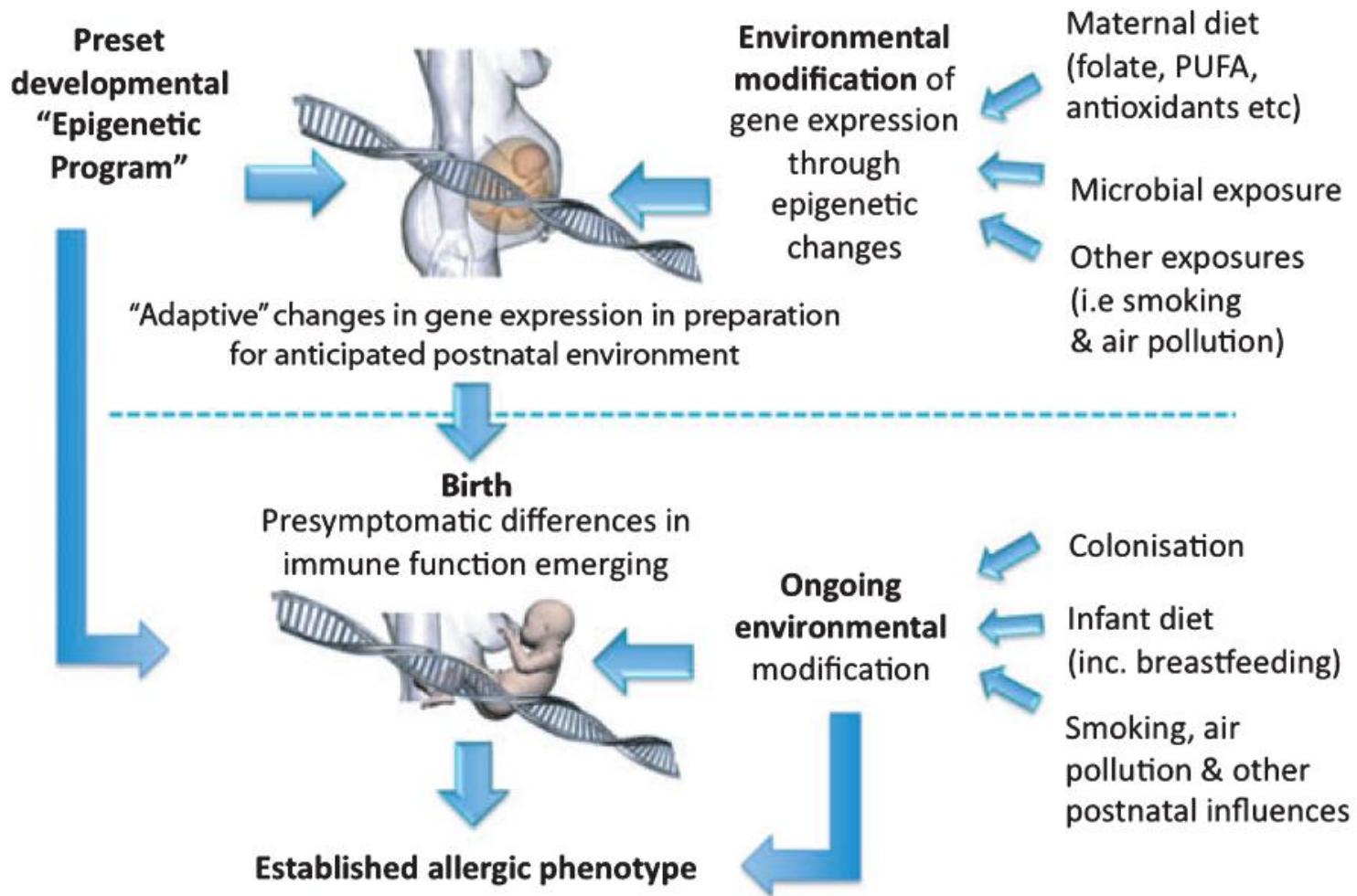
Contact with fetal
skin, gut, airways

Prescott S Early events in allergy development. Not everybody's cup of tea, Milan 2012

Holloway, J. A., et al. *Lancet* 356(9245): 1900-2.
Vance GH, et al. *Clin Exp Allergy* 2005; 35:1318-26.
Szepefalusi Z, et al. *Clin Exp Allergy* 2006; 36:1130-7.

Szepefalusi Z, et al. *Pediatr Res* 2000; 48:404-7.
Loibichler C, et al. *Clin Exp Allergy* 2002; 32:1546-51.

Modulation of gene expression by the pre and post natal environment:



Martino DJ, Prescott SL. Silent mysteries: epigenetic paradigms could hold the key to conquering the epidemic of allergy and immune disease. *Allergy* 2010; 65: 7–15



Breast milk: early source of allergen exposure

- Allergens in breast milk (with TGF β / tolerogenic factors)¹⁻³
- Allergen-IgG complexes (foods & inhalants)⁴
 - antigen-specific Treg cells in animals
 - also detected in human milk

Individual differences in secretion

- DB-RCT lactating women¹
(55g/day egg vs placebo for 21 days)
 - Some (25%) do not secrete OVA



1. Palmer DJ, et al. *Clin Exp Allergy* 2008; 38:1186-91
2. Vance GH, et al. *Clin Exp Allergy* 2005; 35:1318-26
3. Verhasselt, V. et al. *Nat Med* 2008 14 (2): 170-175.
4. Mosconi E, et al. *Mucosal Immunol* 2010; 3:461-74.

Variations in maternal milk (allergens / cytokines / other)
may contribute to the efficacy of oral tolerance



Links between breast milk and the thymus

- IL-7 in breast milk → Important role in generation of thymic Treg¹
- Greater thymus size in breastfeed infants; correlations with breast milk IL-7 levels.²



IL-7 in maternal milk

- crosses the neonatal intestine
- increases T cell production in the thymus ²

breast milk
IL-7

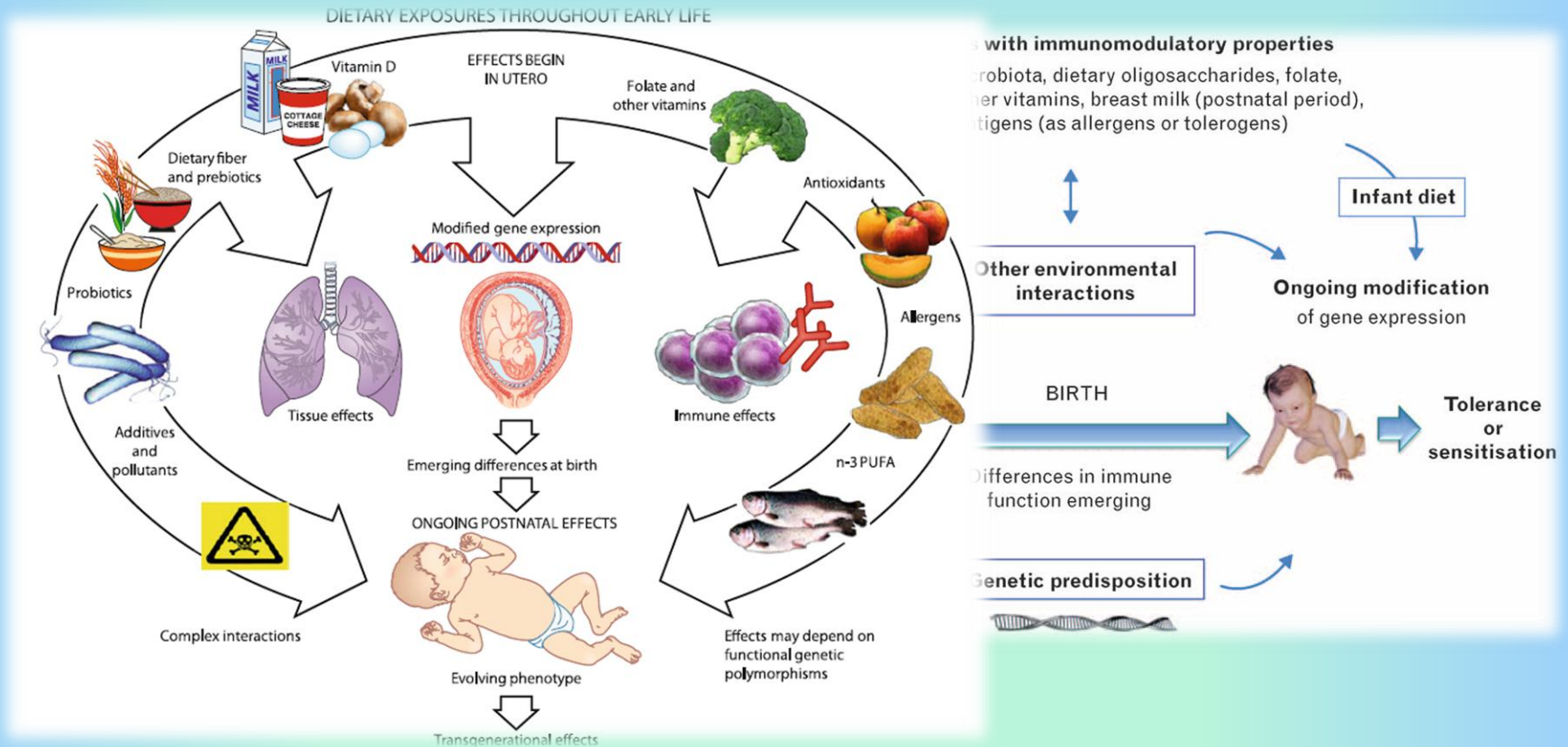
TSLP also in breast milk ³

- Emerging role in oral tolerance⁴
(Not simply a 'Th2' cytokine)

1. Aspinall R, et al. *PLoS One* 2011; 6:e20812.
2. Prentice AM, et al. *Acta Paediatr* 2000; 89:8–12.
3. Macfarlane T, et al. *PAI* 2010; 21:e454-6
4. Spadoni, Il et al. *Mucosal Immunol.* 2012 epub

Suggests a hitherto unrecognized link between gut and systemic tolerance mechanisms: role of milk variations?

Diet & tolerance in allergy development



West CE, Prescott SL. Role of diet in the development of immune tolerance in the context of allergic disease. *Curr Opin Pediatr.* 2010; 22:635-41

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



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CME review article

Supported by a grant fr

Primary diet

Alessandro Fiocchi, MD*; Amiel Warm, MD†; and L

Objective: To present research Data Sources: We conducted with use of the following keyw prevention and food allergy or clinical experience in an allergy

Results: We define a "proact prolonged breast-feeding, and use prevention of food allergy. These in light of epidemiologic evidenc

Conclusions: Inasmuch as nu effective in primary prevention of benefits), delayed (after the six Whether proactive strategies can probiotics as well as microbiolog and randomized clinical trials is



gy

o, MD†;

allergy management. 986 and October 2001 prevention, and dietary e authors' cumulative

estnatal environment, tionist approaches to reduce this distinction nts.

asures that are most ng immunity and other allergenic" formulas. t the scientific use of epidemiologic studies

Immunol. 2003;91:3-13.

The prohibitionist approach



1 NON SARAI CONCEPITO

2 QUALORA CONCEPITO, TUA MADRE NON FUMERA'

3 DURANTE LA GRAVIDANZA, TUA MADRE DIGIUNERA`

4 NON TI NUTRIRAI MEDIANTE LA PLACENTA

5 QUALORA TU NASCA, NON FARLO IN PRIMAVERA NE` IN AUTUNNO

6 DOPO NATO, NON MANGERAI

7 QUALORA MANGI, EVITERAI LATTE, UOVO, GRANO, PESCE, ARACHIDI, FRUTTA SECCA, ed in generale OGNI COSA COMESTIBILE

8 QUALORA MANGI, NON RESPIRERAI

9 QUALORA RESPIRI, NON FARLO IN CITTA`, NE` IN CAMPAGNA

10 QUALORA TU SIA SOPRAVVISSUTO.... LA TUA PROBABILITA` DI NON SVILUPPARE ALLERGIA E` ALMENO DEL 35%!



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Aptamil HA 1 (Milupa)

Aptamil HA 2 (Milupa)

Humana HA 1 (Humana)

Humana HA 2 (Humana)

Mellin HA (Mellin)

Mellin Ipo (Mellin) liquido

Nativà HA 1 (Guigoz)

Nativà HA 2 (Guigoz)

Nidina HA 1 (Nestlè)

Nidina HA 2 (Nestlè)

Nutrilon pepti 1 (Nutricia)

Nutrilon pepti 2 (Nutricia)

Plasmon HA (Plada)

Similac RA (Abbott)

Vivena HA (Dieterba)

Vivena 2 HA (Dieterba)



Nan HA (Nidina active Excel)

Manufacturer	Nestlé SA, Vevey, CH
Labelled for	Reduction of the risk of CMA
Protein source	Whey
Technological process	Hydrolysis
Carbohydrate source	Lactose
Lipid source	Vegetable oils
Price in € per litre	5 €
kCal/L	670



Nutramigen 1 LGG Lipil

Manufacturer	Mead Johnson Nutrilon srl
Labelled for	hypoallergenic infant formula for term infants who are sensitive to the intact proteins in cow's milk and soy formulas, as well as other foods.
Protein source	Casein
Technological process	Enzymatic hydrolysis
Carbohydrate source	86% corn syrup solids, 14% modified corn starch
Lipid source	44% palm oil, 19.5% soy oil, 19.5% coconut oil, 14.5% sunflower oil, 2.5% Lipil



Nutramigen 1 LGG Lipil

Price in € per litre	8 €
kCal/L	672
Omega-3 fatty acids	
Docosahexaenoic acid (DHA), mg/L	116
Alpha - Linolenic acid, g/L	0.44
Omega-6 fatty acids	
Arachidonic acid mg/L	230
Linoleic acid g/L	5.79



Hypolac

Manufacturer	Lactalis
Labelled for	infants and children with known allergies to cow's milk protein and soy - infants and young children with lactose intolerance. From the first week of life.
Protein source	whey
Technological process	Enzymatic hydrolysis



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Cochrane review: formulas containing hydrolysed protein for prevention of allergy and food intolerance in infants

Results

Eighteen trials

Meta-analysis of 4 studies (386 infants) → reduction in allergy incidence in infancy.

One study → reduction in allergy incidence in childhood

Reductions found:

- asthma prevalence in childhood
- eczema incidence in infancy
- eczema prevalence in childhood
- food allergy prevalence in childhood
- CMA incidence in infancy



Cochrane review: formulas containing hydrolysed protein for prevention of allergy and food intolerance in infants

Conclusions

No hydrolysed formula for the prevention of allergy in preference to exclusive breast feeding.

Hydrolysed compared to a cow's milk formula reduces infant and childhood allergy and infant CMA.

Extensive vs. partially hydrolysed formula?

Effects beyond five years?

Costs?

Compliance?



CM vs HA vs Soy

- 1990 – 1994
- Single-blind randomized controlled trial
 - Conventional CMF, pHWF, SF
 - 620 infants
 - Family history of allergic disease
- SPT to milk, egg, peanut, dust mite, grass, & cat dander)
 - 6, 12, and 24 months

PRIMARY OUTCOME:

allergic manifestations in the first 2 years of life.



Formula and risk of allergic disease < 2y

Symptom	CMF	HA	Soy
Any allergic manifestation: 0-1 y	37.3%	37.7%	44.0%
Any allergic manifestation: 1-2 y	48.7%	53.4%	54.5%
Eczema	43.0%	48.7%	46.1%
Food reactions			
Any food	13.5%	15.2%	19.4%
CM	3.1%	1.6%	4.2%
CM SPT+	0.0%	0.5%	1.0%
Peanut SPT+	0.5%	0.0%	0.0%
Egg SPT+	1.0%	0.5%	2.6%

Lowé A. Effect of a partially hydrolyzed whey infant formula at weaning on risk of allergic disease in high-risk children: a randomized controlled trial. *J Allergy Clin Immunol* 2011; 128:360-5



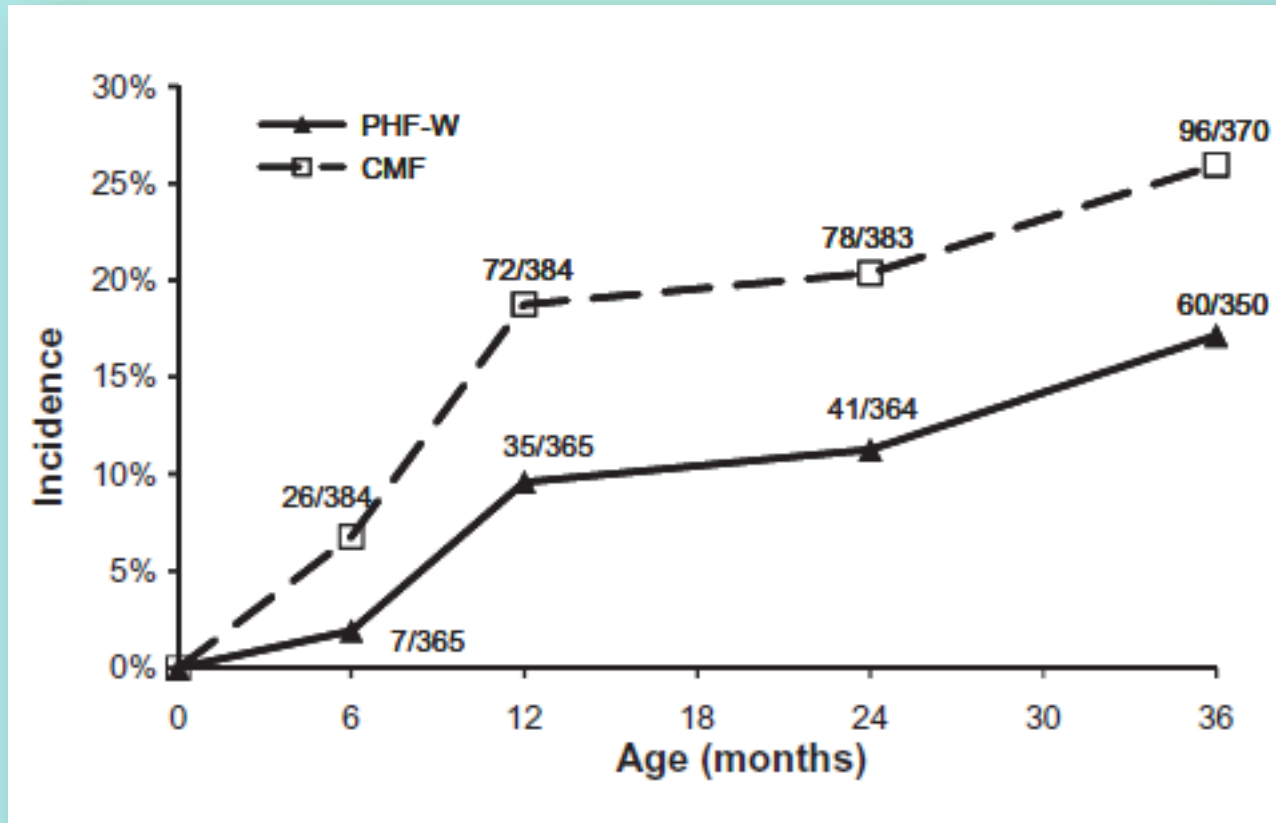
Formula and risk of allergic disease 6-7y

Symptom	CMF	HA	Soy
Eczema	31.5%	33.5%	30.5%
Asthma	32.1%	28.0%	29.7%
Rhinitis	22.2%	22.0%	26.7%
Persistent asthma	25.5%	24.0%	24.2%

Low A. Effect of a partially hydrolyzed whey infant formula at weaning on risk of allergic disease in high-risk children: a randomized controlled trial. *J Allergy Clin Immunol* 2011; 128:360-5



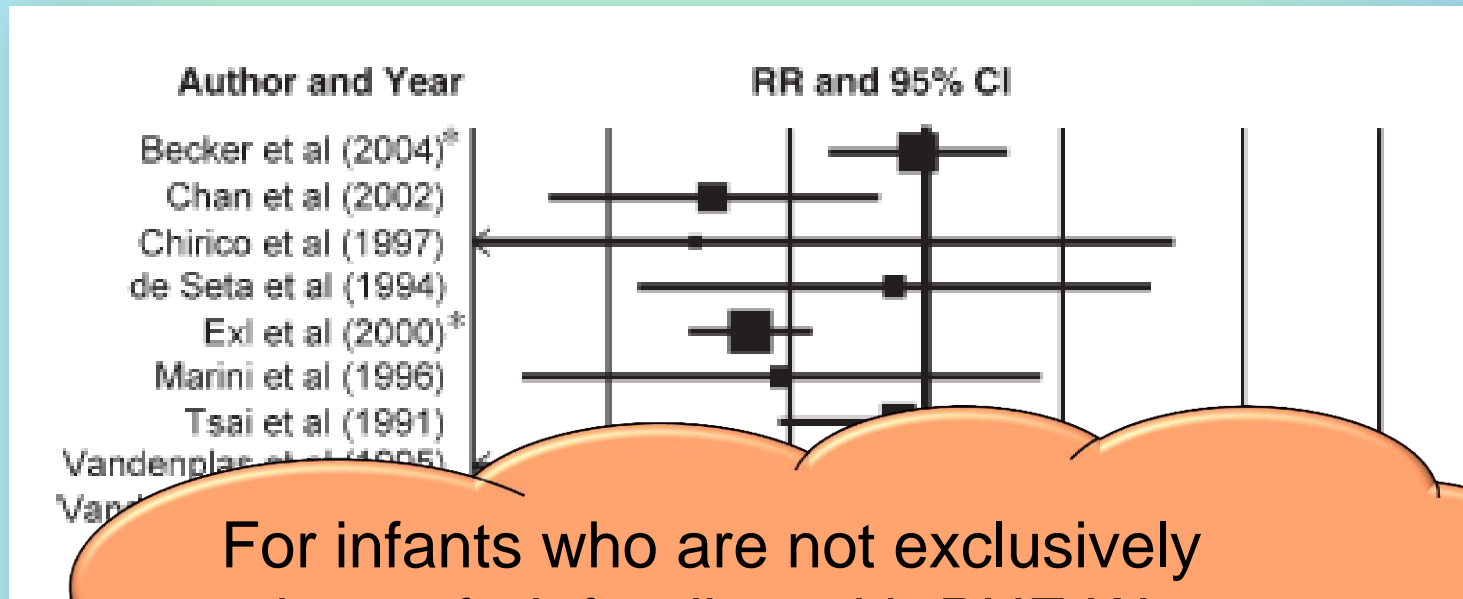
Summed cumulative incidence of atopic dermatitis among infants fed PHF-W and CMF.



Alexander DD. Partially hydrolyzed 100% whey protein infant formula and atopic dermatitis risk reduction: a systematic review of the literature. *Nutr Rev.* 2010;68:232-45



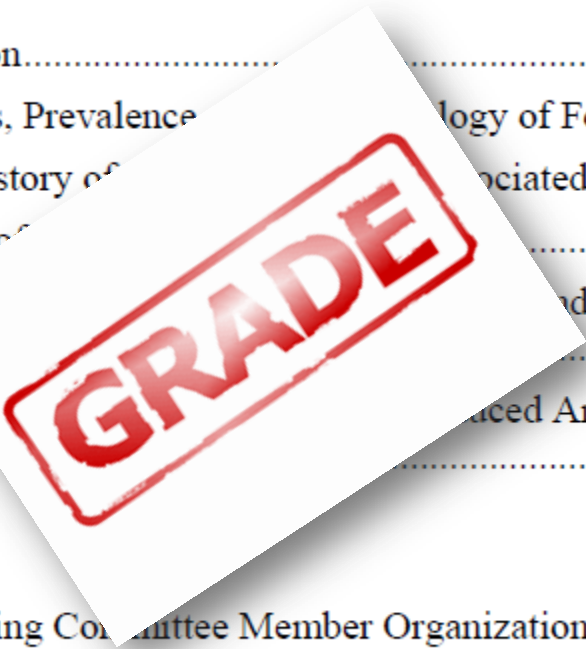
Risk of AD : pHF-W vs CMF



For infants who are not exclusively breastfed, feeding with PHF-W instead of CMF reduce the risk of AD, particularly in infants with a family history of allergy

NIH guidelines for the diagnosis and management of food allergy

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NIH guidelines for the prevention of food allergy

Guideline 32: [...] Patients at risk for developing FA are defined as those with a biological parent or sibling with existing, or history of, allergic rhinitis, asthma, AD, or FA. This definition of “at risk” is used throughout sections 5.2 and 5.3.

NIH guidelines for the prevention of food allergy

Guideline 38: The EP does not recommend using soy infant formula instead of cow's milk infant formula as a strategy for preventing the development of FA or modifying its clinical course in at-risk infants

NIH guidelines for the prevention of food allergy

Guideline 39: The EP suggests that exclusive use of extensively or partially hydrolyzed infant formulas be considered for infants who are not exclusively breastfed and are at risk for developing atopic disease. Cost or availability of extensively hydrolyzed infant formulas may be weighed as prohibitive factors.

NIH guidelines for the prevention of food allergy

Guideline 39:

Practical and considerations of extensively hydrolyzed infant formulas may limit their use to infants who are at risk and not being exclusively breast-fed. There is no evidence to suggest exclusive feeding with a hydrolyzed infant formula is more likely to prevent atopic disease than exclusive breast-feeding.

NIH guidelines for the prevention of food allergy

Guideline 39:

Comparative studies of the various hydrolyzed formulas indicate that not all formulas have the same protective benefit.



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Nutramigen 1 LGG Lipil

Probiotics	
Genus, species	LGG colture
CFU/g powder	10^6 CFU/g

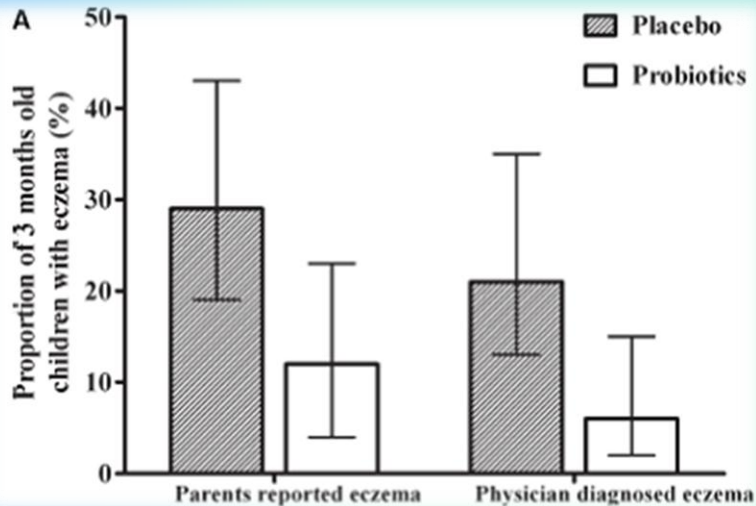


Nan HA (Nidina active Excel)

Omega-3 fatty acids	
Docosahexaenoic acid (DHA), mg/L	79
Alpha - Linolenic acid, g/L	0.64
Omega-6 fatty acids	
Arachidonic acid mg/L	79
Linoleic acid g/L	5.3
Probiotics	
Genus, species	B. lactis
CFU/g powder	10 ⁷ CFU/g



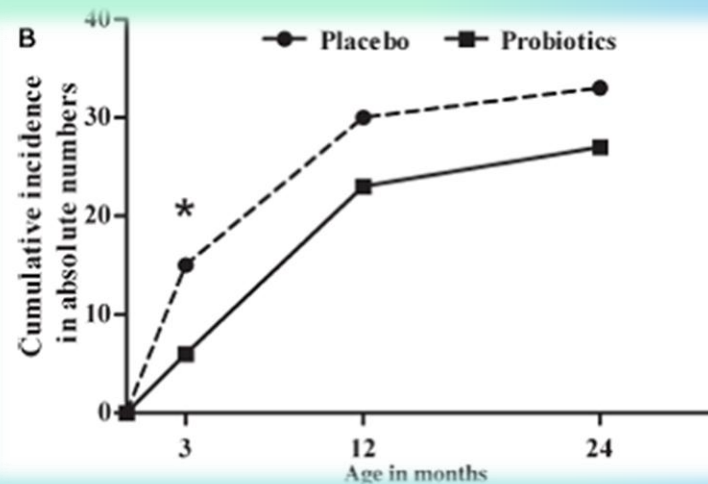
Ecologic PandA and eczema



AD:

6/50 (12%) in treated vs. 15/52 (29%) in placebo. $P = 0.035$

RR reduction: 58%



Njers R. the effects of selected probiotic strains on the development of eczema . The PandA study. Allergy 2009; 64:256-61

The idea that supplemental probiotic bacteria can be used to manipulate allergy homeostatic mechanisms remains a hypothesis

Pre

They
home
towa

- prevention
- treatment.



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Prebiotics (non-digestible, fermentable oligosaccharides)

Initial studies using prebiotics in cow-milk-based formula showed reduced cumulative incidence of allergic outcomes in **high-risk children** at 2 years:

- atopic dermatitis
- recurrent wheezing
- allergic urticaria
- reduced respiratory tract infections
- fever episodes and antibiotic prescriptions

Moro G. A mixture of prebiotic oligosaccharides reduces the incidence of atopic dermatitis during the first six months of age. *Arch Dis Child* 2006; 91: 814–9

Arslanoglu S. Early dietary intervention with a mixture of prebiotic oligosaccharides reduces the incidence of allergic manifestations and infections during the first two years of life. *J Nutr* 2008; 138: 1091–5



Prebiotics (non-digestible, fermentable oligosaccharides)

Subsequent studies

⇒ reduced risk of AD in children **at low risk** of allergic disease

Gruber C. Reduced occurrence of early atopic dermatitis because of immunoactive prebiotics among low-atopy-risk infants. *J Allergy Clin Immunol* 2010; 126: 791–7

Mechanisms of effect:

- promoting colonisation with healthy commensal bacteria?
- direct effects on the immune system?



Prebiotics (naturally in breast milk)

There is encouraging evidence that prebiotics have a number of health-promoting effects, including immune effects, which may reduce the risk of allergic and infectious outcomes; the **results** of several large multicentre studies are **awaited** with interest as there are still relatively few studies to report on allergy outcomes



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n-3 PUFA (fish oil)

Epidemiological studies suggest dietary n-3 PUFA exposure in pregnancy and early childhood may protect against asthma and allergic disease

n-3 PUFA \Rightarrow anti-inflammatory properties

Calvani M. Consumption of fish, butter and margarine during pregnancy and allergy in the offspring: role of maternal atopy. *Pediatr Allergy Immunol* 2006; 17: 94-102

Romieu I. Maternal fish intake during pregnancy and atopy and asthma in infancy. *Clin Exp Allergy* 2007; 37: 518-25

Kull I. Fish consumption during the first year of life and development of allergic diseases during childhood. *Allergy* 2006;61: 1009-15

Calder PC. The relationship between the fatty acid composition of immune cells and their function. *Prostaglandins Leukot Essent Fatty Acids* 2008; 79: 101-8



n-3 PUFA (fish oil)

RCT using fish oil in pregnancy \Rightarrow immunological effects

RCT using fish oil in pregnancy and lactation \Rightarrow immunological effects

Postnatal interventions with fish oil have not shown consistent or long-term benefits.

Olsen L. Fish oil supplementation during pregnancy and asthma in the offspring: 10-year follow-up of a randomized controlled trial. *Am J Clin Nutr* 2008; 88:167–75

Furuhjelm C. Fish oil supplementation in pregnancy and lactation may decrease the risk of infant allergy. *Acta Paediatr* 2009; 98: 1461–7

Schouten L. Cow milk allergy symptoms are reduced in mice fed dietary synbiotics during oral sensitization with whey. *J Nutr* 2009; 139: 1398–1403

Almqvist C. Omega-3 and omega-6 fatty acid exposure from early life does not affect atopy and asthma at age 5 years. *J Allergy Clin Immunol* 2007; 119:1438–44



n-3 PUFA & infants' allergies in first year of life

Dietary n-3 long chain polyunsaturated fatty acid (LCPUFA) supplementation of pregnant women with a fetus at high risk of allergic disease

706 infants

Intervention group (n=368): fish oil capsules (900 mg of n-3 LCPUFA daily) from 21 weeks' gestation until birth

Control group (n=338) vegetable oil capsules without n-3 LCPUFA.

Outcome measure: IgE-associated allergic disease (eczema or food allergy with sensitisation) at 1 year of age.

Palmer DJ, Sullivan T, Gold MS, Prescott SL, Heddle R, Gibson RA, Makrides M. Effect of n-3 long chain polyunsaturated fatty acid supplementation in pregnancy on infants' allergies in first year of life: randomised controlled trial. *BMJ*. 2012 Jan 30;344:e184



n-3 PUFA & infants' allergies in first year of life

Infants with IgE-associated allergic disease: 9 vs 13%, ns

Infants with AD & allergy 7 vs 12%, $p=0.06$

Infants with egg sensitisation 9 vs. 15%, $p=0.02$

Infants with food allergy 17 vs 16%, $p=ns$

Palmer DJ, Sullivan T, Gold MS, Prescott SL, Heddle R, Gibson RA, Makrides M. Effect of n-3 long chain polyunsaturated fatty acid supplementation in pregnancy on infants' allergies in first year of life: randomised controlled trial. *BMJ*. 2012 Jan 30;344:e184



n–3 PUFA (fish oil)

Allergy-protective effects of increasing n–3 PUFA status
– if any – are more likely to be greatest in pregnancy

Due to the differential effects of n–3 PUFA in the
antenatal versus the postnatal period, future systematic
reviews should examine these interventions separately



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Reducing stress!!?

Stress affects immune function

- effects in pregnancy
- long-term effects in offspring
- some evidence in humans

Maternal stress and allergies

- higher IgE levels in newborns
- risk of wheeze and asthma

Infant stress levels

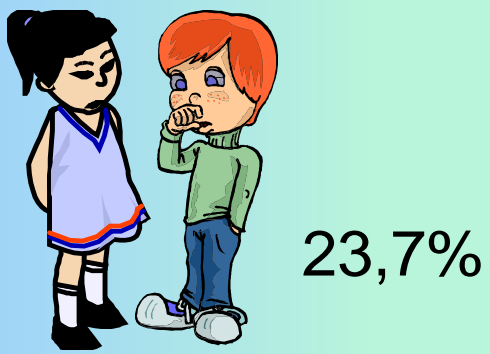
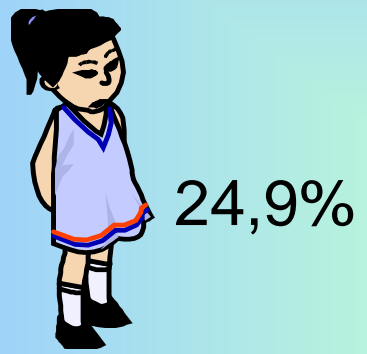
- cortisol levels indicate stress in babies, and higher allergy risk!



Logical to reduce stress for many health benefits



Sibship size, birth order, and atopy in Italy



9,3%



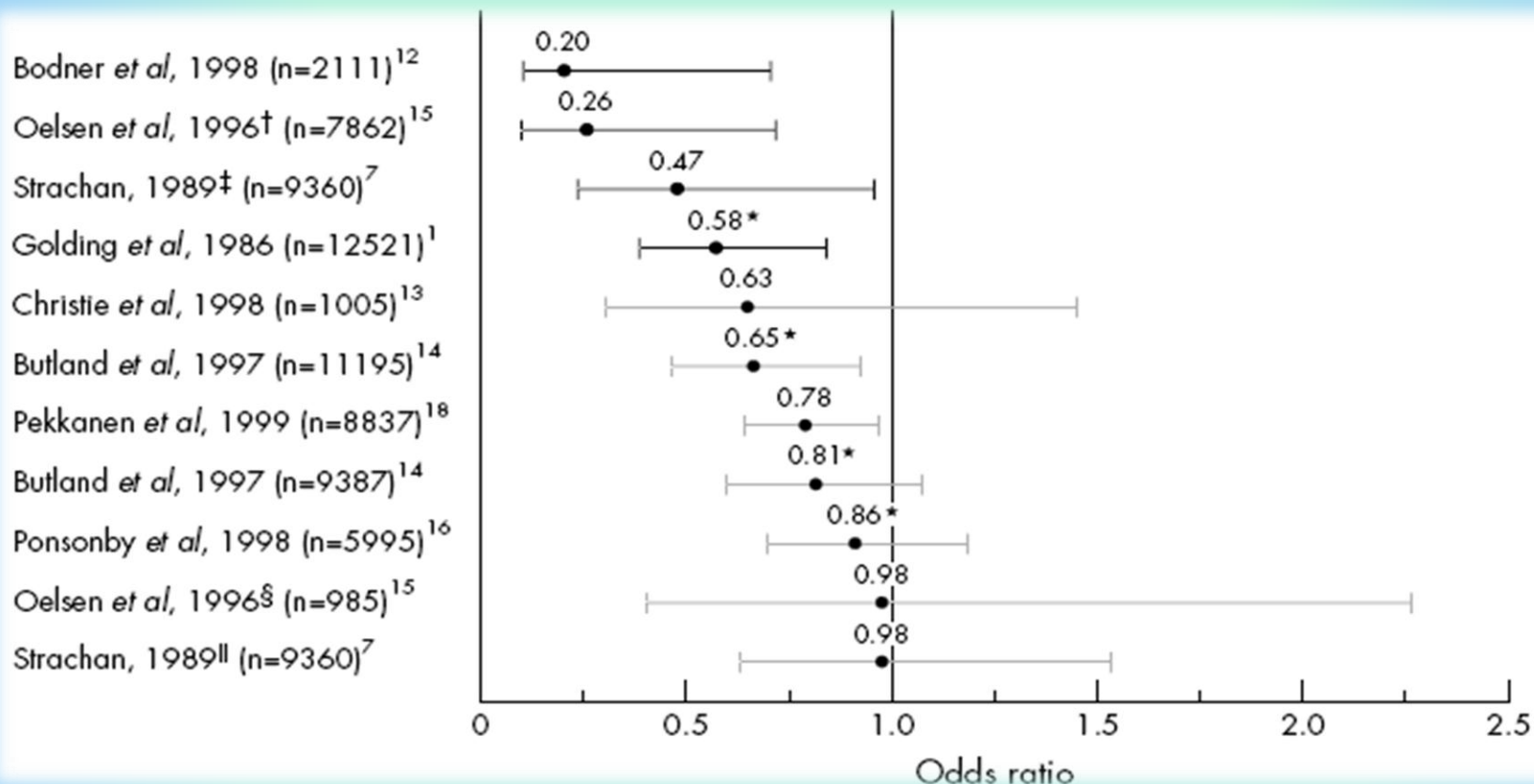
18,9%



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



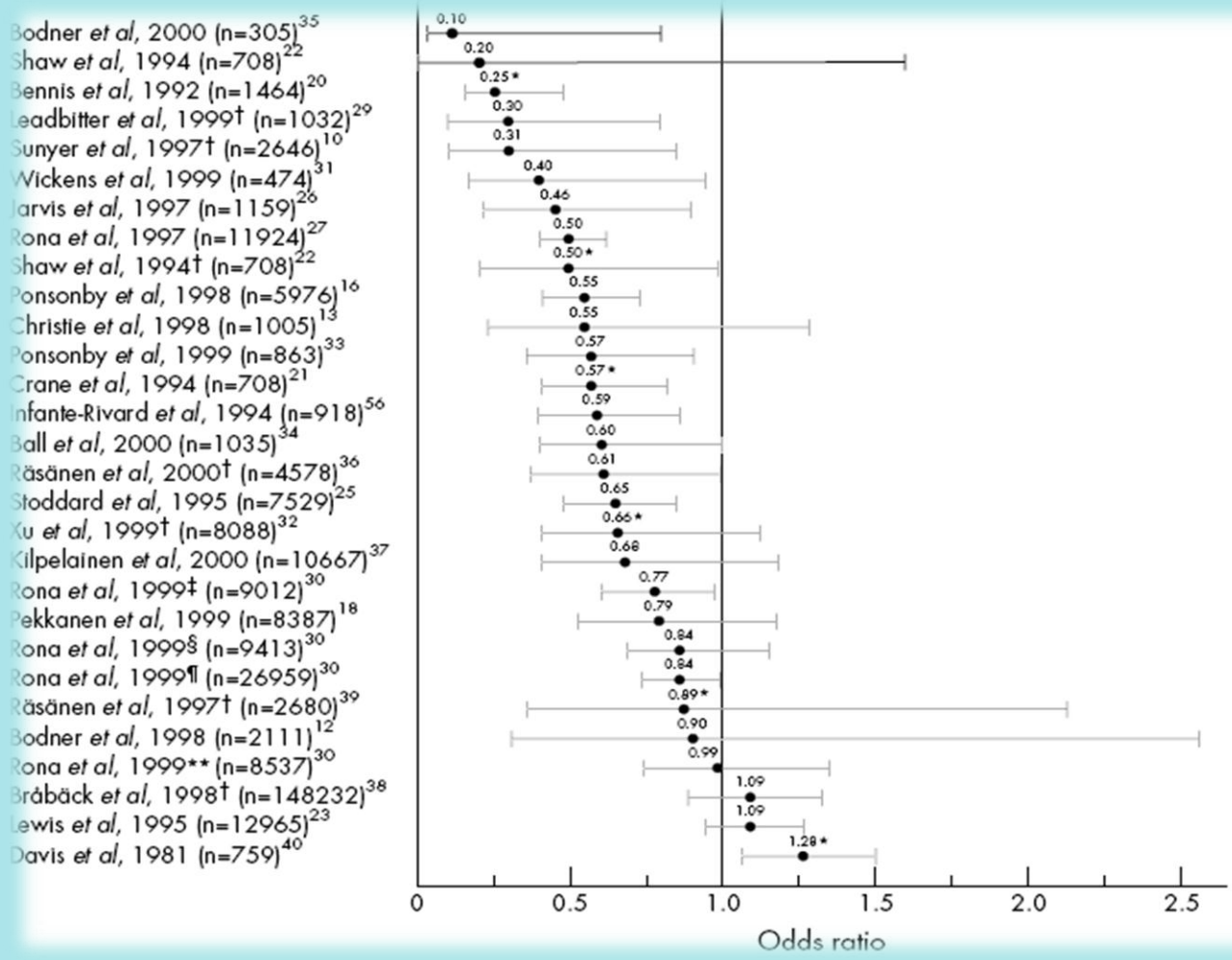
Eczema and number of siblings: 3+ vs. none



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



Asthma and number of siblings: 3+ vs. none

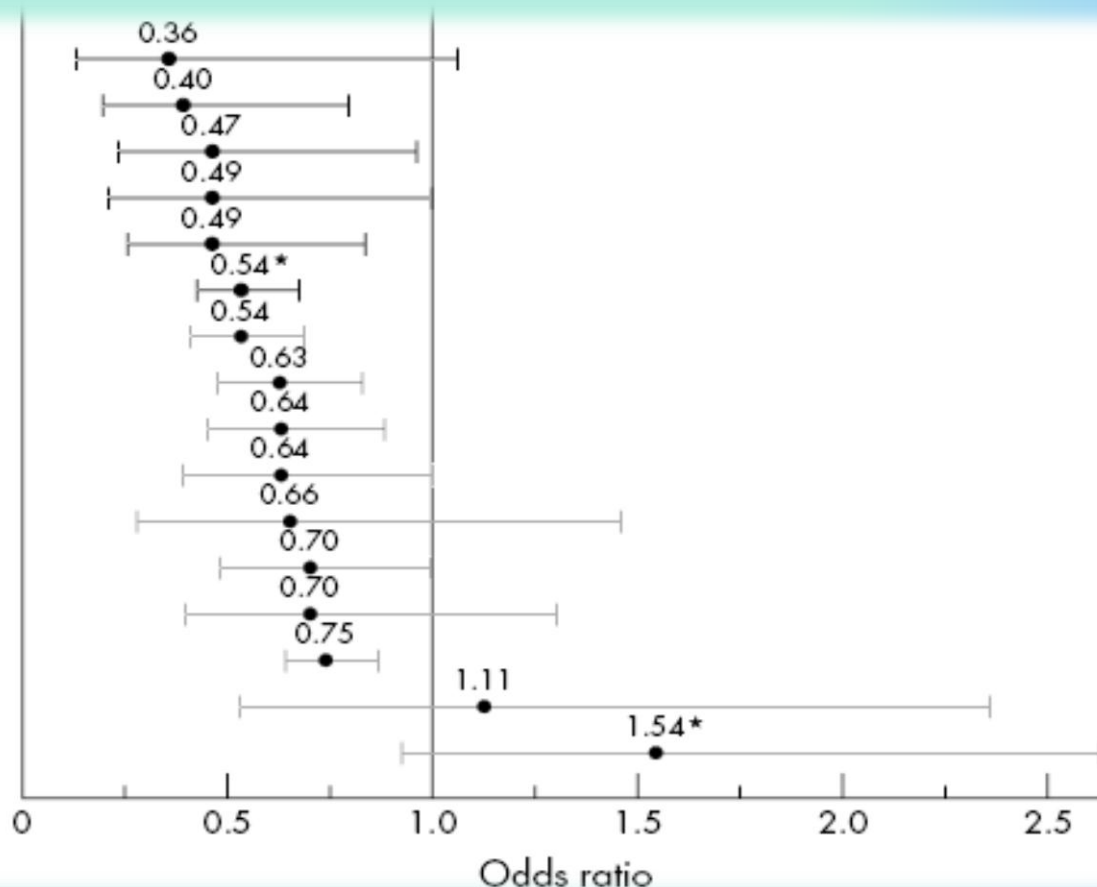


Karmaus W. Does an higher number of siblings protect against the development of allergy and asthma? *J. Epidemiol. Community Health* 2002;56;209-217



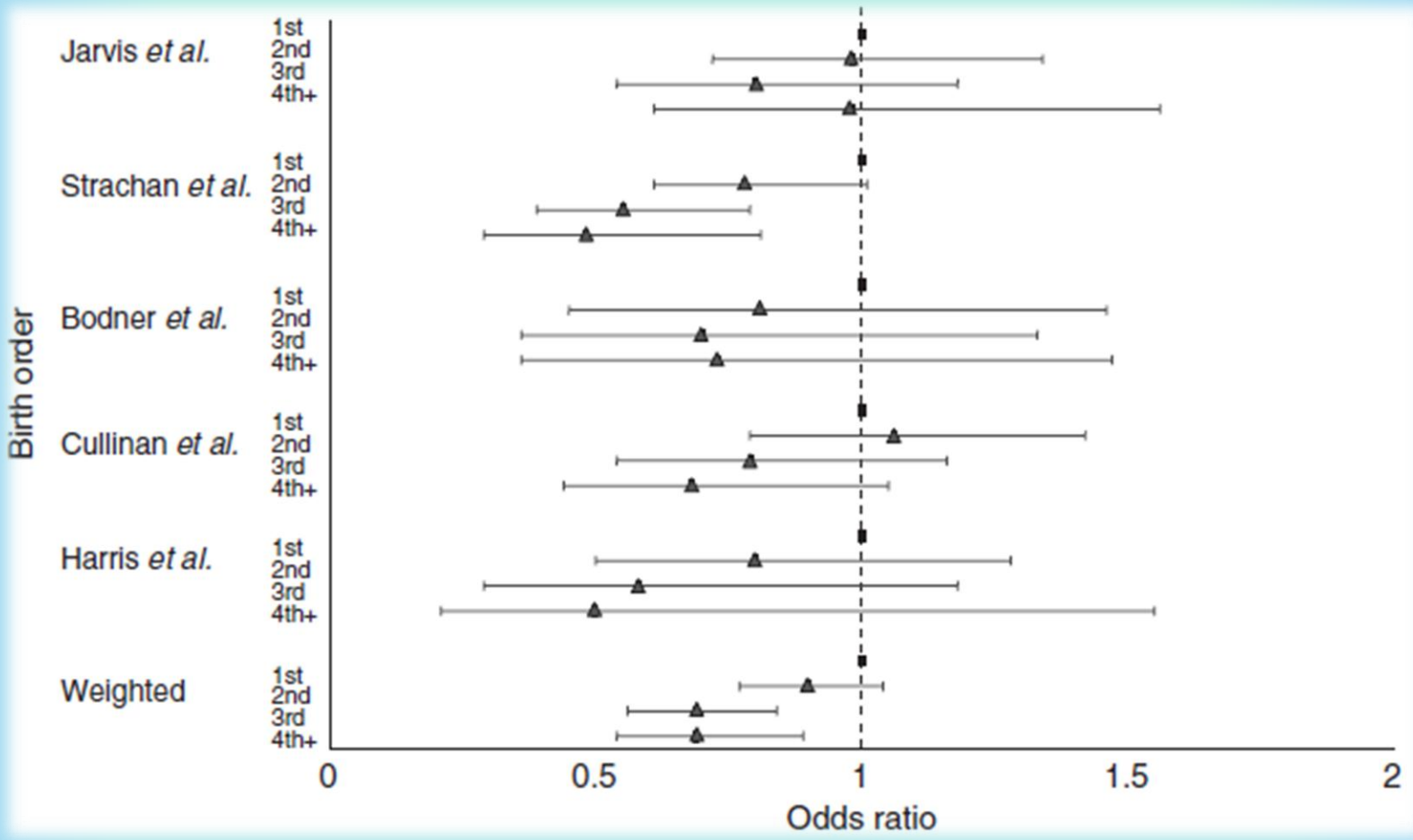
SPT+ and number of siblings: 3+ vs. none

- Forastiere *et al*, 1997 (n=2226)⁴⁹
- Storm *et al*, 1998 (n=1470)⁵¹
- Matricardi *et al*, 1997† (n=1659)⁵⁰
- Strachan *et al*, 1996 (n=723)⁸
- Strachan *et al*, 1997† (n=1369)⁴⁸
- von Mutius *et al*, 1994 (n=6248)⁴⁴
- Matricardi *et al*, 1998† (n=11371)⁶
- Matricardi *et al*, 1998‡ (n=11371)⁶
- Nowak *et al*, 1996 (n=1702)⁴⁶
- Strachan *et al*, 1997‡ (n=1369)⁴⁸
- Matricardi *et al*, 1997‡ (n=1659)⁵⁰
- Jarvis *et al*, 1997 (n=907)²⁶
- Leadbitter *et al*, 1999 (n=714)²⁹
- Svanes *et al*, 1999 (n=13932)¹¹
- Haby *et al*, 2000 (n=650)⁵²
- Davis *et al*, 1981 (n=759)⁴⁰





Atopy by order of birth



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



Food allergy prevention

1. Fattori nutrizionali implicati nell'incremento delle allergie
2. L'approccio proibizionistico
3. Quali sono le formule ipoallergeniche in commercio?
4. Quali studi sono stati fatti sulla efficacia delle formule ipoallergeniche?
5. Cosa ci dicono le reviews sistematiche sulla efficacia preventiva delle formule ipoallergeniche?
6. Possiamo contare sui probiotici?
7. Fibre solubili e prebiotici
8. Acidi grassi essenziali
9. Ridurre lo stress
10. Riequilibrare il metabolismo della vitamina D
11. Conviene fare la prevenzione dell'allergia al latte?
12. Il ruolo dello svezzamento precoce nel bambino a rischio allergico?



Vitamin D

- recognized immunoregulatory effects
 - declining levels with sedentary lifestyles
- ⇒ a candidate factor in the rise in 'autoimmune' & 'allergy'

↑↑ maternal vitamin D ⇒ ↓↓ asthma & AR in children

↑↑ vitamin D ⇒ ↑↑ risk of allergic disease?

Camargo CA . Cord-blood 25-hydroxyvitamin D levels and risk of respiratory infection, wheezing, and asthma. *Pediatrics* 2011; 127:e180–7

Erkkola M. Maternal vitamin D intake during pregnancy is inversely associated with asthma and allergic rhinitis in 5-year-old children. *Clin Exp Allergy* 2009; 39: 875–882

Krstić G: Asthma prevalence associated with geographical latitude and regional insolation in the United States of America and Australia. *PLoS One* 2011; 6:e18492

Back O. Does vitamin D intake during infancy promote the development of atopic allergy? *Acta Derm Venereol* 2009; 89: 28–32.



Vitamin D

There is a sound basis for further investigating the role of changing vitamin D status in the rising rates of allergy

RCT are needed:

- several pregnancy trials are underway
- the findings of these are awaited with great interest



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Conviene?

Fattori da considerare:

- a. Valori e preferenze del medico
- b. Valori e preferenze del paziente
- c. Costi
- d. Palatabilità
- e. Indici nutrizionali



Resource utilisation (costs)

Milk/formula	Cost per liter (Euro)	Cost per 6 months (Euro)
normal cow's milk	0.9	129
normal formula	2.0	288
HA formula	5	720
eHF	6	864
soy formula	5	720
rice formula	6	864
amino acid formula	14	2016

Fiocchi A, Schunemann H. Diagnosis and Rationale for Action against Cow's Milk Allergy. The WAO DRACMA guideline. WAO Journal 2010; S1 (April), 1-105.









Suggested retail prices in Italy

Milk/formula	Cost per liter (Euro)	Cost per 6 months (Euro)
normal cow's milk	1.0	144
normal formula (powder)	3.1	446
normal formula (liquid)	5.8	835
HA formula	5	720
eHF: Nutramigen	8	1152
eHF: Hypolac	8	1152
amino acid formula	14	2016
soy formula	4.5	680

Retail prices obtained from a local drugstore



Palatability of formulae - total

	Cow's milk	11.90
	Starting formula	9.88
	Partial hydrolysate	9.54
	Soy formula	8.44
	Hydrolised rice formula	7.94
	Hydrolised soy formula	7.62
	Whey hydrolysate	6.38
	Casein hydrolysate	5.74

Pedrosa M, Palatability of hydrolysates and other substitution formulas for cow's milk-allergic children: a comparative study of taste, smell, and texture evaluated by healthy volunteers. *J Investig Allergol Clin Immunol.* 2006;16:351-6



Growth pattern of healthy infants fed Nutramigen

Children fed Nutramigen thinner.

Taste?

Hydrolised proteins satiate > whole proteins?

AA satiate > whole proteins?

Mennella JA. Differential growth patterns among healthy infants fed hydrolysate or cow-milk formulas. Pediatrics. 2011;127



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12. Conclusioni



Conclusions

Current recommendations for allergy prevention:

1. avoidance of cigarette smoke
2. promotion of breastfeeding
3. use of hydrolysed formula

Future studies are likely to provide clearer insights:

- probiotics?
- prebiotics?
- specific dietary nutrients?...