Weaning: the Optimal Time for Solid Food Introduction for Allergy Prevention

Attilio Boner

University of Verona, Italy

- ✓ introduction
- ✓ starting point
- ✓ old reccomendations
- ✓ new findings
- ✓ dietary antigens properties
- ✓ development of tolerance
- ✓ other possible mistakes
- ✓ not only allergy
- ✓ allergy development?
- ✓ what can be done?
- ✓ conclusions

Early-life environmental determinants of allergic diseases and the wider pandemic of inflammatory noncommunicable diseases.

Prescott SL. J Allergy Clin Immunol. 2013;131:23-30.

- The increase in a diverse range of **chronic noncommunicable diseases (NCDs) is one of the major global challenges of the 21st century.**

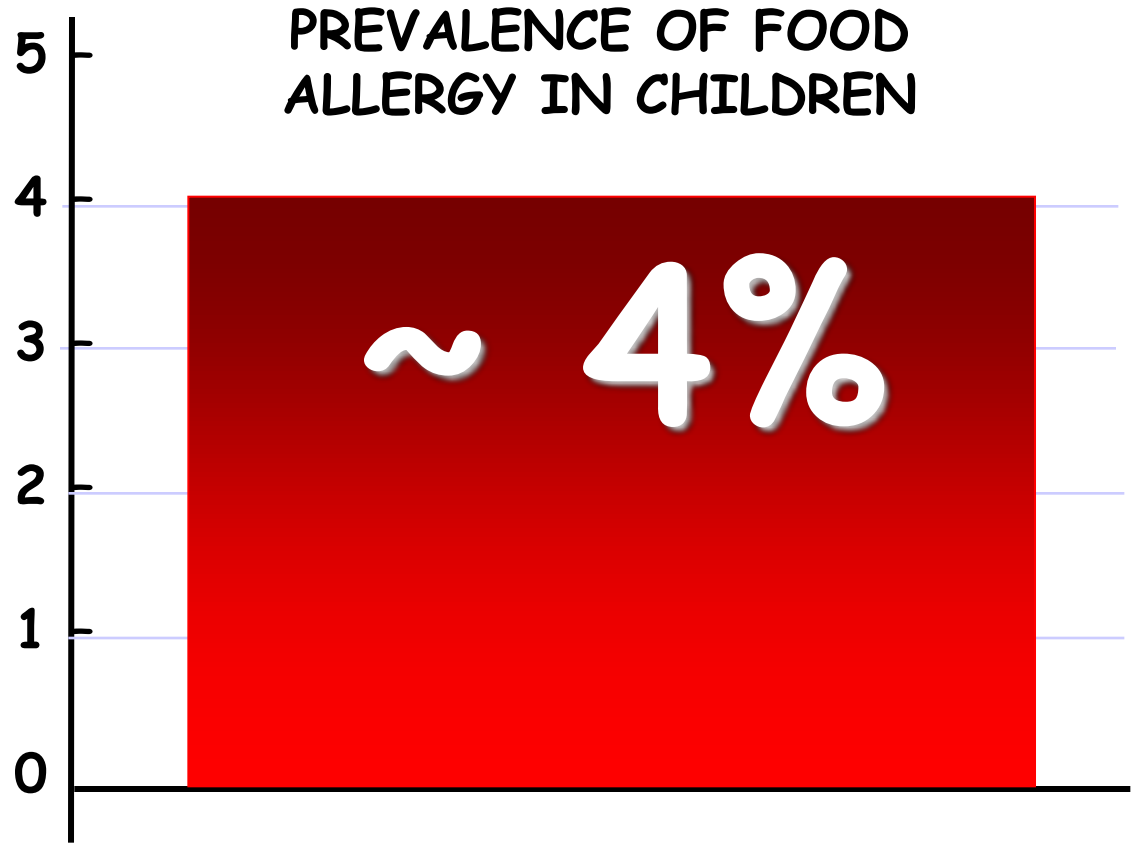
- The dominant focus of the NCDs agenda is usually on "the big four":

1) cardiovascular disease,
2) metabolic disease (obesity and type 2 diabetes),
3) cancer, and
4) chronic lung disease & allergy

Food Allergy Among Children in the United States

Branum Pediatrics 2009;124:1549

- ✓ A cross-sectional survey of data on food allergy among children <18 yrs
- ✓ in the 1997–2007



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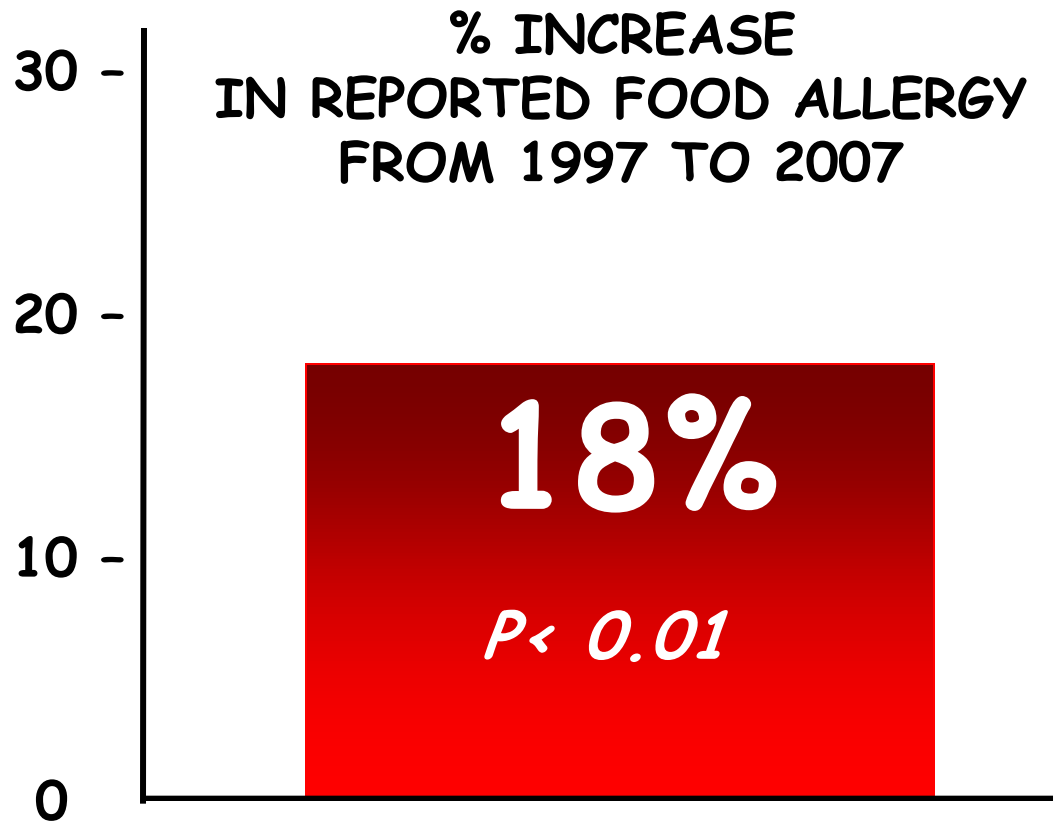

Spontaneous development of clinical tolerance to foods

Vickery BP JACI 2011;127:576

✓In general, resolution of allergy to egg, milk, wheat, and soy can be expected, although sensitivity can persist into the second decade of life, which is longer than previously appreciated.

✓In contrast,most patients allergic to peanut, tree nuts, and seafood will not outgrowtheir disease and must maintain strict elimination diets.

Evolving concepts on natural history and dietary avoidance/early introduction of food allergens

Jones SM, JACI 2013;131:3

Studies of the natural history of several food allergies in children

- *Savage JH, J Allergy Clin Immunol. 2007;120:717–719*
- *Savage JH, J Allergy Clin Immunol. 2010;125:683–686*
- *Skolnick HS, J Allergy Clin Immunol. 2001;107:367–374*
- *Skripak JM, J Allergy Clin Immunol. 2007;120:1172–1177*
- *Wood RA. Pediatrics. 2003;111:1631–1637*

even food allergies that are not classically "lifelong" (eg, milk, egg, wheat, and soy) are present well into the school-age years for many patients

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Risk factors in childhood eczema.

Fergusson D M, JEpidemiol Community Health 1982;36:118-22.

- ✓a birth cohort of 1265 New Zealand infants
- ✓early diverse solid-food diet
- ✓incidence of eczema by age 3 yrs

Cumulative rates % (number studied) of eczema by milk and solid food diet during the first four months

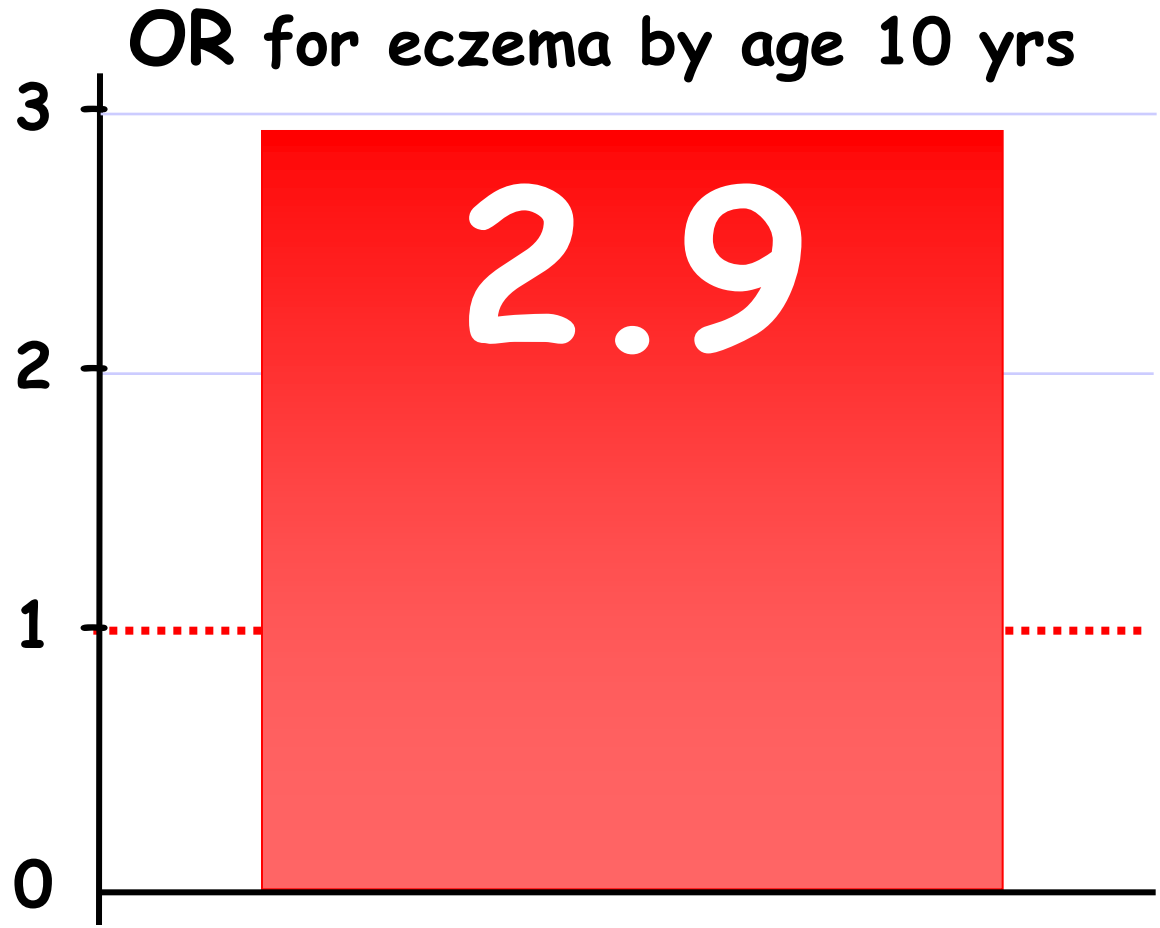
	First year			
	Solid food diet (No of different foods)			
Milk diet	*None*	*1–3*	*≥4*	*Total*
Bottle only	4·1 (49)	3·7 (188)	5·4 (37)	4·0 (274)
Breast and bottle	6·3 (143)	8·4 (464)	12·9 (85)	8·5 (692)
Breast only	6·2 (129)	11·5 (78)	0·0 (2)	8·1 (209)
Total	5·9 (321)	7·5 (730)	10·5 (124)	7·4 (1175)

number of solid foods p <0.01

Early solid feeding and recurrent childhood eczema: a 10-year longitudinal study.

Fergusson DM, Pediatrics. 1990;86:541-6.

- ✓a birth cohort of New Zealand children
- ✓early solid feeding practices
- ✓risks of recurrent or chronic eczema in childhood was examined
- ✓follow-up to age 10 yrs



in children exposed to ≥ 4 different types of solid food before 4 months

Comments to the New Zealand Fergusson's studies

Fergusson DM, Clin Allergy 1981;11:325-31.
Fergusson DM, J Epidemiol Community Health 1982;36:118-22.
Fergusson DM, Pediatrics 1990;86:541-6.

- **At 2 years of age, eczema** was significantly **more frequent** in infants **fed solids before 4 months of age** than in those fed no solids (18% vs 13%).

- Furthermore, **the association was found to be dose dependent**; the prevalence of eczema increased with the number of different food types from **13% for no foods**, **16% for 1 to 3**, and up to **20% for 4 and more** food types.

- Feeding practices substantially differed **at that time** (1970s and 1980s), with a **much lower breast feeding rate** (on average, only exclusively **18%** were breast fed in comparison to more than **49%** in 2000s) *Filipiak J Pediatr 2007;151:352*

Comments to the New Zealand Fergusson's studies

Fergusson DM, Clin Allergy 1981;11:325-31.
Fergusson DM, J Epidemiol Community Health 1982;36:118-22.
Fergusson DM, Pediatrics 1990;86:541-6.

- **In the New Zealand cohort there was a much earlier introduction of solids** with higher diversity compared with the following studies (*Filipiak J Pediatr 2007;151:352*).

- For example, **solids were introduced in the first 4 months** in 34% children of the German cohort (*Filipiak J Pediatr 2007;151:352*), whereas the proportion **in the New Zealand cohort was 72%** (where cereals were introduced in 56%, vegetables in 43%, fruits in 44%, and egg in 13% of participants).

- In the New Zealand cohort, **the very early introduction of solids within the first 4 months in the absence of human milk** may produce a different immunologic response than solid introduction after 3 or even 4 months of age in the presence of breast feeding.

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Reccommended Approaches to Allergy Prevention

Pediatrics 2000;106:346

- ✓No maternal dietary restriction during pregnancy, (peanuts?)
- ✓ breastfeeding,
- ✓dietary restrictions while breastfeeding,
- ✓the use of hypoallergenic formulas, and
- ✓delays in the introduction of certain foods into the infant's diet

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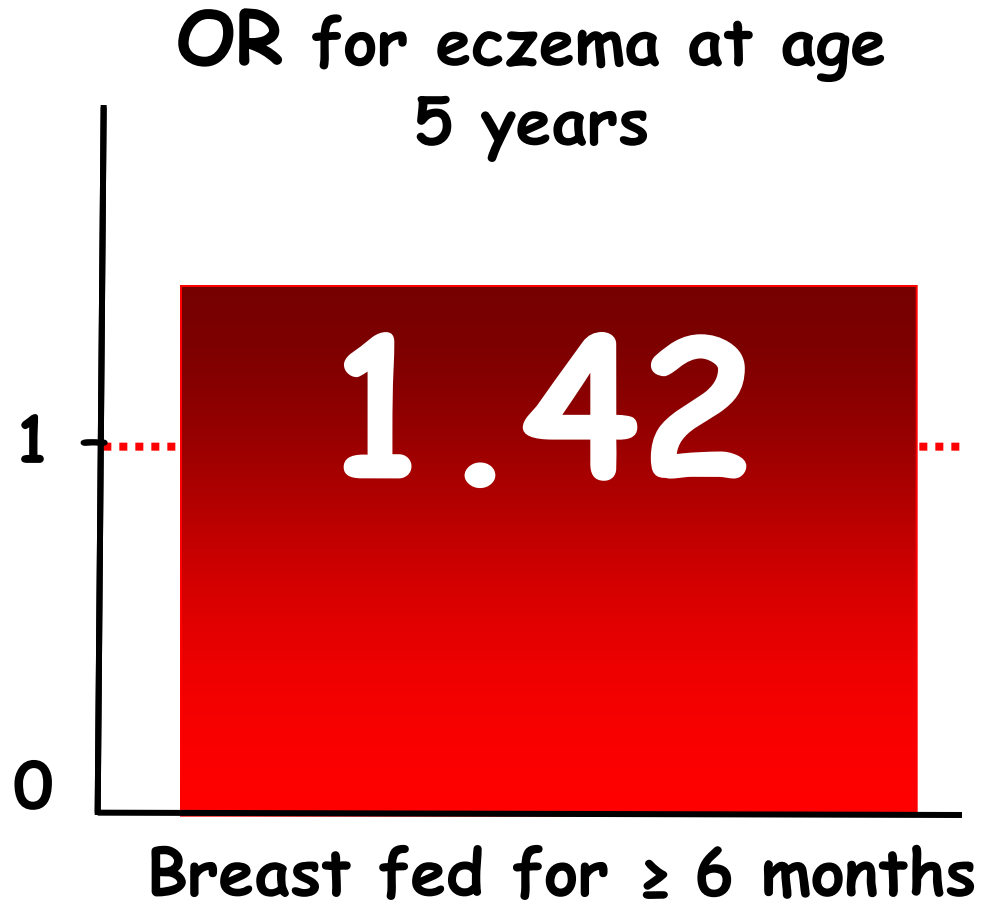
Breast feeding

The association between infant feeding practices and subsequent atopy among children with a family history of asthma. *Mihrshahi S Clin Exp Allergy. 2007;37:671-9.*

- ✓A cohort of 516 children with a **family history of asthma** in Sydney, Australia,
- ✓followed from birth to age 5 years



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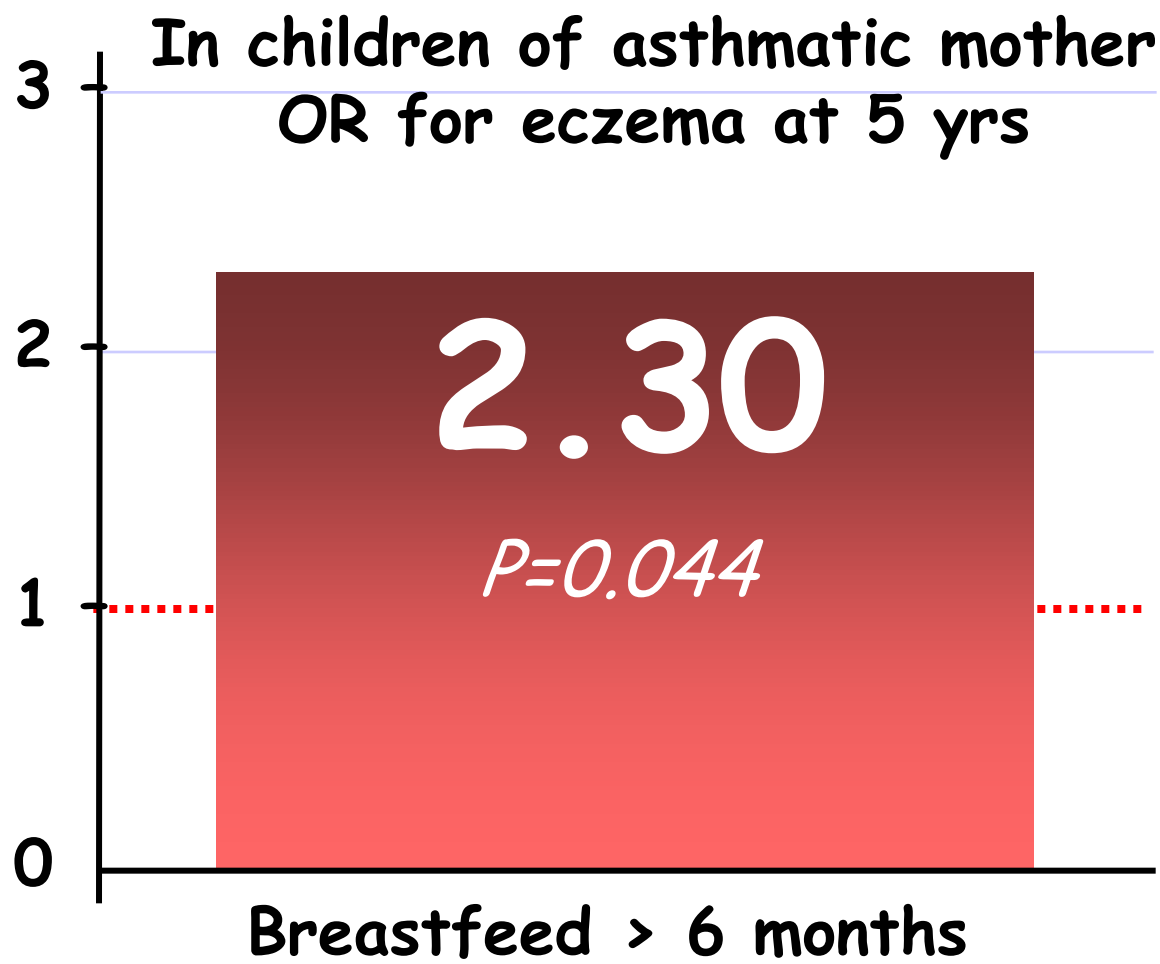
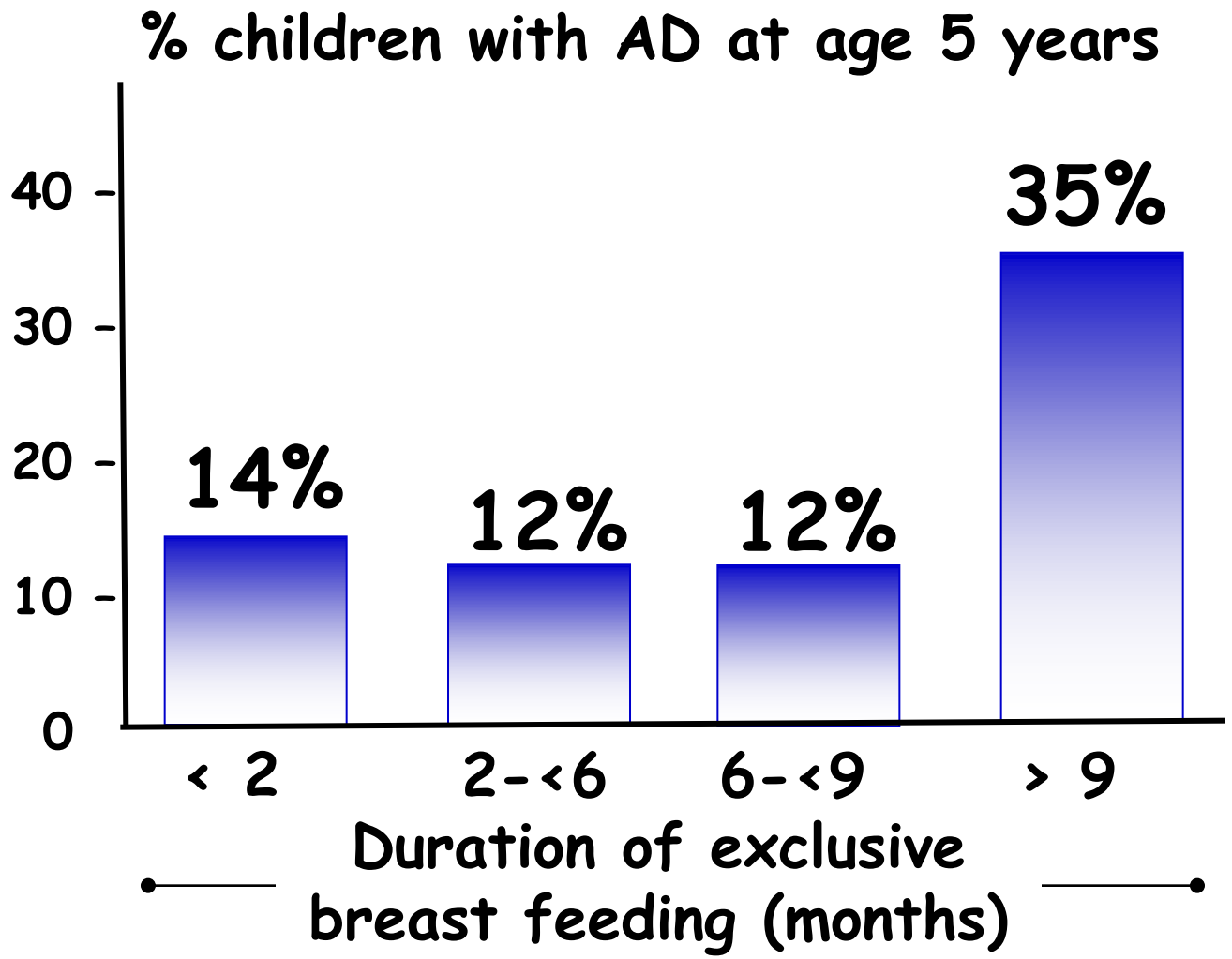


Prolonged exclusive breastfeeding is associated with increased atopic dermatitis: a prospective follow-up study of unselected healty newborns from birth to age 20 years.

Person ClinExpAll 2006;36:1011

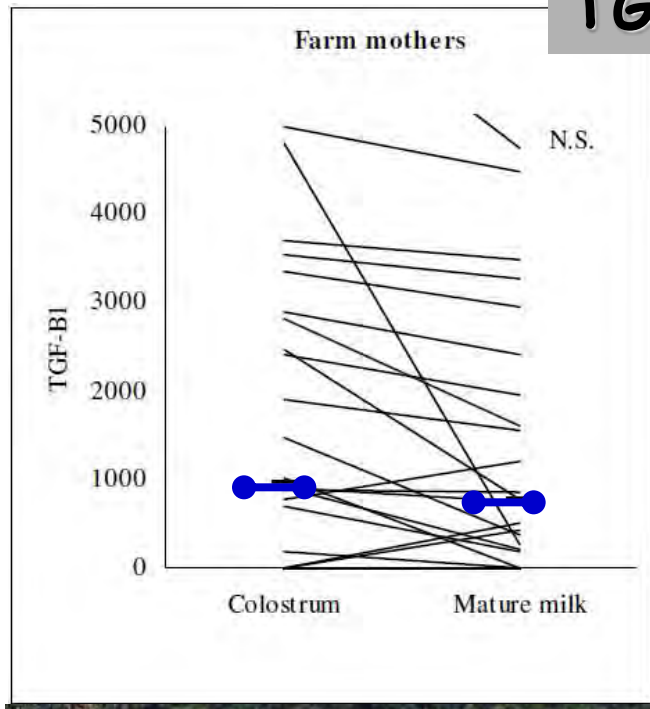
- ✓ 200 unselected healthy newborns (42% has a family history of allergy)
- ✓ Follow up at ages 5 (n=163), 11 (n=150) and 20 years (n=164) with clinical examination and skin prick testing

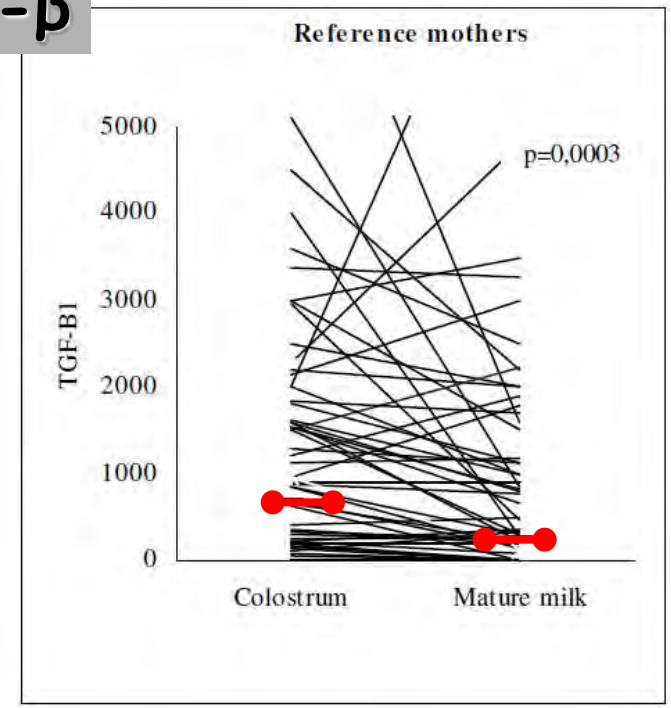


Farming and immune regulatory cytokines in milk of lactating women. *D.G. Peroni, L. Pescollderungg, PAI 2010;21:977*

- ✓TGF-β1 and IL-10 in colostrum and mature milk of mothers living in a farm in comparison to reference mothers living in town.
- ✓Samples within three days postpartum (colostrum) and at the first month of life (mature milk).
- ✓ELISA assays were performed to quantify TGF-β1 and IL-10

TGF-β

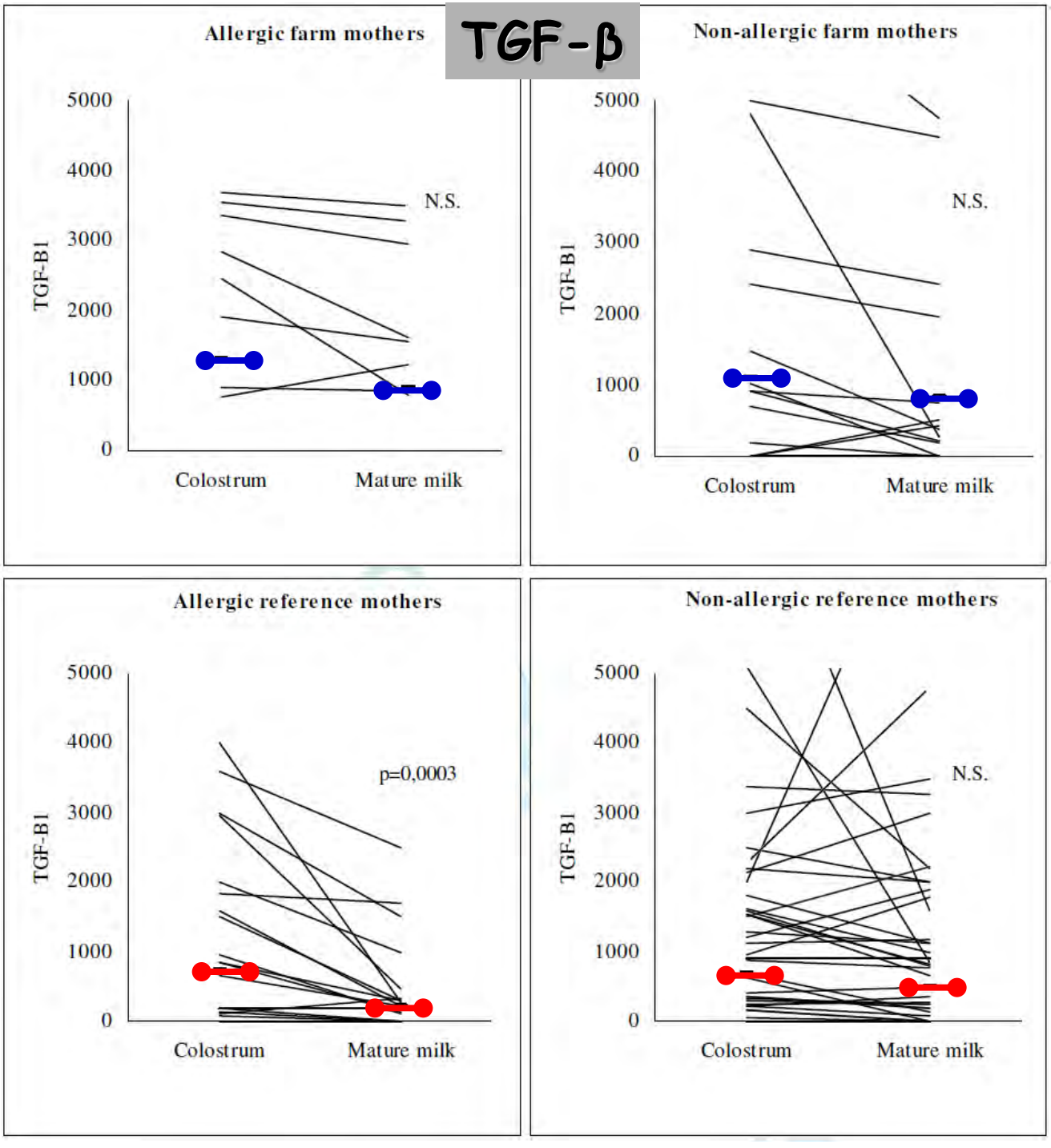




Farming and immune regulatory cytokines in milk of lactating women.

D.G. Peroni,
L. Pescollderungg,
Ped Allergy Immunol
2010;21:977

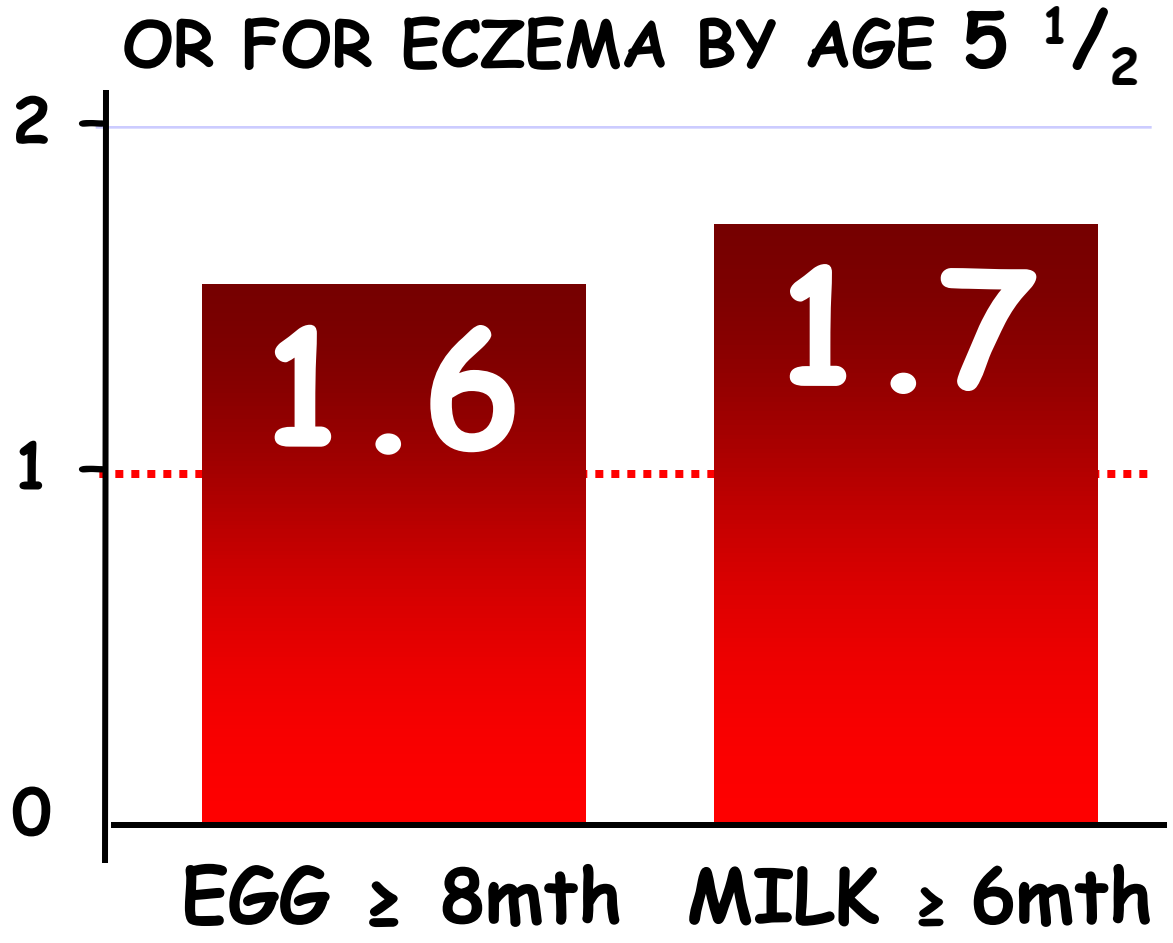
The reduction of TGF-β in the milk of allergic mother might be an explanation



Solid foods: Milk - Egg

The Introduction of Solids in Relation to Asthma and Eczema *Zutavern Arch Dis Child 2004;89:303*

- ✓ 642 children recruited before birth and followed to the age 5 $^1/_2$ years
- ✓ Retrospective evaluation of solid foods introduction perfommed at age 12 months



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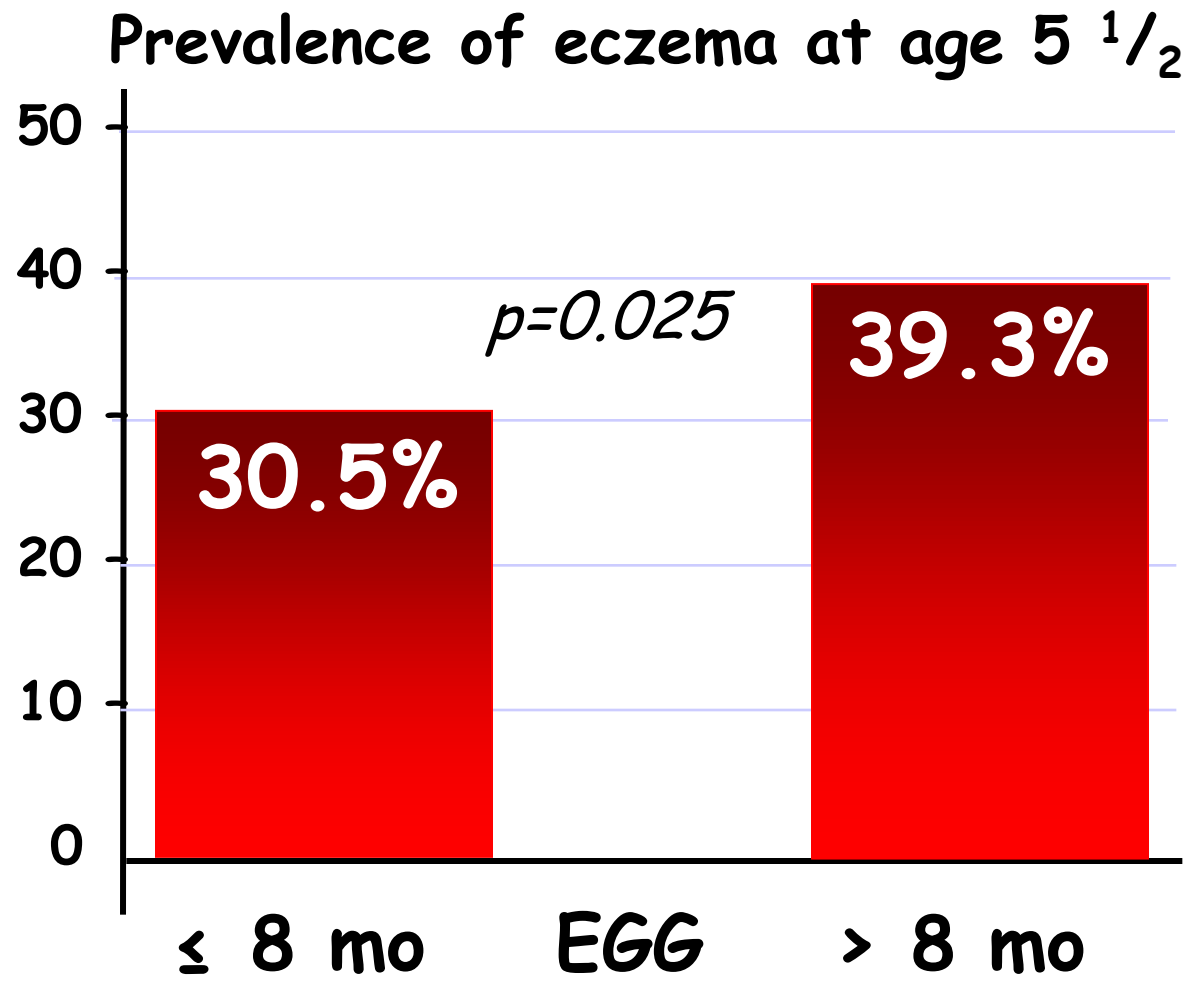

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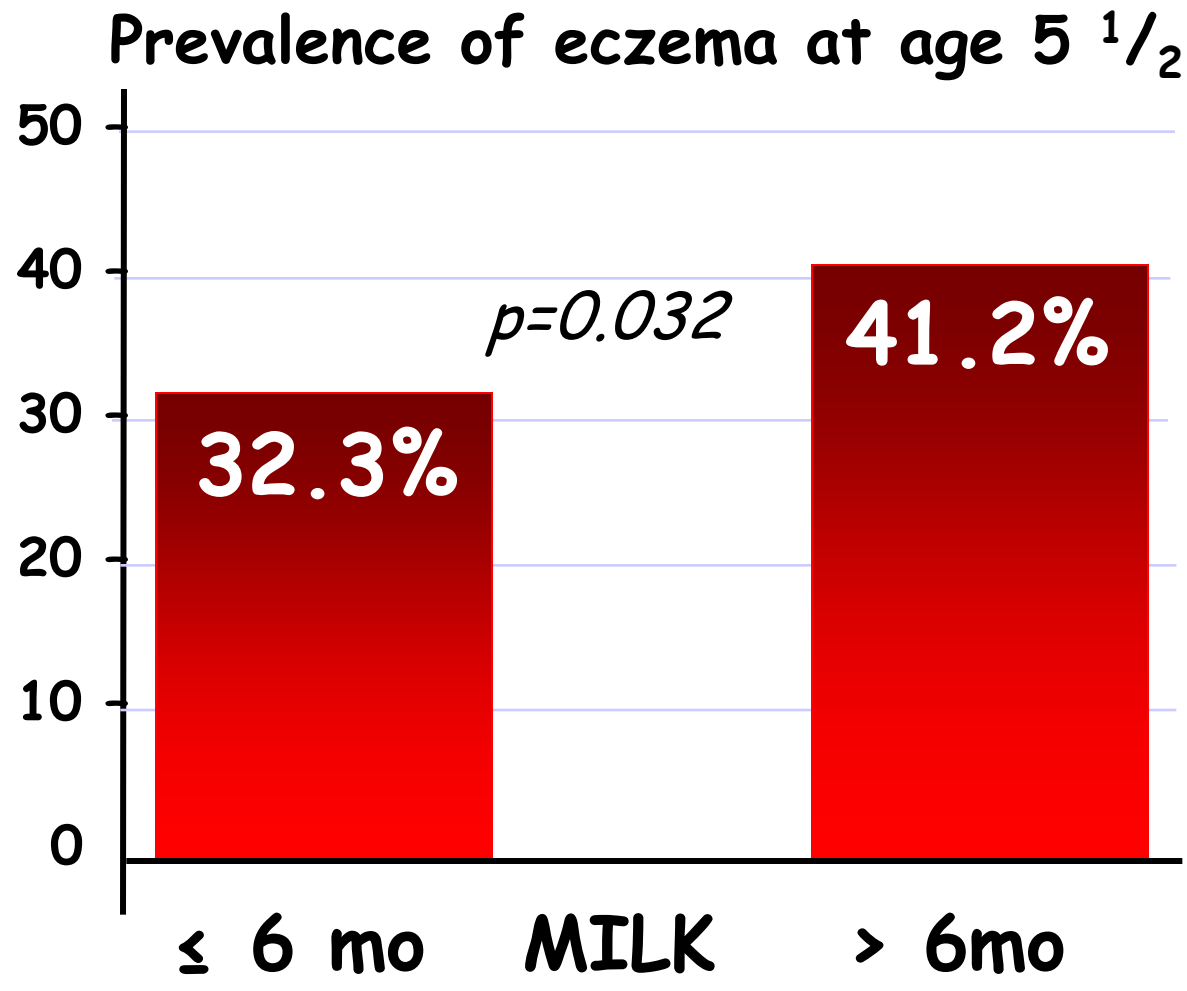


Solid Food Introduction in Relation to Eczema; Results from a Four-Year Prospective Birth Cohort Study.

Filipiak J Pediatr 2007;151:352

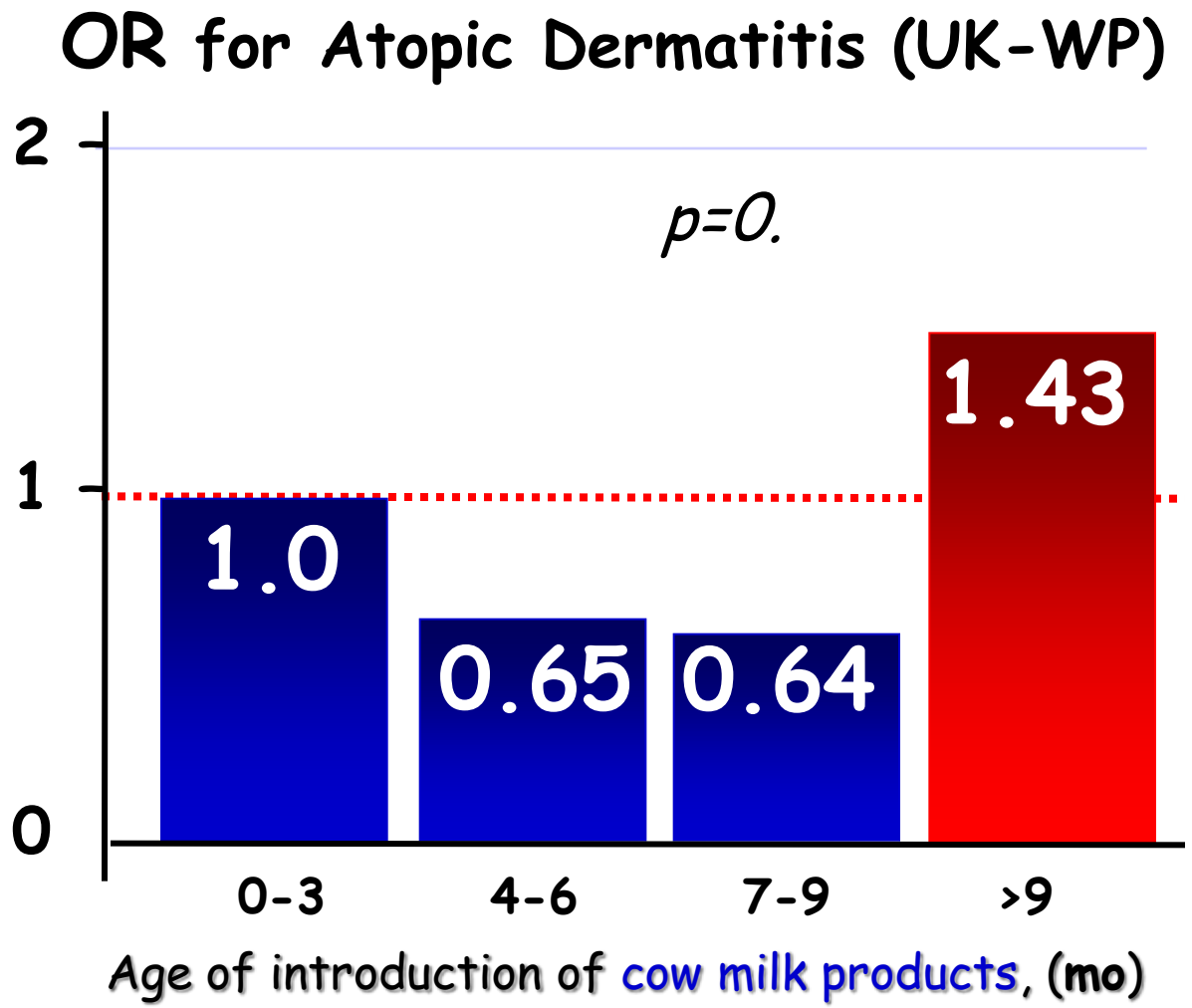
- ✓ Introduction of solid foods in the first 12 months (birth cohort)
- ✓ Occurrence of eczema during the first 4 years of life
- ✓ an intervention group (n=2252) (allergenic food such as cow's milk and dairy products,eggs, fish, tomatoes, nuts, soy products, and citrus fruits were to be avoided entirely during the first year)
- ✓ nonintervention group (n=3739).

In this large population-based prospective birth cohort study, there was **no evidence for a protective effect** in relation to eczema **from delayed introduction of solids beyond the fourth month and of most potentially allergenic solids beyond the sixth month of life.**

Age at first introduction of cow milk products and other food products in relation to infant atopic manifestations in the first 2 years of life: the KOALA Birth Cohort Study.

Snijders BE, Pediatrics 2008; 122:e115–e122.

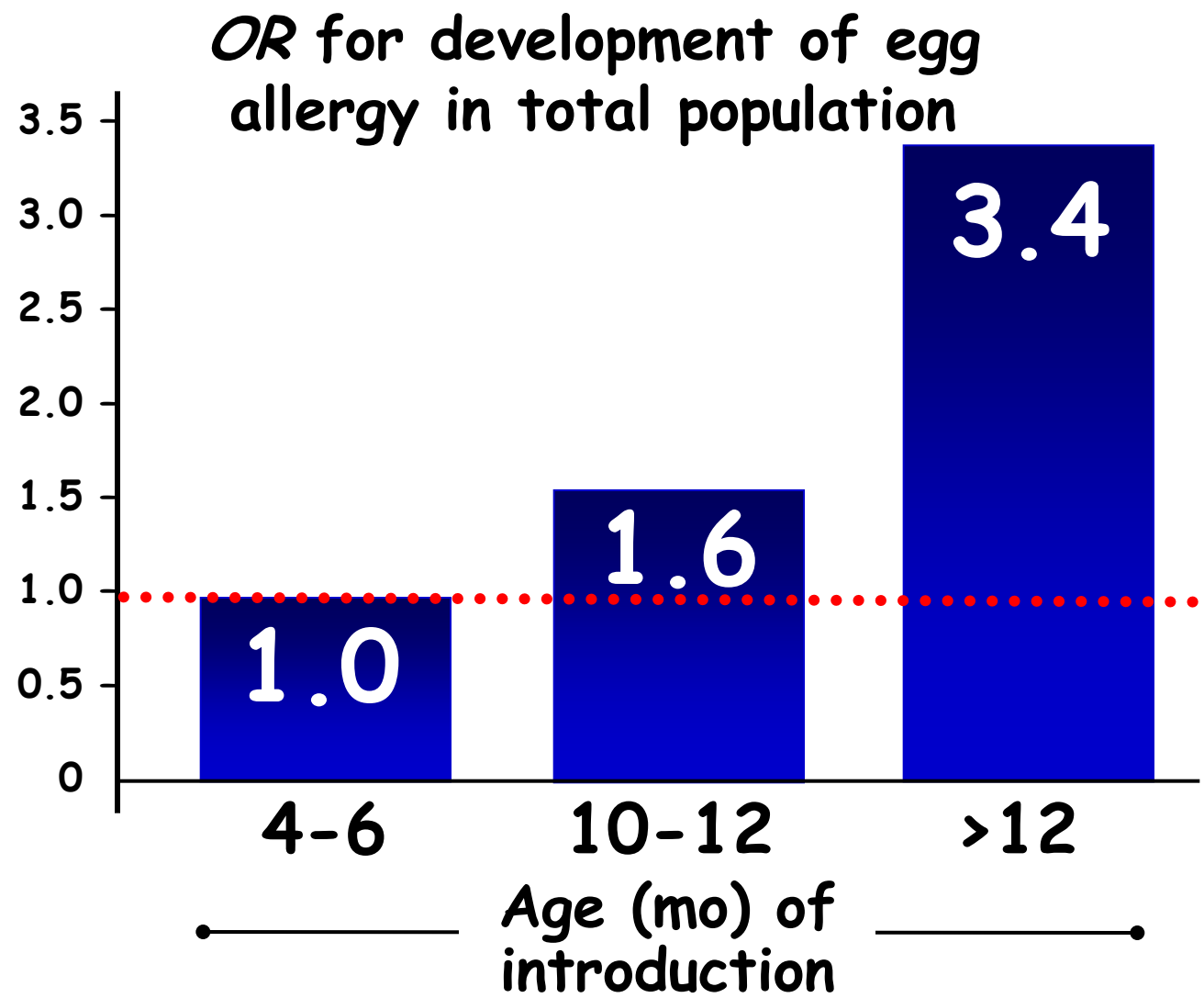
- ✓2558 infants in an ongoing prospective birth cohort study in the Netherlands
- ✓introduction of cow milk products and other food products
- ✓Follow-up: 2 years



Can early introduction of egg prevent egg allergy in infants? A population-based study

Koplin JACI 2010;126:807

- ✓ Population-based cross-sectional study.
- ✓ 2589 infants.
- ✓ To determine whether confirmed egg allergy in 12-month-old infants is associated with:
  (1) duration of breast-feeding and
  (2) ages of introducing egg and solids



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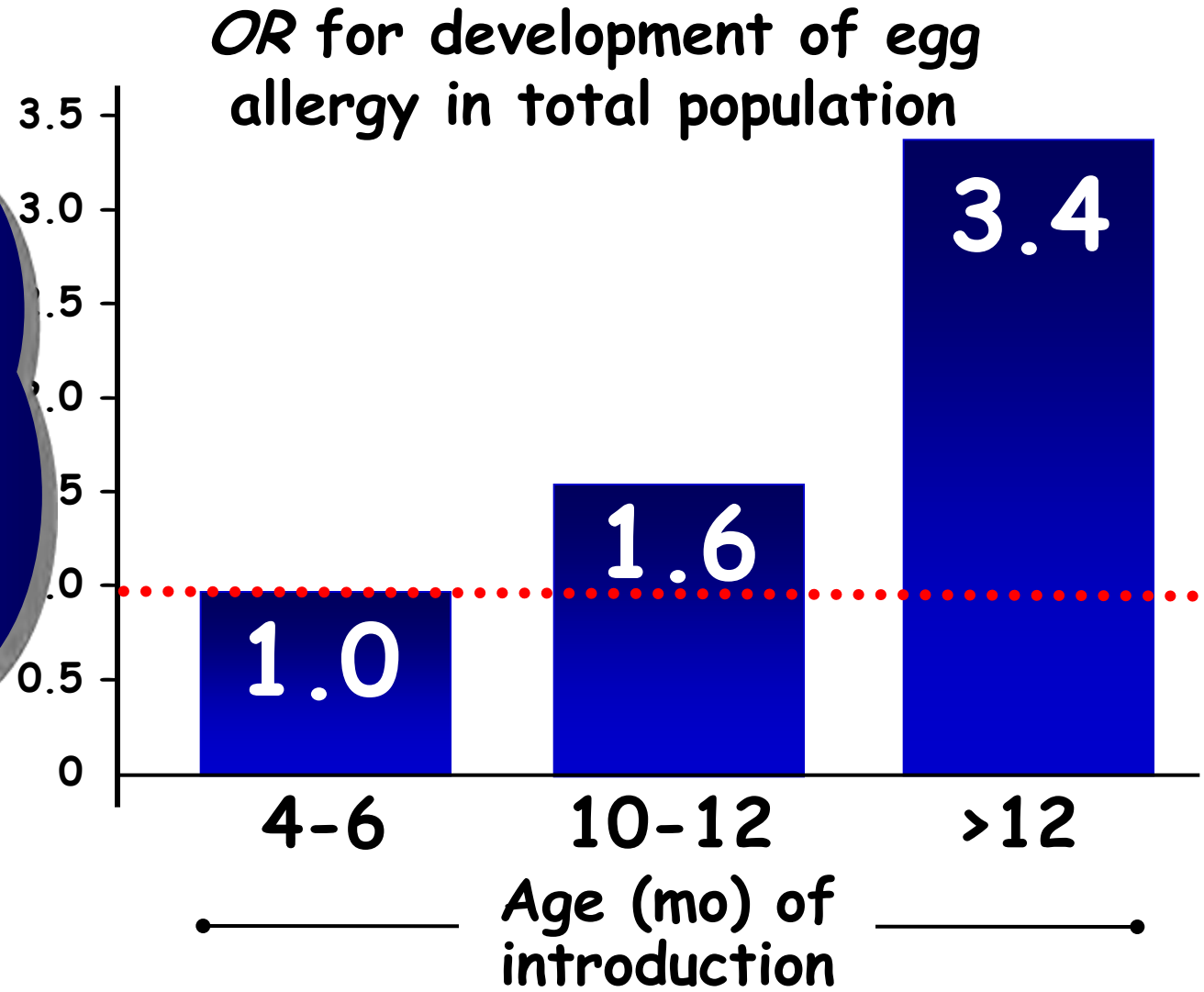
- ✓ Populati
  s
- ✓
  eg

These findings persisted even in children without risk factors (OR = 3.3; 10-12 mo.)



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OR for development of egg allergy in total population

In children exposed at age 4 to 6 months to cooked eggs vs those exposed to eggs in backed goods

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Age at the Introduction of Solid Foods During the First Year and Allergic Sensitization at Age 5 Years

Nwaru Pediatrics 2010;125:50

- ✓ 994 children
- ✓ age at the introduction of solid foods
- ✓ adjustment for potential confounders
- ✓ allergen-sIgE at 5 years

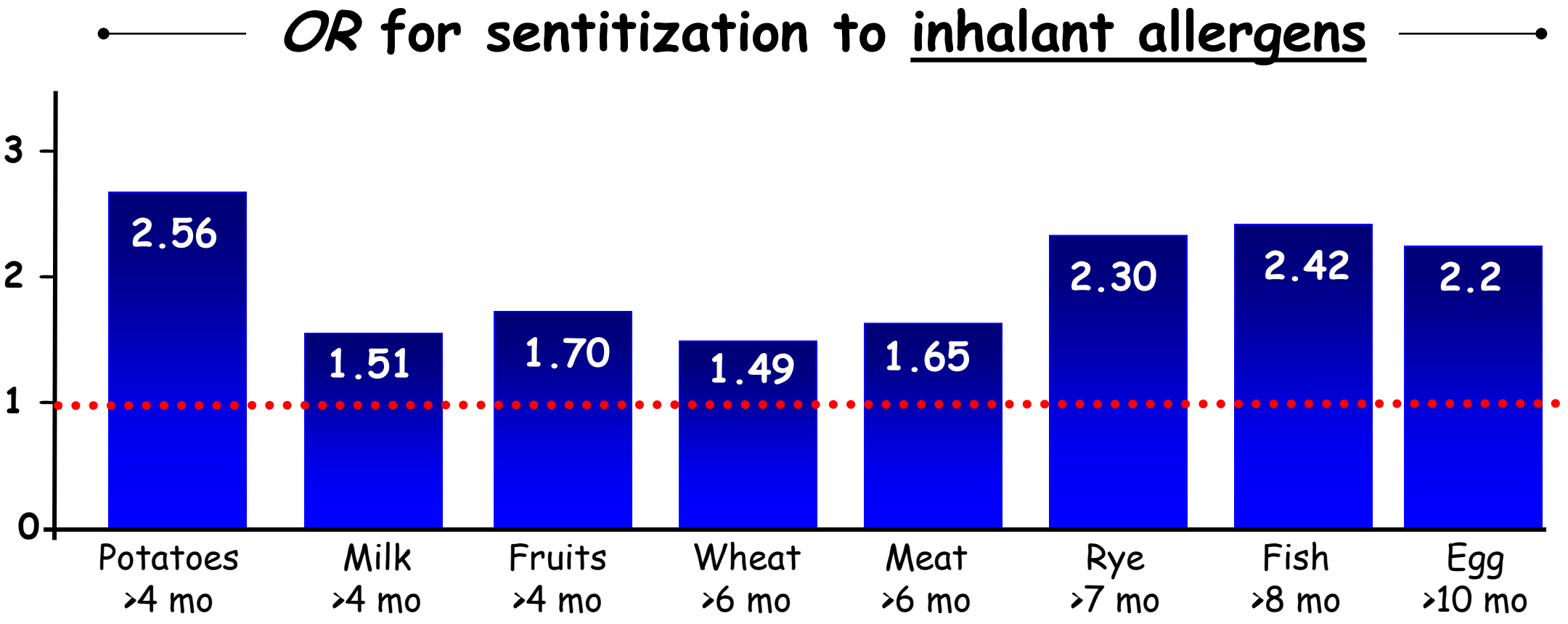
Late introduction of:

- **potatoes (>4 months),**
- **oats (>5 months),**
- **rye (>7 months),**
- **wheat (>6 months),**
- **meat (>5.5 months),**
- **fish (>8.2 months),**
- **eggs (>10.5 months)**

was significantly directly associated with sensitization to food allergens.

Age at the Introduction of Solid Foods During the First Year and Allergic Sensitization at Age 5 Years

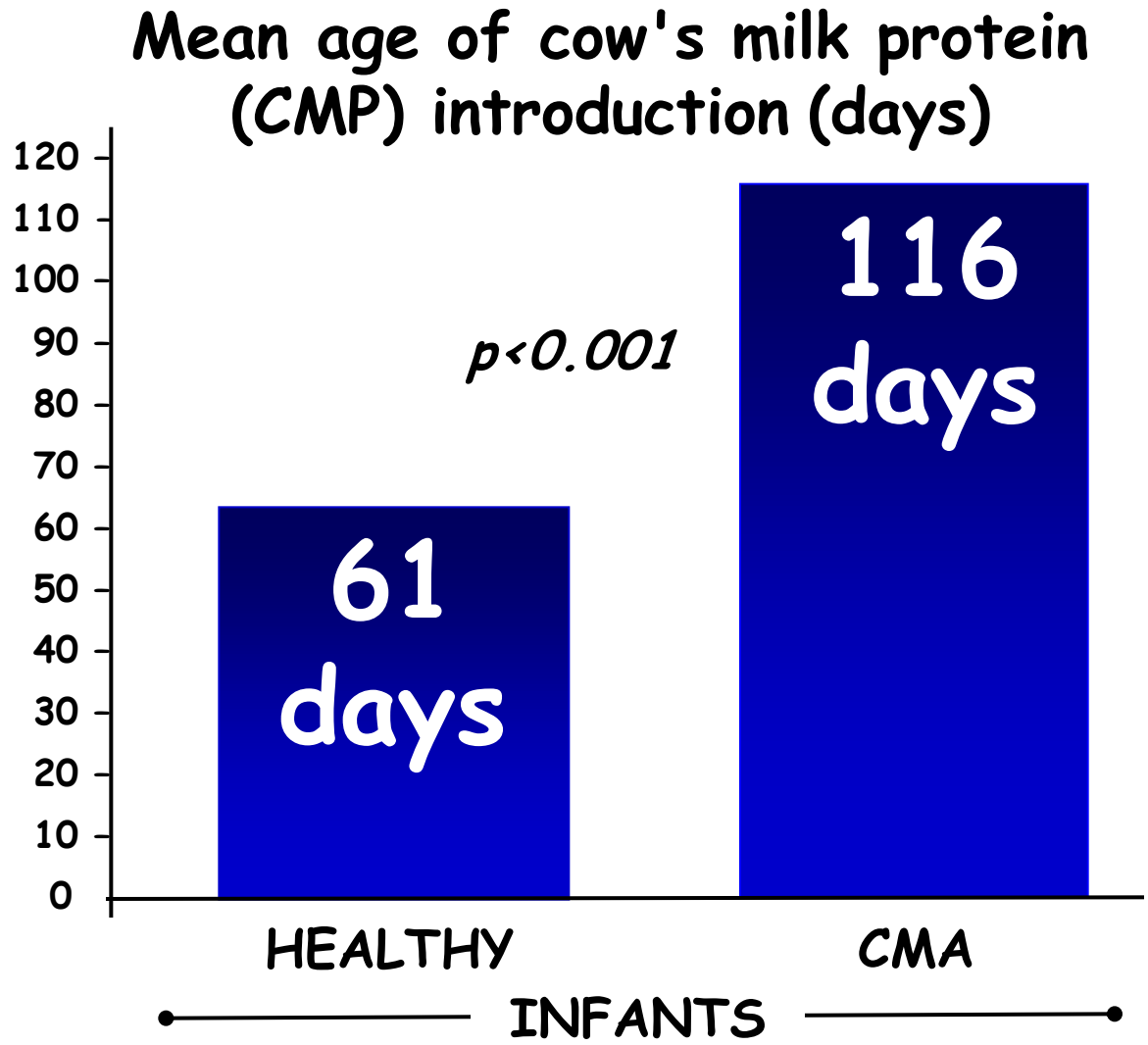
Nwaru Pediatrics 2010;125:50



Early exposure to cow's milk protein is protective against IgE-mediated cow's milk protein allergy

Katz JACI 2010;126:77

- ✓13,019 infants.
- ✓Telephone interview.
- ✓Skin prick tested, and challenged orally in probable cases.



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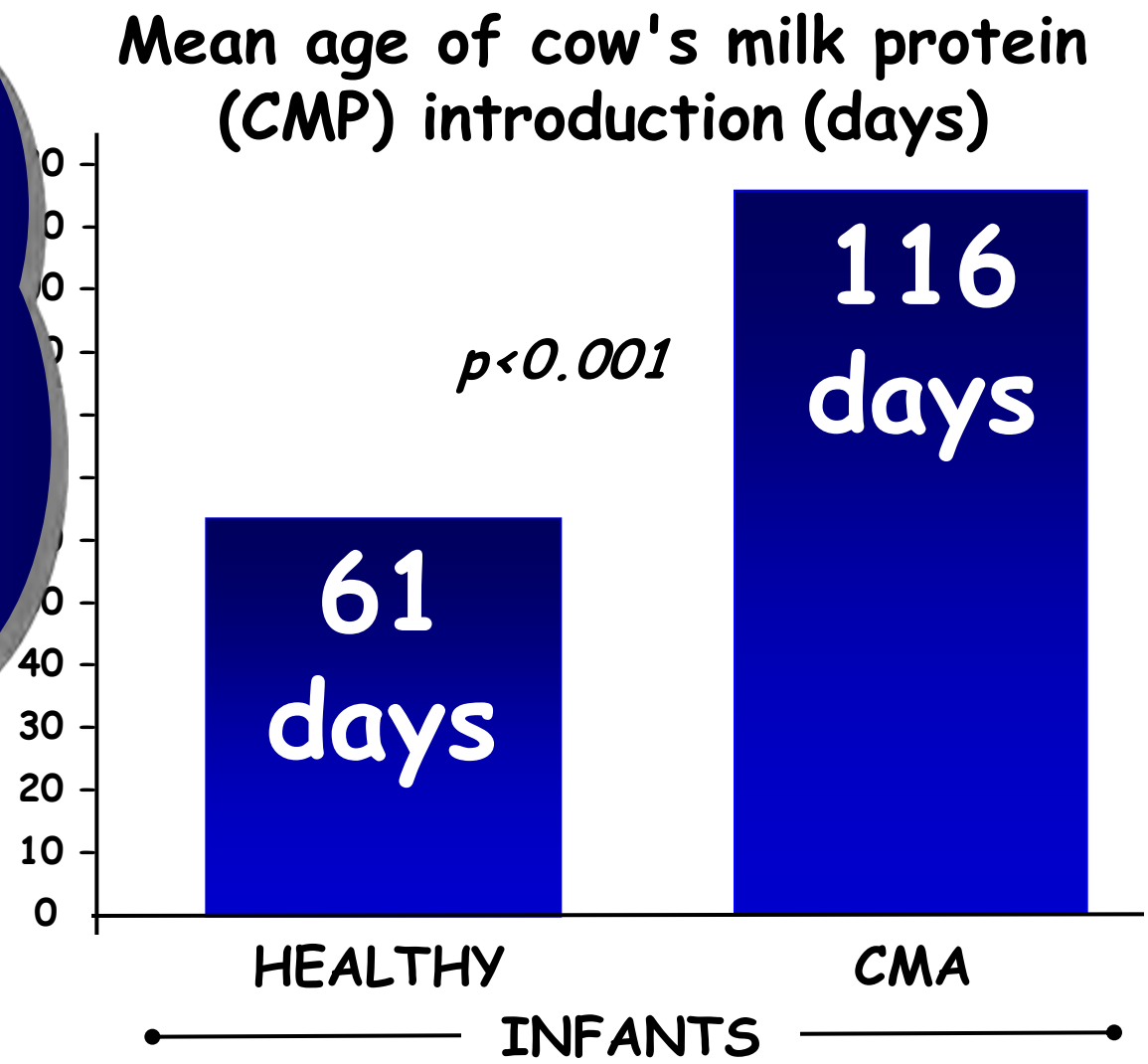
JACI 2010;126:77

Early exposure to CMP as a supplement to breast-feeding might promote tolerance.

+

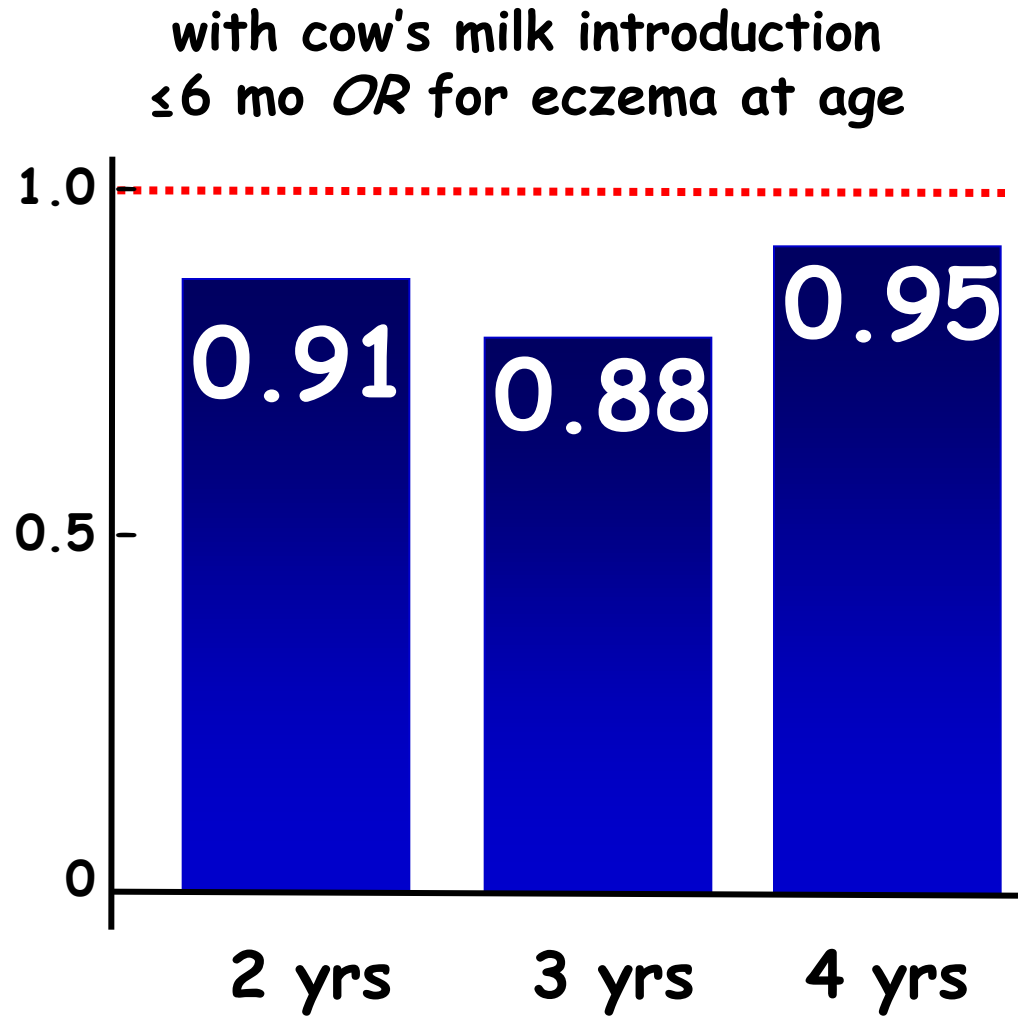
= Tolerance



The introduction of allergenic foods and the development of reported wheezing and eczema in childhood

Tromp APAM 2011;165:933

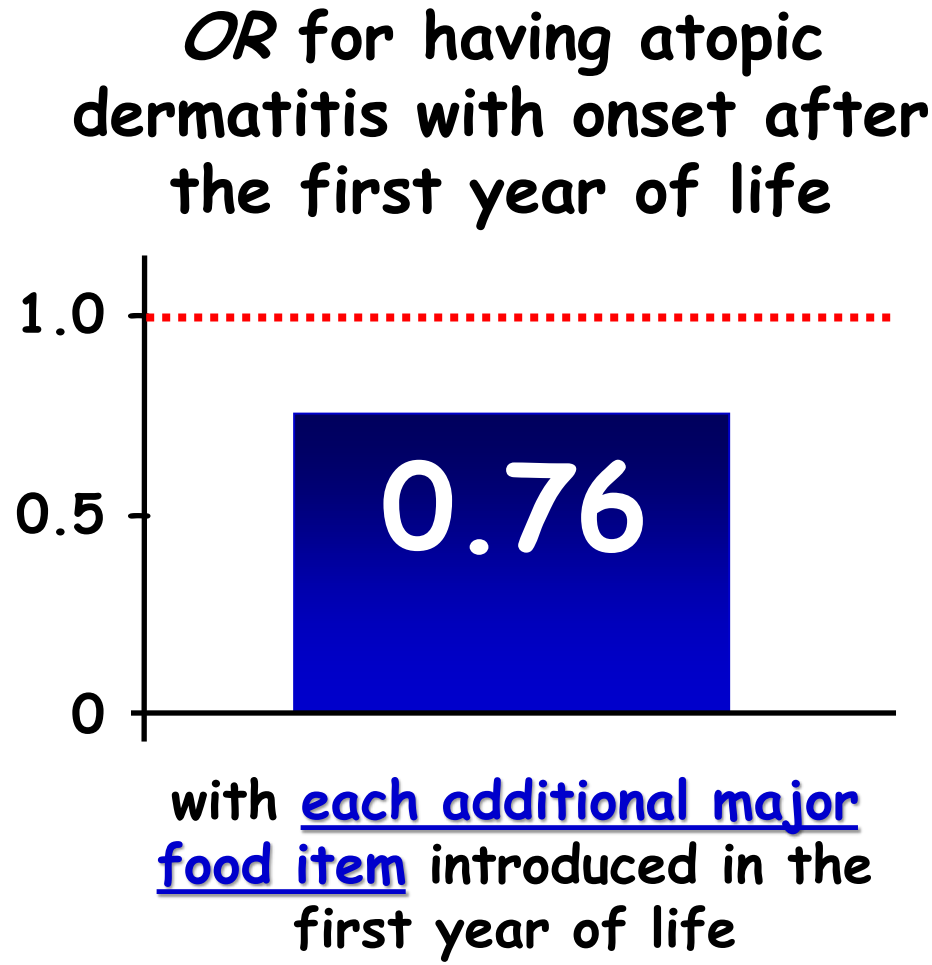
- ✓ 605 preschool children.
- ✓ Timing of introduction of cow's milk, hen's egg, peanuts, tree nuts, soy, and gluten collected by questionnaires at 6 and 12 months of age.



Development of atopic dermatitis according to age of onset and association with early-life exposures

Roduit JACI 2012;130:130

- ✓ Introduction to complementary food in the first year of life.
- ✓ Development of atopic dermatitis, taking into account the reverse causality.
- ✓ 1041 children birth cohort study.
- ✓ Feeding practices reported by parents in monthly diaries between the 3rd and 12th months of life.



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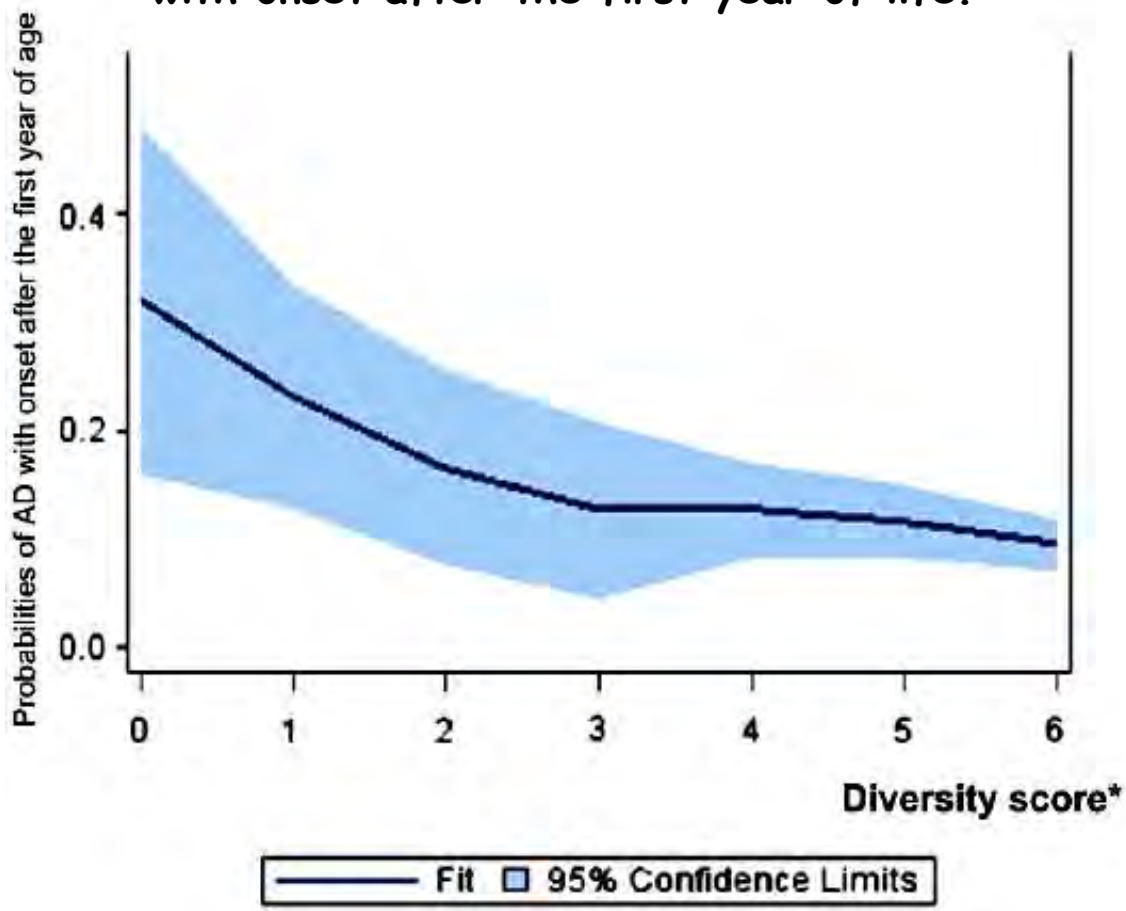
Association between increasing numbers of different major food items (n = 6) introduced in the first year of life and atopic dermatitis *(AD)* with onset after the first year of life.



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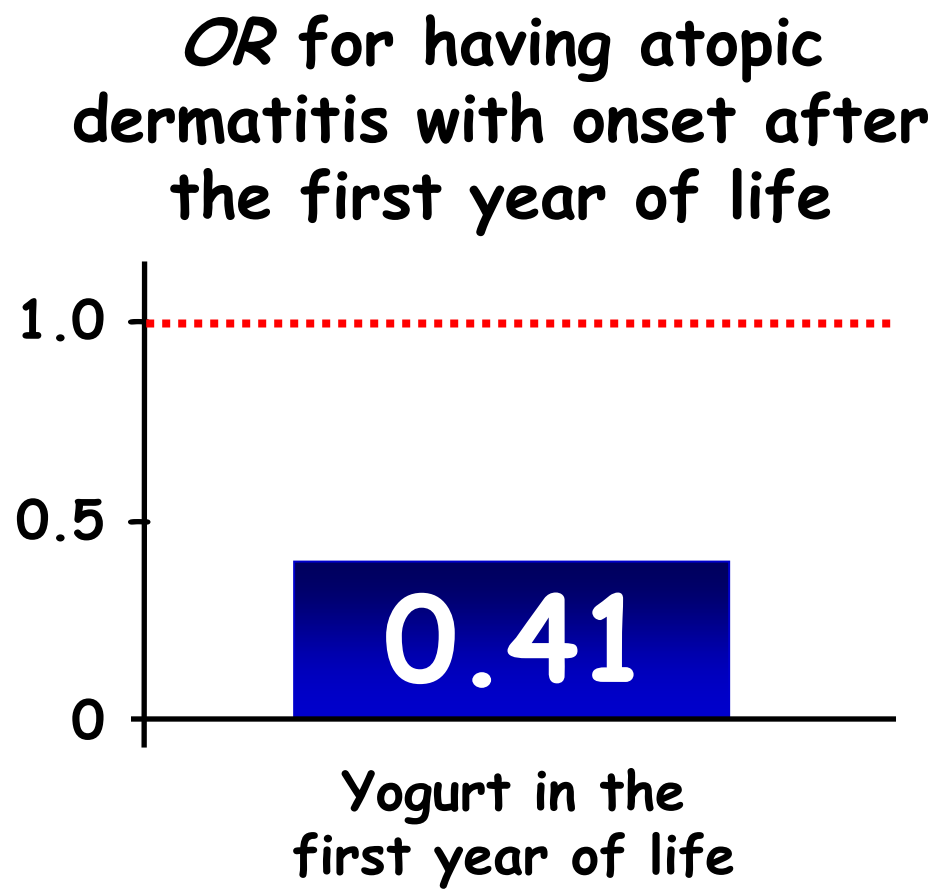
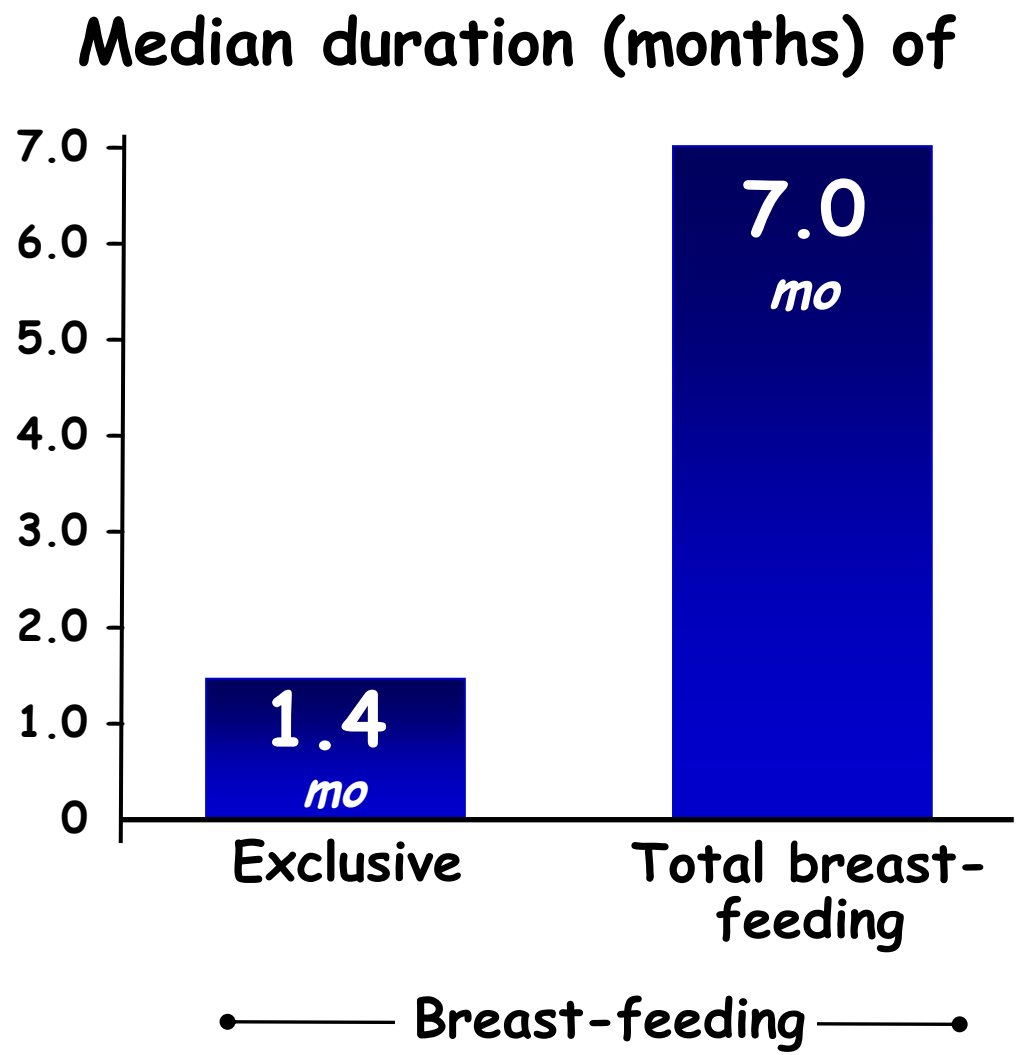


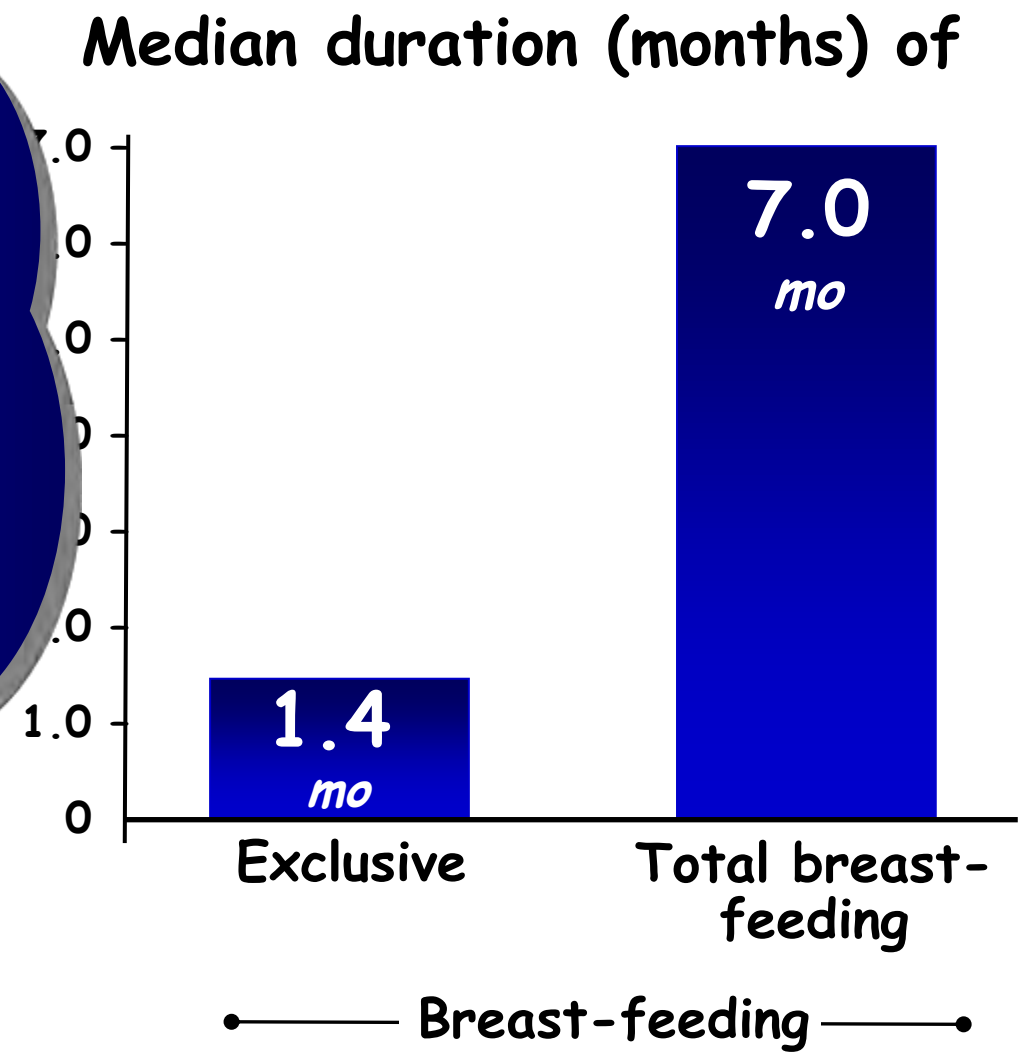
Timing of infant feeding in relation to childhood asthma and allergic diseases. *Nwaru JACI 2013;131:78*

- ✓ 3781 consecutively born children.
- ✓ Dietary exposures.
- ✓ Asthma, allergic rhinitis, and atopic eczema, IgE antibodies at the age of 5 years.



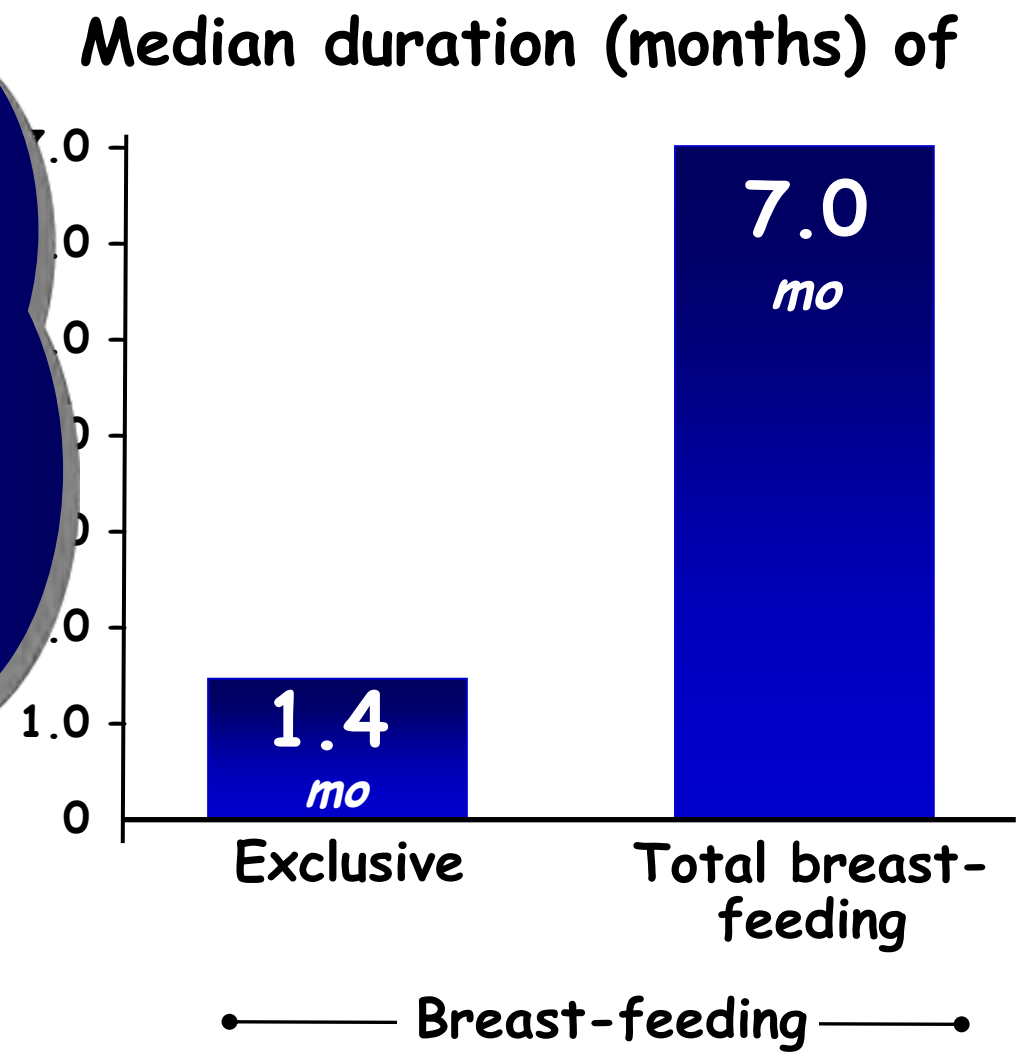
Timing of infant feeding in relation to childhood asthma and allergic diseases. *Nwaru JACI 2013;131:78*

✓ Introduction of wheat, rye, oats, or barley <u>at 5 to 5.5 months</u> was inversely associated with asthma and allergic rhinitis, whereas introduction of other cereals at less than 4.5 months increased the risk of atopic eczema.



Timing of infant feeding in relation to childhood asthma and allergic diseases. *Nwaru JACI 2013;131:78*

✓ Introduction of egg at <u>11 months or less</u> was inversely associated with asthma, allergic rhinitis, and atopic sensitization, whereas introduction of fish <u>at 9 months or less</u> was inversely associated with allergic rhinitis and atopic sensitization.



gluten

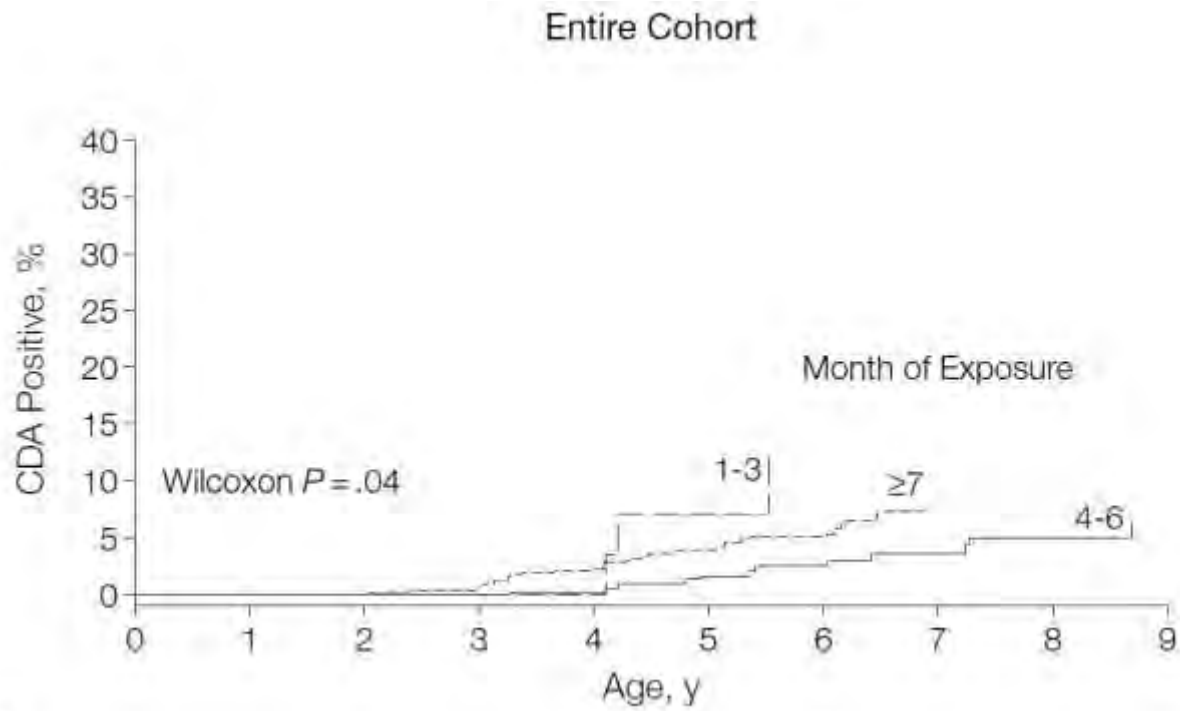
Risk of celiac disease autoimmunity and timing of gluten introduction in the diet of infants at increased risk of disease. *Norris JM, JAMA. 2005;293:2343-2351*

✓development of celiac disease autoimmunity (CDA)

✓1560 children at increased risk for celiac disease or type 1 diabetes, as defined by possession of either HLA-DR3 or DR4 alleles, or having a first-degree relative with type 1 diabetes.

✓ follow-up: 4.8 years.

% children developing celiac disease autoimmunity (CDA).



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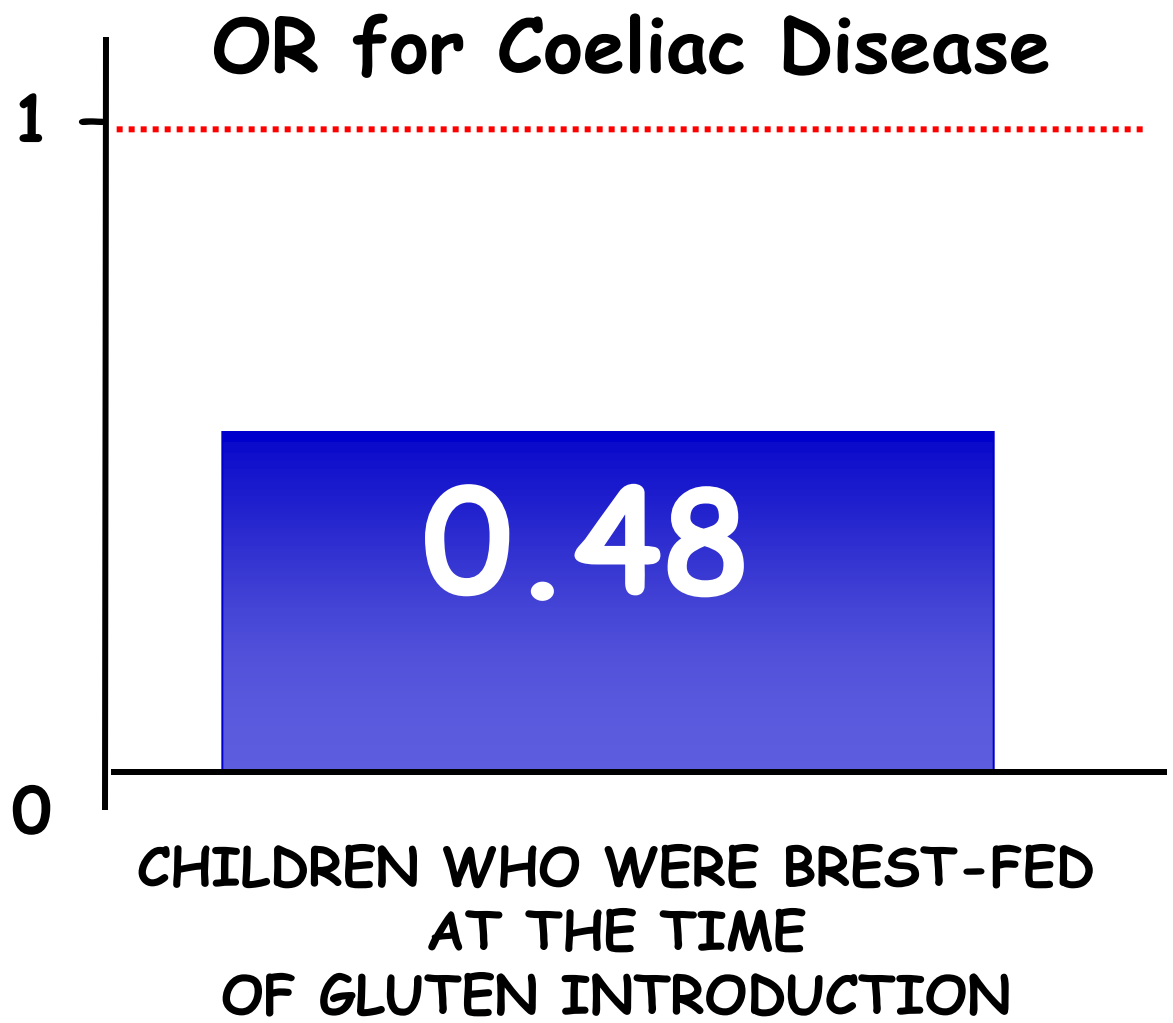
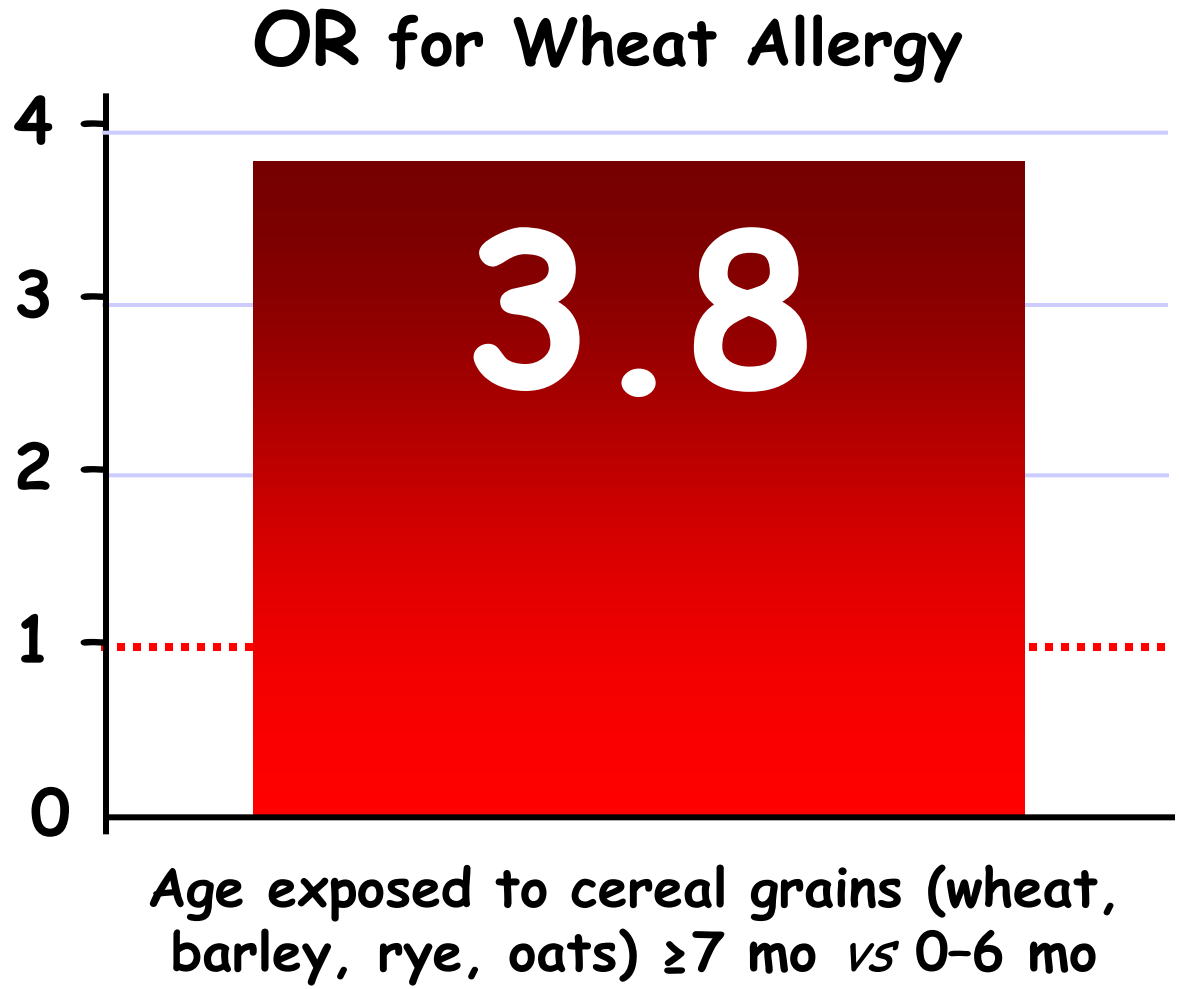
EFFECT OF BREAST FEEDING ON RISK OF COELIC DISEASE: A SYSTEMATIC REVIEW AND META-ANALYSIS OF OBSERVATIONAL STUDIES *Akobeng Arch Dis Child 2006; 91: 39*

- ✓ Meta-analysis observational studies published between 1966 and June 2004;
- ✓ 6 case-control studies



Timing of initial exposure to cereal grains and the risk of wheat allergy. *Poole JA, Pediatrics 2006; 117:2175–2182.*

- ✓1612 children enrolled at birth
- ✓followed to the mean age of 4.7 years.
- ✓Questionnaire data and dietary exposures were obtained at 3, 6, 9, 15, and 24 months and annually thereafter.

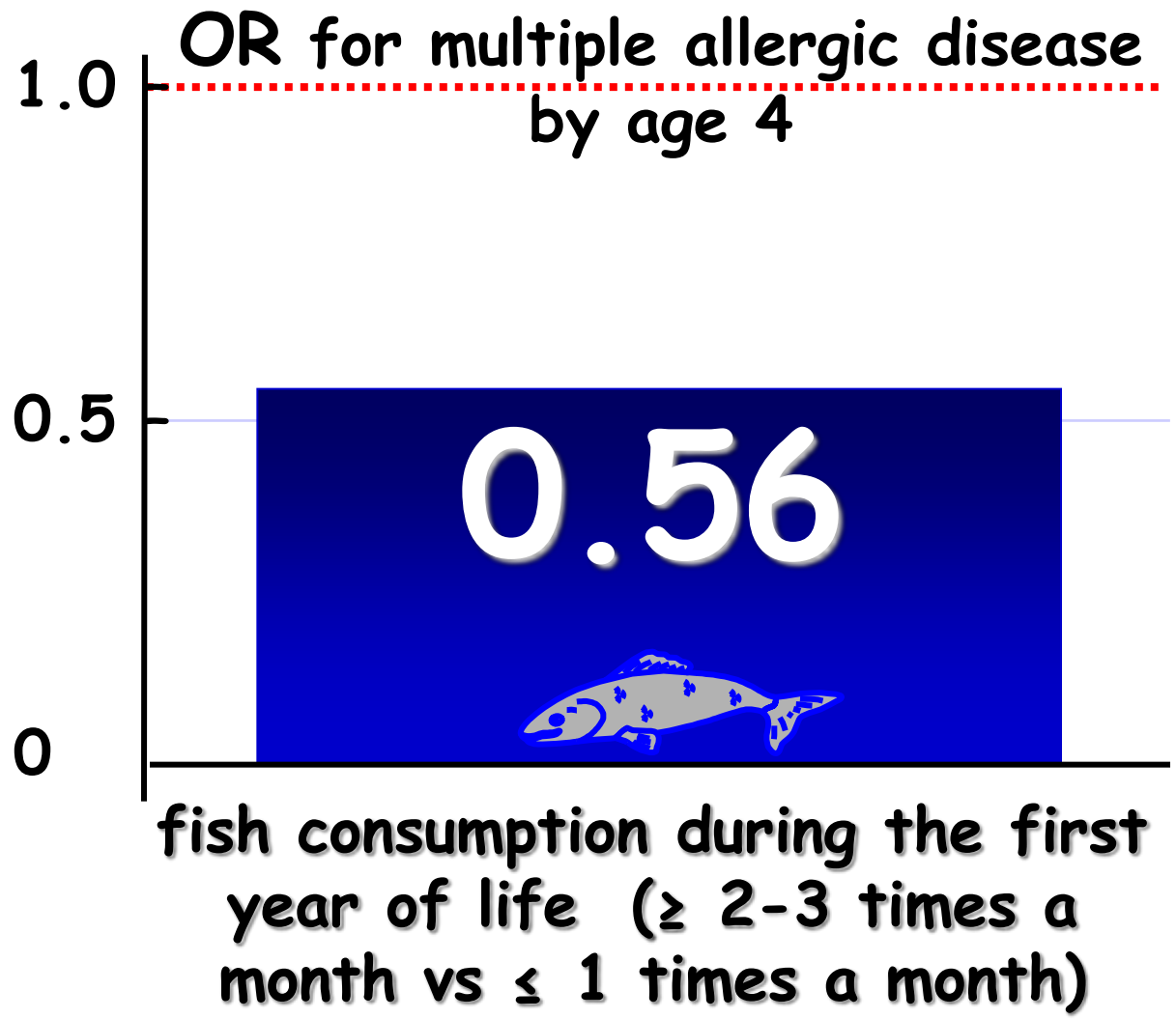


fish

Fish consumption during the first year of life and development of allergic diseases during childhood.

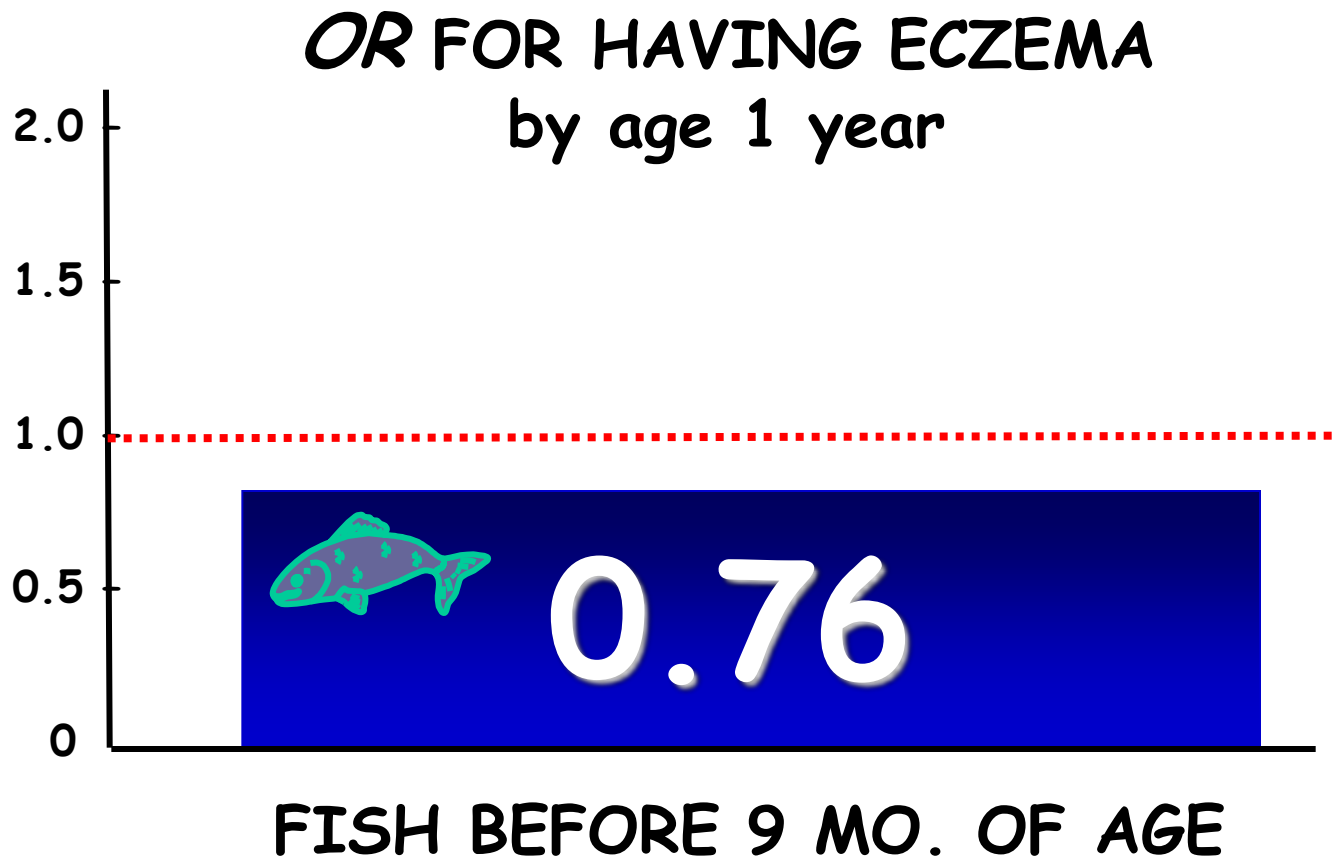
Kull I. Allergy. 2006;61:1009-15

- ✓birth cohort of 4089 new-born infants in Sweden
- ✓follow-up: 4 years
- ✓Parental questionnaires at ages 2 months, 1, 2 and 4 years



Early introduction of fish decreases the risk of eczema in infants *Alm Arch Dis Child 2009;94:11*

- ✓ Infants born in Sweden in 2003.
- ✓ 8176 families.

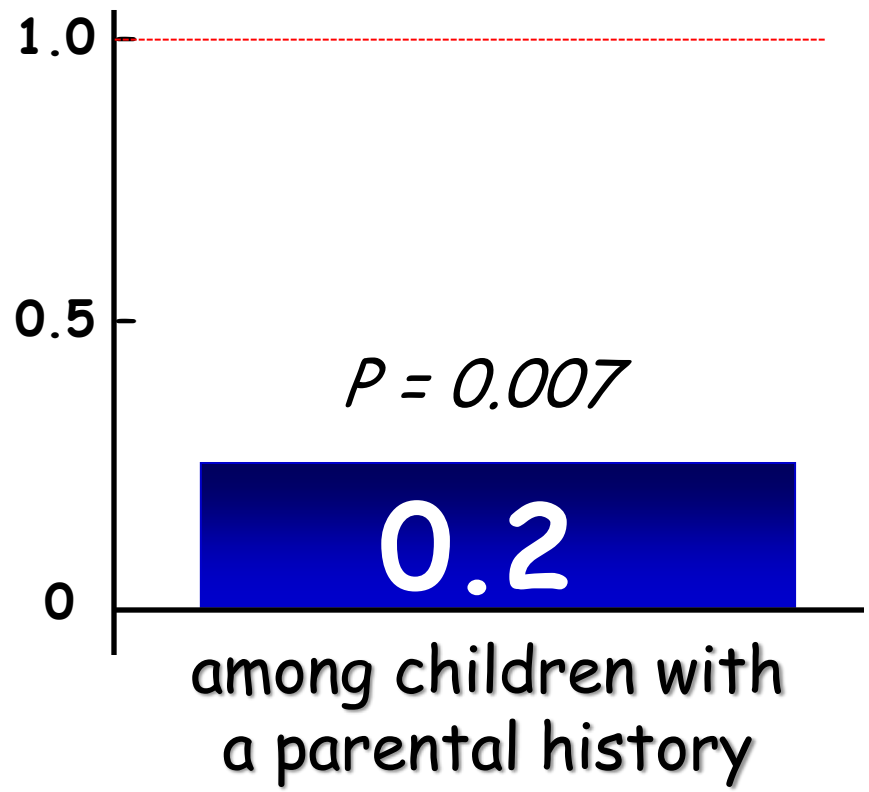


peanut

Early complementary feeding and risk of food sensitization in a birth cohort. *Joseph JACI 2011;127:1203*

- ✓ Introduction of complementary food <4 months.
- ✓ IgE to egg, milk, and peanut allergen at 2 yrs.
- ✓ 594 maternal-infant pairs.

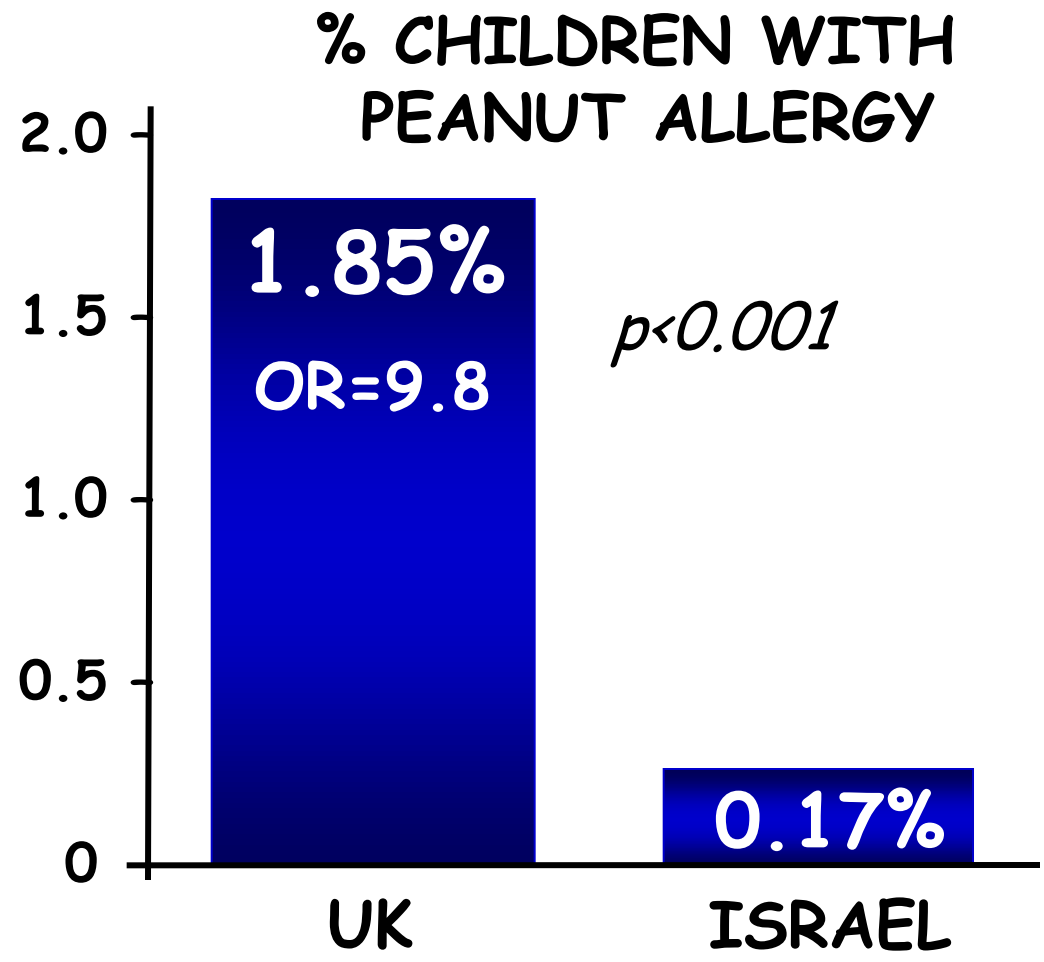
early feeding reduced the risk of peanut sensitization OR



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

Du Toit JACI 2008;122:984

- ✓ Questionnaire.
- ✓ Primary schoolchildren (5171 in the UK and 5615 in Israel).
- ✓ Peanut consumption and weaning in Jewish infants (77 in the UK and 99 in Israel).



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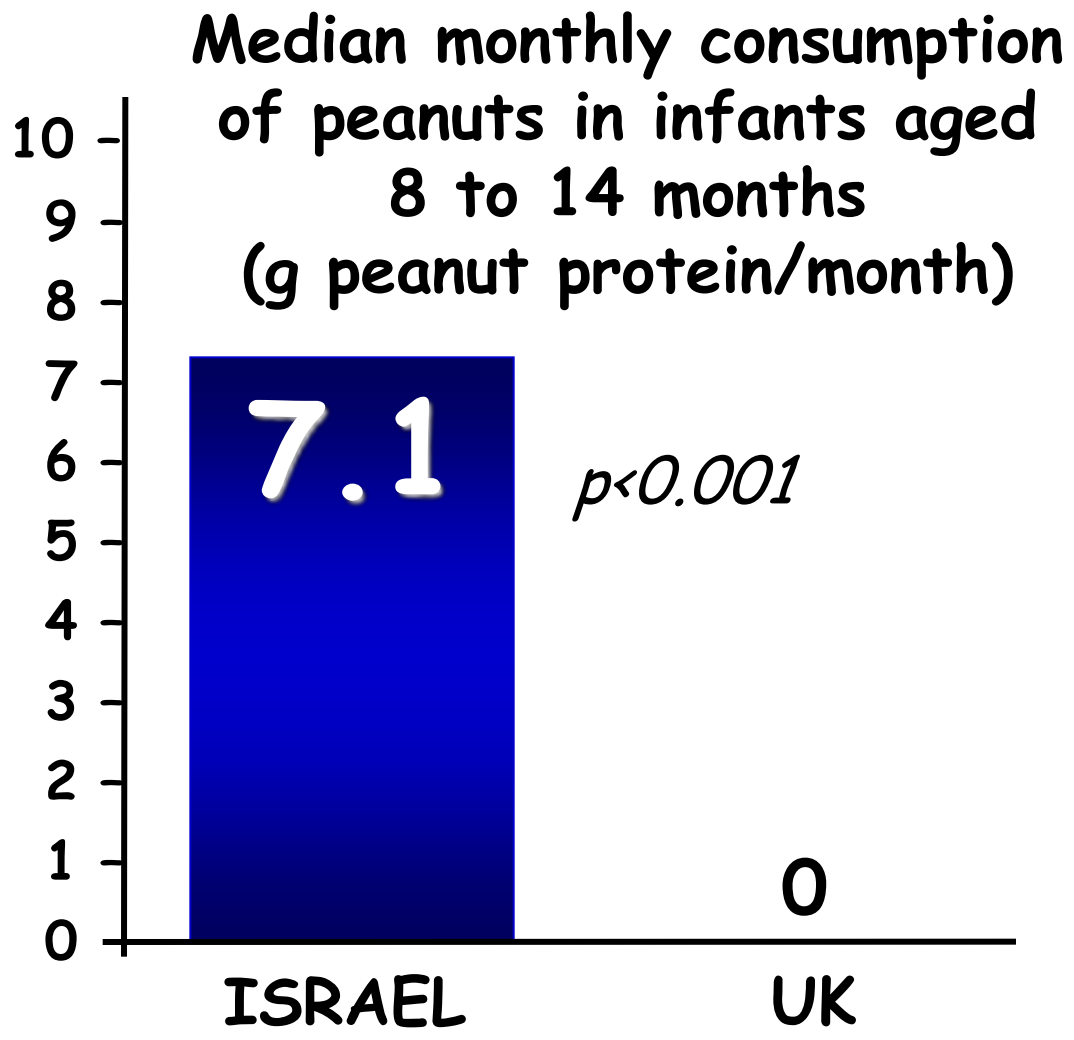


Household peanut consumption as a risk factor for the development of peanut allergy

Fox JACI 2009; 123:417

Background:

Most children with peanut allergy (PA) react on first known oral exposure to peanut.

Recent data suggest cutaneous exposure as a route of sensitization.

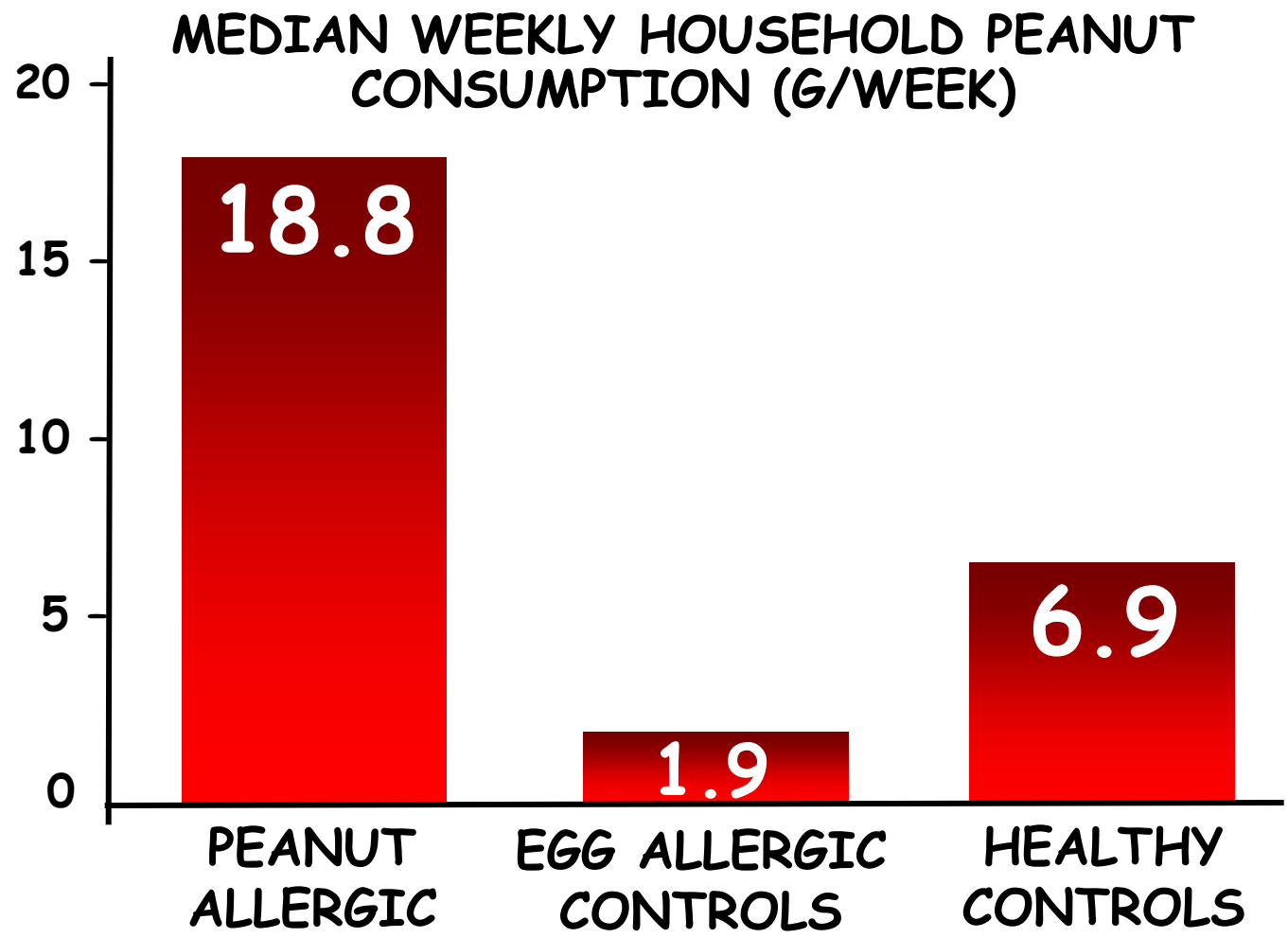
Objectives:

This study aimed to establish the relevant route of peanut exposure in the development of allergy.

Household peanut consumption as a risk factor for the development of peanut allergy

Fox JACI 2009; 123:417

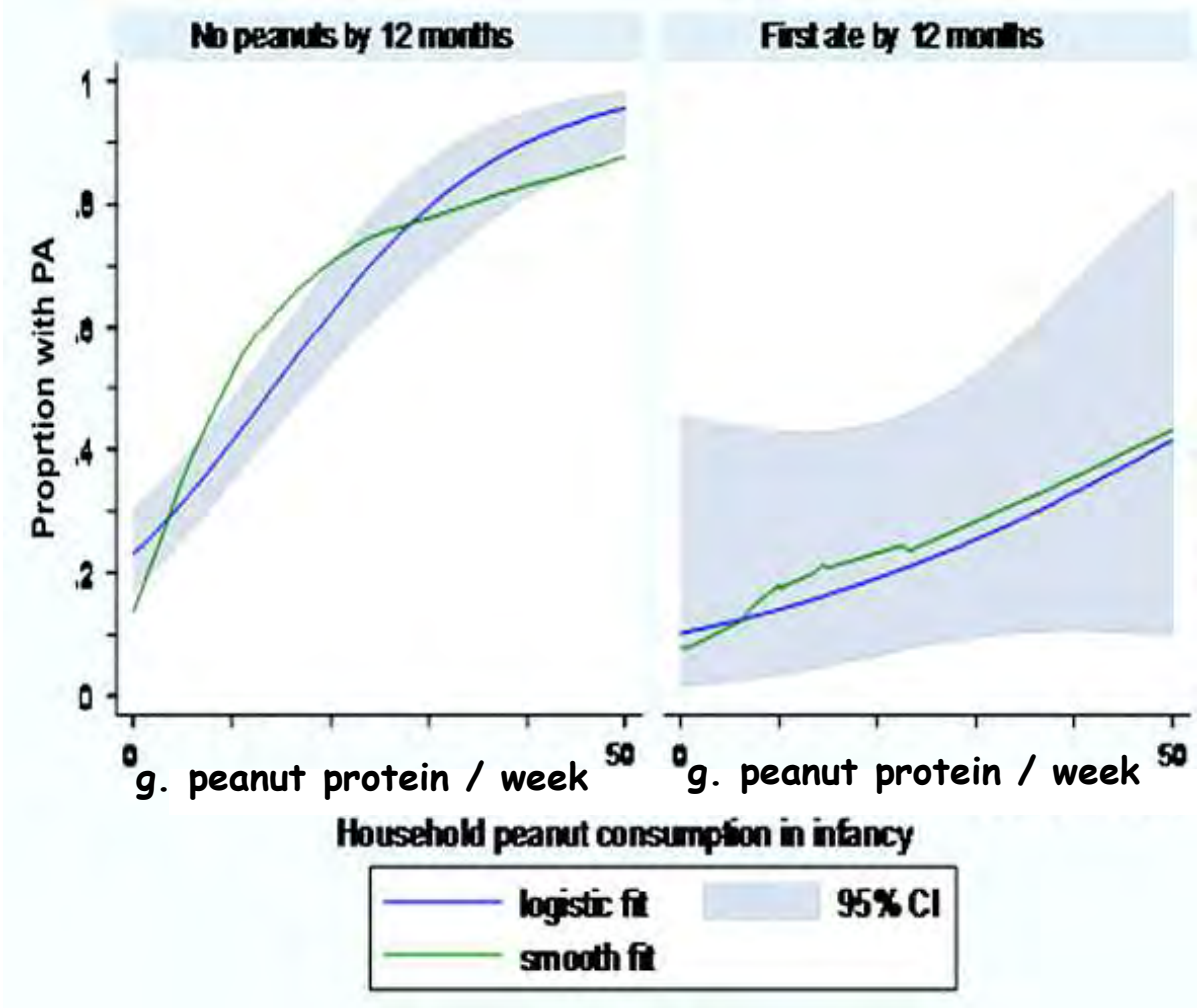
- ✓ Questionnaires to children with PA and to high-risk controls (with egg allergy) and controls without allergy.



Household peanut consumption as a risk factor for the development of peanut allergy

Fox JACI 2009; 123:417

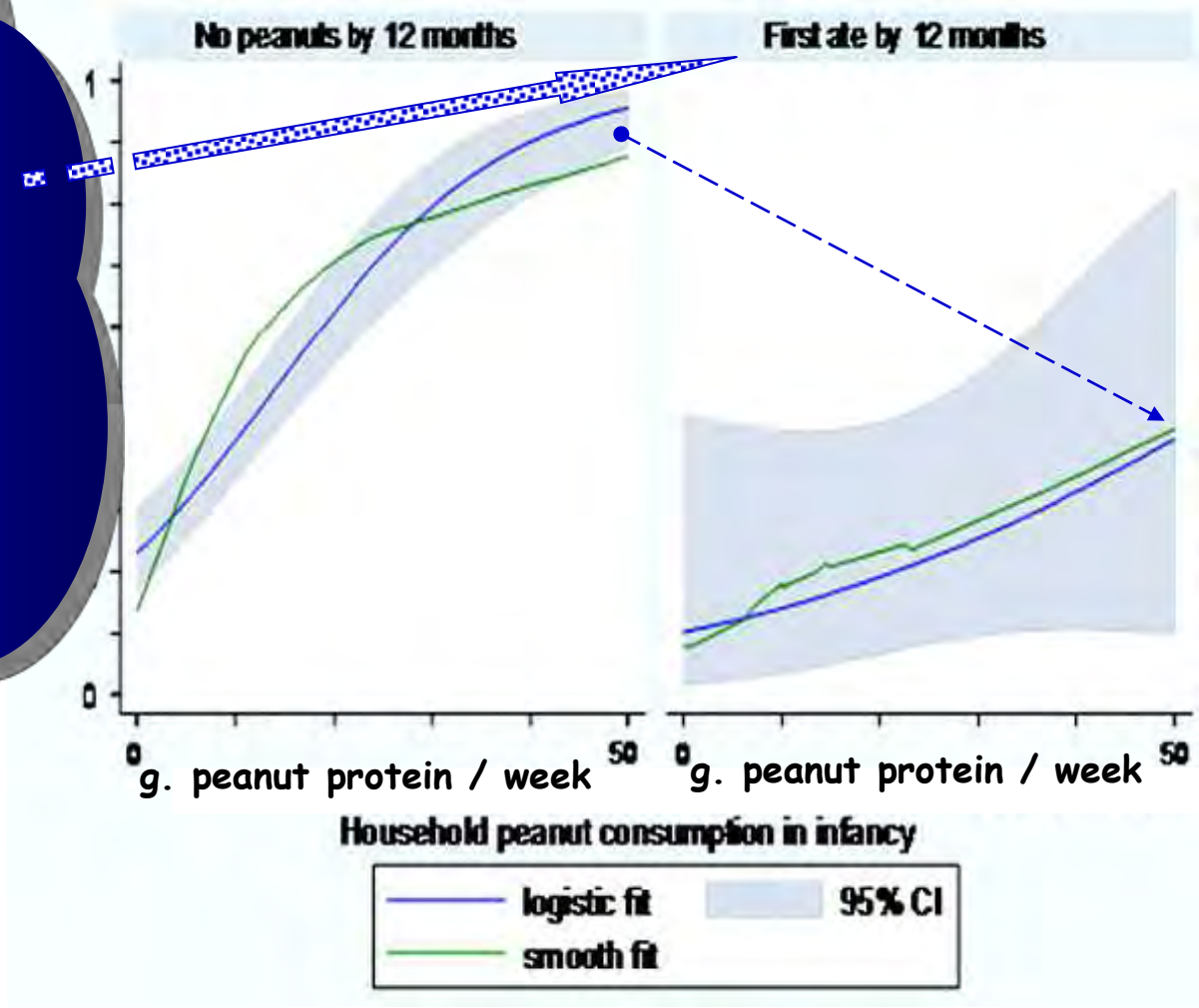
Peanut allergy among children with food allergy (n= 293) as a function of environmental exposure depending on whether child first ate peanuts by 12 months.



Household peanut consumption as a risk factor for the development of peanut allergy

JACI 2009; 123:417

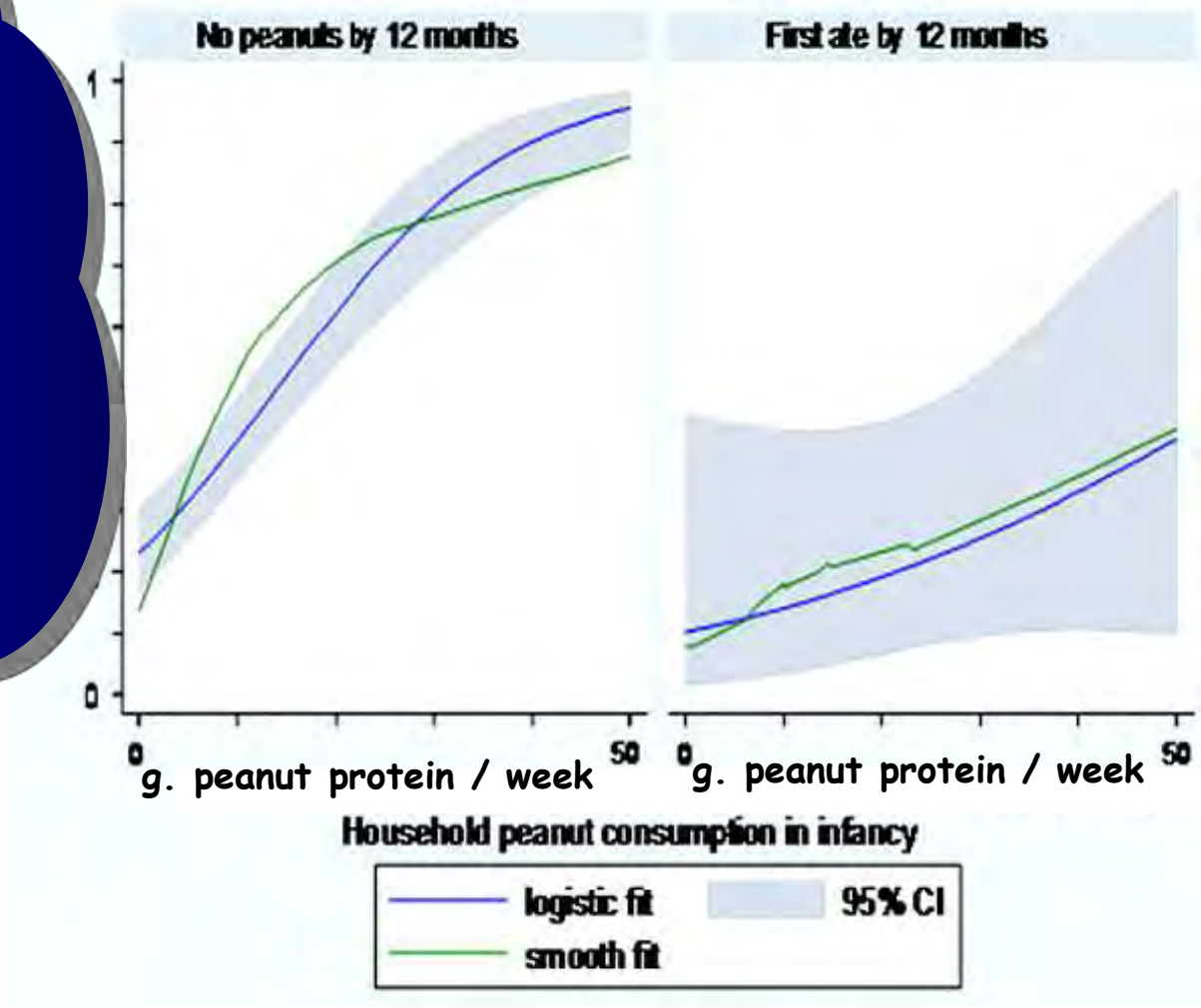
Early oral exposure to peanut in infants with high environmental peanut exposure may have had a protective effect against the development of PA.



Household peanut consumption as a risk factor for the development of peanut allergy

JACI 2009; 123:417

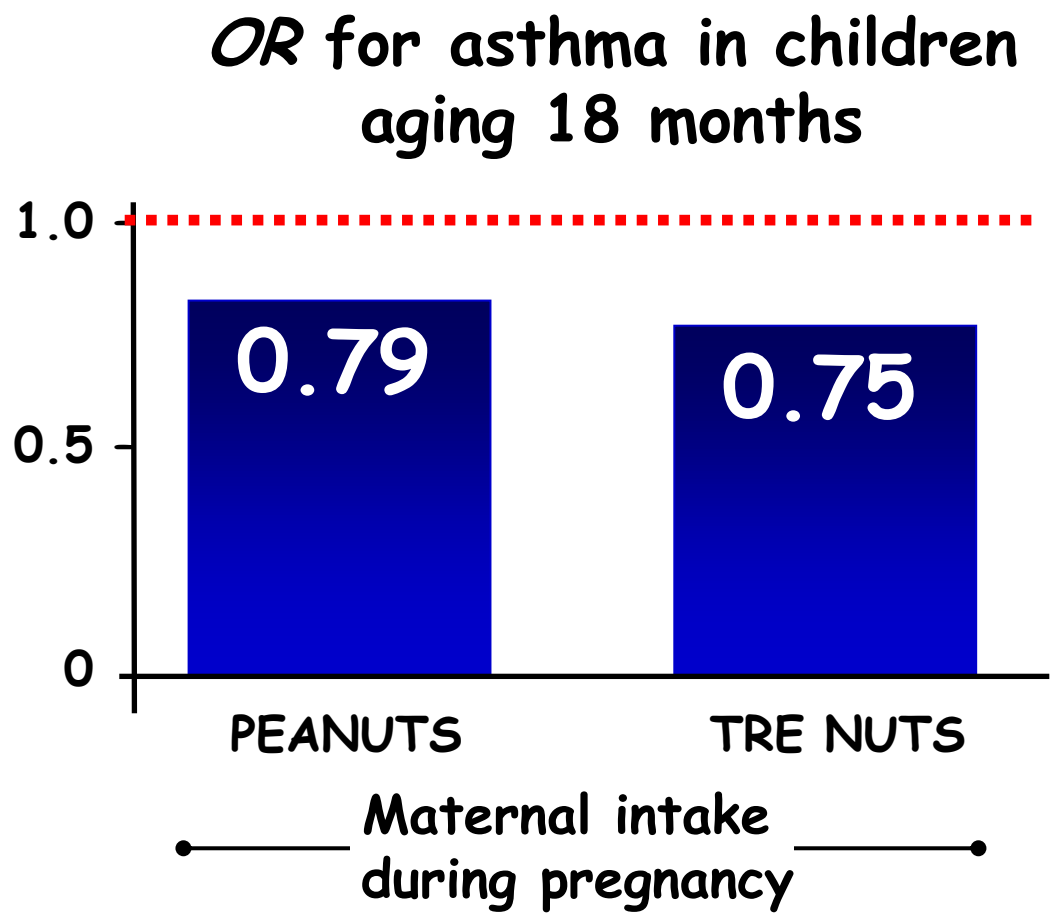
Better cleaning may reduce prevalence of PA?



Peanut and tree nut consumption during pregnancy and allergic disease in children—should mothers decrease their intake? Longitudinal evidence from the Danish National Birth Cohort.

Maslova JACI 2012;130:724

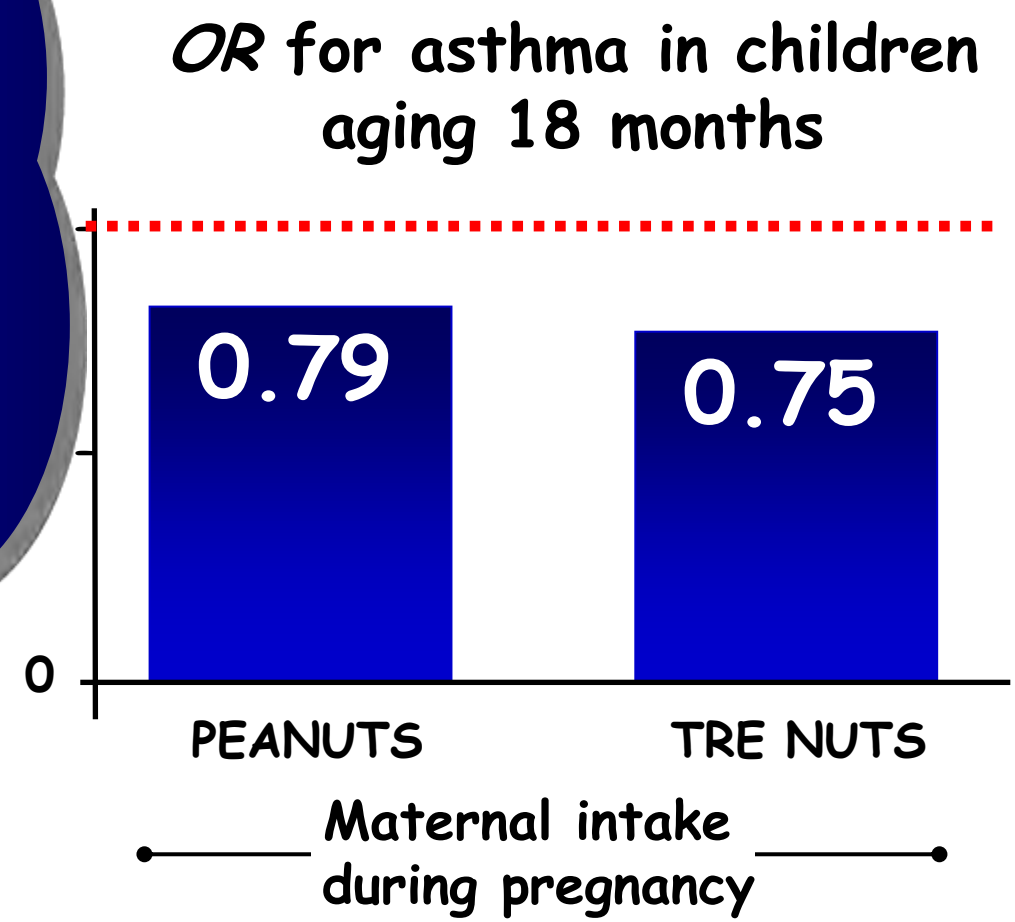
- ✓ Danish National Birth Cohort (n=61,908).
- ✓ Maternal peanut and tree nut intake during pregnancy and allergic outcomes in children at 18 months and 7 years of age.



Peanut and tree nut consumption during pregnancy and allergic disease in children—should mothers decrease their in[illegible]dinal evidence from the Danish N[illegible]

Maslova JACI 2012;130:724

✓ Higher tree nut intake was inversely associated with a medication-related asthma diagnosis (OR, 0.81) and self-reported allergic rhinitis (OR, 0.80).



- fruits

Infant feeding and childhood atopy: does early introduction of nonmilk fluids matter?

Andreasyan K, Pediatr Allergy Immunol 2007; 18:250–257.

- ✓497 infants
- ✓introduction of fruit syrup, orange juice, sterilized water, vitamins and honey at 1 month
- ✓development of child atopic disease up to 8 years

- **Sterilized water** was introduced to the majority (62%) and
- **fruit syrup** to 15% of children at 1 month of age.
- **orange juice** was given to only 3% of the infants.

Infant feeding and childhood atopy: does early introduction of nonmilk fluids matter?

Andreasyan K, Pediatr Allergy Immunol 2007; 18:250–257.

- ✓497 infants
- ✓introduction of fruit syrup, orange juice, sterilized water, vitamins and honey at 1 month
- ✓development of child atopic disease up to 8 years

None of the non-milk fluids appeared to be a significant predictor of atopic sensitization

Infant feeding and childhood atopy: does early introduction of nonmilk fluids matter?

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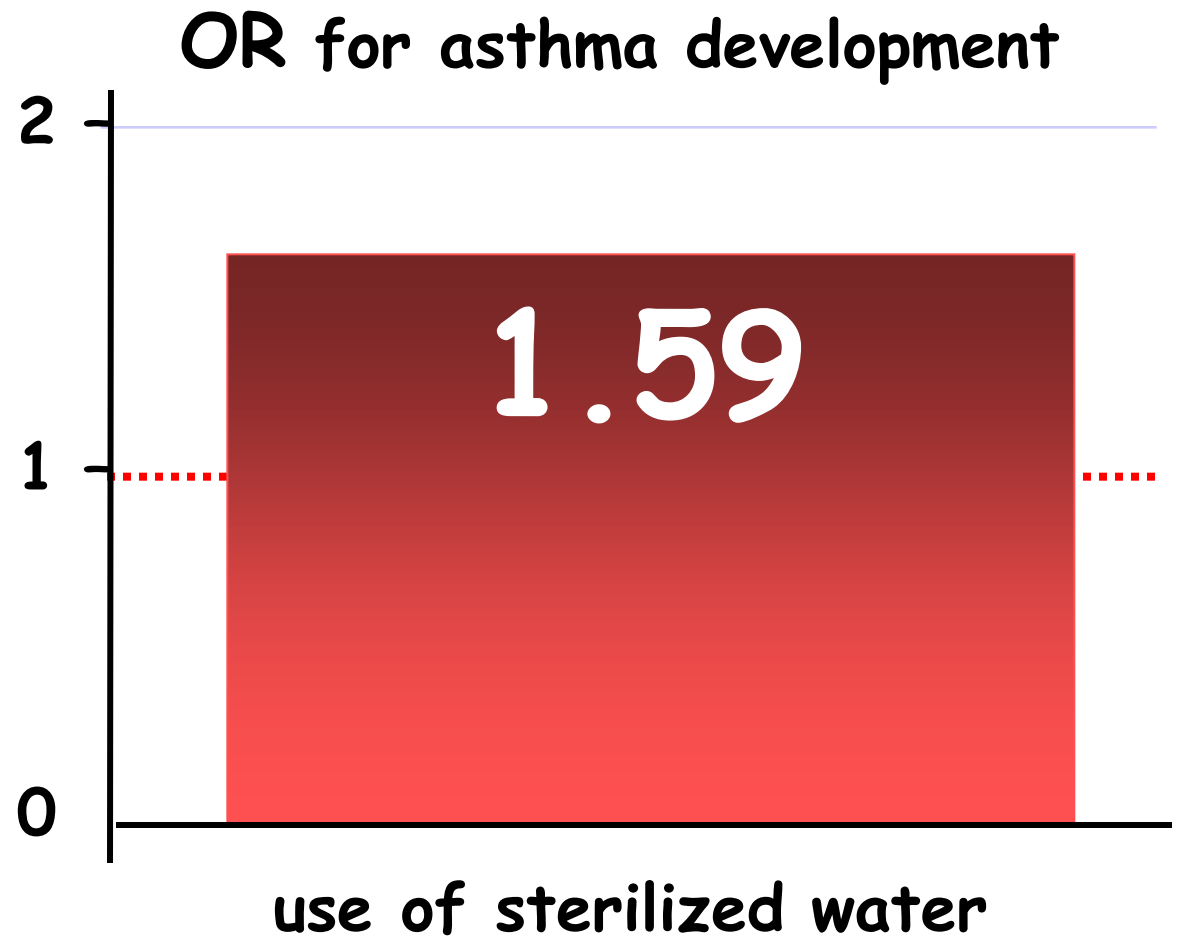

Infant feeding and childhood atopy: does early introduction of nonmilk fluids matter?

Andreasyan K, Pediatr Allergy Immunol 2007; 18:250–257.

Effect on gut flora?