# Highlights in Pediatric Allergy & Pulmonolgy

***Attilio Boner***
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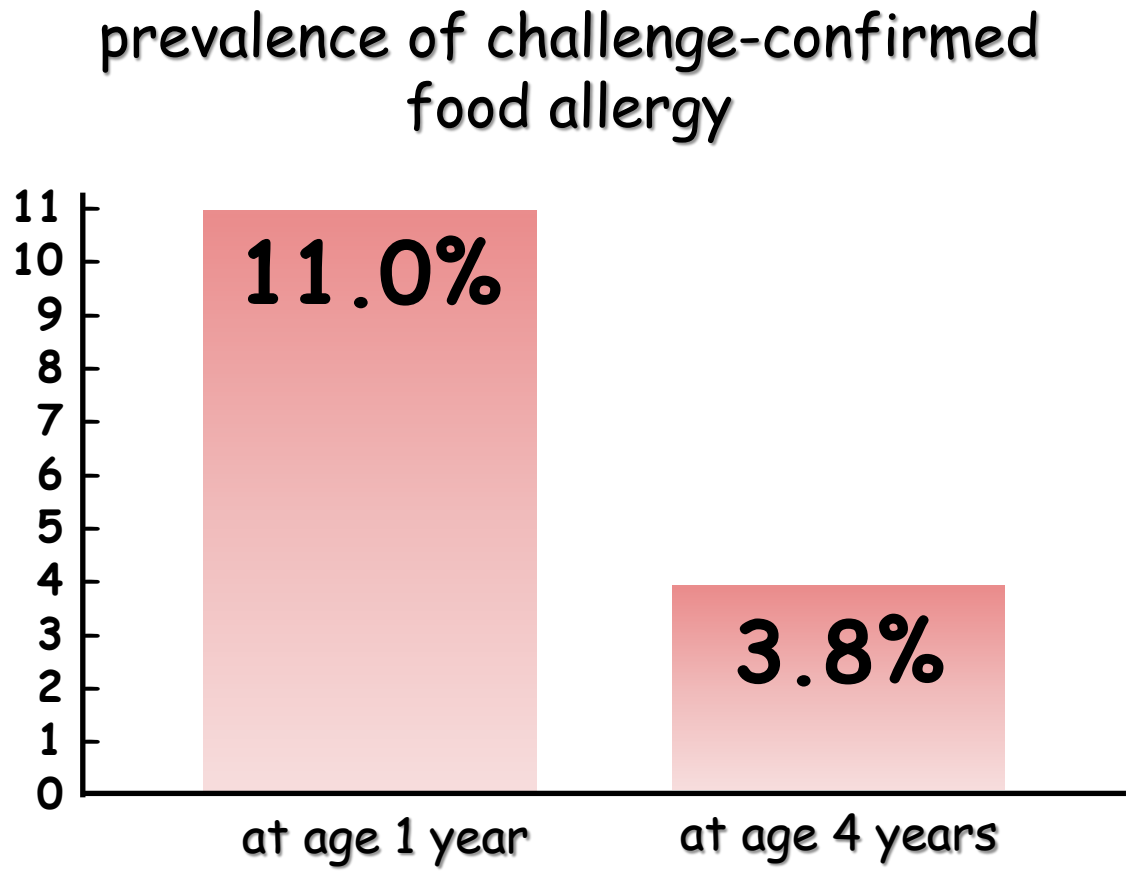
- ✓ Epidemiology
- ✓ Atopic Dermatitis
- ✓ Food allergy
- ✓ Bronchiolitis & Asthma
- ✓ Allergic rhinitis
- ✓ Unexpected burden
- ✓ Summary & Conclusions

# The prevalence of food allergy and other allergic diseases in early childhood in a population-based study: HealthNuts age 4-year follow-up.

*Peters RL, J Allergy Clin Immunol. 2017 Jul;140(1):145-153.e8.*

✓HealthNuts is a population-based cohort study with baseline recruitment of **5276 one-year-old children** in Melbourne, Australia

✓SPTs to 4 food allergens and those with detectable SPT results had formal food challenges

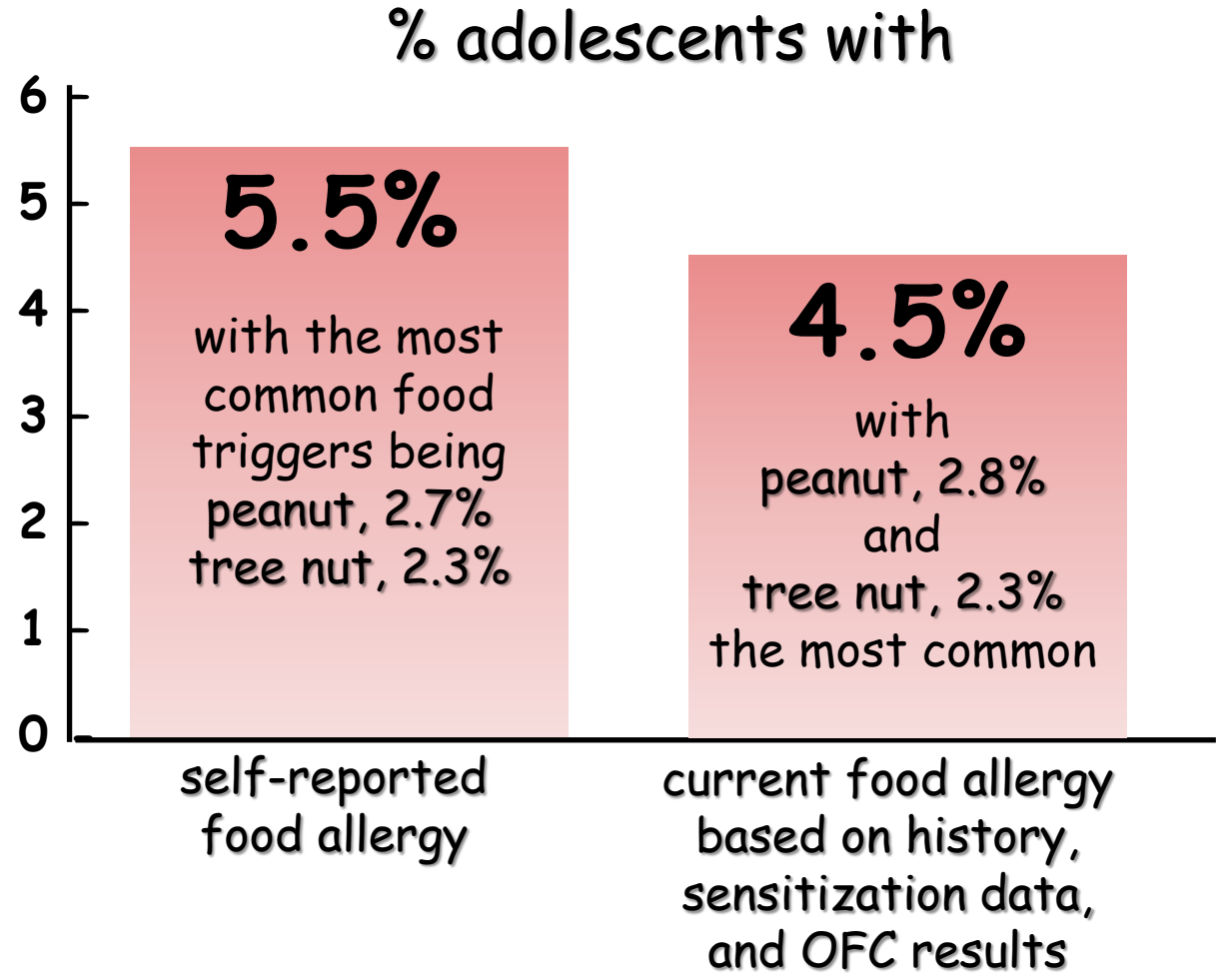


# Prevalence of clinic-defined food allergy in early adolescence: The SchoolNuts study.

*Sasaki M, J Allergy Clin Immunol. 2018 Jan;141(1):391-398.e4.*

✓Schools randomly selected from greater metropolitan Melbourne, Australia.


✓5016 students aged 10 to 14 years, and their parents, were asked to complete a questionnaire regarding the adolescent's food allergy or food-related reactions.



# Prevalence of clinic-defined food allergy in early adolescence: The SchoolNuts study.

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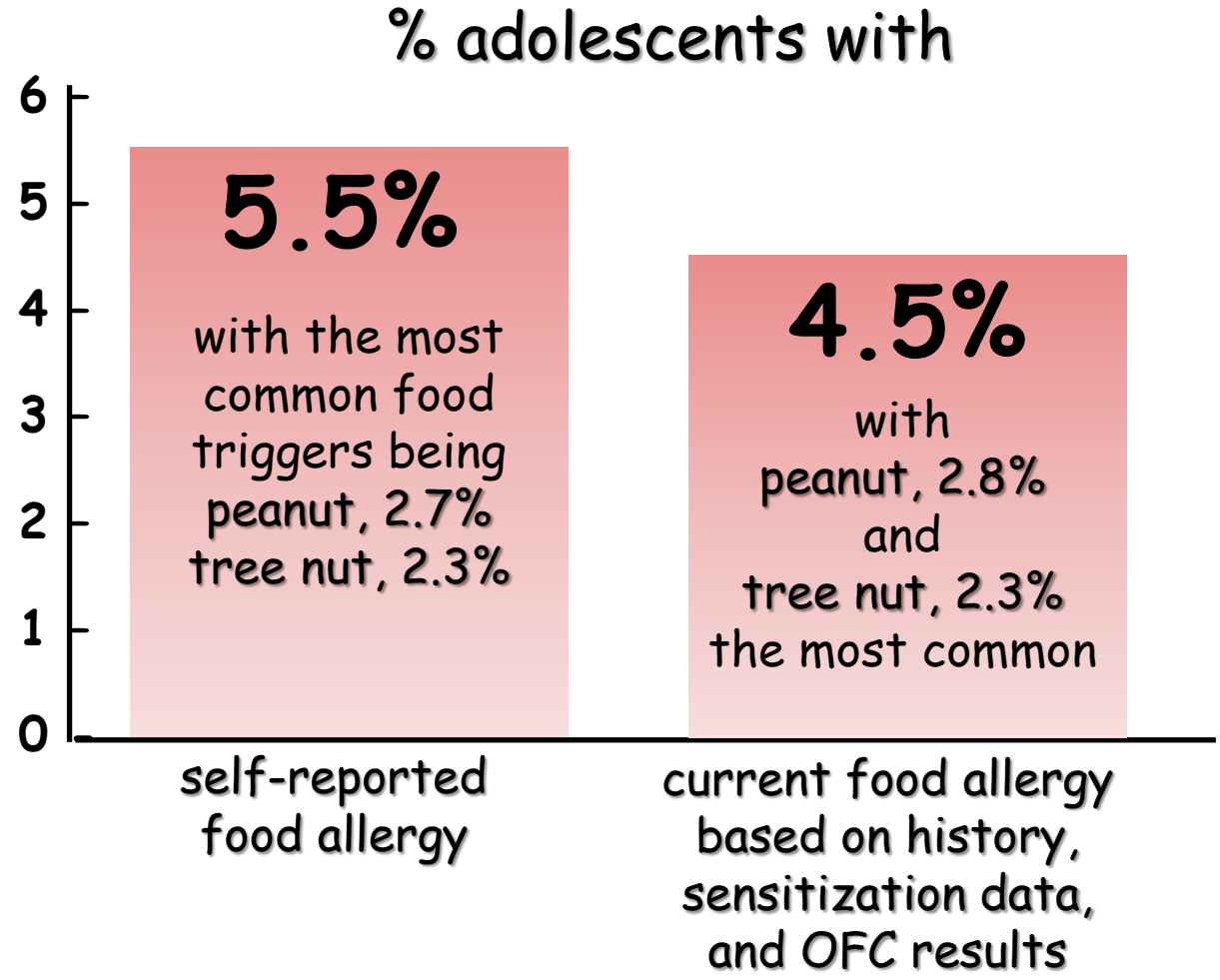
Approximately
**1 in 20**
10- to 14-year-old school students in Melbourne has current food allergy.



# Epidemiology of anaphylaxis

*Tejedor Alonso M. A.  Clin Exp Allergy 2015;45:1027–1039*

**Incidence of anaphylaxis (per 100 000 person-years)**

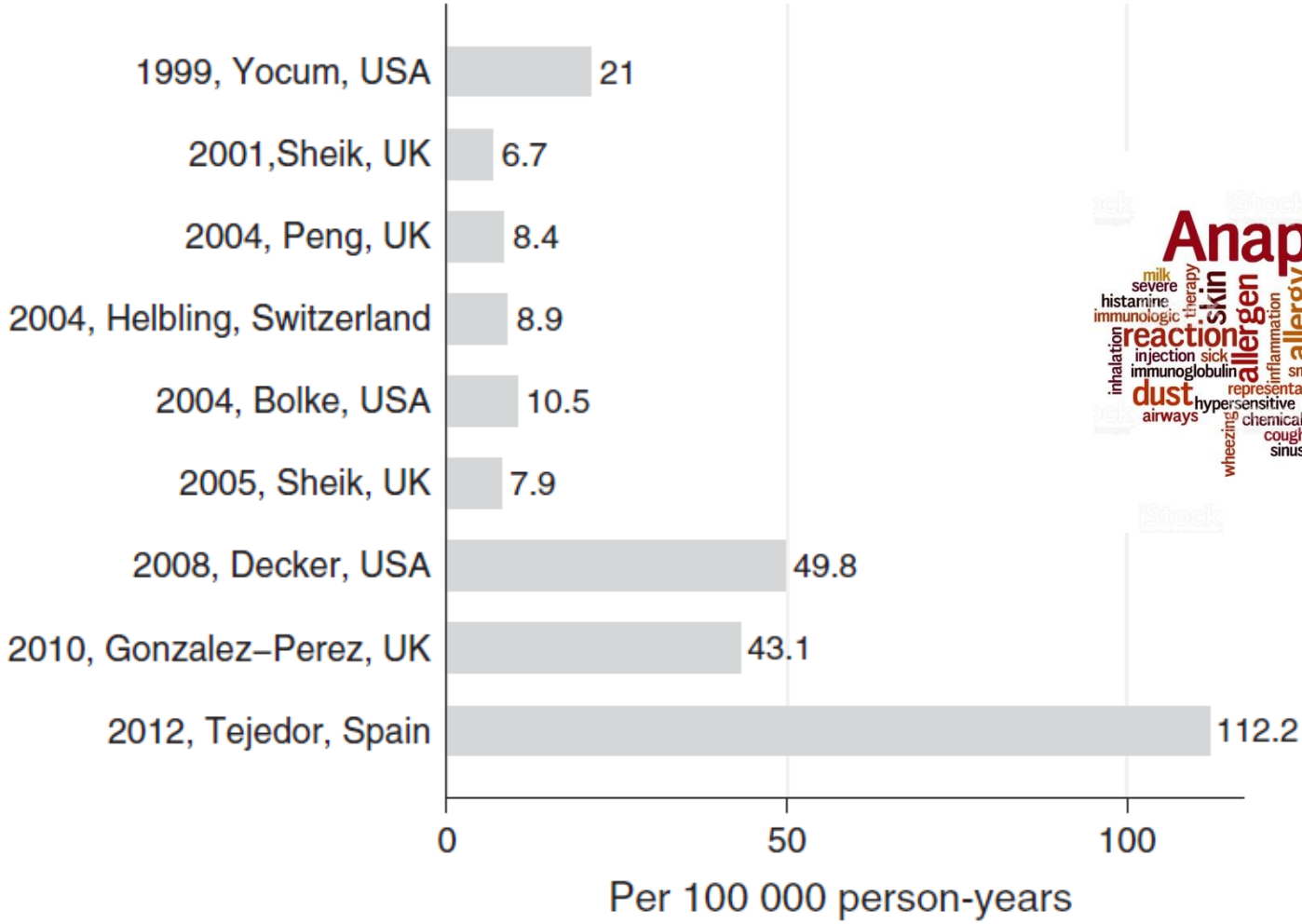
in different series from the general population

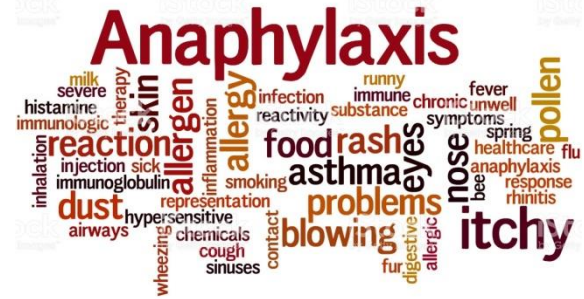
(primary care databases or databases of large health maintenance organizations).

1999

+ + + + + +

2012



# Phenotypes of Atopic Dermatitis Depending on the Timing of Onset and Progression in Childhood

*C Roduit, JAMA Pediatr. 2017;171:655-662*

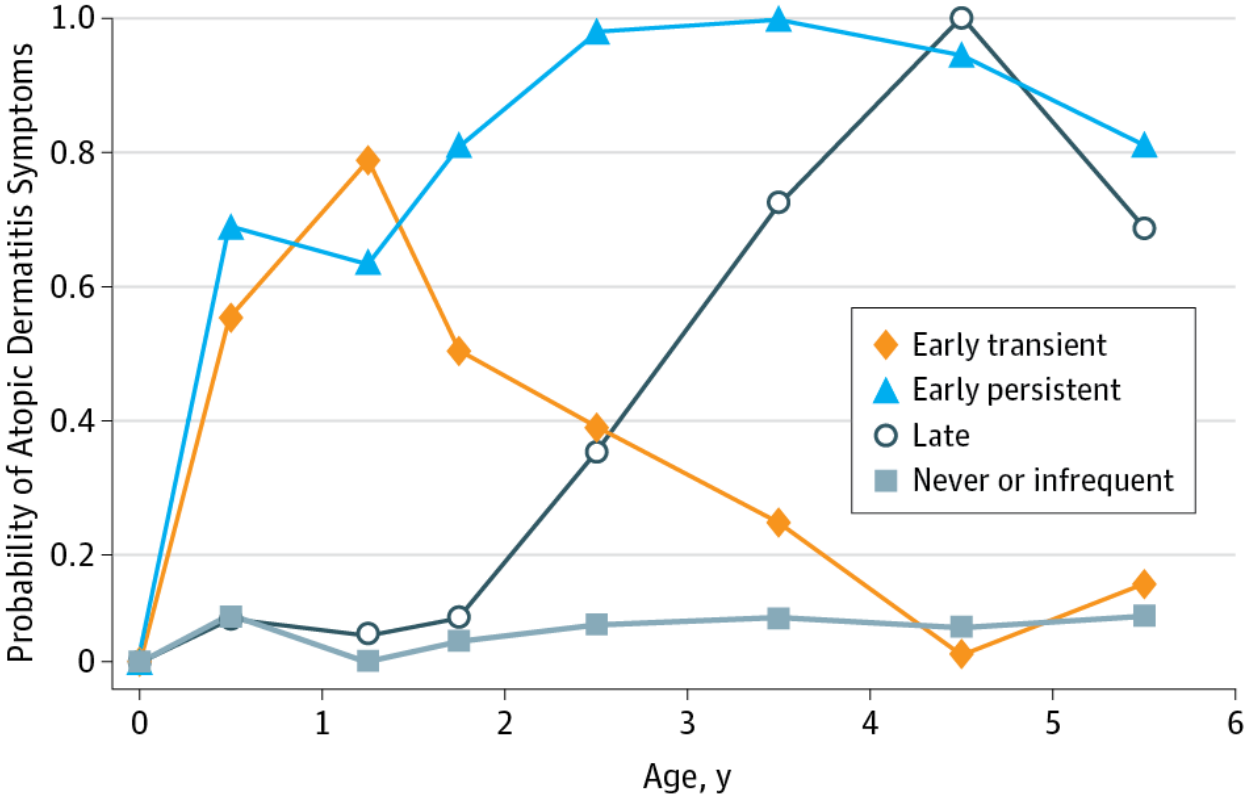
- ✓ The Protection Against Allergy Study in Rural Environments (PASTURE) is a European birth cohort where pregnant women were divided in 2 groups dependent on whether they lived on a farm.
- ✓ 1038 children followed to 6 years of age.

- ➢ Latent class analysis model separated 4 phenotypes of atopic dermatitis in childhood:
- 2 early phenotypes with onset before age 2 years (early transient [9.2%] and early persistent [6.5%]), } 15.7%
- the late phenotype with onset at age 2 years or older (4.8%), and
- the never/infrequent phenotype (79.5%), defined as children with no atopic dermatitis.

# Phenotypes of Atopic Dermatitis Depending on the Timing of Onset and Progression in Childhood

*C Roduit, JAMA Pediatr. 2017;171:655-662*

Estimated Probabilities of Atopic Dermatitis Symptoms at Each Time Point From Birth to 6 Years of Age for Each Atopic Dermatitis Phenotype in the 4-Class Model




The prevalences of the phenotypes are:

- 9.2% for early transient (n = 96),
- 6.5% for early persistent (n = 67),

15.7%

- 4.8% for late (n = 50),
- 79.5% for never/infrequent (n = 825).

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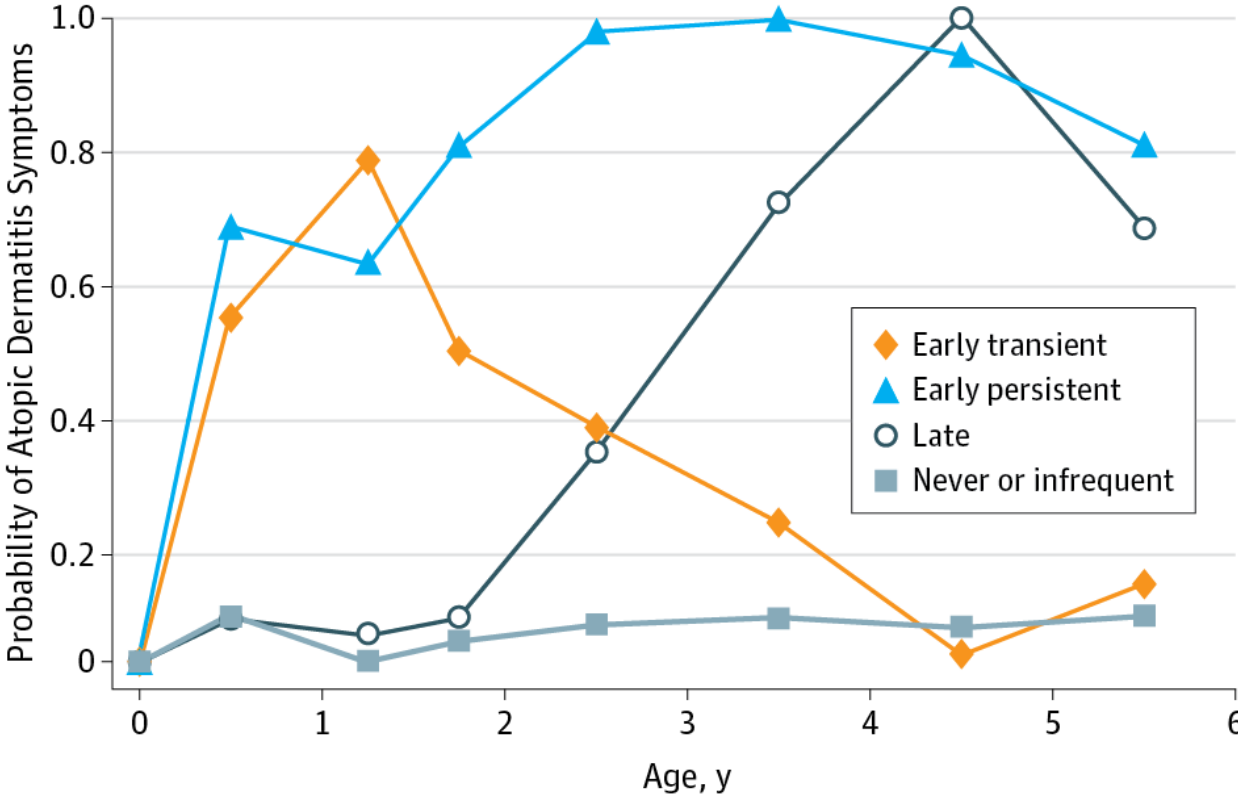


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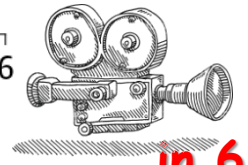


**The incidence of AD in 6 yr old children is ≈ 20%**

# Identification of atopic dermatitis subgroups in children from 2 longitudinal birth cohorts.

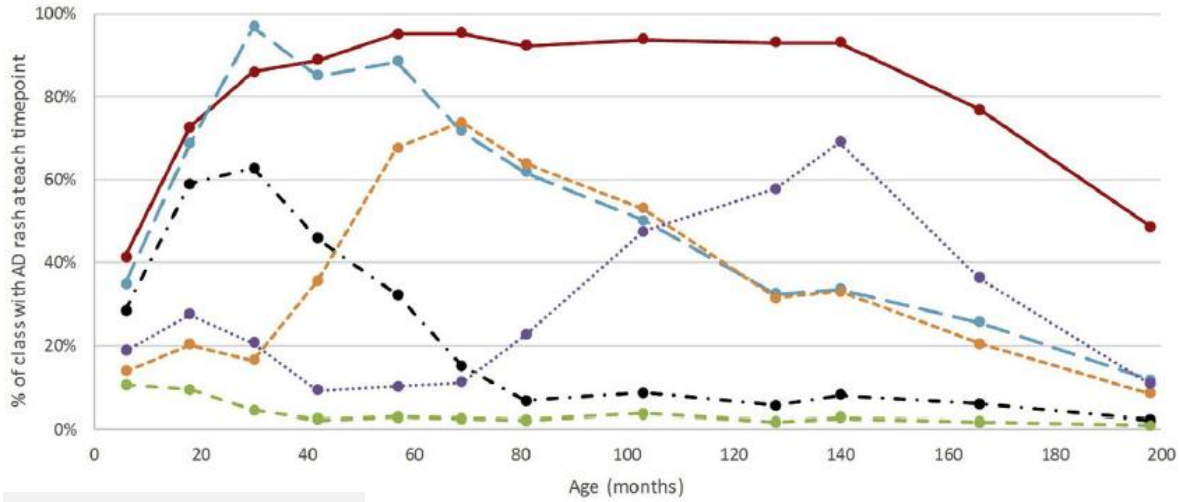
*Paternoster L, J Allergy Clin Immunol. 2018 Mar;141(3):964-971.*

✓2 birth cohort studies including **9894 children** from the United Kingdom (ALSPAC) and **3652** from the Netherlands (PIAMA).

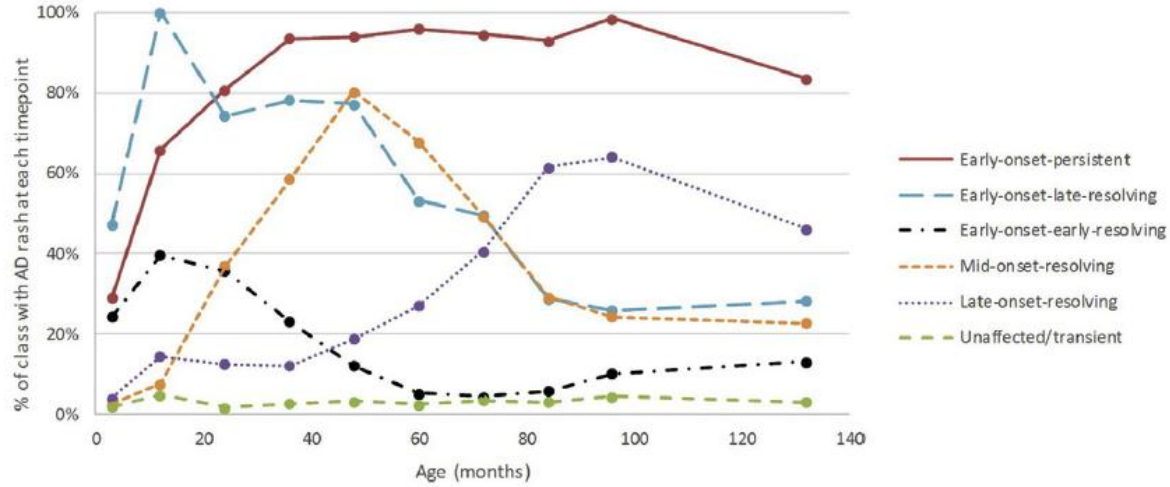
✓AD was defined by parental report of a typical itchy and/or flexural rash.

✓patterns of AD from birth to the age of 11 to 16 years.

A, ALSPAC (n = 9894




B, PIAMA (n = 3652).



# Identification of atopic dermatitis subgroups in children from 2 longitudinal birth cohorts.

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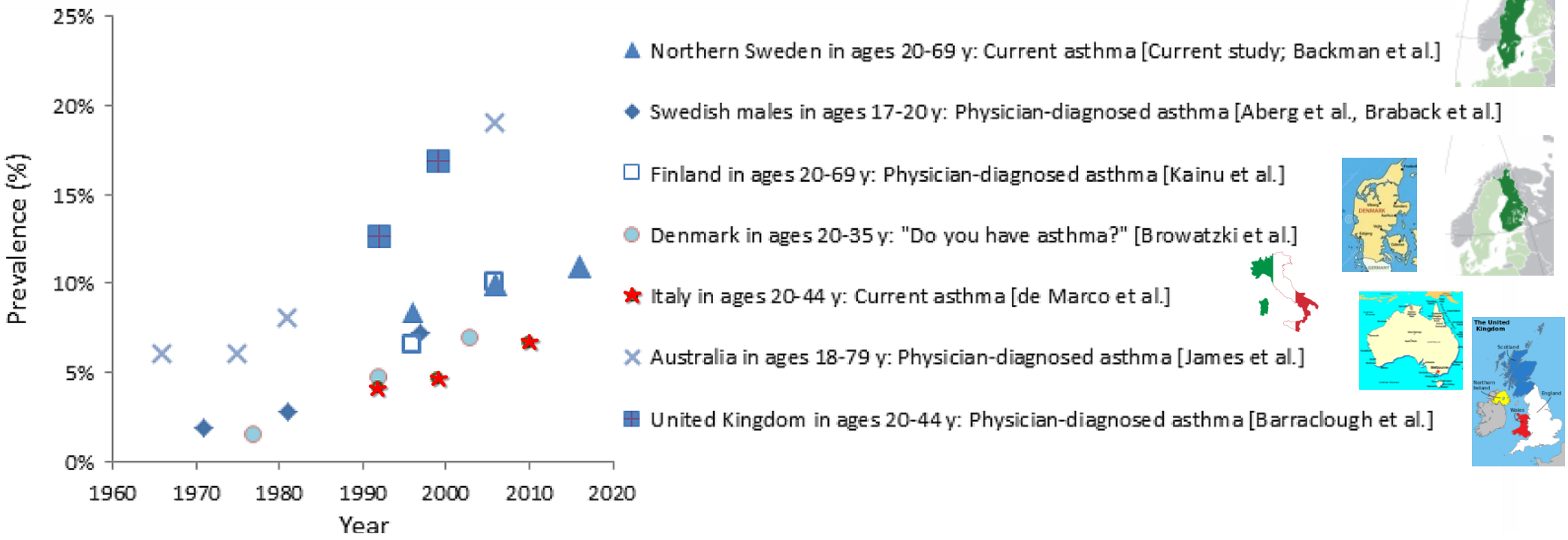
## Descriptions and prevalences of the classes in 2 independent cohorts

| Class | Description of class in ALSPAC | ALSPAC prevalence | PIAMA prevalence |
|---|---|---|---|
| Unaffected individuals or transient AD | 64% of this class never had reported rash, others had 1 or 2 isolated occasions of rash; ~10% reported rash consistent with AD at 6-18 mo and this declined with age | 58.0% | 62.9% |
| Early-onset-persistent AD | At age 30 mo, ~85% of this class had reported rash, increasing to >90% prevalence until 12 y; it then steadily declined to ~50% at 16.5 y | 7.3% | 4.9% |
| Early-onset-late-resolving AD | In this class the prevalence of rash rose steeply to >95% at 30 mo and then steadily declined to ~10% by 16.5 y | 7.0% | 3.8% |
| Early-onset-early-resolving AD | ~60% of children in this class had reported rash at 18 and 30 mo; this declined to 10% by 6-7 y | 12.9% | 15.4% |
| Mid-onset-resolving AD | In this class there was a 10%-20% prevalence of rash until 30 mo, steeply rising to 75% prevalence at 5-6 y, and steadily declining to <10% prevalence by 16.5 y | 7.0% | 6.5% |
| Late-onset-resolving AD | In this class, ~30% reported rash at 18 mo, declining to ~10% prevalence at 5-6 y, steadily rising to ~70% prevalence by 12 y and finally declining to 10% by 16.5 y | 7.9% | 6.5% |

Lifetime prevalence of AD up to adolescence is ≈ 40 %

# Increased prevalence of allergic asthma from 1996 to 2006 and further to 2016 - results from three population surveys. *H Backman, CEA 2017;47:1426-1435*

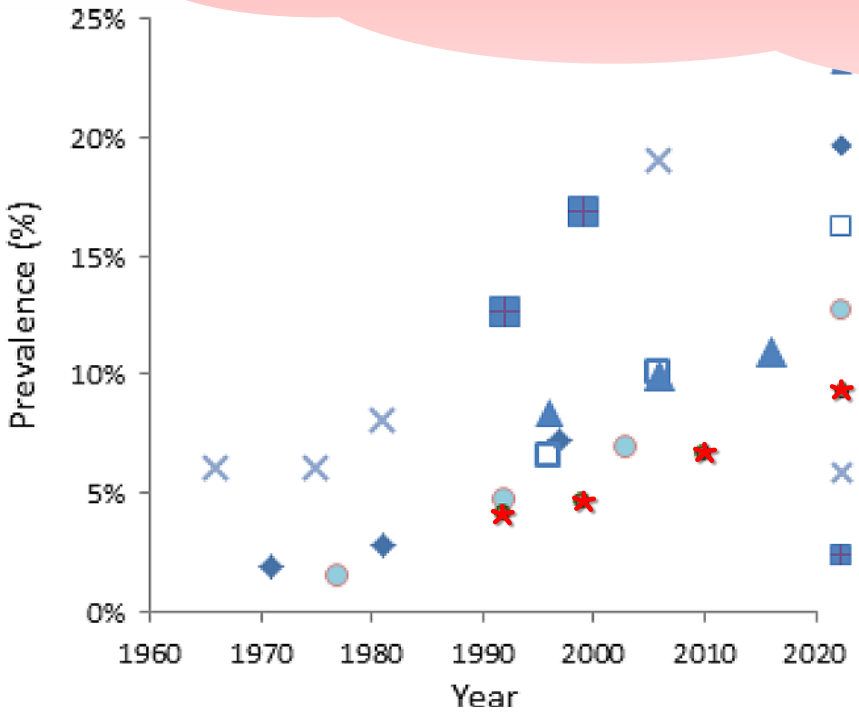
Repeated surveys of asthma prevalence among adults in the general population, with the same methods within the same age-span and area.



# Increased prevalence of allergic asthma from 1996 to 2006 and further to 2016 - results from three population surveys. *H Backman, CEA 2017;47:1426-1435*

Repeated ... ulation,

Clinicians should be aware that the previously observed increase in prevalence of allergic asthma is still ongoing.




20-69 y: Current asthma [Current study; Backman et al.]

Swedish males in ages 17-20 y: Physician-diagnosed asthma [Aberg et al., Braback et al.]

Finland in ages 20-69 y: Physician-diagnosed asthma [Kainu et al.]

Denmark in ages 20-35 y: "Do you have asthma?" [Browatzki et al.]

Italy in ages 20-44 y: Current asthma [de Marco et al.]

Australia in ages 18-79 y: Physician-diagnosed asthma [James et al.]

United Kingdom in ages 20-44 y: Physician-diagnosed asthma [Barraclough et al.]

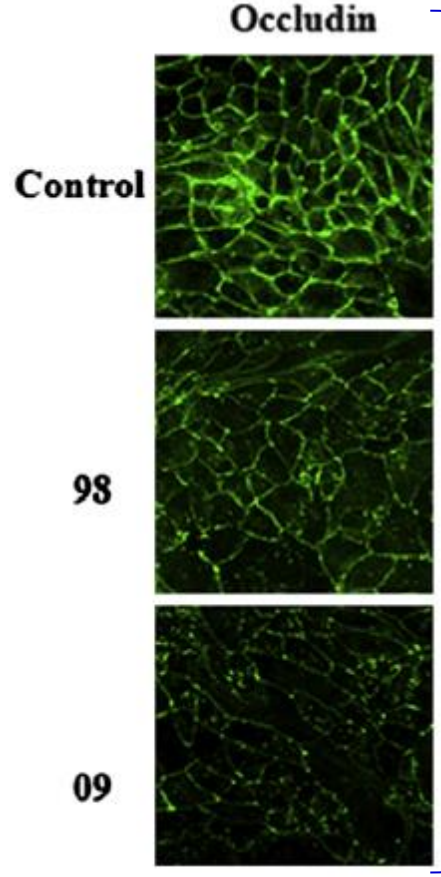

# Environmental changes could enhance the biological effect of Hop J pollens on human airway epithelial cells.

*Lee SI, J Allergy Clin Immunol 2014;134:470-72*

- ✓ Collected Japanese hop luppolo del Giappone (Hop J) pollens in 1998 and 2009.

- ✓ Prepared 2 pollen extracts (the 1998 and 2009 extracts).

**Occludin degradations induced by protease activity of Hop J pollen extracts**




human airway epithelial cells culture

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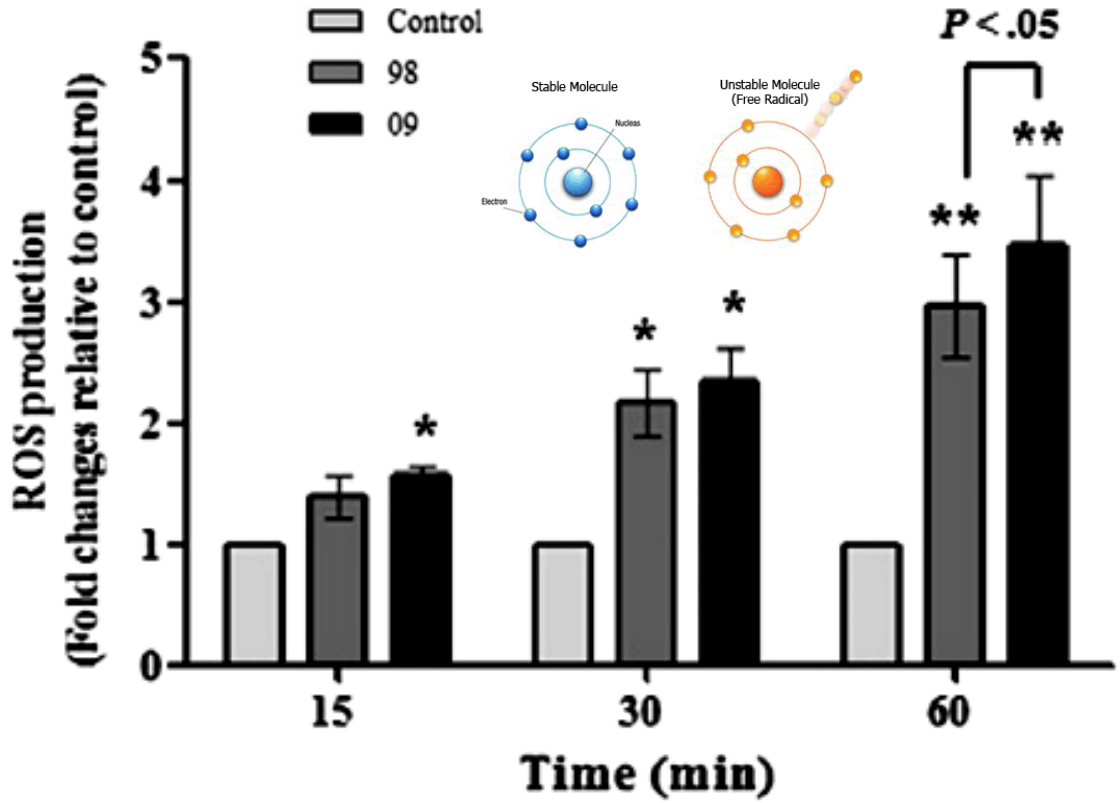
**ROS production (oxidase activity) induced by the 98 and 09 extracts**



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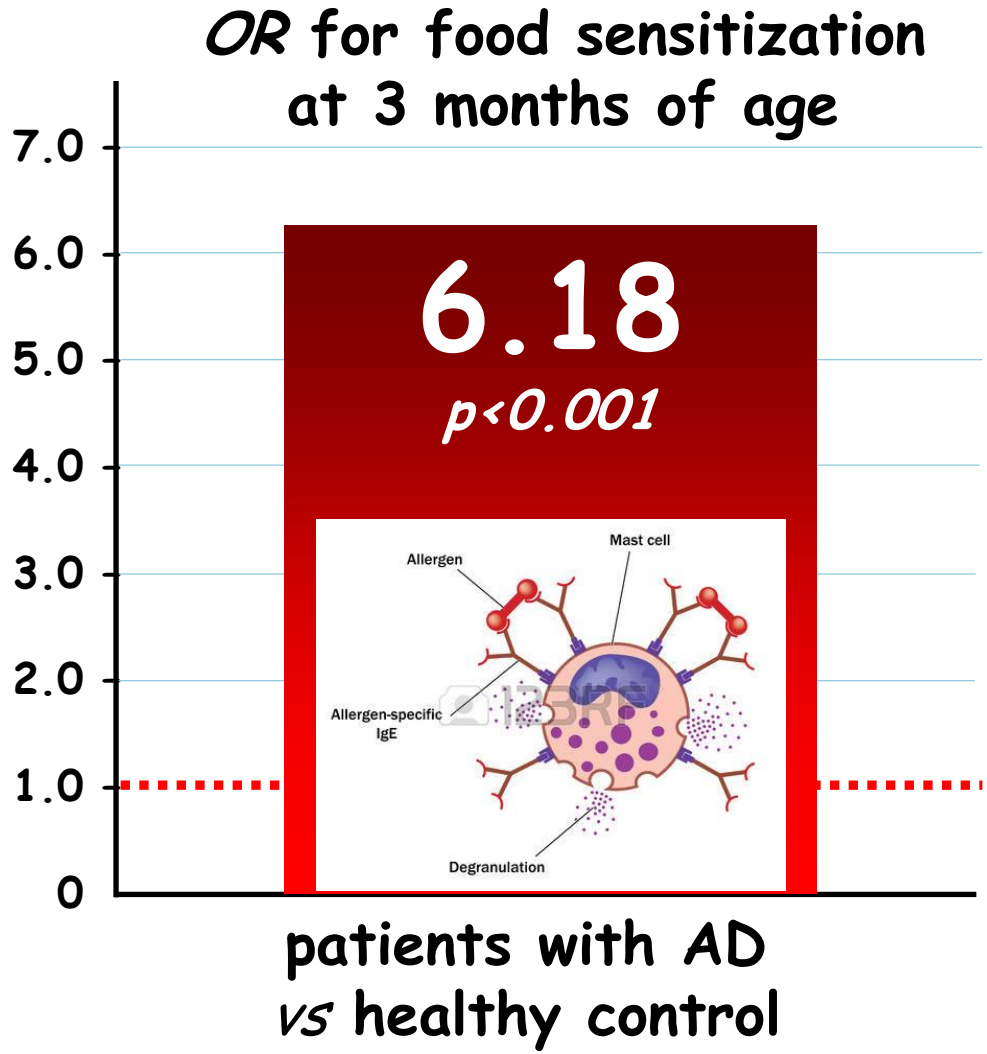
# Does atopic dermatitis cause food allergy?
## A systematic review *Tsakok T, JACI 2016;137:1071-1078.*

- ✓ 66 studies:
  18 population-based,
  8 used high-risk cohorts,
  and the rest comprised
  patients with either
  established AD or FA;

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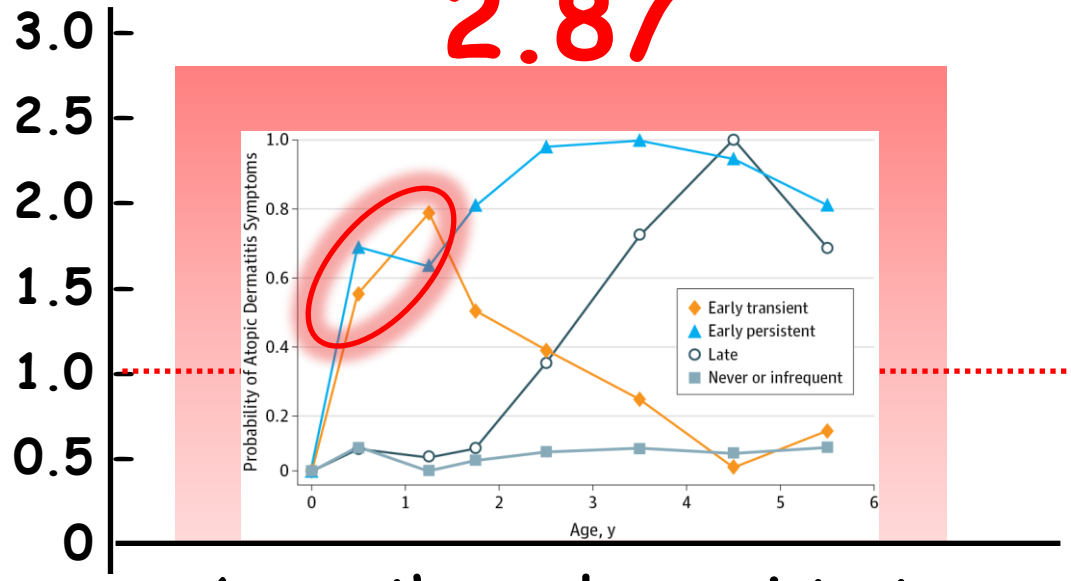
- ✓ The Protection Against Allergy Study in Rural Environments (PASTURE) is a European birth cohort where pregnant women were divided in 2 groups dependent on whether they lived on a farm.
- ✓ 1038 children followed to 6 years of age.

**OR developing asthma**

**2.87**

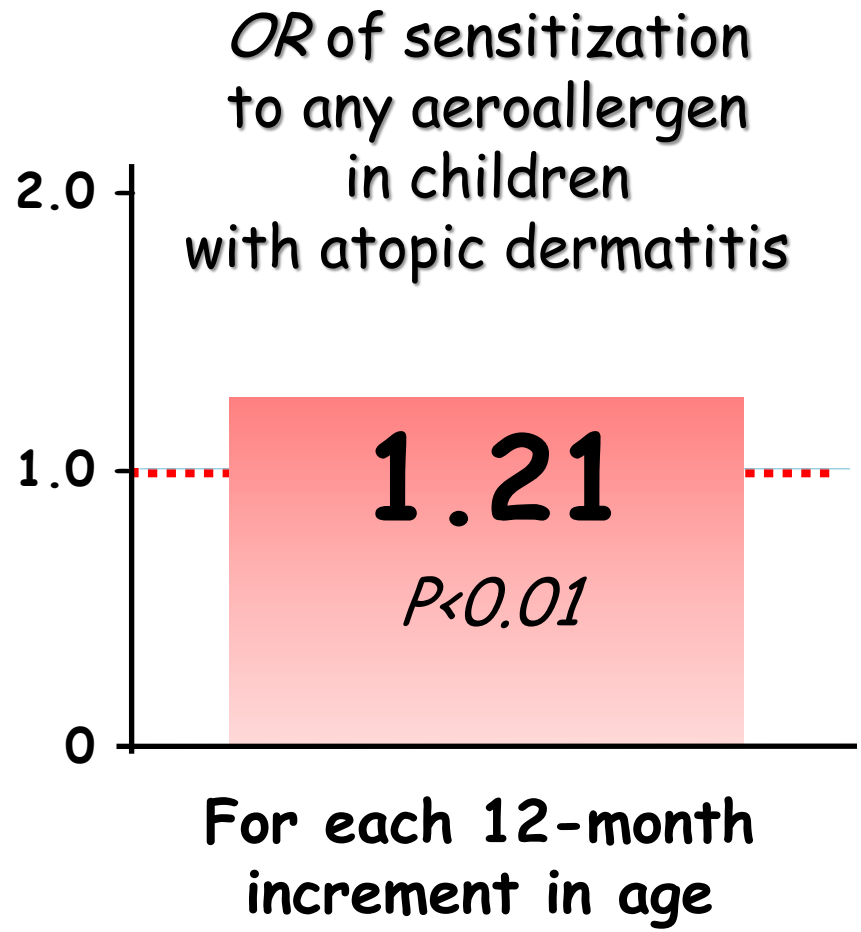



**Among the early-persistent phenotype of atopic dermatitis**

# Sensitization to food and inhalant allergens in relation to age and wheeze among children with atopic dermatitis

*Wisniewski JA, Clin Exp Allergy. 2013 Oct;43(10):1160-70.*

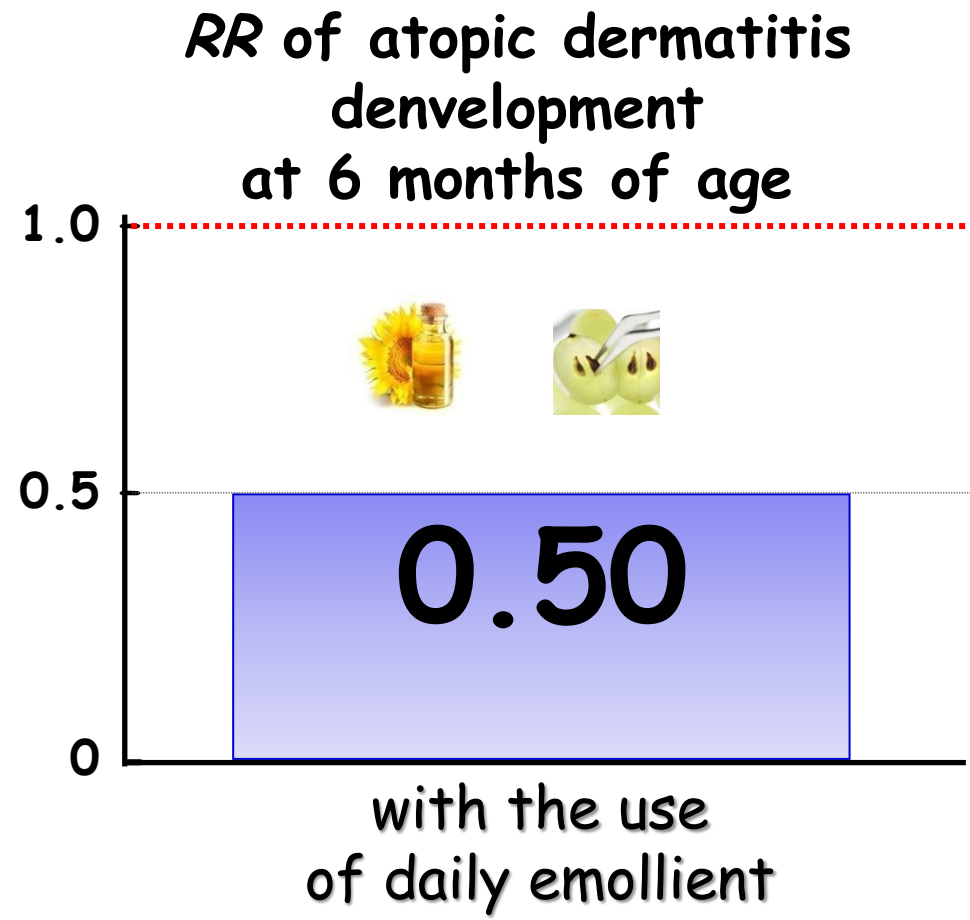
- ✓ IgE antibodies to food and inhalant allergens
- ✓ children with active atopic dermatitis (AD) (5 mo.-15 yrs, n = 66), with and without history of wheeze



# Emollient enhancement of the skin barrier from birth offers effective atopic dermatitis prevention

*Simpson EL, J Allergy Clin Immunol 2014;134:818-23*

- ✓ 124 neonates at high risk for atopic dermatitis.
- ✓ Parents in the intervention arm were instructed to apply full-body emollient therapy at least once per day starting within 3 weeks of birth.
- ✓ Parents in the control arm were asked to use no emollients.
- ✓ Incidence of atopic dermatitis at 6 months.



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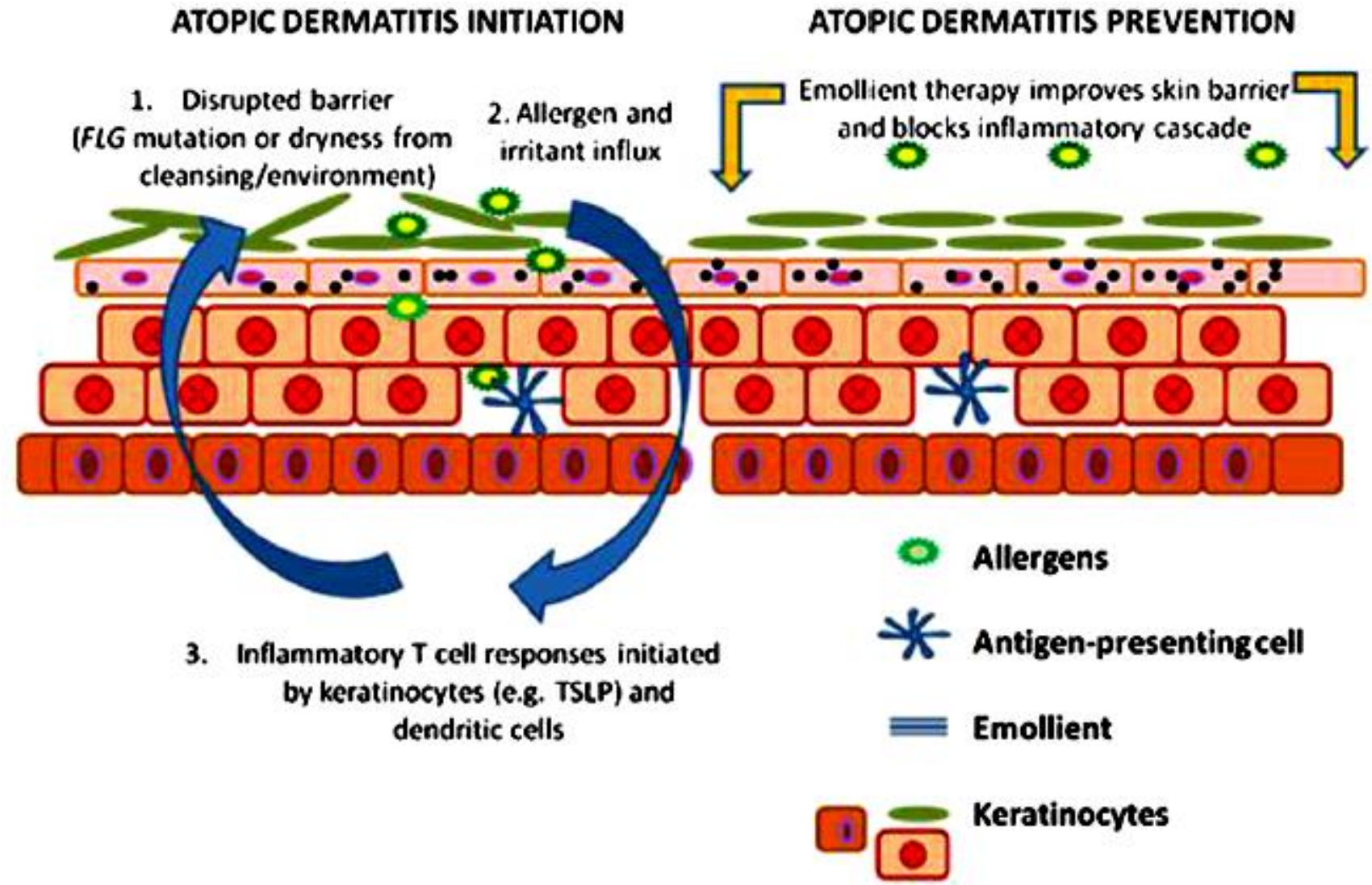
Skin barrier protection might prevent atopic dermatitis development.

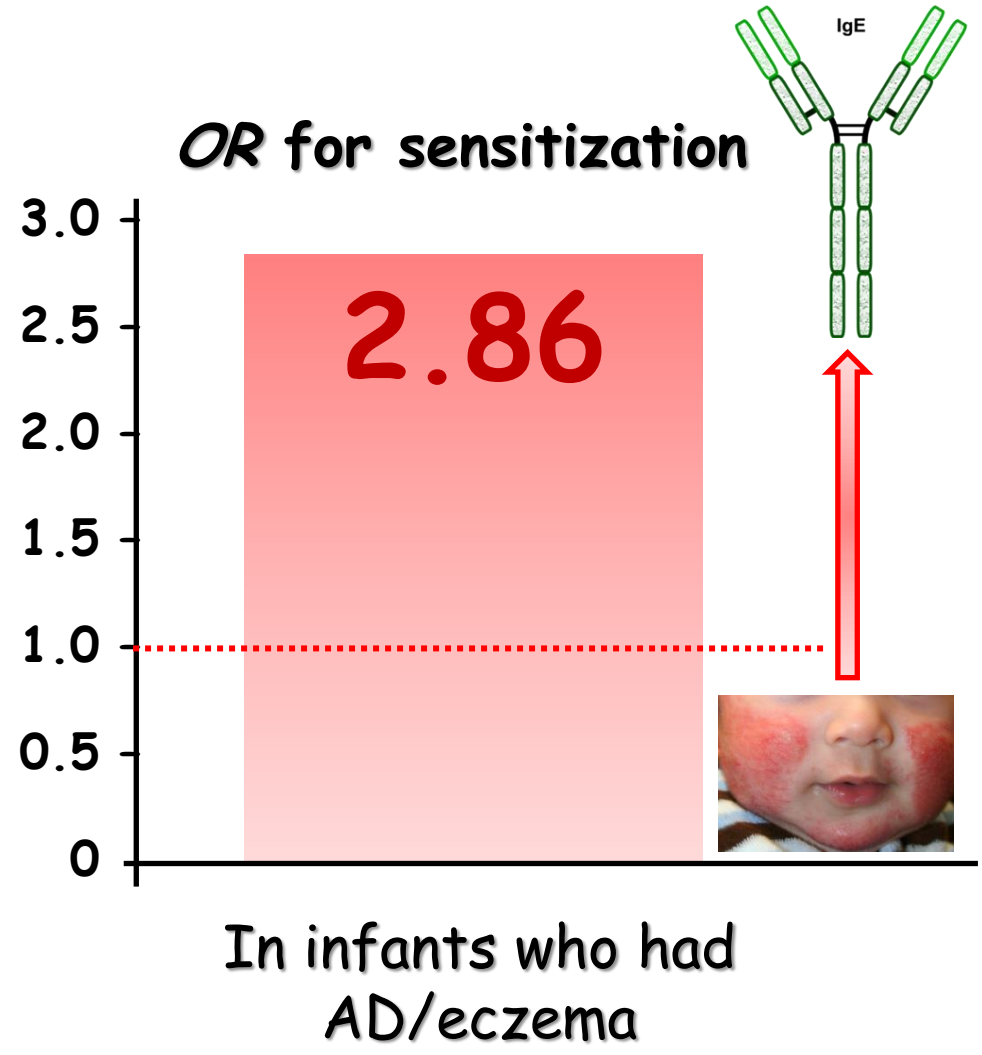
*FLG*, Filaggrin.



# Application of moisturizer to neonates prevents development of atopic dermatitis

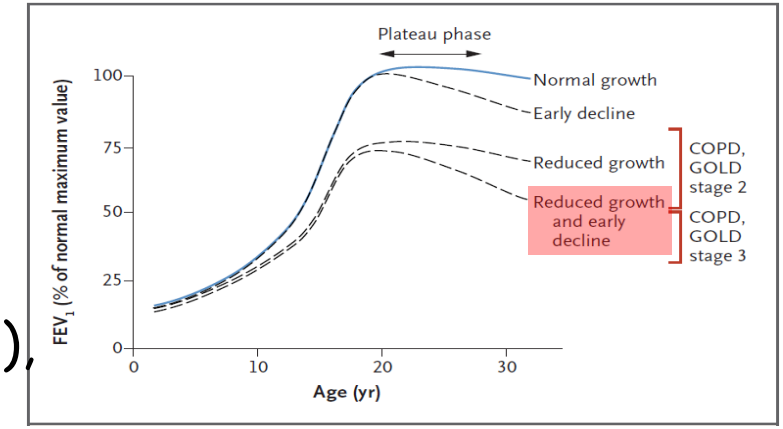
*Horimukai K, J Allergy Clin Immunol. 2014 Oct;134(4):824-830.e6*

- ✓ Emulsion-type moisturizer applied daily during the first 32 weeks of life to 59 of 118 neonates at high risk for AD (based on having a parent or sibling with AD).
- ✓ Onset of AD (eczematous symptoms lasting >4 weeks) and eczema (lasting >2 weeks).
- ✓ Cumulative incidence of (AD/eczema) at week 32 of life.
- ✓ Serum levels of allergen-specific IgE.



# Patterns of Growth and Decline in Lung Function in Persistent Childhood Asthma

*McGeachie MJ, N Engl J Med 2016;374:1842-52*




- Participants with reduced growth and an early decline, as compared with those who had normal growth, had:
  - lower $FEV_1$ lung function at enrollment (OR, 0.85),
  - a lower bronchodilator response (OR, 0.91), and
  - increased airway hyperresponsiveness (OR, 0.66);
  - were more likely to be male (OR, 3.07);
  - were younger at enrollment (OR, 0.62 per year); and
  - had a lower level of parental education (OR, 0.43 for at least a college degree vs. a lower level; *P = 0.01* ),
  - a greater number of positive skin tests at enrollment (OR for ≥3 positive tests vs. <3, 2.42; *P = 0.03* ).

Primary & Secondary Prevention !

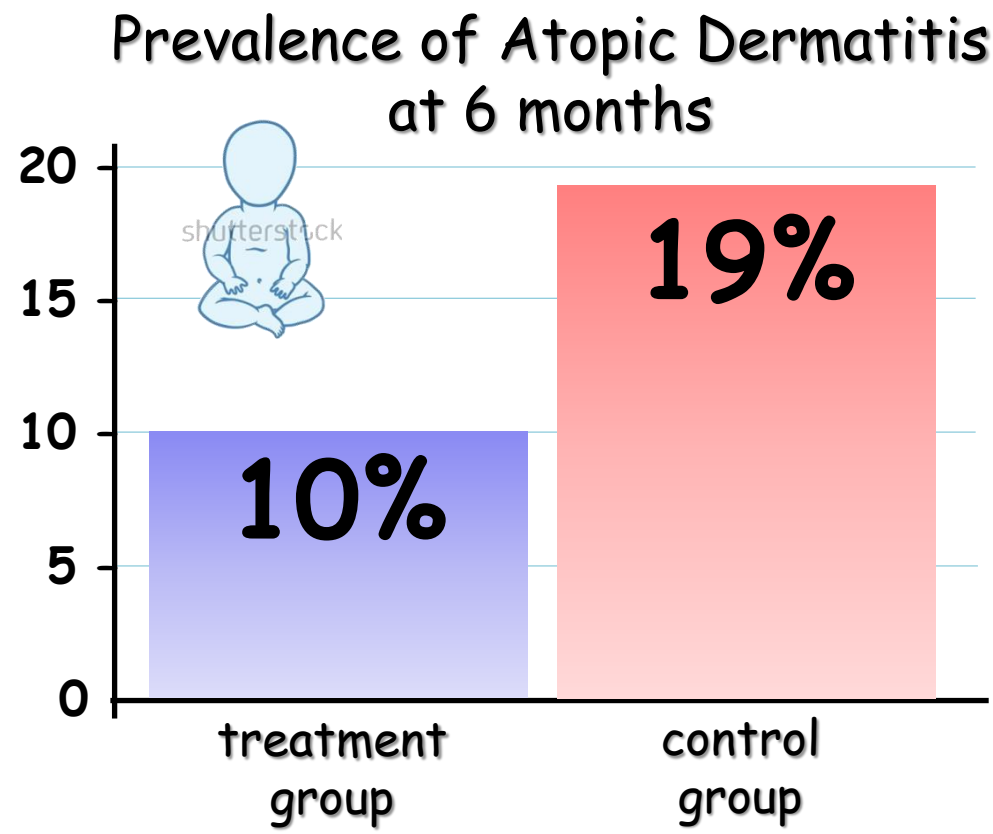
# A randomized trial of a barrier lipid replacement strategy for the prevention of atopic dermatitis and allergic sensitization: the PEBBLES pilot study.

*Lowe AJ, Br J Dermatol. 2018 Jan;178(1):e19-e21.*

✓twice-daily application of a ceramide-dominant emollient (EpiCeram™) for the first 6 months of life in 80 infants

✓parents of infants in the intervention group were shown how to apply approximately 6 g of EpiCeram to the full skin surface of their child twice per day.

✓Treatment was to commence within the first 3 weeks.



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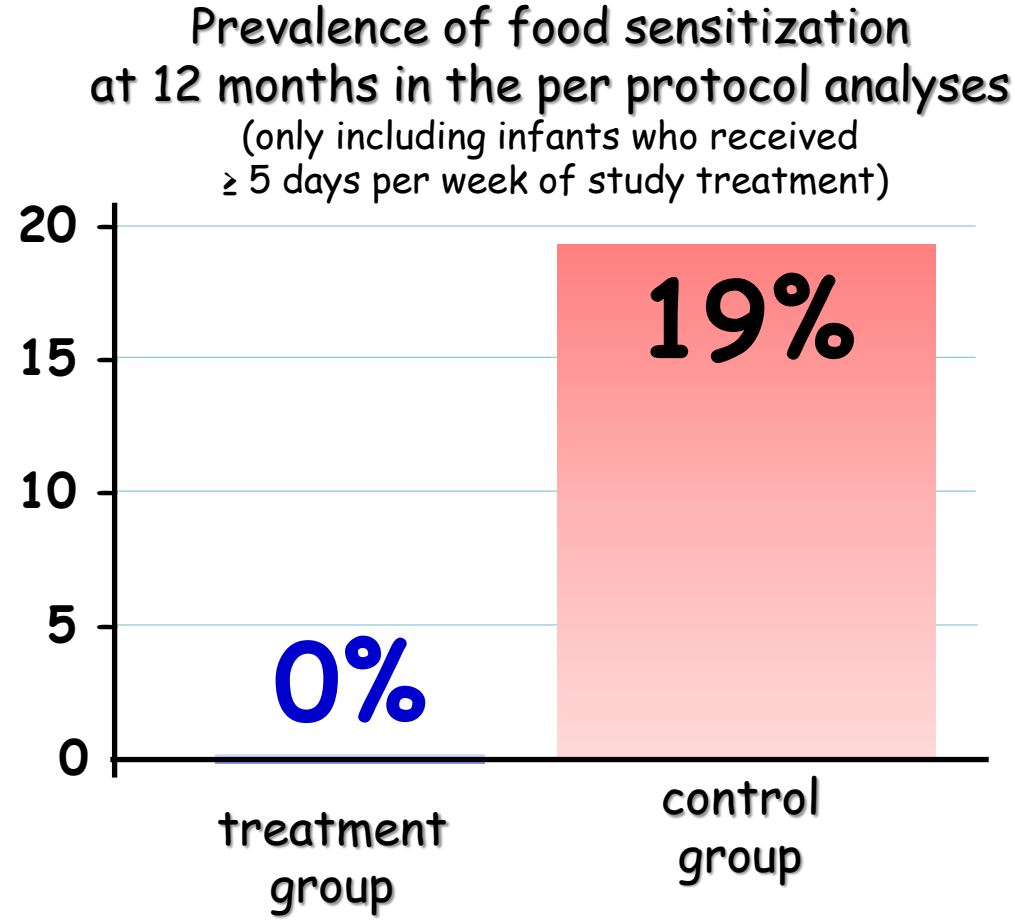
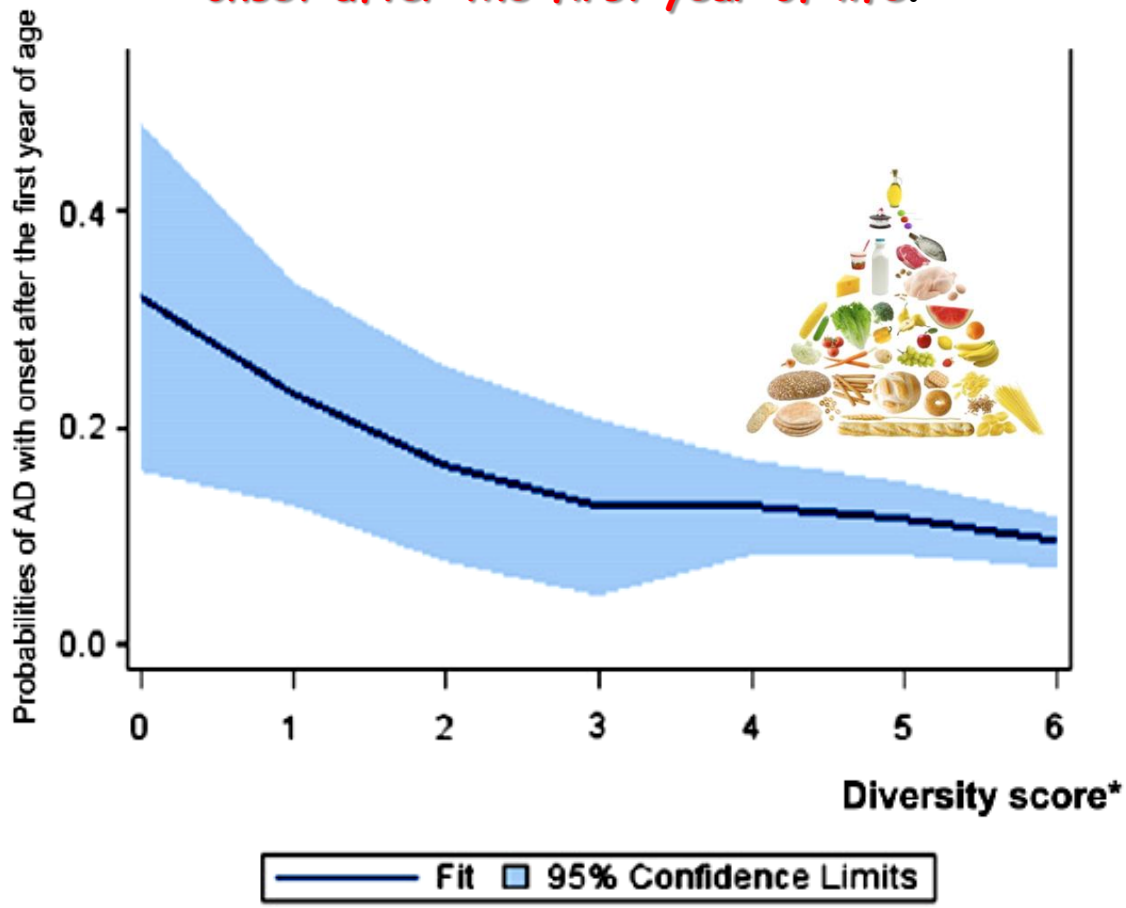


# Development of atopic dermatitis according to age of onset and association with early-life exposures

*Roduit C. J Allergy Clin Immunol. 2012 Jul;130(1):130-6.e5.*

- ✓ 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.

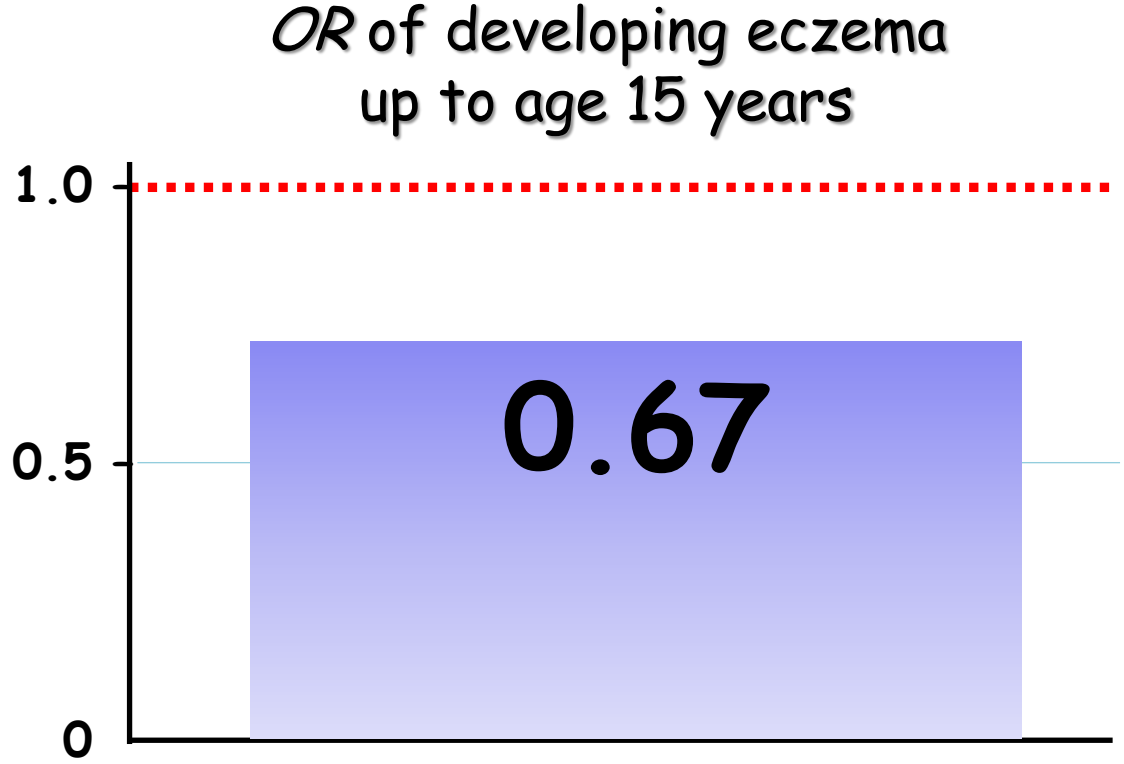
**Association between increasing numbers of different major food items (n = 6) introduced in the first year of life and atopic dermatitis with onset after the first year of life.**



# Food diversity during the first year of life and allergic diseases until 15 years.

*Markevych I, J Allergy Clin Immunol. 2017 Dec;140(6):1751-1754.e4.*

- ✓from the population-based German birth cohort LISAplus (recruited from 1997 to 1999)
- ✓food diversity within the first 6 months of life
- ✓allergic outcomes until the age of 15 years




children in the highest quartile who were introduced to all 8 food groups during the first year of life *vs* children in the lowest quartile with a maximum of 5 food groups

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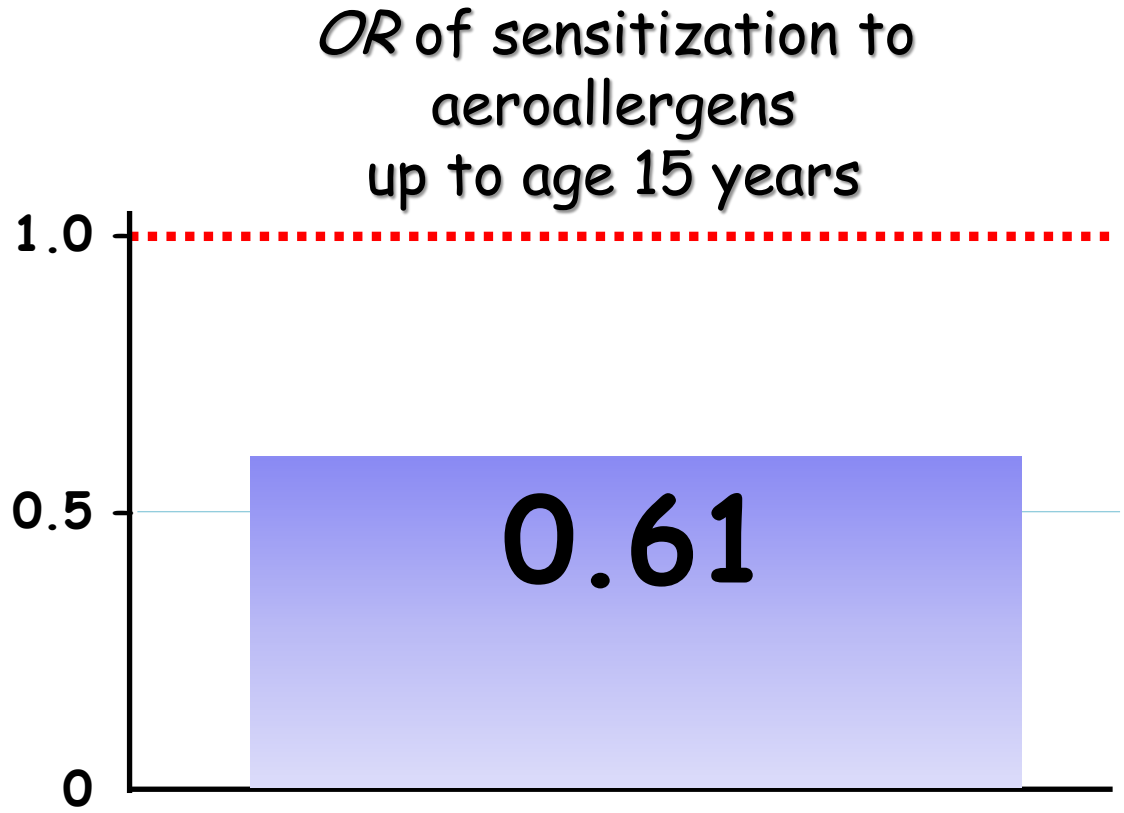


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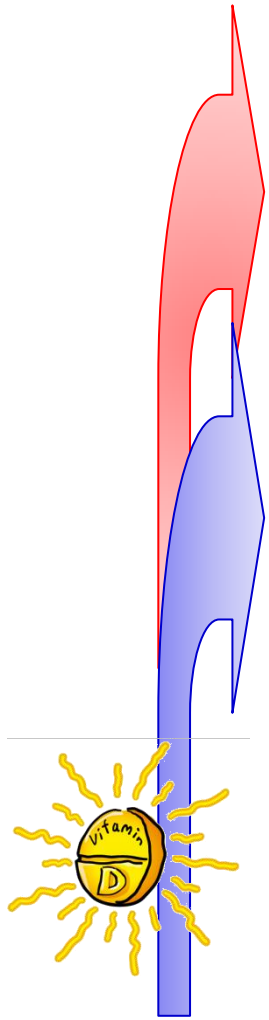
# Is vitamin D level associated with the natural course of atopic dermatitis?

*Dogru M. Allergol Immunopathol (Madr). 2018 Mar 17. pii: S0301*

✓69 patients with AD and 70 healthy children

✓SPTs , eosinophil counts, sIgE and serum 25OHD3 levels

✓After at least 4 years of follow-up, patients were re-evaluated for natural course of AD.




- There was a negative correlation between 25OHD3 levels and severity of AD (r=-0.480; p=0.001).

- **In patients reassessed after 4 years**: age, the age of AD onset, vitamin D deficiency, SCORAD level and severe AD were higher in the persistent group vs. remission group, **25OHD3 levels were higher in the remission group vs. persistent group** *(p<0.05).*

# Is vitamin D level associated with the natural course of atopic dermatitis?

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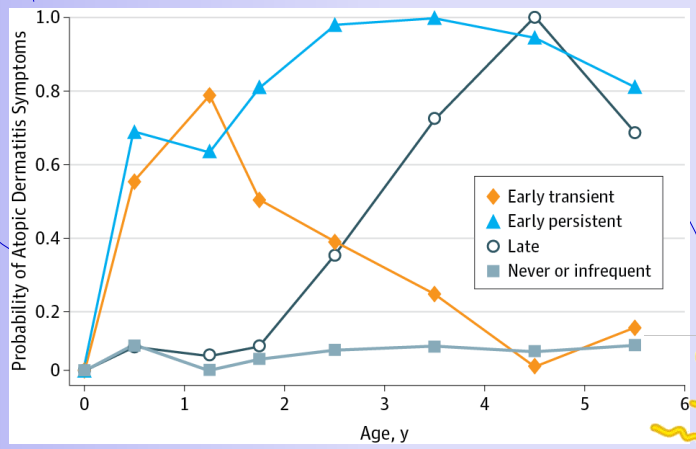
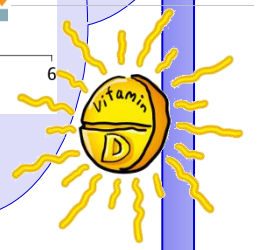
Vitamin D may affect the natural course of atopic dermatitis.

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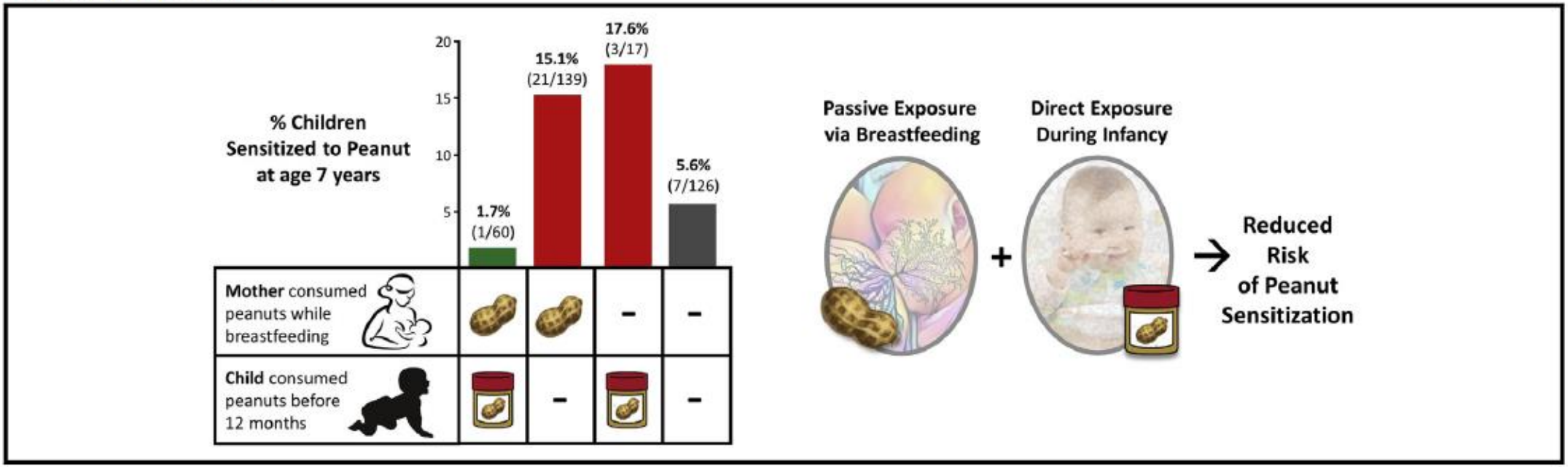
# Reduced risk of peanut sensitization following exposure through breast-feeding and early peanut introduction.

*Pitt TJ, J Allergy Clin Immunol. 2018 Feb;141(2):620-625.e1*

GRAPHICAL ABSTRACT




Maternal peanut consumption while breast-feeding paired with direct introduction of peanuts in the first year of life was associated with the lowest risk of peanut sensitization, compared with all other combinations of maternal and infant peanut consumption.

# Timing of food introduction and development of food sensitization in a prospective birth cohort

*MM Tran, PAI 2017;28:471-477*

- ✓ Sensitization to foods at age 1 year in the Canadian Healthy Infant Longitudinal Development (CHILD) birth cohort study (n=2124).
- ✓ Nutrition questionnaire prospectively collected at age 3, 6, 12, 18, and 24 months.

➢ Delaying introduction of cow's milk products, egg, and peanut beyond the first year of life significantly increased the odds of sensitization to that food:

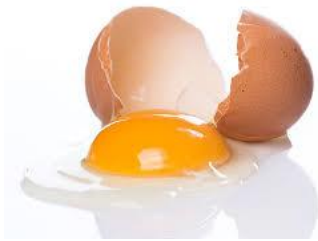

- cow's milk *aOR* = 3.69;
- egg *aOR* = 1.89;

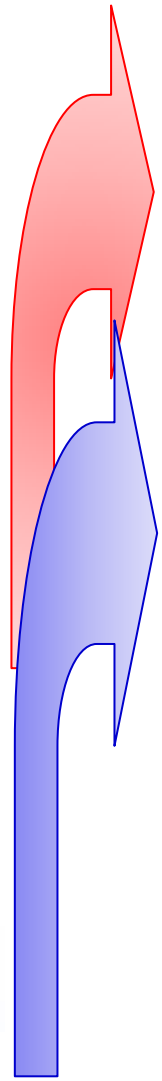
- peanut *aOR* = 1.76.

# Early life innate immune signatures of persistent food allergy.

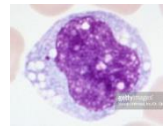
*Neeland MR, J Allergy Clin Immunol. 2018 Sep;142(3):857-864.e3*

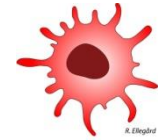
✓Longitudinally collected PBMC samples from a population-based cohort of challenge-confirmed egg-allergic infants with either persistent or transient egg allergy outcomes in childhood to phenotype and quantify the functional innate immune response associated with clinical phenotypes of egg allergy.





- infants with persistent egg allergy exhibit an increased numbers of circulating monocytes and dendritic cells that produce more inflammatory cytokines .





- follow-up analysis revealed that this unique innate immune signature continues into childhood in those with persistent egg allergy and that increased serum vitamin D levels correlate with changes in innate immune profiles observed in children who developed natural tolerance to egg.

# Early life innate immune signatures of persistent food allergy.

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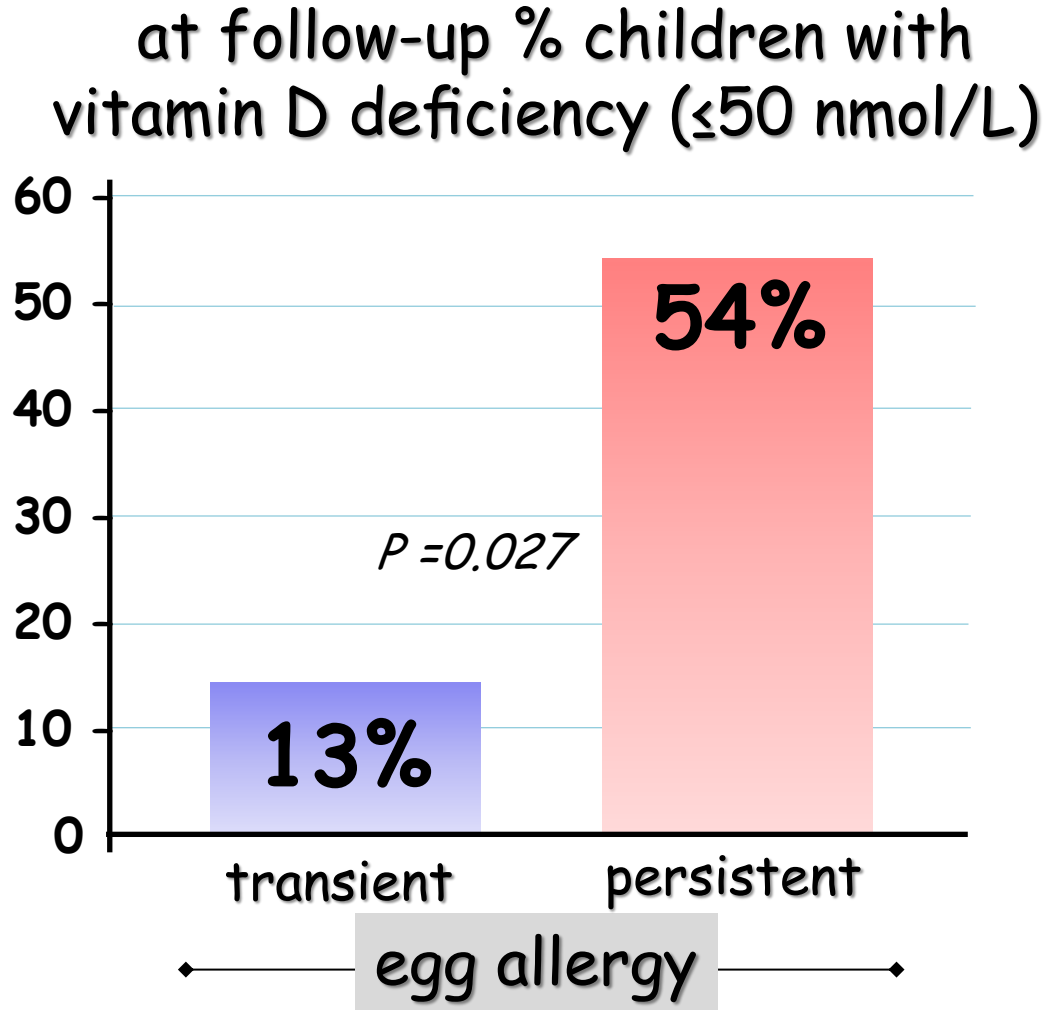
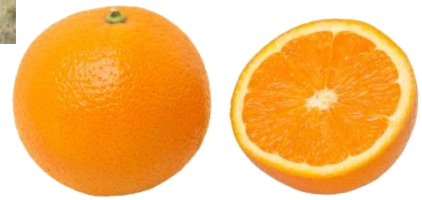


# A new allergen family involved in pollen food-associated syndrome: Snakin/gibberellin-regulated proteins.

*Sénéchal H, J Allergy Clin Immunol. 2018 Jan;141(1):411-414.e4.*

•4 snakin/GRPs (gibberellin-regulated protein*) from fruits were shown to be allergens (www.allergen.org) :



Pru p 7 in peach,

Pun g 7 in pomegranate,

Pru m 7 in Japanese apricot

Cit s 7 in sweet orange,

*Because Pru p 7 shares more than 80% sequence identity with snakin-1 and more than 95% with other fruit GRP allergens, BP14 in Cupressus sempervirens pollen should be considered as the cross-reactive allergen in the 2 documented PFAS involving peach and/or citrus.

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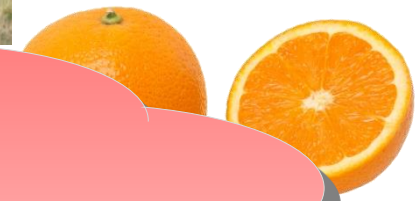


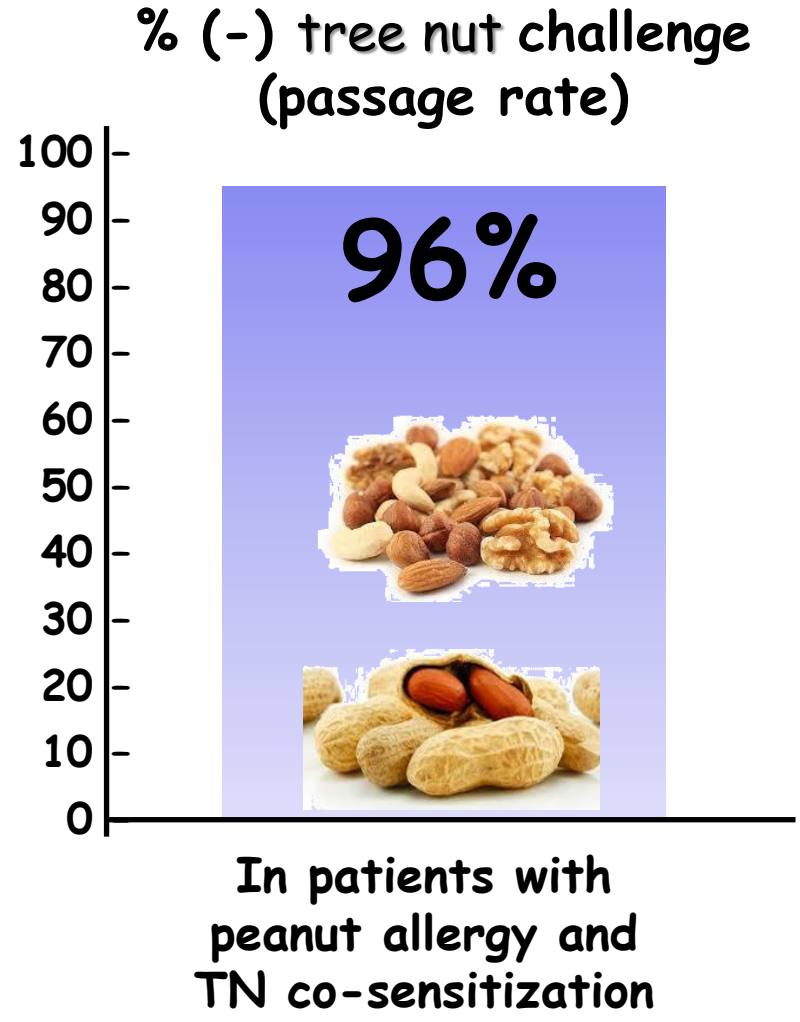
*Bec d more sempervirens ve allergen in the 2 documented PFAS involving p and/or citrus.

Snakin/GRP sensitization was reported to be clinically associated with eyelid edema, systemic reaction, or food-dependent exercise-induced anaphylaxis.

# Characteristics of tree nut challenges in tree nut allergic and tree nut sensitized individuals

*C Couch, Ann Allergy Asthma Immunol 2017;118:591-596*

- ✓ Open tree nut (TN) oral food challenges (OFCs) performed from 2007 through 2015.
- ✓ Outcome based on SPT wheal size, sIgE, peanut co-allergy, and TN sensitization only
  *vs*
  TN allergy with sensitization to other TNs.



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*C Couch, Ann Allergy Asthma Immunol 2017;118:591-596*

- ✓ Open tree
  fo
  p
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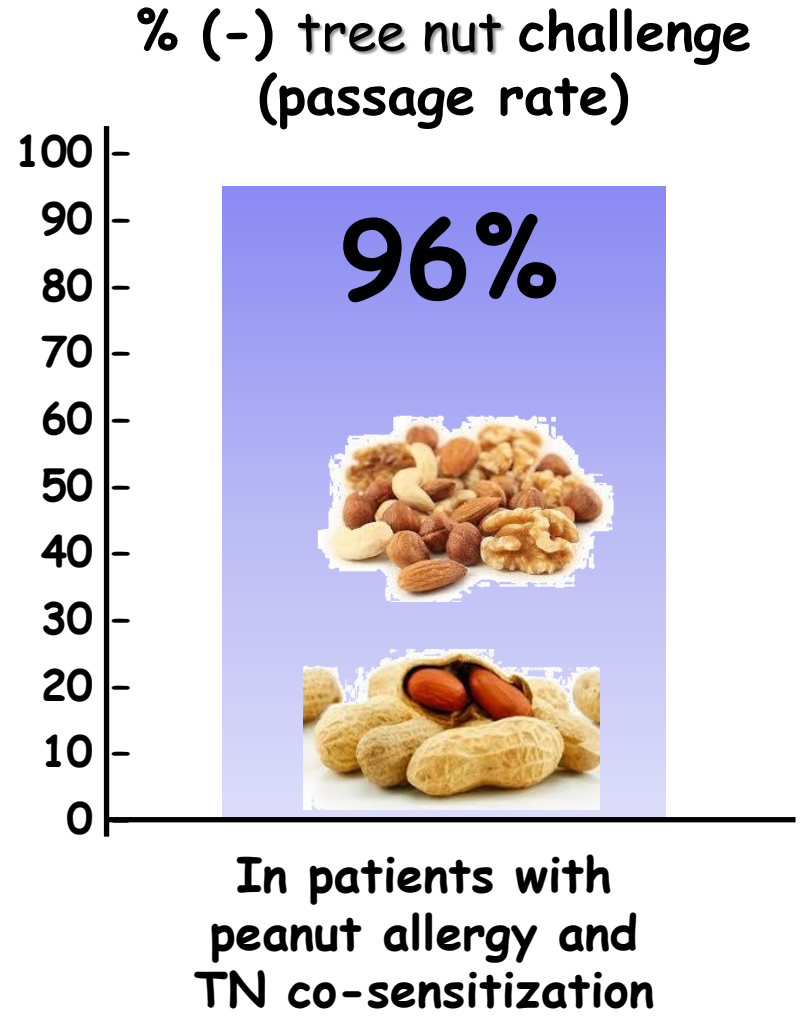
Nearly all patients with peanut allergy and TN co-sensitization passed the TN challenge, questioning the clinical relevance of "co-allergy."



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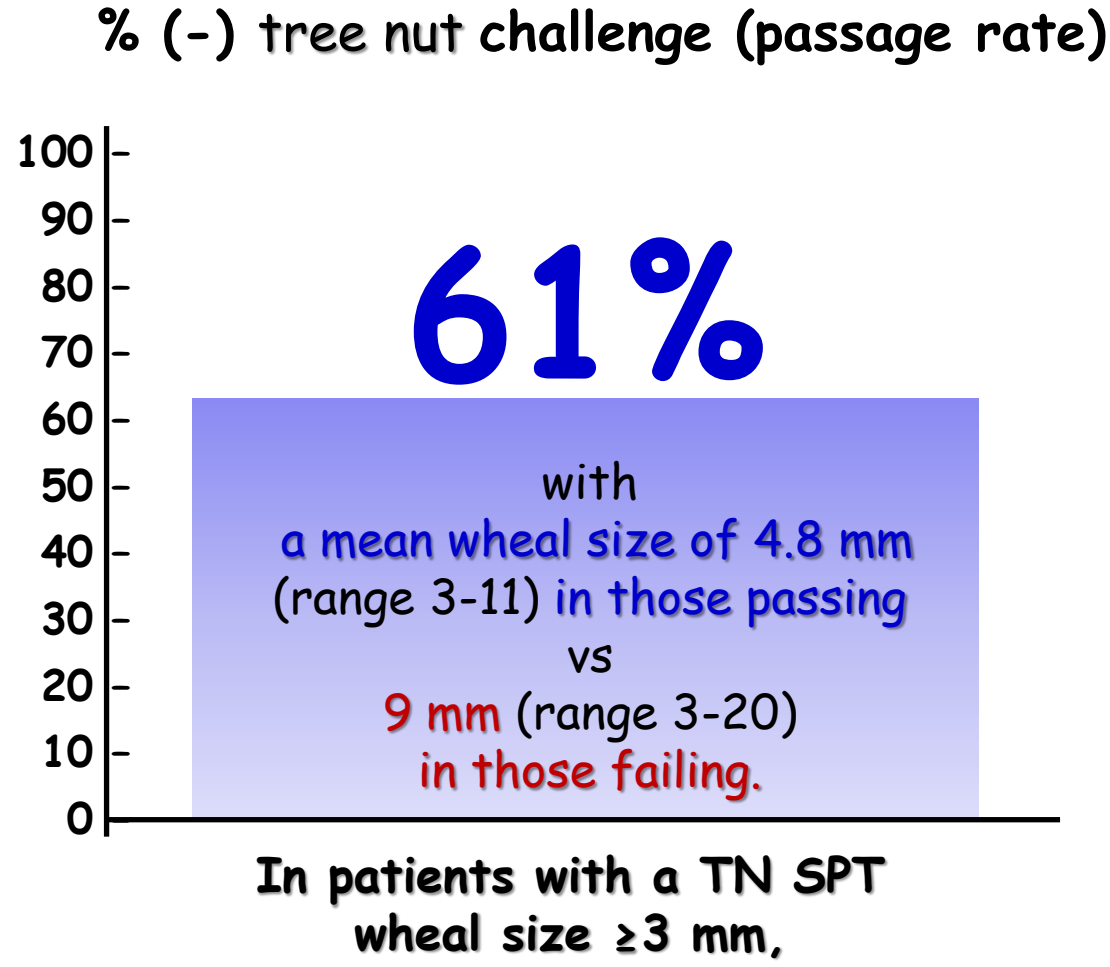


# NUT Co Reactivity - ACquiring Knowledge for Elimination Recommendations (NUT CRACKER) study.

*Elizur A, Allergy. 2018 Mar;73(3):593-601.*

✓83 patients with a history of previous reactions to walnut, pecan, cashew, pistachio, hazelnut, and almond allergy

✓SPTs using finely ground tree-nut solution and basophil activation tests (BAT)

- over 50% of patients were allergic to only 1-2 tree-nuts.

- the rate of co-allergy for most tree-nuts was <30%

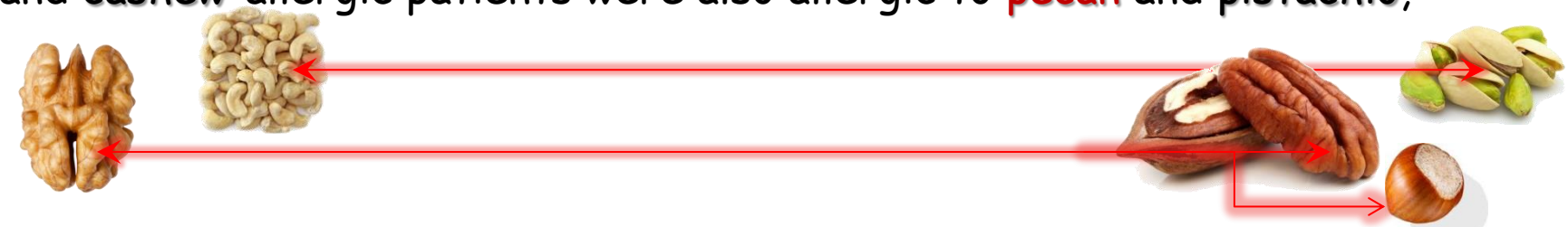
# NUT Co Reactivity - ACquiring Knowledge for Elimination Recommendations (NUT CRACKER) study.

*Elizur A, Allergy. 2018 Mar;73(3):593-601.*

## Rate of co-allergy between tree-nuts

| | Other tree-nut allergies | | | | | |
|---|---|---|---|---|---|---|
| Tree-nut | Walnut | Pecan | Cashew | Pistachio | Hazelnut | Almond |
| Walnut (n = 53) | - | 34 (64.2%) | 20 (37.7%) | 11 (20.8%) | 11 (20.8%) | 0 |
| Pecan (n = 34) | 34 (100%) | - | 14 (41.2%) | 6 (17.6%) | 10 (29.4%) | 0 |
| Cashew (n = 40) | 20 (50%) | 14 (35%) | - | 26 (65%) | 6 (15%) | 0 |
| Pistachio (n = 26) | 11 (42.3%) | 6 (23.1%) | 26 (100%) | - | 3 (11.5%) | 0 |
| Hazelnut (n = 14) | 11 (78.6%) | 11 (78.6%) | 6 (42.9%) | 3 (21.4%) | - | 0 |
| Almond (n = 1) | 0 | 0 | 0 | 0 | 0 | - |

All of walnut- and cashew-allergic patients were also allergic to pecan and pistachio, respectively,



while

Two-thirds pecan- and pistachio-allergic patients were allergic to walnut and cashew, respectively.

# Tree nuts oral challenges and induction of tolerance

**Dose**

1mg

5mg

10 mg

20 mg

40 mg

80 mg

160 mg

200 mg

400mg

600 mg

800 mg – 1,1 g

1,1 g

ogni 20 minuti,
ogni 30 se storia di anafilassi

La dose cumulativa da raggiungere è di 4,5 g di frutta a guscio corrispondenti all'incirca a

1 noce,

4 nocciole,

20 pinoli,

10 pistacchi,

3 mandorle,

5 arachidi,

2 anacardi.

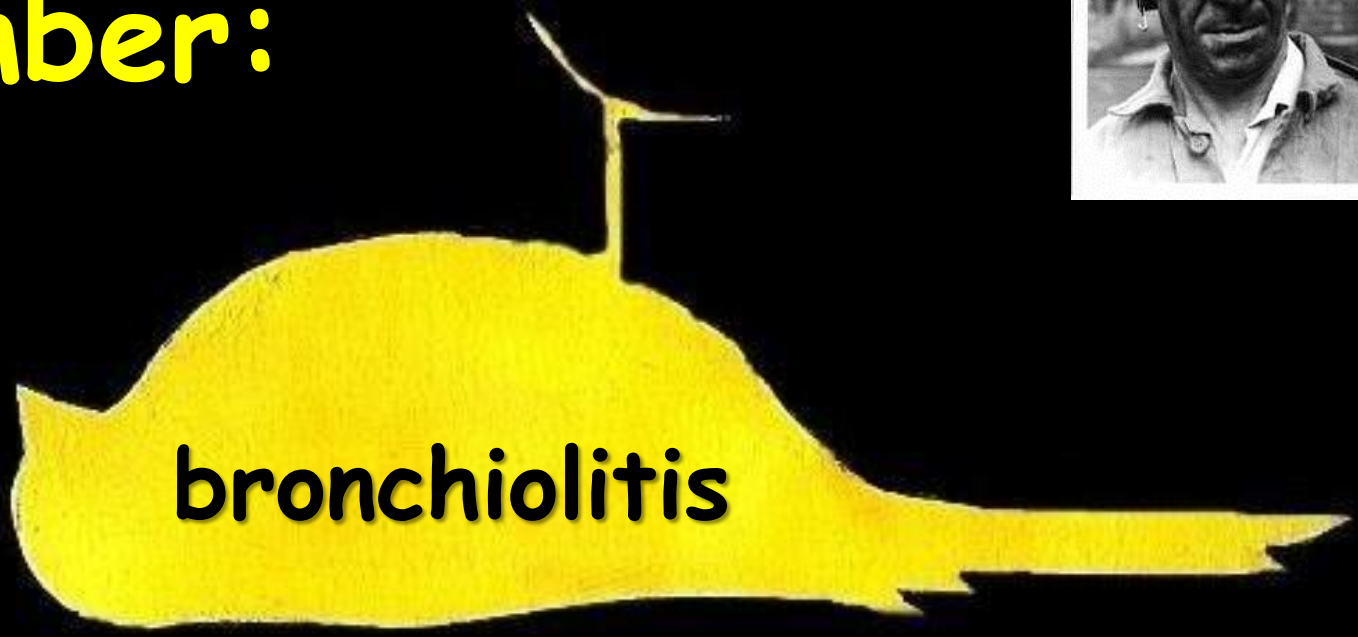

Challenges are discontinued and considered positive in case of objective symptoms or if suggestive subjective symptoms occurr at 3 subsequent doses or a subjective symptom lasted for more than 45 minutes.

# Highlights in Pediatric Allergy & Pulmonolgy

**Attilio Boner**
**University of Verona, Italy**
attilio.boner@univr.it

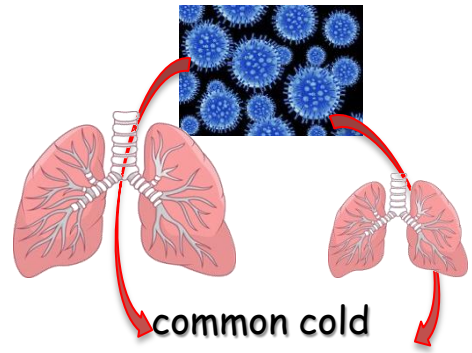
- ✓ Epidemiology
- ✓ Atopic Dermatitis
- ✓ Food allergy
- ✓ **Bronchiolitis & Asthma**
- ✓ Allergic rhinitis
- ✓ Unexpected burden
- ✓ Summary & Conclusions

# Remember:




is our canary in the hospital
to suggest predisposition to:
wheezy bronchitis, asthma and COPD

# Several data support the possibility that premorbid lung function may be abnormal among infants who have severe bronchiolitis in the first year of life.




- **Reduced lung function both before bronchiolitis and at 11 years.** *Turner SW, Arch Dis Child. 2002;87(5):417-20.*

- **Diminished lung function, RSV infection and respiratory morbidity in prematurely born infants** *Broughton S, Arch. Dis. Child 2006;91:26-30*

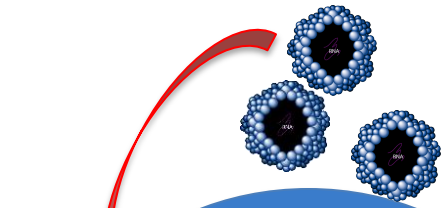

- **Diminished lung function as a predisposing factor for wheezing respiratory illness in infants.** *Martinez FD, N Engl J Med 1988; 319: 1112-7.*

- **Lung function in prematurely born infants after viral lower respiratory tract infections.** *Broughton S, Pediatr Infect Dis J 2007;26:1019-24.*

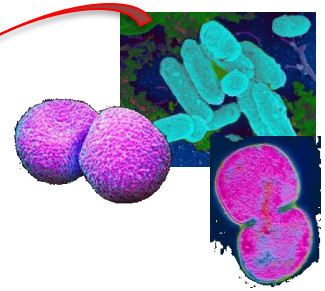
- **Lung function prior to viral lower respiratory tract infections in prematurely born infants.** *Drysdale SB, Thorax 2011;66:468-73.*

- **Decreased lung function precedes severe respiratory syncytial virus infection and post-respiratory syncytial virus wheeze in term infants** *Zomer-Kooijker K, ERJ 2014;44:666-674*

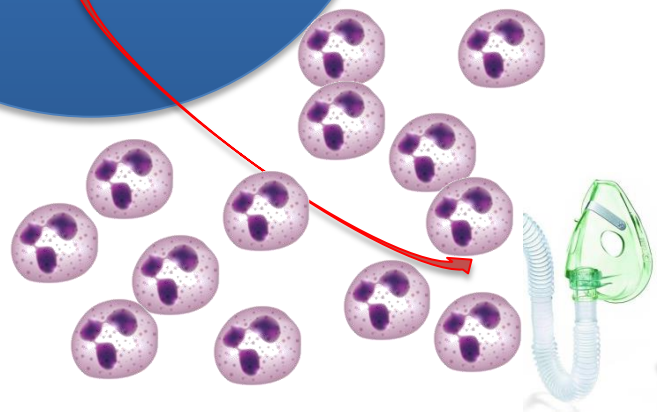
# The Wheezy Bronchis & Protracted Bacterial Bronchitis Vicious Circle in Young Children:



Wheezy bronchitis



Early risk



Wheezy Bronchitis + PBB

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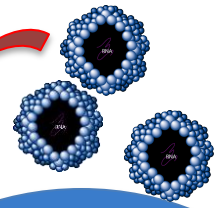

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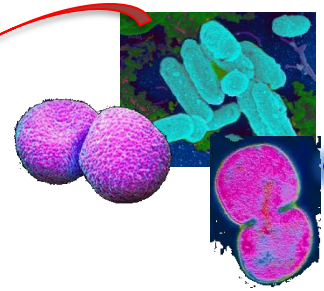
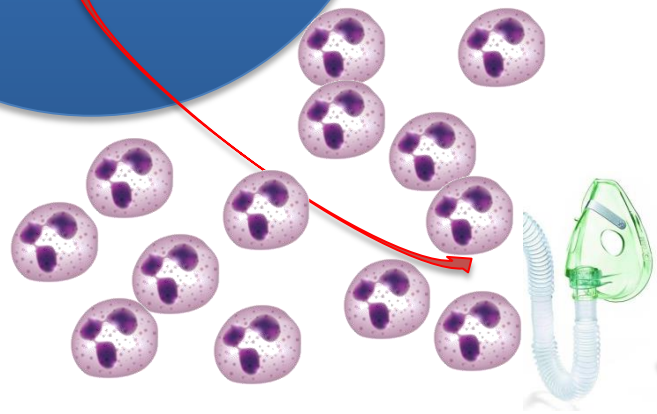


Month 20

| Sunday | Monday | Tuesday | Wednesday | Thursday | Friday | Saturday |
|---|---|---|---|---|---|---|
| dry cough | dry cough | dry cough | dry cough | dry cough | dry cough | dry cough |
| Dry Wet cough | Dry Wet cough | Dry Wet cough | Dry Wet cough | Wet cough | Wet cough | Wet cough |
| Wet cough | Wet cough | Wet cough | Wet cough | Wet cough | Wet cough | Wet cough |
| Wet cough | Wet cough | Wet cough | Wet cough | Wet cough | Wet cough | Wet cough |
| Wet cough | Wet cough | Wet cough | Wet cough | Wet cough | Wet cough | Wet cough |
| | | | | | | |



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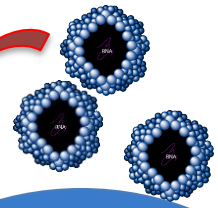
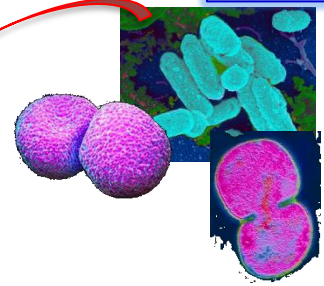


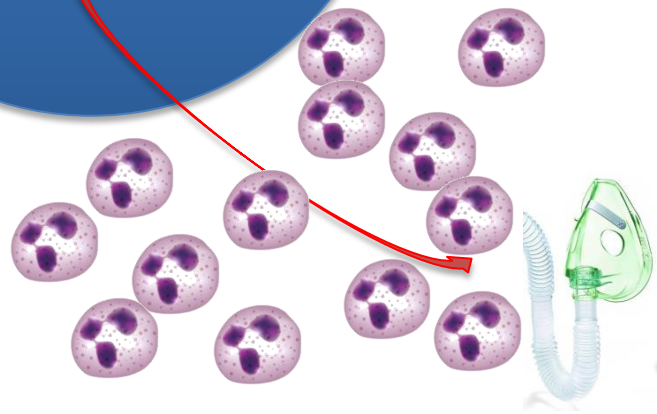
Wheezy bronchitis



antibiotic

Month 20

| Sunday | Monday | Tuesday | Wednesday | Thursday | Friday | Saturday |
|---|---|---|---|---|---|---|
| dry cough | dry cough | dry cough | dry cough | dry cough | dry cough | dry cough |
| Dry Wet cough | Dry Wet cough | Dry Wet cough | Dry Wet cough | Wet cough | Wet cough | Wet cough |
| Wet cough | Wet cough | Wet cough | Wet cough | Wet cough | Wet cough | Wet cough |
| Wet cough | Wet cough | Wet cough | Wet cough | Wet cough | Wet cough | Wet cough |
| Wet cough | Wet cough | Wet cough | Wet cough | Wet cough | Wet cough | Wet cough |
| | | | | | | |



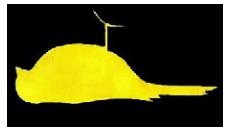
Wheezy Bronchitis + PBB

# Respiratory health outcomes 1 year after admission with severe lower respiratory tract infection

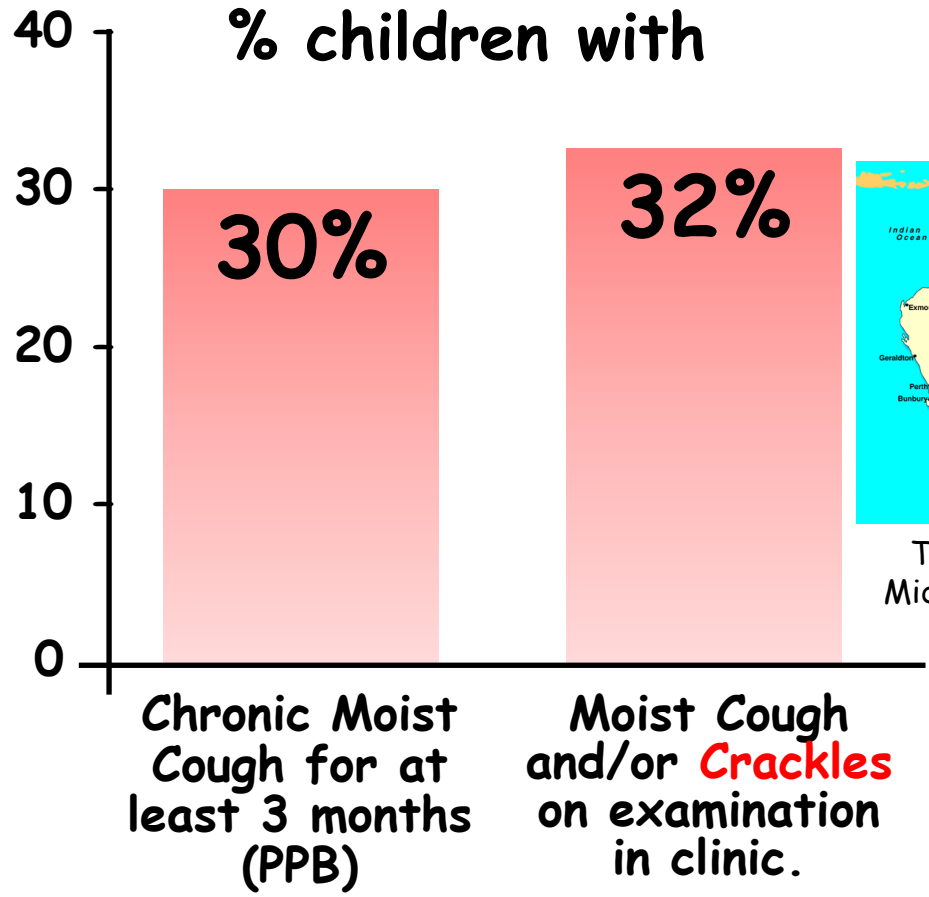
*Trenholme AA, Pediatr Pulmonol 2013;48:772*

THE BEGINNING

- ✓ 94 children aged < 2 years hospitalized for severe bronchiolitis or pneumonia with no co-morbidities.



- ✓ Assessed 1 year post index admission.
- ✓ Examination, pulse oximetry, and chest X-ray (CXR).



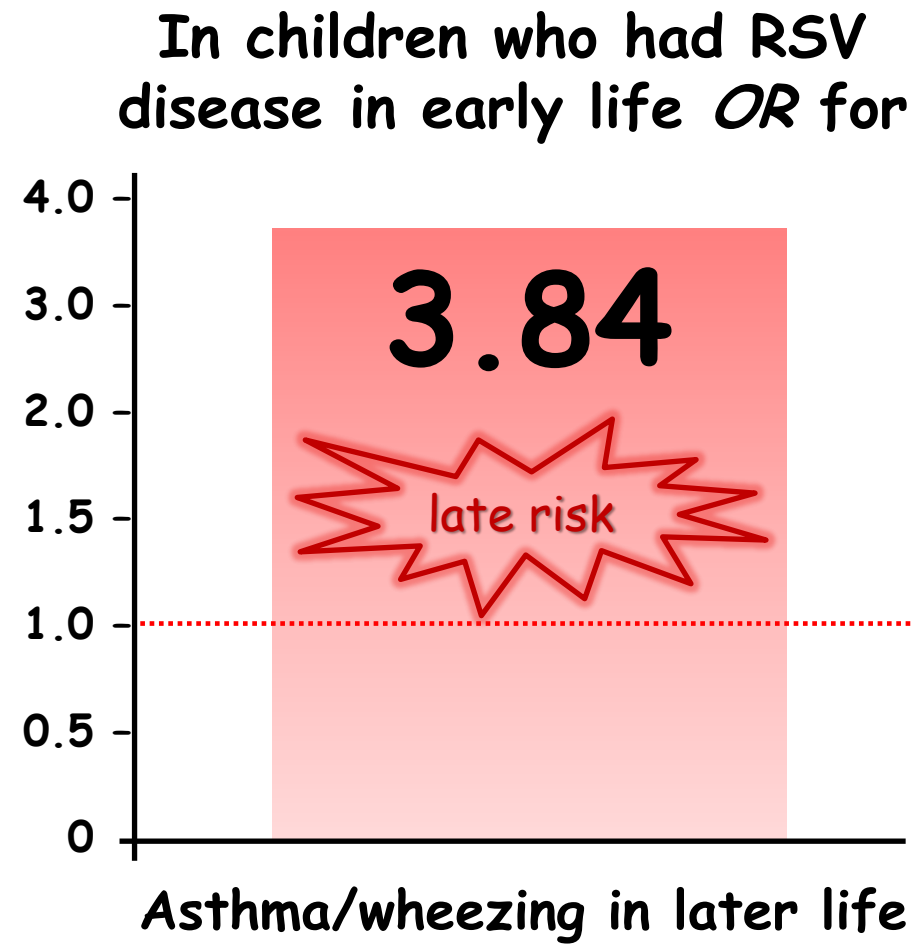


The University of Auckland, Middlemore Hospital, Auckland, New Zealand

# Association between respiratory syncytial virus hospitalizations in infants and respiratory sequelae: systematic review and meta-analysis

*Régnier SA, Pediatr Infect Dis 2013;32:820-826*

- ✓ 15 studies assessed the association between RSV-confirmed hospitalization for up to 3 years of age and asthma/wheezing later in life.
- ✓ 82,008 unique individuals (including 1533 with RSV-confirmed hospitalization)

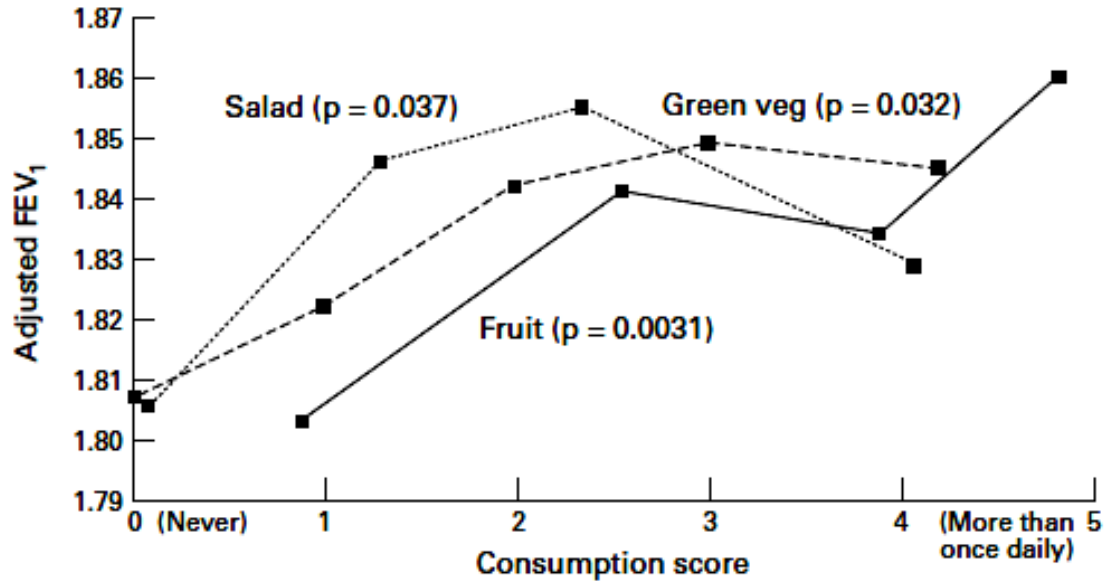


# Effect of fresh fruit consumption on lung function and wheeze in children

*Cook DG, Thorax 1997;52:628-633*

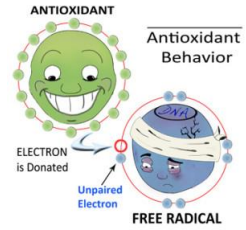
- ✓ 2650 children aged 8-11 yrs from 10 towns in England and Wales
- ✓ $FEV_1$
- ✓ A food frequency questionnaire

**Relationship between frequency of consumption of fresh fruit, salad, and green vegetables and $FEV_1$**



# Dietary total antioxidant capacity in early school age and subsequent allergic disease.

*Gref A, Clin Exp Allergy. 2017;47(6):751-759*




✓2359 children from the Swedish birth cohort BAMSE

✓Dietary total antioxidant capacity (TAC) at age 8 years estimated by combining information on the child's diet the past 12 months from a food frequency questionnaire with a database of common foods analysed with the oxygen radical absorbance capacity method.

✓asthma and rhinitis was based on questionnaires, and serum IgE antibodies were measured at 8 and 16 years.

**aOR of sensitization to inhalant allergens by adolescence**


TAC of the diet for the 3rd compared to the 1st tertile at age 8 years

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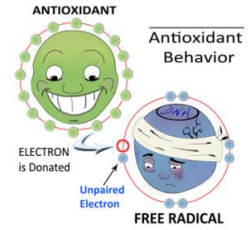


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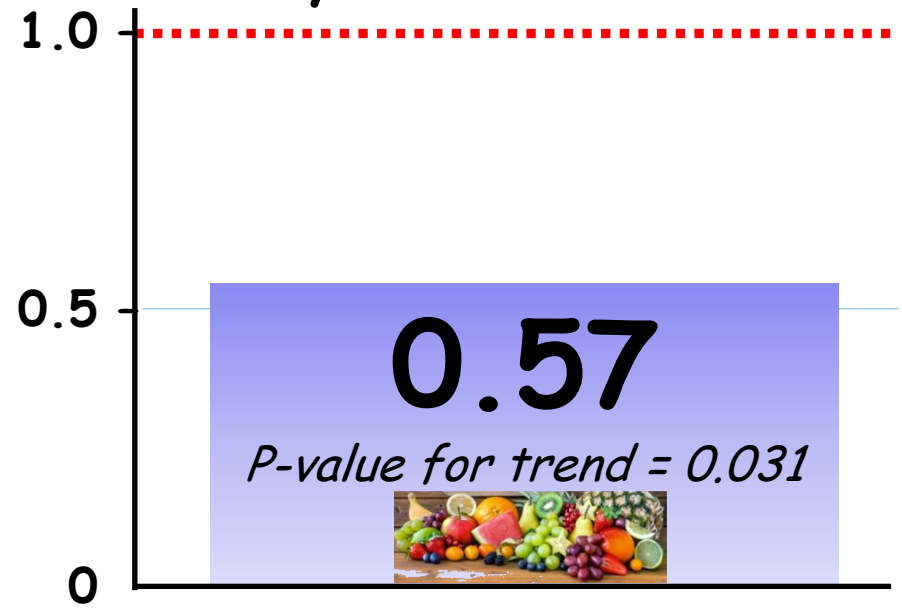
**aOR of allergic asthma by adolescence**

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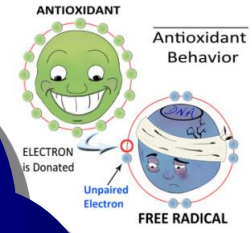



✓2359 children f… birth co…

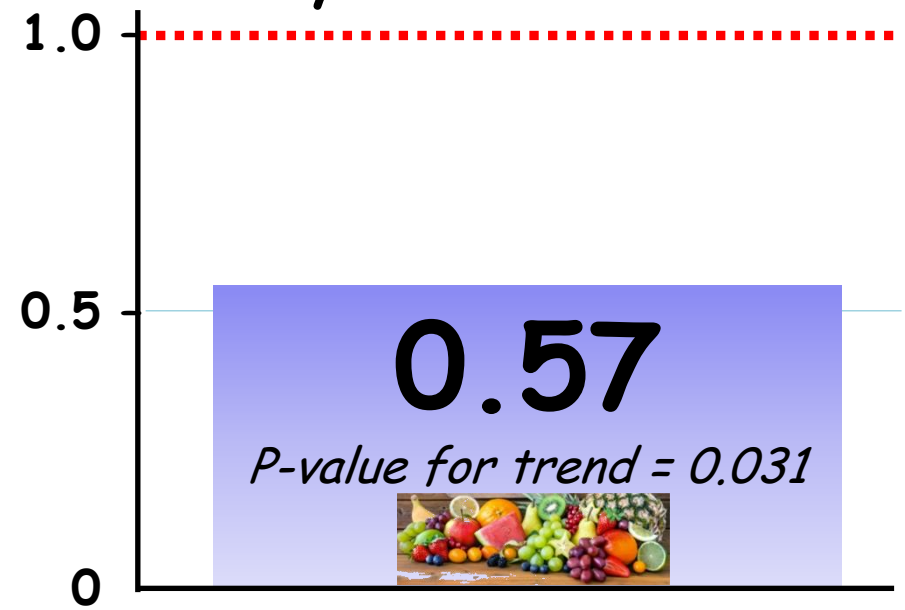
✓Di… (TA… co…

o… o… r…

✓as… questi… were mea… …bodies …years.

**These findings indicate that implementing an antioxidant-rich diet in childhood may contribute to the prevention of allergic disease.**

**aOR of allergic asthma by adolescence**

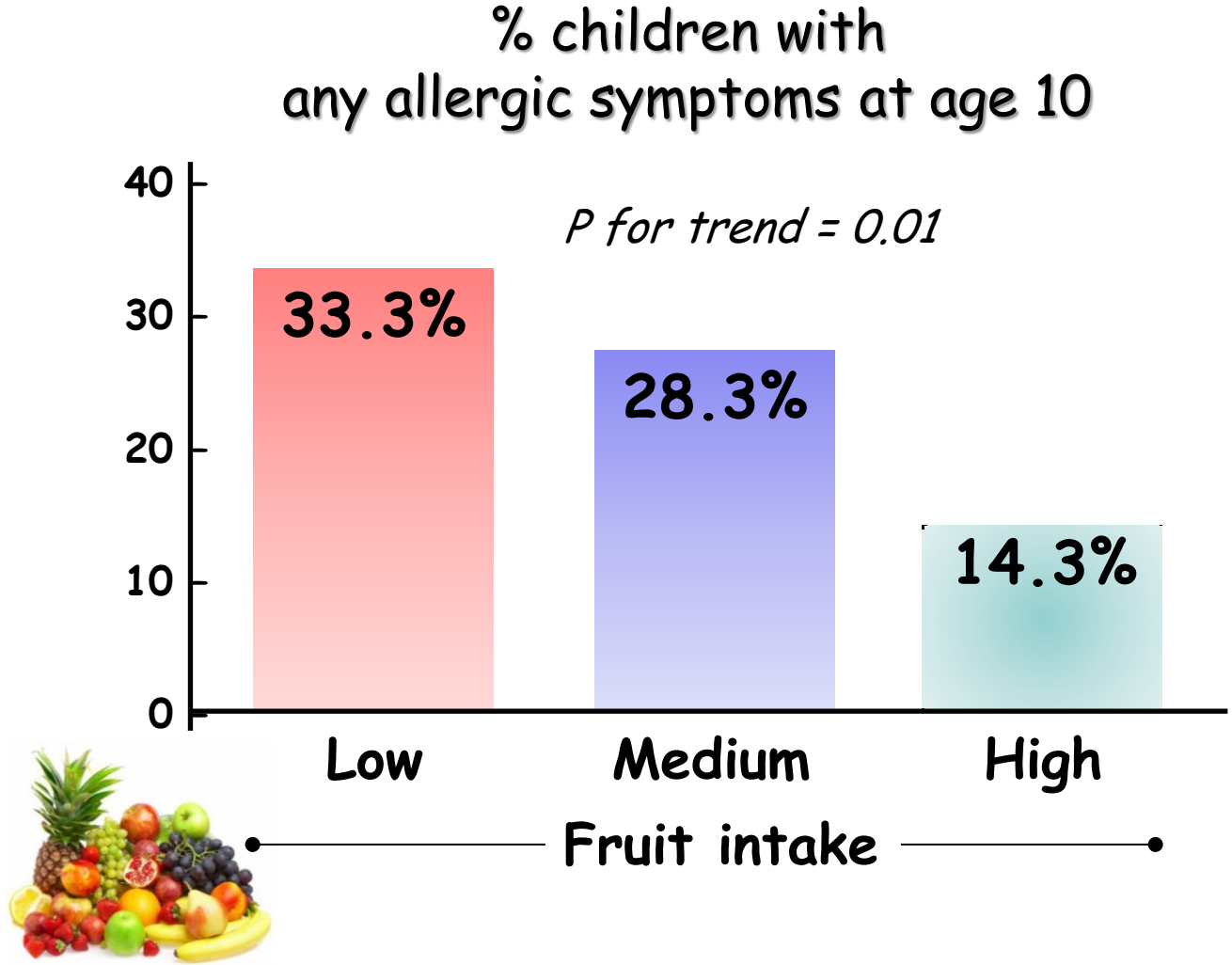



TAC of the diet for the 3rd compared to the 1st tertile at age 8 years

# Fruit intake reduces the onset of respiratory allergic symptoms in schoolchildren

*T Kusunoki, PAI 2017;28:793-800*

- ✓ A prospective cohort study on primary schools in Japan.
- ✓ Questionnaires regarding allergic symptoms and diet distributed to the parents of all 759 7-year-old schoolchildren for 4 consecutive years, from 2011 to 2014.
- ✓ sIgE to inhalant allergens at 10 years of age.



# Fruit intake reduces the onset of respiratory allergic symptoms in schoolchildren

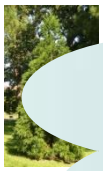
*T Kusunoki, PAI 2017;28:793-800*

Fruit intake and sensitization to inhalant allergens at 10 years of age

| Allergen | Fruit intake | Positive rate (%) | Multivariate OR[a] (95% CI) | *P* for trend |
|---|---|---|---|---|
| House dust mites | Low | 32/57 (56.1) | Ref. | .24 |
| | Medium | 200/375 (53.3) | 0.79 (0.44–1.42) | |
| | High | | | |
| Jap | | | | .82 |
| | | | | .17 |
| | | | (0.25–1.27) | |
| Ragweed | Low | 15/57 (26.3) | Ref. | .046 |
| | Medium | 63/375 (16.8) | 0.48 (0.25–0.93) | |
| | High | 8/59 (13.6) | 0.40 (0.15–1.05) | |
| Any allergen | Low | 40/57 (70.2) | Ref. | .13 |
| | Medium | 272/375 (72.5) | 0.97 (0.51–1.83) | |
| | High | 35/59 (59.3) | 0.55 (0.25–1.24) | |

Sensitization was defined as the level of specific immunoglobulin E ≥ 0.7 A/mL.

[a] Sex, season of birth weight, birth order, patient's allergies, breastfeeding, and experience of food avoidance were included as confounding factors



higher intake of fruit can help prevent sensitization in schoolchildren.

# Fruit intake reduces the onset of respiratory allergic symptoms in schoolchildren

*T Kusunoki, PAI 2017;28:793-800*

Fruit intake and % allergic symptoms in schoolchildren that existed at the start of the study and disappeared by the end of the study (recovered symptoms)

| Symptom | Fruit intake | Prevalence of recovered symptom (%) | Multivariate *OR*[a] (95% CI) | *P* for trend |
|---|---|---|---|---|
| Asthma (n = 60) | Low | 3/8 (37.5) | Ref. | .02 |
| | Medium | 31/51 (60.8) | 5.57 (0.96–32.17) | |
| | High | 1/1 (100.0) | 16.5 (0.38–718.50) | |
| Eczema (n = 95) | Low | 5/10 (50.0) | Ref. | .21 |
| | Medium | 32/76 (42.1) | 1.18 (0.26–5.28) | |
| | High | 6/9 (66.7) | 4.09 (0.49–34.09) | |
| Rhinitis (n = 142) | Low | 5/16 (31.3) | Ref. | .18 |
| | Medium | 35/112 (31.3) | 1.10 (0.34–3.60) | |
| | High | 7/14 (50.0) | 3.16 (0.63–15.72) | |
| Any (n = 219) | Low | 12/27 (44.4) | Ref. | .17 |
| | Medium | 84/172 (48.8) | 1.37 (0.57–3.29) | |
| | High | 12/20 (60.0) | 2.46 (0.69–8.71) | |

[a] Sex, season of birth, low birthweight, birth order, parent's allergies, breastfeeding, and experience of food avoidance were included as confounding factors.

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higher intake of fruit can help decrease respiratory allergic symptoms in schoolchildren.

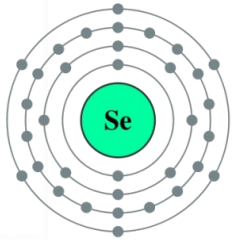
[a] Sex, season of birth, low birthweight, birth order, parent's allergies, breastfeeding, and experience of food avoidance were included as confounding factors.

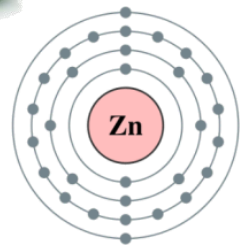
# Fruits and vegetables in general health

curcumin

soy

sulforaphane



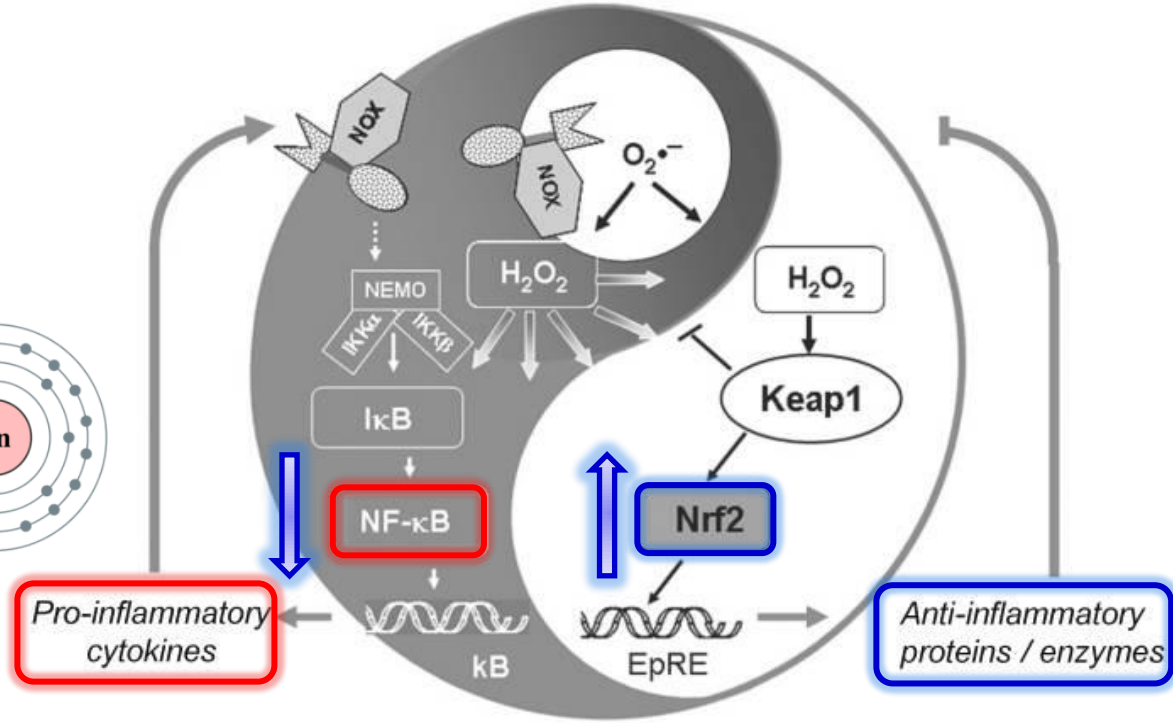





quercitin

resveratrol

Transcription factors involved in the process of converting, or transcribing, DNA into RNA.




**NF-κB** = nuclear factor kappa-light-chain-enhancer of activated B cells

**Nrf2** = Nuclear factor (erythroid-derived 2)-like 2

# Higher serum 25(OH)D concentrations are associated with improved $FEV_1$ and FVC in adolescence.

*Flexeder C, Eur Respir J 2017;49:1601804*


✓German birth cohorts GINIplus and LISAplus,

✓spirometry and 25(OH)D measurements during the 15-year follow-up in 2607 adolescents.

❑Serum 25(OH)D concentrations were significantly associated FVC, $FEV_1$ and $FEV_1$/FVC measured before bronchodilation after adjustment for potential confounders:

- $FEV_1$ increased by 10 mL,
- FVC by 20 mL
- $FEV_1$/FVC decreased by 0.177%

per 10 nmol·L−1 (4 ng/mL) increase in 25(OH)D concentrations.

# A population-based prospective cohort study examining the influence of early-life respiratory tract infections on school-age lung function and asthma.

*van Meel ER, Thorax. 2018 Feb;73(2):167-173.*

✓a population-based prospective cohort study of 5197 children born between April 2002 and January 2006

✓Information on physician-attended upper and lower respiratory tract infections at age ≤ 3 and >3–6 years obtained by annual questionnaires.

✓Spirometry and physician-diagnosed asthma assessed at age 10 years.

Compared with children without lower respiratory tract infections ≤3 years,

- children with lower respiratory tract infections ≤3 years of age had a lower:

- $FEV_1$,
- FVC,
- $FEV_1$/FVC and
- $FEF_{75}$ (forced expiratory flow at 75% of FVC)

at age 10 years

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*van Meel ER, Thorax. 2018 Feb;73(2):167-173.*

✓a po
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✓Sp
diagno
at age 10 ye

**"As the twig is bent, the tree inclines" (perhaps)**

*Burrows B, Taussig LM. Am Rev Respir Dis. 1980 Dec;122(6):813-6.*


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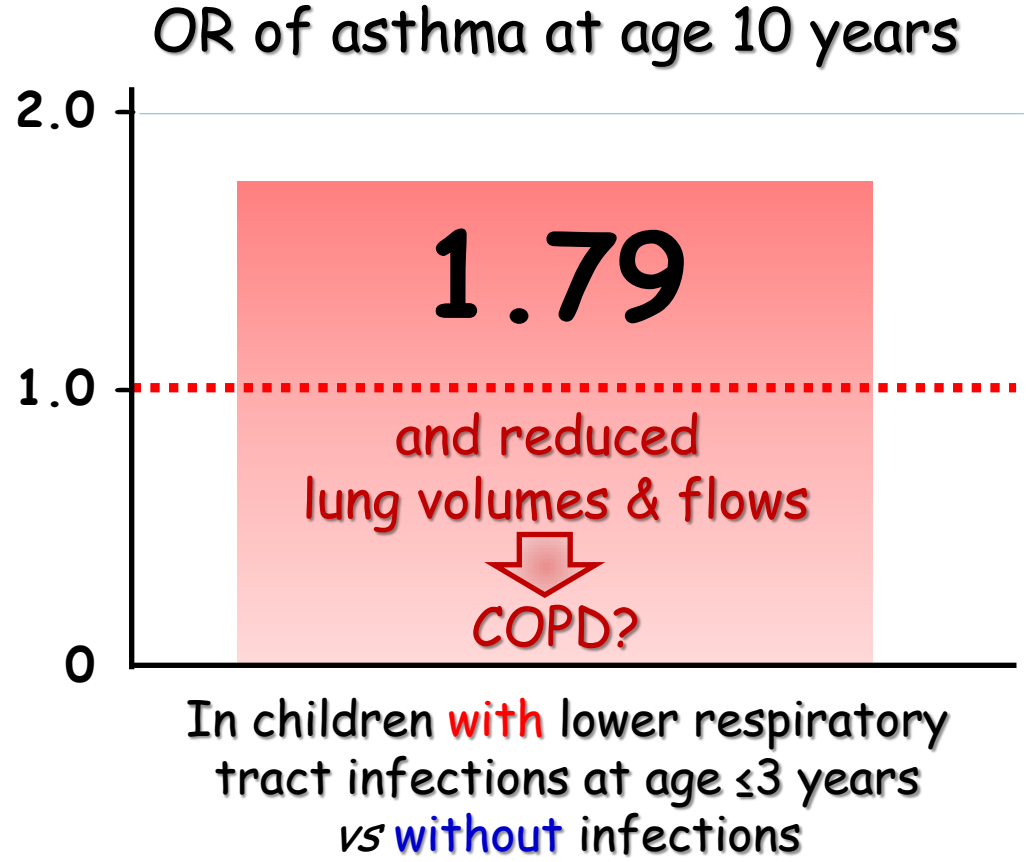
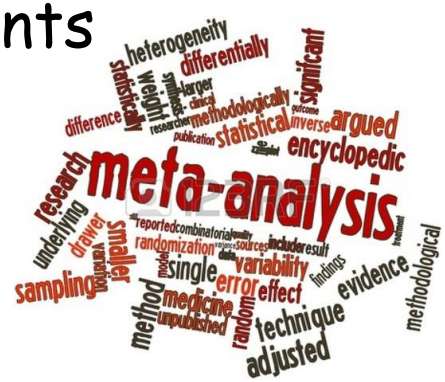
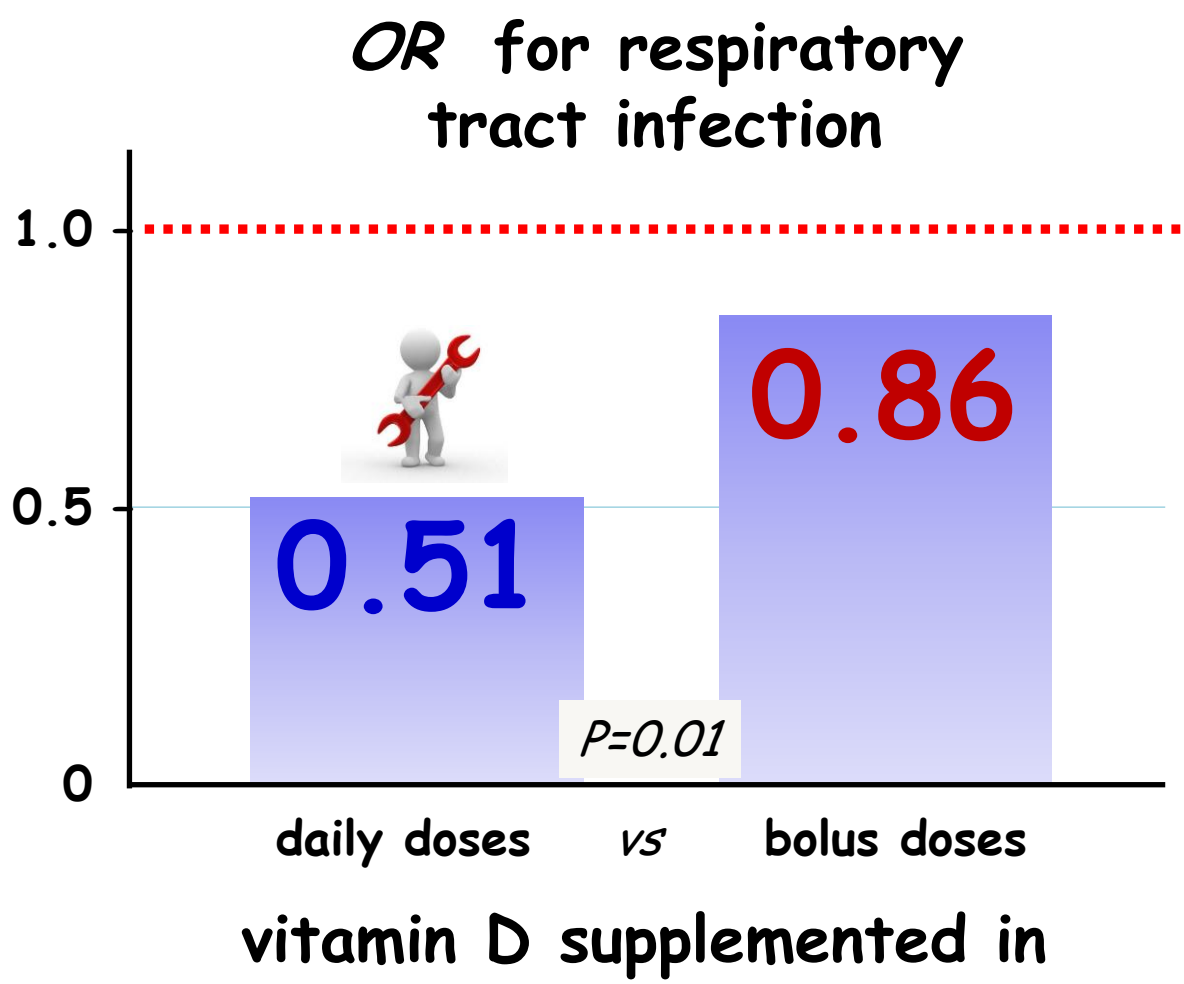


# Vitamin D and respiratory tract infections: A systematic review and meta-analysis of randomized controlled trials.

*Bergman P, PLoS One 2013; 8:e65835*

- ✓meta-analysis of 11 placebo-controlled studies
- ✓5660 patients included

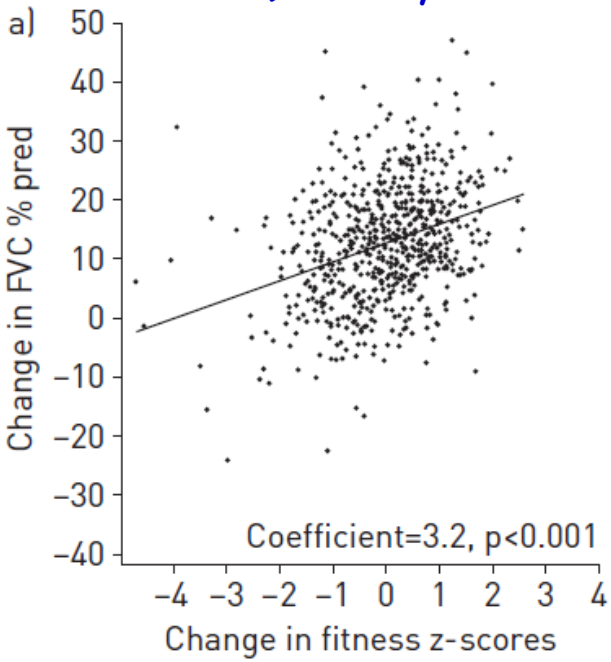


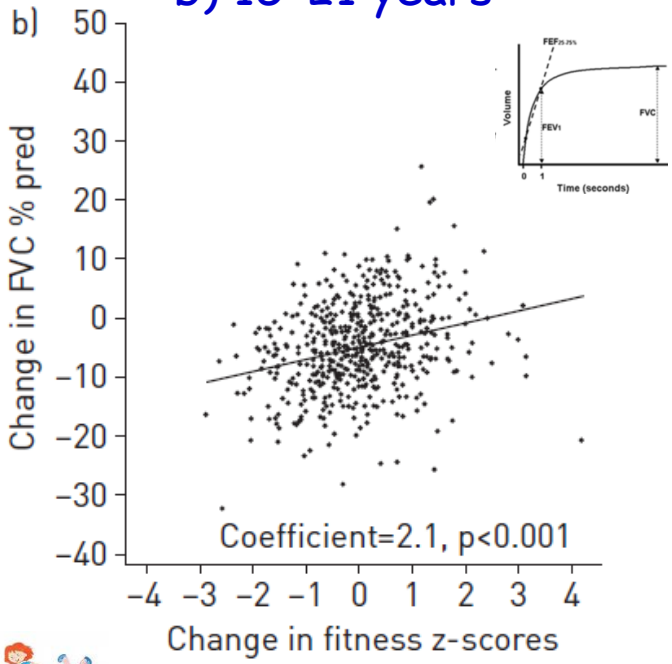
# Does physical fitness enhance lung function in children and young adults? *Hancox RJ, Eur Respir J 2018;51:1701374*


Change in FVC % predicted with sex-specific changes in aerobic fitness (maximal oxygen uptake (V'O2max) z-scores) between each age in the Odense study

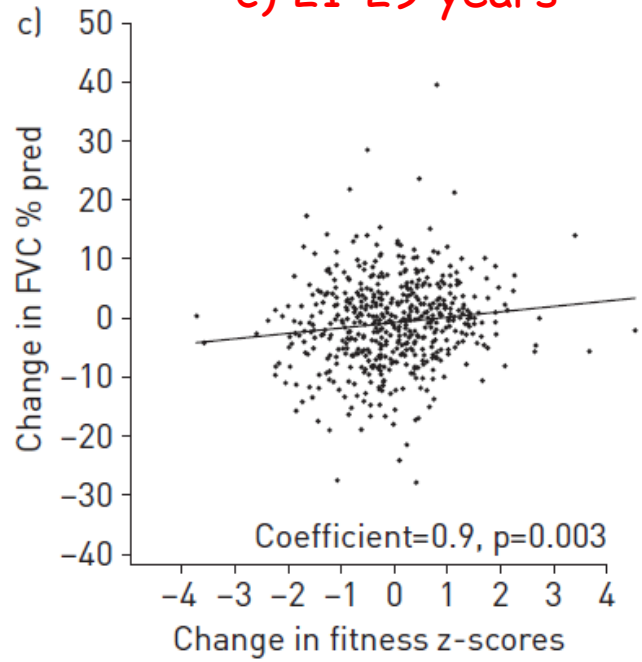
a) 9–15 years




b) 15–21 years




c) 21–29 years

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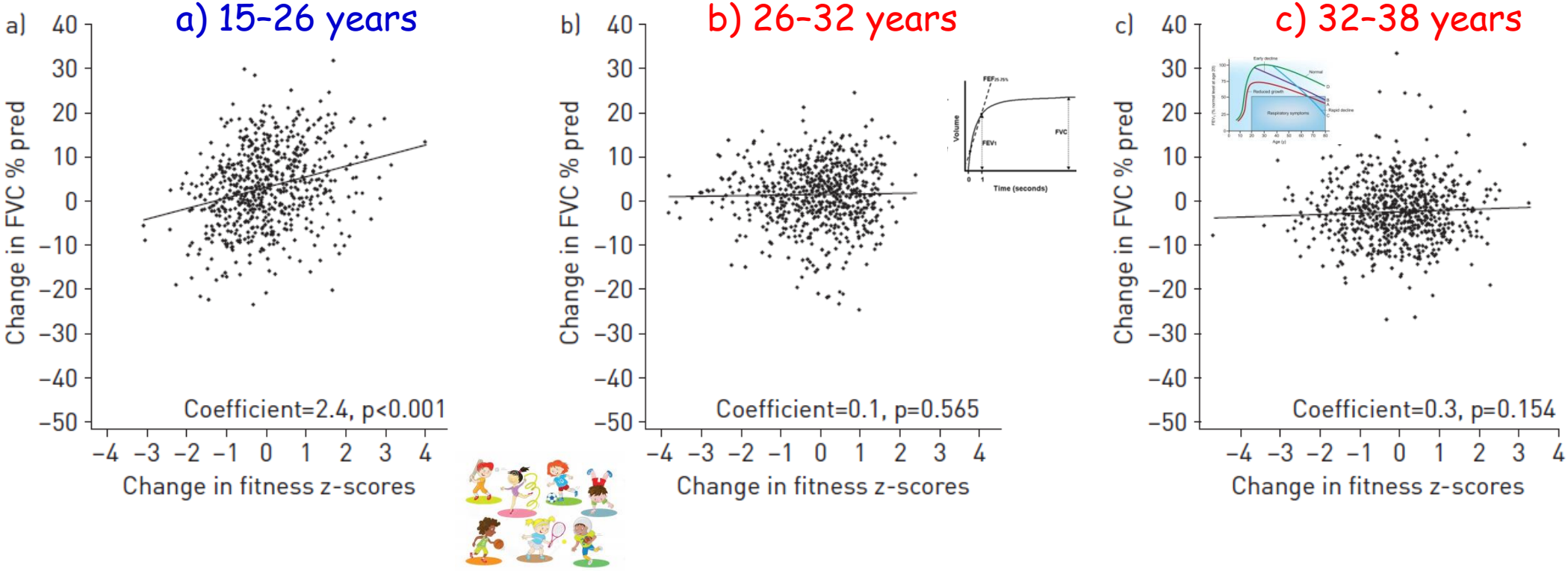
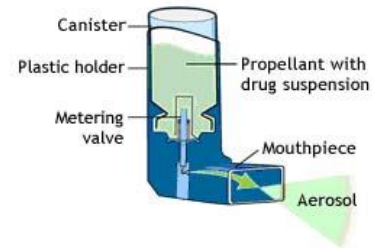


# Inhaler Errors in the CRITIKAL Study: Type, Frequency, and Association with Asthma Outcomes

*Price DB, JACI Pract 2017; 5:1071-1081*

- ✓ Between 2011 and 2014 and captured data from more than 5000 patients.
- ✓ Inhaler errors observed by purposefully trained health care professionals.

- In metered-dose inhaler users without spacer,
- actuation before inhalation (24.9% of patients) was associated with uncontrolled asthma (aOR 1.55).



# Inhaler Errors in the CRITIKAL Study: Type, Frequency, and Association with Asthma Outcomes

*Price DB, JACI Pract 2017; 5:1071-1081*

- The CRITIKAL study is the first study to observe associations between specific inhaler errors and poorer asthma outcomes, including increased likelihood of having uncontrolled symptoms and increased exacerbation rate.

- **Over the past 40 years the frequency and type of inhaler errors have not changed.**

- Generic errors, such as not exhaling, not holding the breath, insufficient speed of inhalation, dose preparation errors for DPIs, and coordination problems with MDIs, were the most common.

- One critical error in this study was insufficient inspiratory effort when using a DPI. All DPIs demonstrate flow-dependent dose emission and therefore the generic instruction when using these is to inhale as fast as possible.

# Inhaler Errors in the CRITIKAL Study: Type, Frequency, and Association with Asthma Outcomes

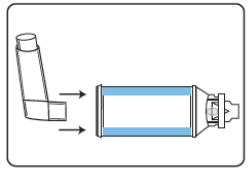
*Price DB, JACI Pract 2017; 5:1071-1081*

- The critical MDI error found in this study was poor coordination between the start of an inhalation and actuation of the dose (actuation coming before inhalation- MDI without a chamber).

- The CRITIKAL study results also highlighted "exhaling into the mouthpiece or not holding the inhaler upright" as a critical MDI error.

**FASE 1:**

Inserire lo spray nel distanziatore Respiro®



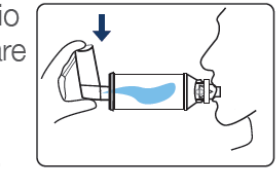
**FASE 2:**

**Agitare bene lo spray** inserito nel distanziatore prima di ogni spruzzo.


**FASE 3:**

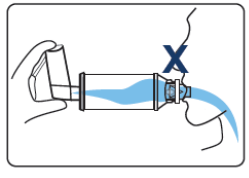
**Espirare profondamente.**

Mettere il boccaglio in bocca ed erogare nel distanziatore una sola dose di farmaco alla volta.



**FASE 4:**

**Inspirare profondamente** e lentamente dalla bocca, tenendo le labbra chiuse sul boccaglio fino alla fine dell'inspirio.



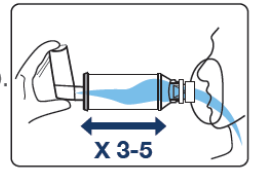
**FASE 5:**

*RIPETERE QUESTI PASSAGGI PER 2 VOLTE*

**Trattenere il respiro per 10 secondi** ed espirare lentamente dal naso per ridurre i sintomi della rinite con il farmaco che altrimenti andrebbe buttato. Sciacquare bene la bocca.


**FASE 5:**
**(per soggetti non collaboranti)**

**Per i bambini in età prescolare** si deve usare una mascherina che aderisca bene al viso. Far eseguire 3-5 atti respiratori.




+

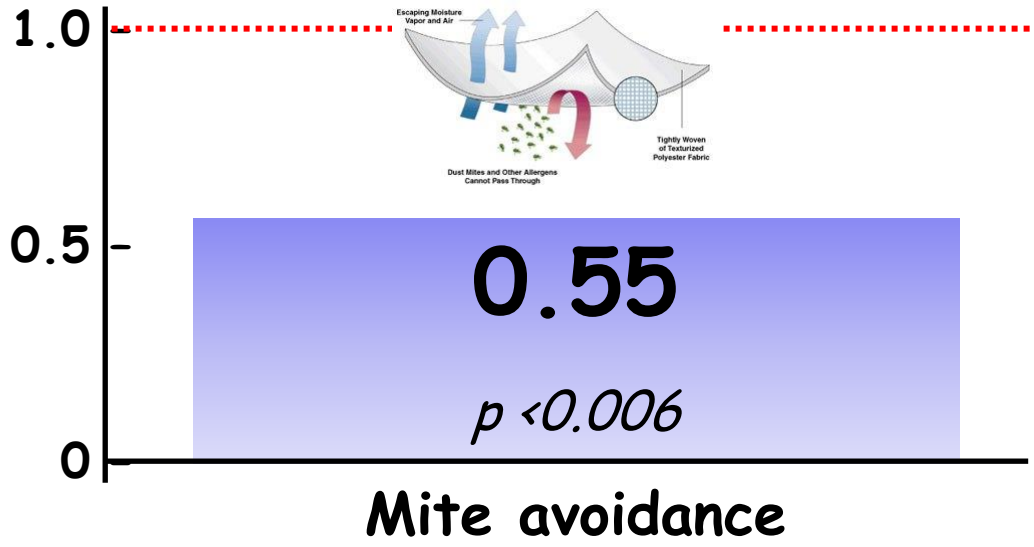
"Let me see how you use it"

# Preventing Severe Asthma Exacerbations in Children. A Randomized Trial of Mite-Impermeable

*Murray CS, Am J Respir Crit Care Med. 2017;196:150-158*

- ✓ Mite-sensitized children with asthma (ages 3-17 yr) after an emergency hospital attendance with an asthma exacerbation.
- ✓ Mite-impermeable (active group, n=46) or control (placebo group, n=138) bed encasings.


**HR for emergency hospital attendance**



# Mite Avoidance as a Logical Treatment for Severe Asthma in Childhood. Why Not? *Editorial*

*Platts-Mills TAE, Am J Respir Crit Care Med. 2017; 196:119-121*

The relevance of allergen exposure at critical steps in the development of severe exacerbations of asthma in at-risk children

**INCREASED RISK**

Allergen exposure (mite, cat, cockroach, and other)

*Continued relevant allergen exposure*

Rhinovirus infection

RNA rhinovirus

*Sensitization*

- Skin prick test
- Serum IgE

*Bronchial inflammation*

- Airway hyperreactivity
  - methacholine
  - histamine
  - exercise

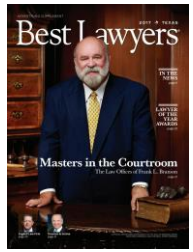
*Severe exacerbations or wheezing*

**DECREASED RISK or PROTECTION**

- Minimal / no allergen exposure
- Other environmental exposures (e.g., high endotoxin)
- ↓ allergen exposure
- Anti-IgE therapy
- Immunotherapy
- Pharmacology
- Regular aerobic exercise

# Something new in the air: Paying for community-based environmental approaches to asthma prevention and control.

*Tschudy MM, J Allergy Clin Immunol. 2017 Nov;140(5):1244-1249.*




- Several pilot programs across the United States are underway, and as they prove their value and as payment increasingly becomes aligned with better outcomes at lower cost, these efforts should have a bright future

## Home Bases Environmental Interventions: Spectrum of Intensity

Examples of Interventions

**Minor:**
- Environmental Assessment
- Pillow & Mattress Covers

**Moderate:**
- IPM supplies & services (Integrated Pest Management)
- Cleaning Kits
- HEPA Furnace filters, vacuums, & air purifiers

**Major:**
- Vent/heating retrofits
- Re-roofing
- Insulation
- Removal of water damaged materials

Source: CDC Task Force on Community Preventative Services. "Asthma Control: Home-Based Multi-Trigger, Multicomponent Environmental Interventions Summary Evidence Tables – Economic review:

# Highlights in Pediatric Allergy & Pulmonolgy

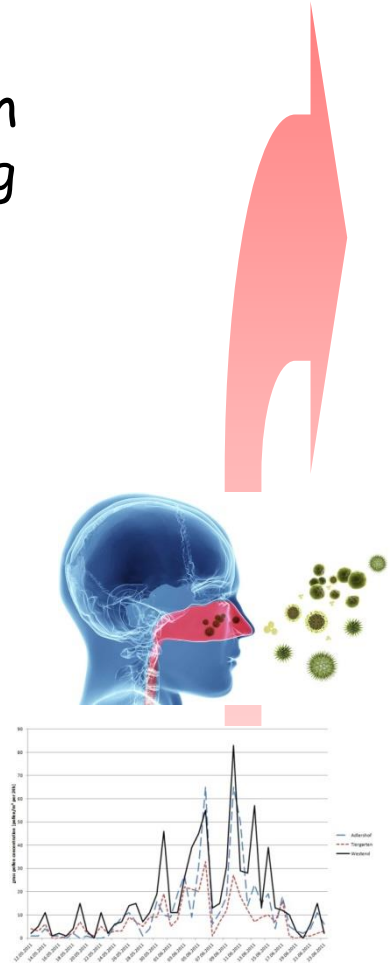
***Attilio Boner***
***University of Verona, Italy***
*attilio.boner@univr.it*

- ✓ Epidemiology
- ✓ Atopic Dermatitis
- ✓ Food allergy
- ✓ Bronchiolitis & Asthma
- ✓ **Allergic rhinitis**
- ✓ Unexpected burden
- ✓ Summary & Conclusions

# Memory and multitasking performance during acute allergic inflammation in seasonal allergic rhinitis

*K Trikojat, CEA 2017;47:479-487*

- ✓ Influence of seasonal allergic rhinitis (SAR) on memory and multitasking performance.
- ✓ Non-medicated patients with SAR (*n* = 41) and healthy non-allergic controls performed a verbal learning and memory test during and out of symptomatic allergy periods (pollen *vs.* non-pollen season).



- During the symptomatic allergy period, patients showed:
  - (1) poorer performance in word list-based learning *(P = 0.028)*
  - (2) a general slowing in:
    -processing speed *(P < 0.001)*
    and
    -a shift in processing strategy *(P < 0.001)* in multitasking.

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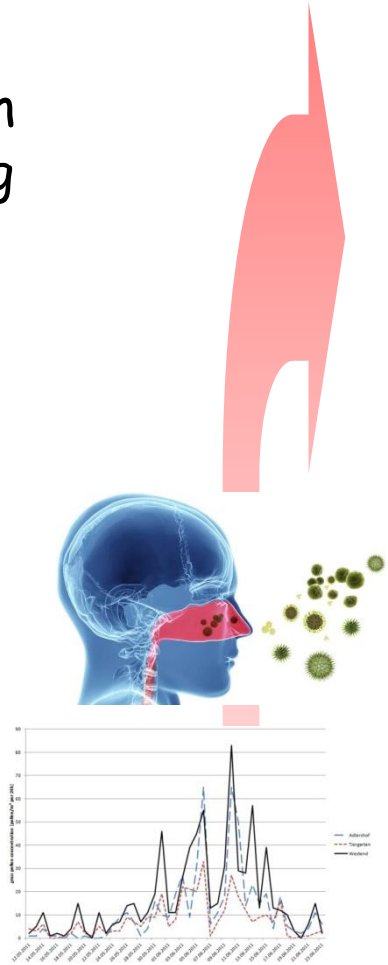
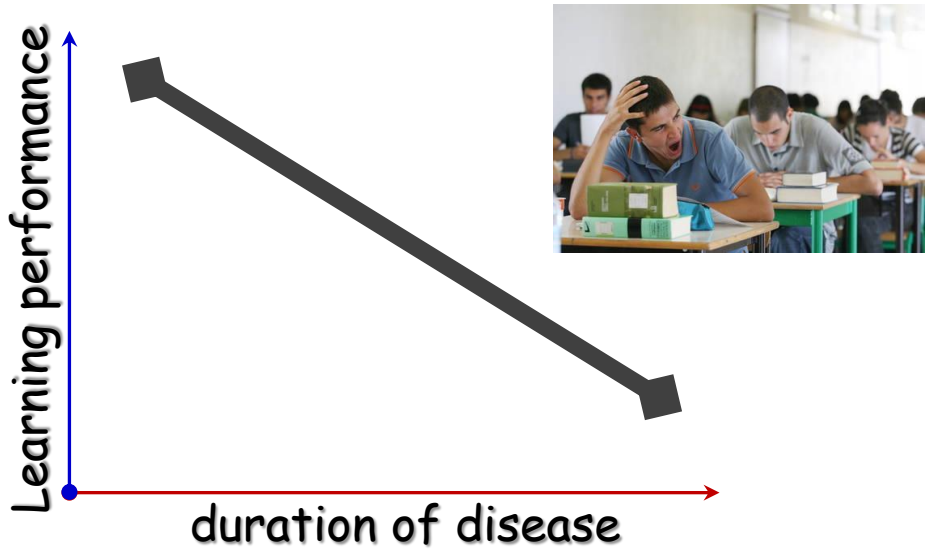


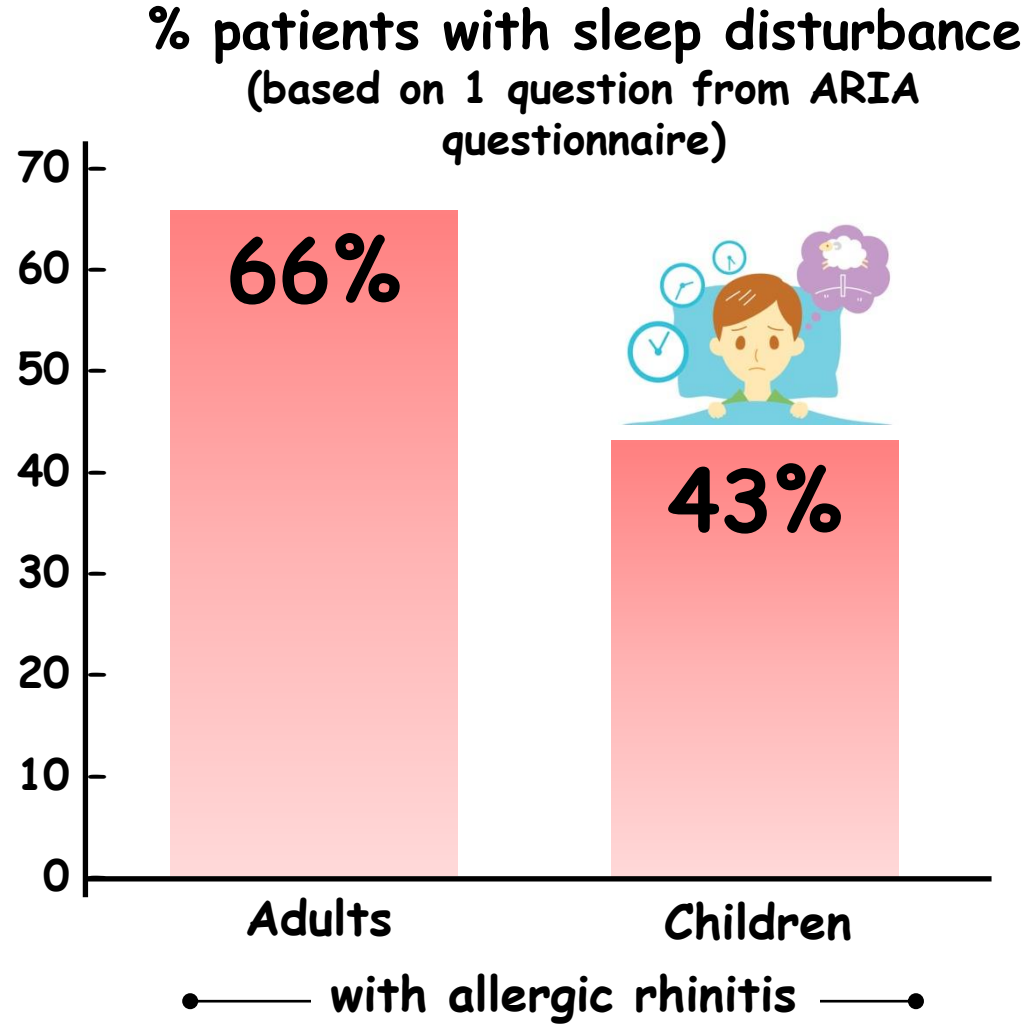
- A significant negative association was found between learning performance and duration of disease *(r = –0.451, P = 0.004).*



# Assessment of sleep disturbance in children with allergic rhinitis

*Dass K, Ann Allergy Asthma Immunol 2017;118:505-506*

- ✓ Patients aged 8 to 30 years old (n = 144) with controlled asthma.
- ✓ Completed the following questionnaires:
  - ARIA disease severity questions,
  - PROMIS profile,
  - modified Epworth Sleepiness Scale (ESS),
  - Pediatric Perceived Cognitive Function/Applied Cognition-General Concerns, and
  - Sino-Nasal Outcome Test (SNOT-22).



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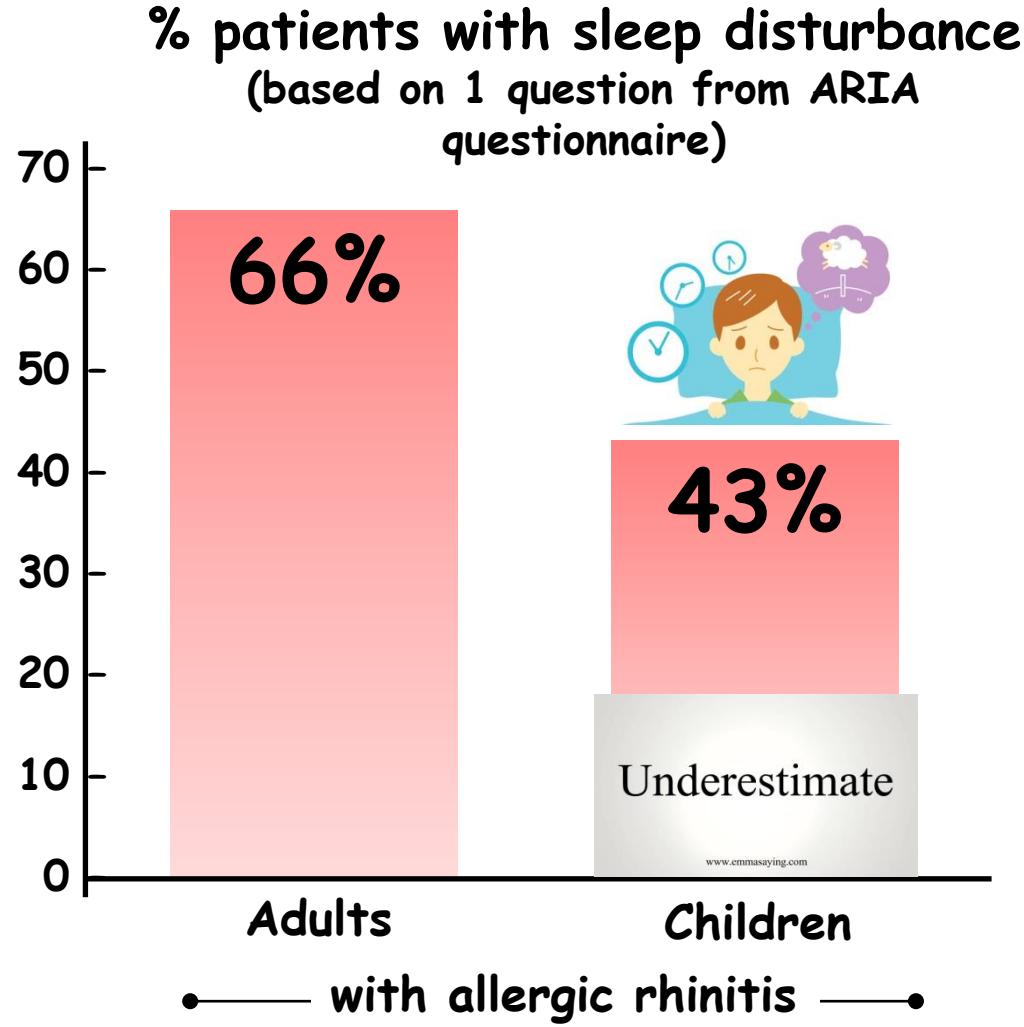


# Assessment of sleep disturbance in children with allergic rhinitis

*Dass K, Ann Allergy Asthma Immunol 2017;118:505-506*

Conclusions:

- 1 question assessment of sleep disturbance is inadequate in screening for sleep disturbance or sleep-related impairment.

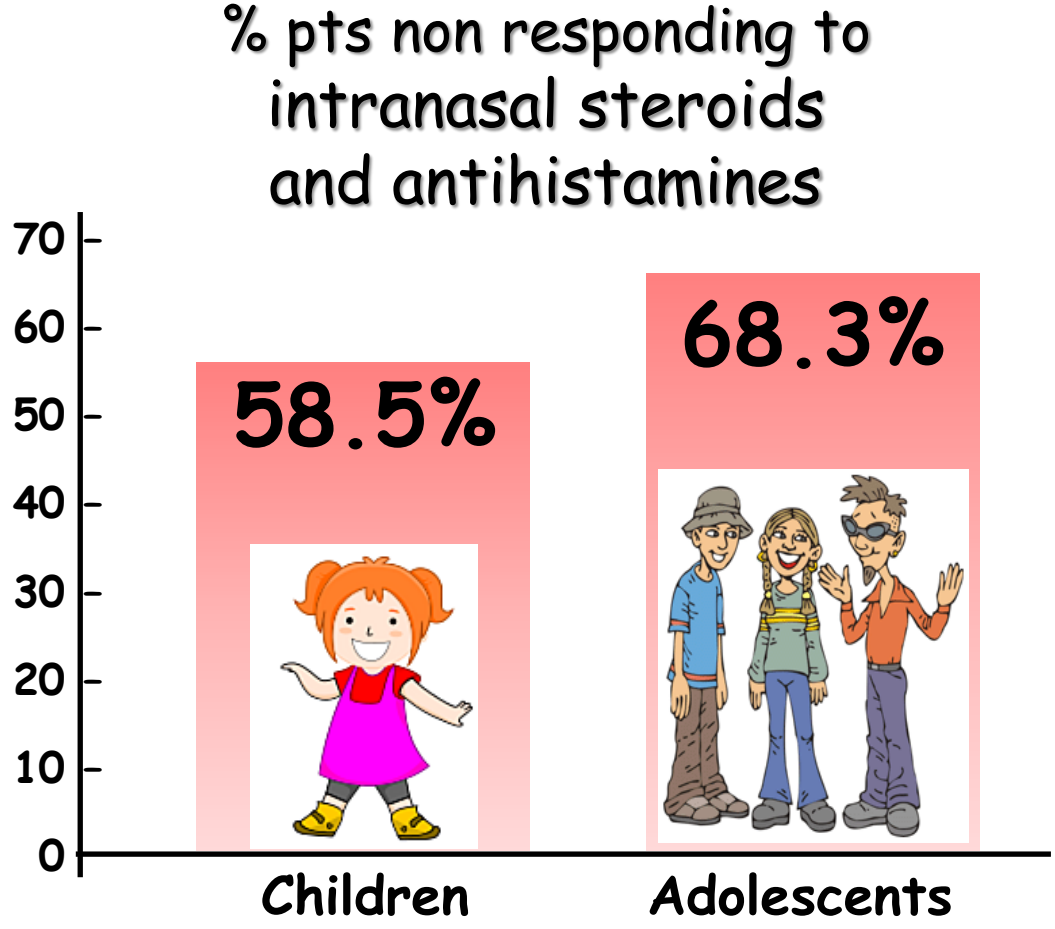
- In the pediatric age group specifically, sleep disturbance can manifest in other forms, such as:
  - in peer relationships
  - daytime functioning,

  } which are not currently assessed in ARIA.

- PROMIS is the only tool that can assess sleep disturbance and capture other quality-of-life measures.

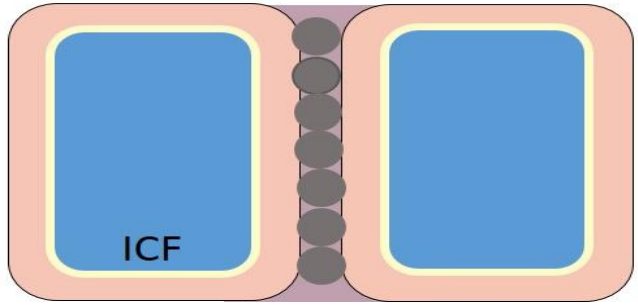
# Nasal obstructive disorders impair health-related quality of life in adolescents with persistent allergic rhinitis: A real-life study. *M Valls-Mateus, PAI 2017;28:438-445*

- ✓ 142 patients (41 children, 6-11 years old and 101 adolescents, 12-17 years old) with moderate and severe persistent allergic rhinitis (PER).
- ✓ After 2 months of intranasal steroids and antihistamines, patients were asked whether their symptoms had improved (yes/no) and classified accordingly in R, responders and NR, non-responders.

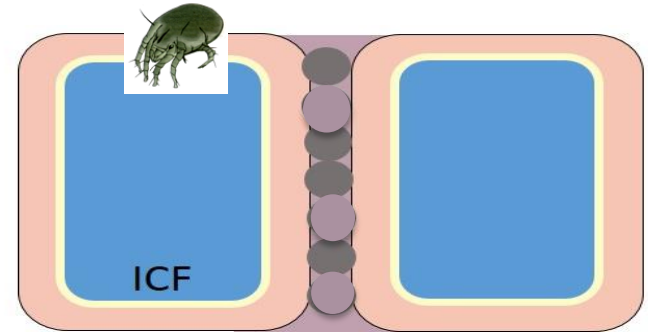


# Impaired barrier function in patients with house dust mite–induced allergic rhinitis is accompanied by decreased occludin and zonula occludens-1 expression

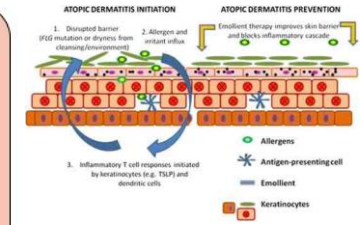
*Steelant B, JACI 2016;137:1043-1053.*




Primary nasal epithelial cells of control subject.

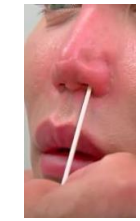



Primary nasal epithelial cells of patients with HDM-induced AR.




AR symptoms correlated inversely with resistance in patients with HDM-induced AR.

decreased transepithelial resistance with increased fluorescein isothiocyanate-dextran 4 kDa (FD4) permeability and reduced occludin and zonula occludens-1 expression.



# Highlights in Pediatric Allergy & Pulmonolgy

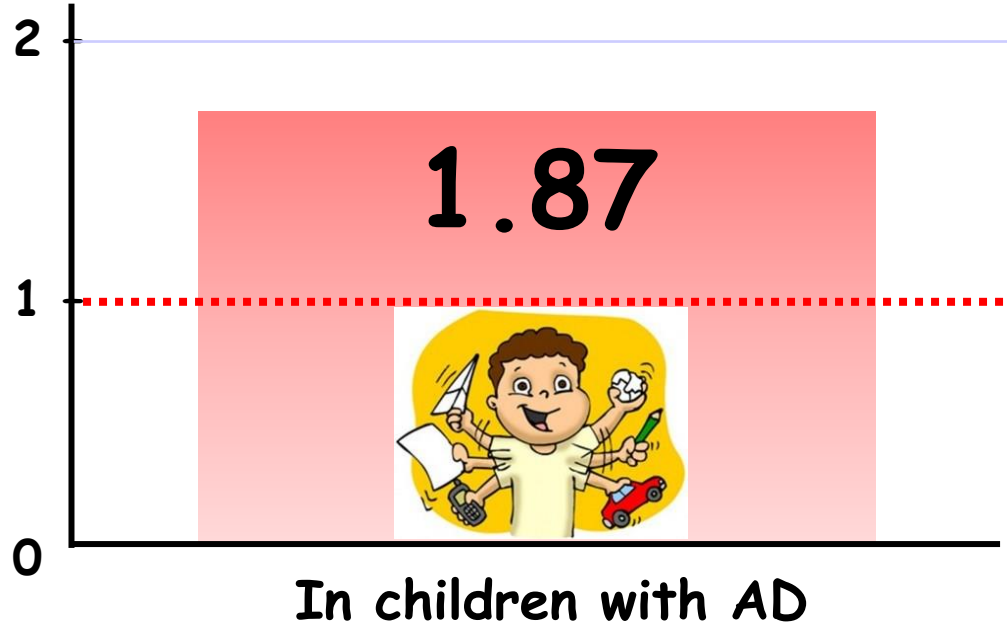
***Attilio Boner***
***University of Verona, Italy***
*attilio.boner@univr.it*

- ✓ Epidemiology
- ✓ Atopic Dermatitis
- ✓ Food allergy
- ✓ Bronchiolitis & Asthma
- ✓ Allergic rhinitis
- ✓ Unexpected burden
- ✓ Summary & Conclusions

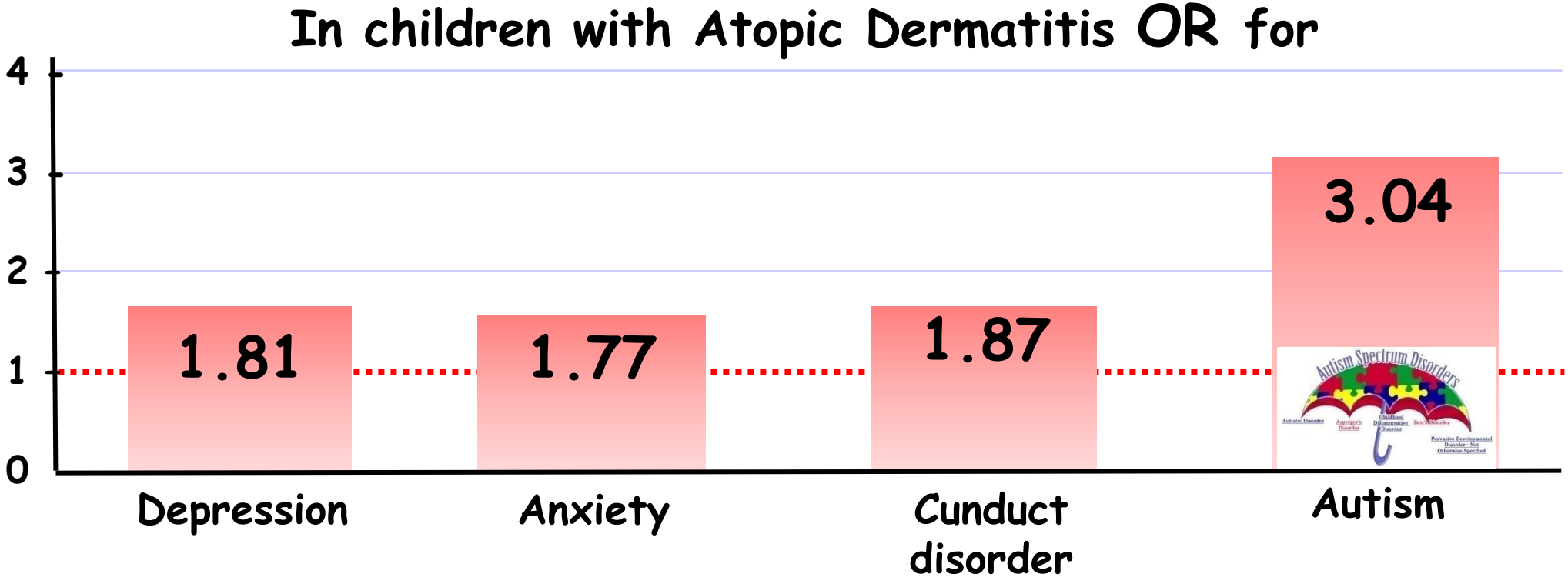
# Mental health comorbidity in patients with atopic dermatitis *Yaghmaie P, JACI 2013;131:428-33*

- ✓ 92642 noninstitutionalized children aged 0 to 17 years.
- ✓ Lifetime prevalence of provider-diagnosed **mental health conditions** for those with and without a history of AD.

**OR** of having attention deficit hyperactivity disorder



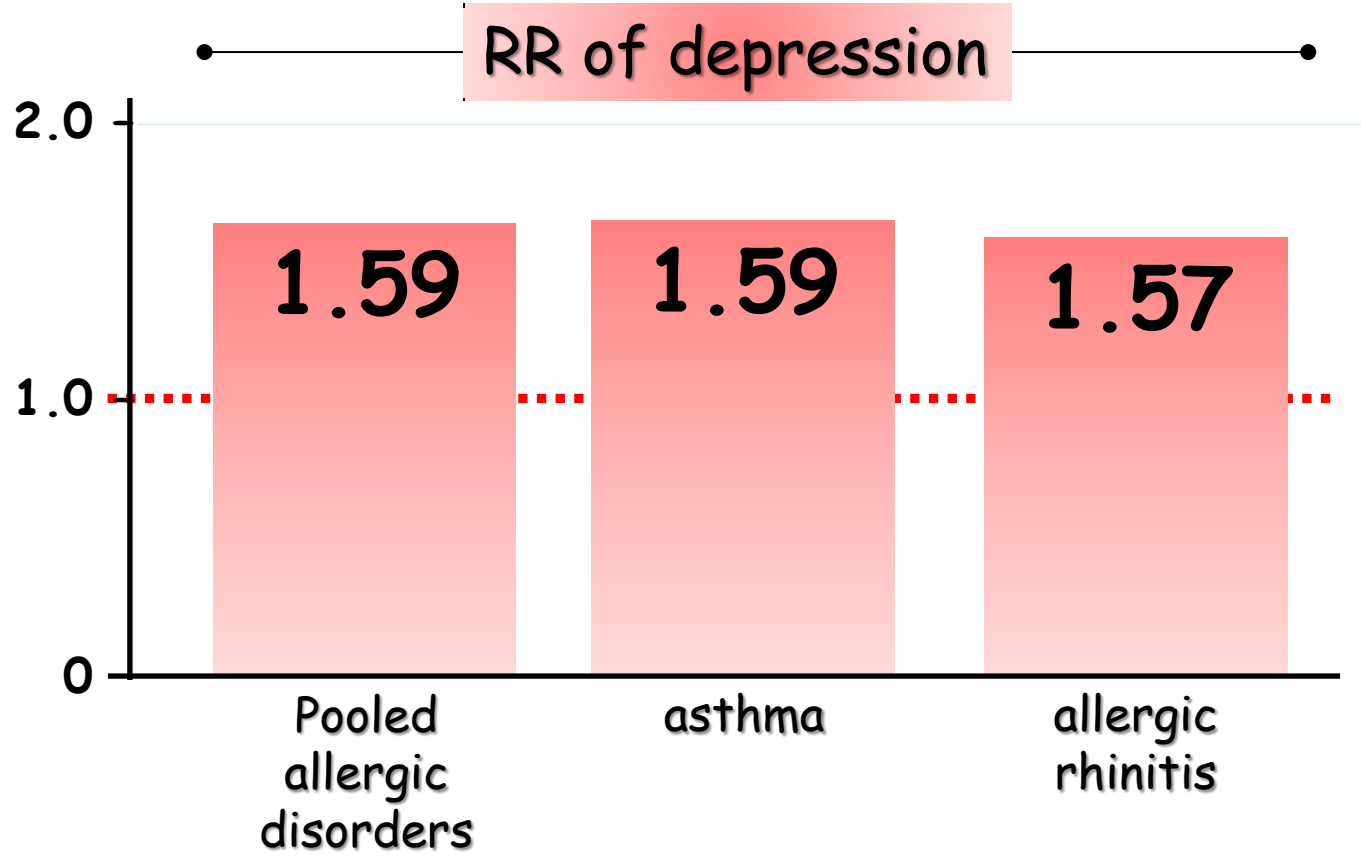
# Mental health comorbidity in patients with atopic dermatitis *Yaghmaie P, JACI 2013;131:428-33*



# Allergic disorders and risk of depression: A systematic review and meta-analysis of 51 large-scale studies.

*Lu Z. Ann Allergy Asthma Immunol. 2018 Mar;120(3):310-317.e2.*

✓51 studies including > 2.5 million participants



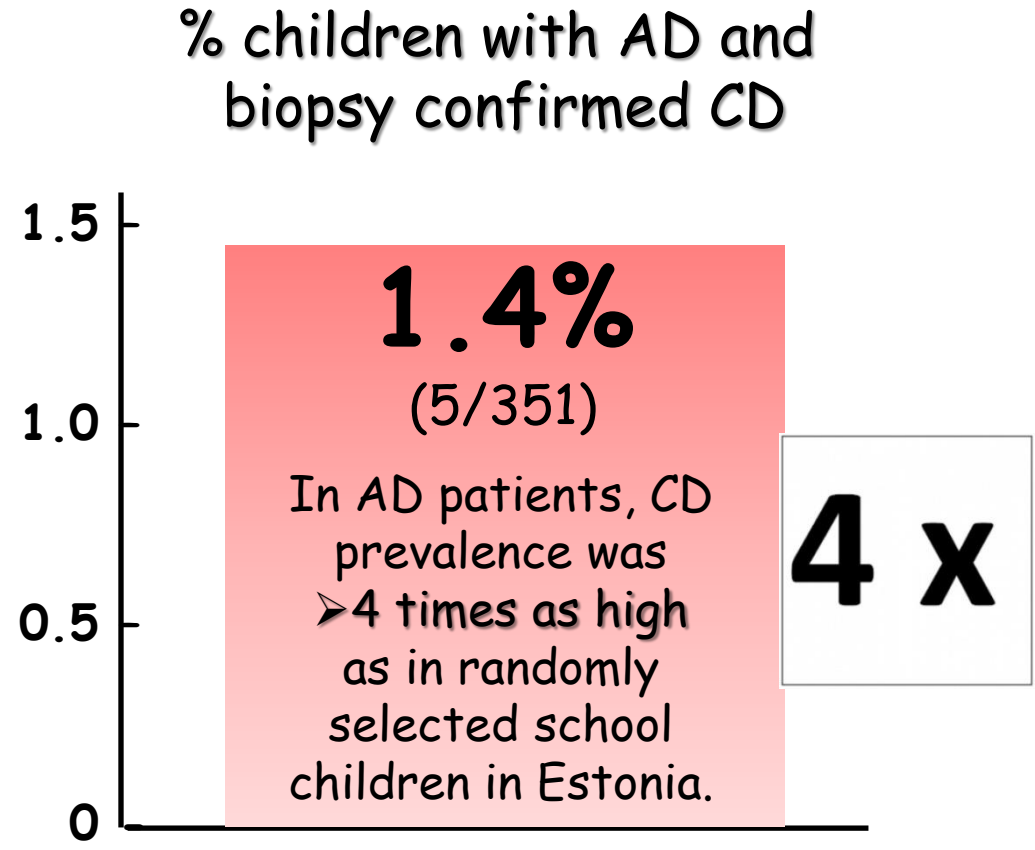
# Celiac disease in children with atopic dermatitis.

*Ress K, Pediatr Dermatol. 2014;31(4):483-8.*

✓351 consecutive Estonian children with active atopic dermatitis (AD), (mean age 5.8 yrs)

✓total serum IgA, IgA- and IgG-type autoantibodies to tissue transglutaminase (IgA-anti-TG2, IgG-anti-TG2) and to deamidated gliadin peptides (IgA-anti-DGP, IgG-anti-DGP).

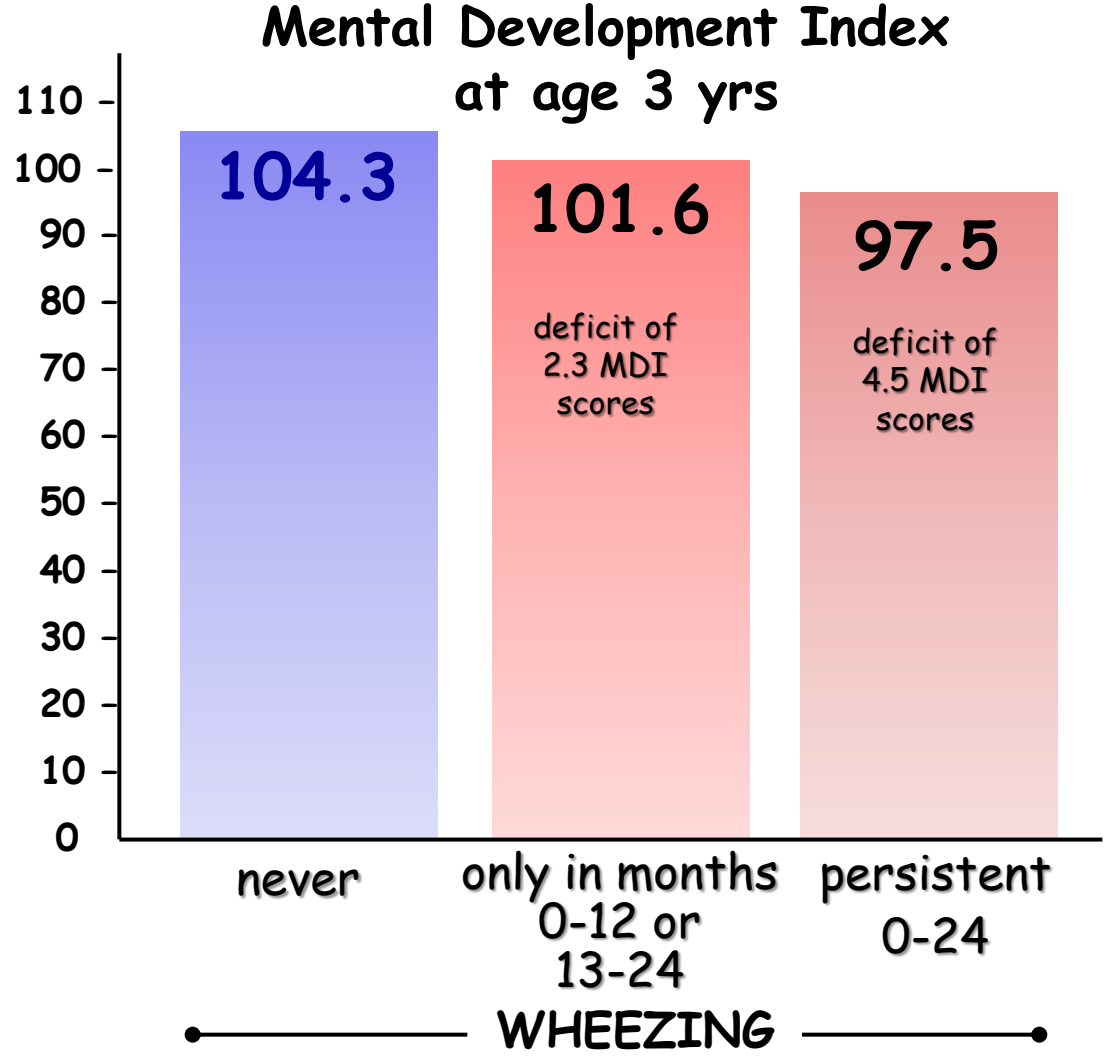
✓diagnosis of CD confirmed by small intestine biopsy



# Early wheezing phenotypes and cognitive development of 3-yr-olds. Community-recruited birth cohort study

*Jedrychowski W. Pediatr Allergy Immunol. 2010;21:550-6*

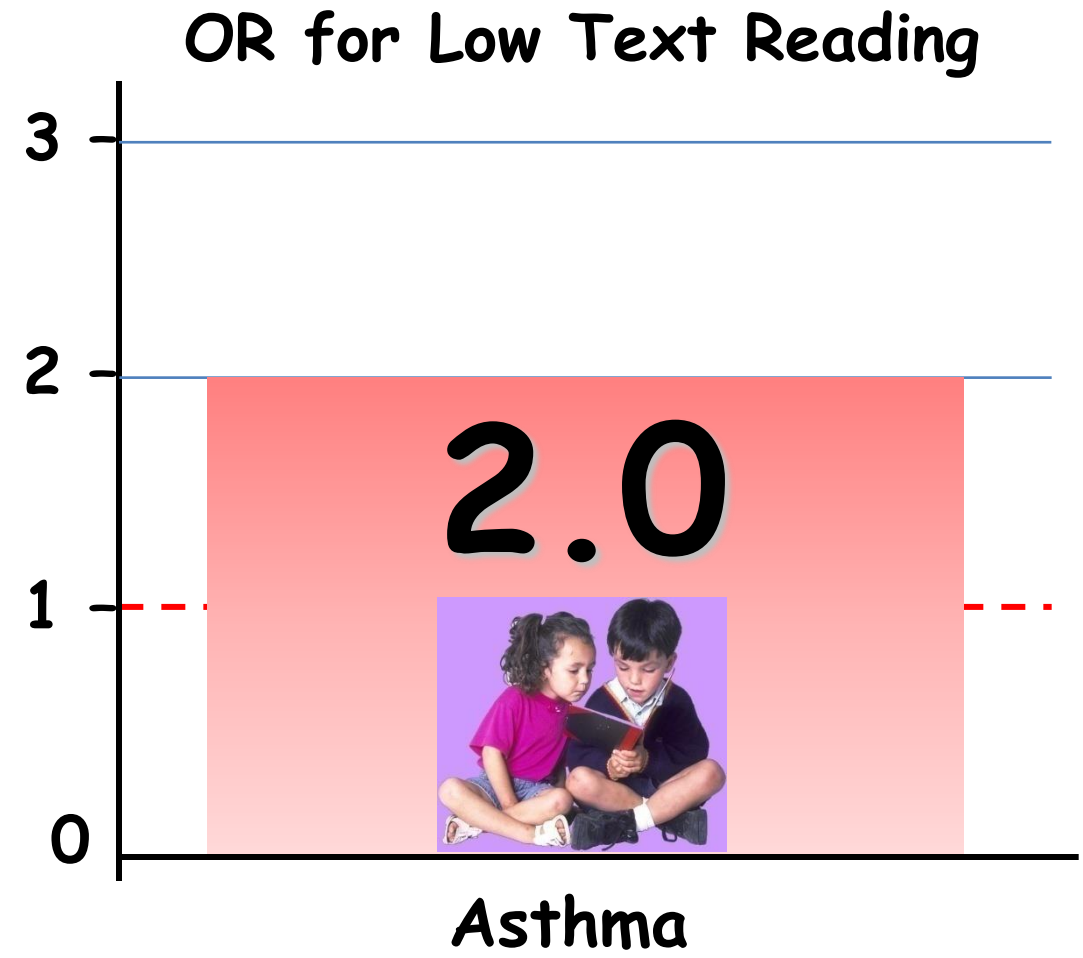
- ✓Birth cohort (n=468).
- ✓Wheezing symptoms over first two years.
- ✓Cognitive status of children at the age of 3 yr with the Bayley Mental Development Index (MDI).



# Beginning school with asthma independently predicts low achievement in a prospective cohort of children

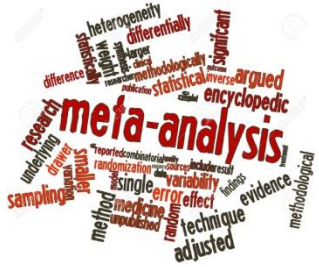
*Liberty CHEST 2010;138:1349*

- ✓ A child cohort (n=**298**) in New Zealand
- ✓ Physician reports for asthma
- ✓ Children's achievement in reading and math at school entry and after 12 months.

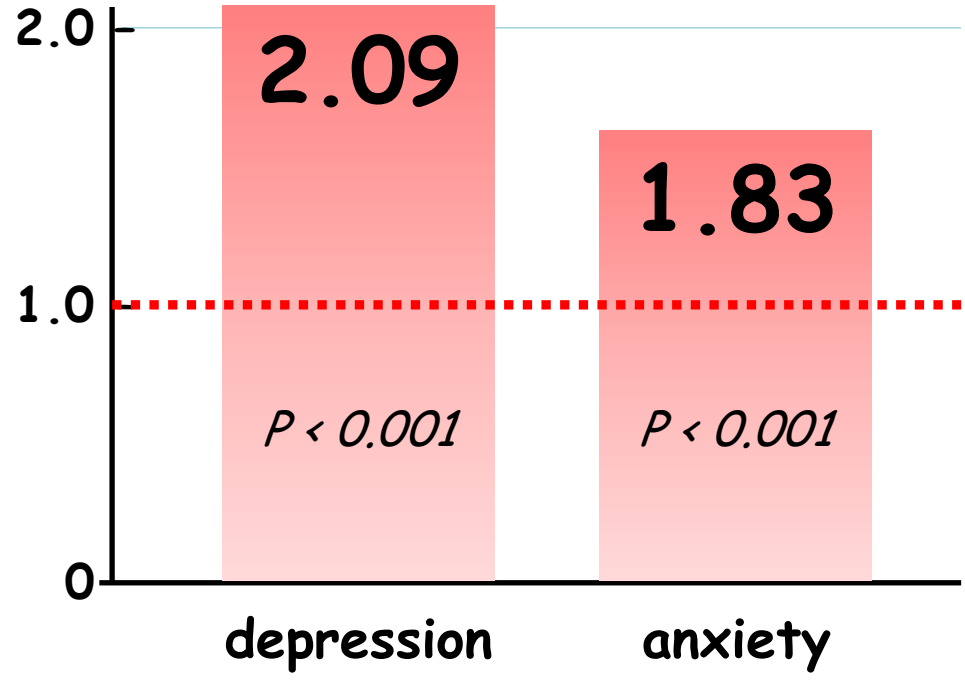


# Prevalence of anxiety and depressive symptoms in adolescents with asthma: A meta-analysis and meta-regression *Lu Y., Pediatr Allergy Immunol 2012; 23:707-15*

- ✓ 8 studies for analysis.
- ✓ 3546 adolescents with asthma.
- ✓ 24,884 controls.



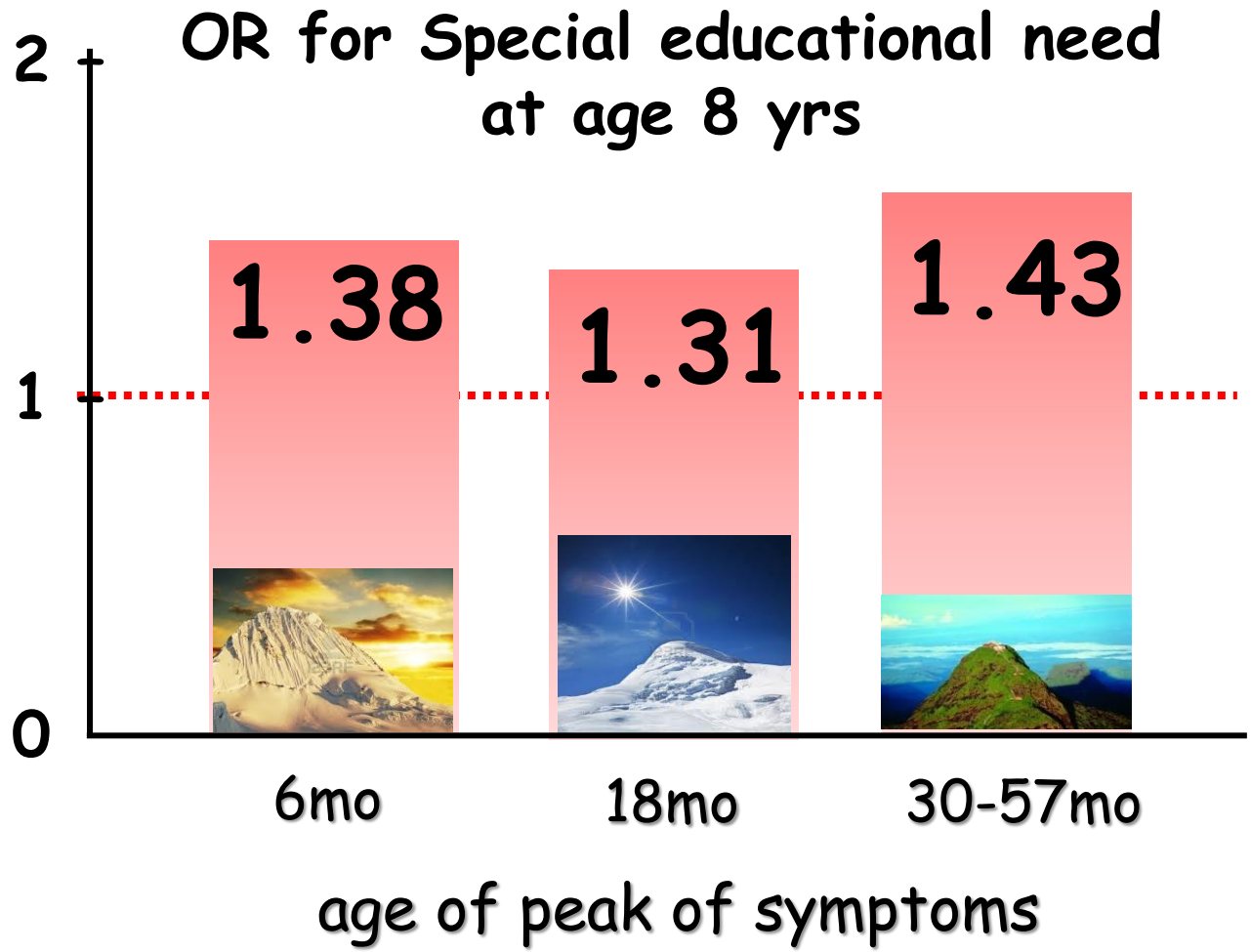

in asthmatic adolescents OR for developing




# Pediatric Sleep Disorders and Special Educational Need at 8 Years: A Population-Based Cohort Study

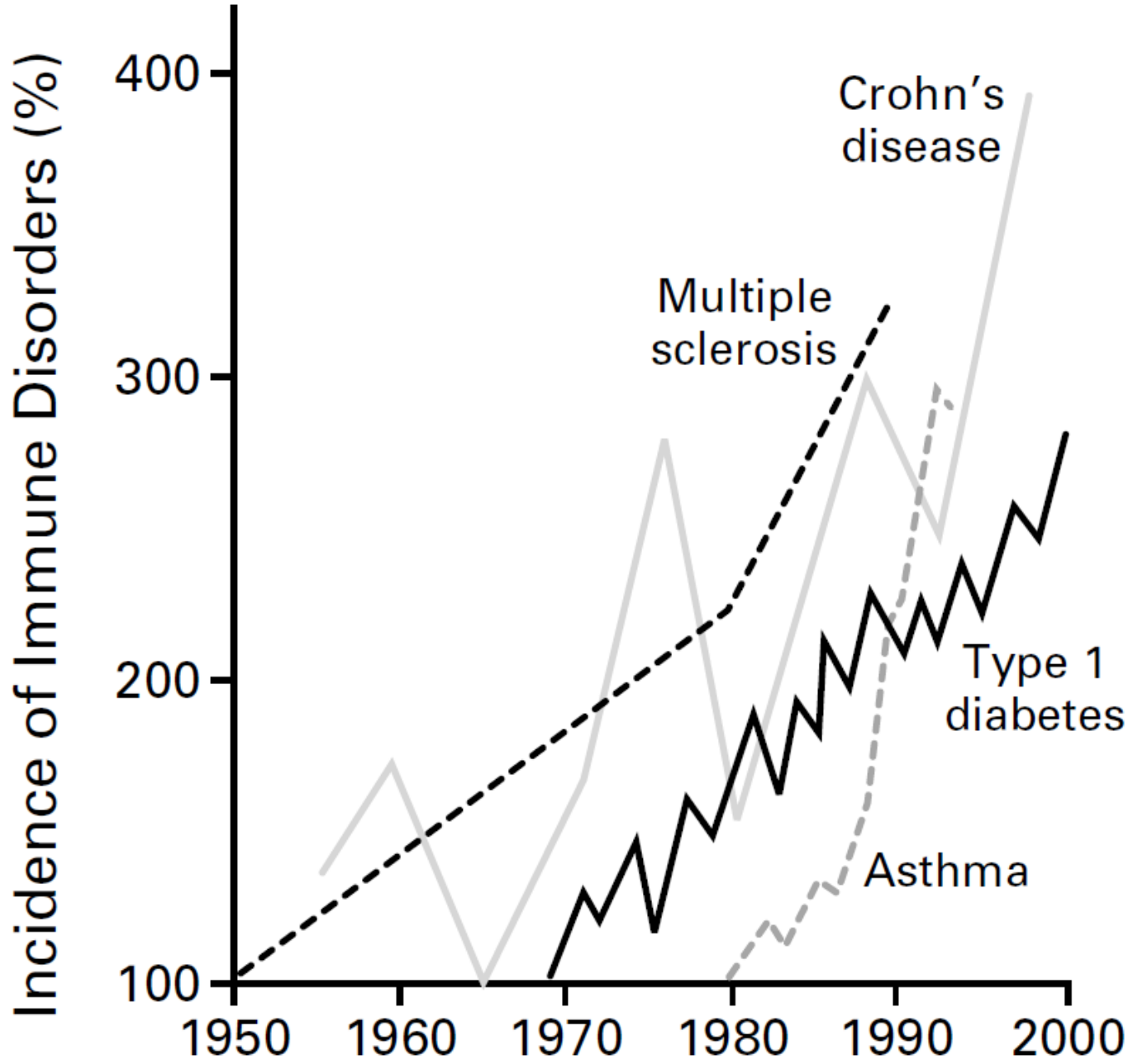
*Bonuck K. Pediatrics 2012;130:634*

- ✓ Sleep disordered breathing (SDB) through 5 years of age (11 049 children).
- ✓ Special educational need (SEN) at 8 years.
- ✓ Parents reported on children's snoring, witnessed apnea, and mouth-breathing at 6, 18, 30, 42, and 57 months.



# The increased Incidence of Immune Disorders from 1950 to 2000 in different part of the world.

*Bach JF.*
*N Engl J Med.*
*2002;347(12):911-20*




*by a courtesy of Prof. Hans Bisgaard*

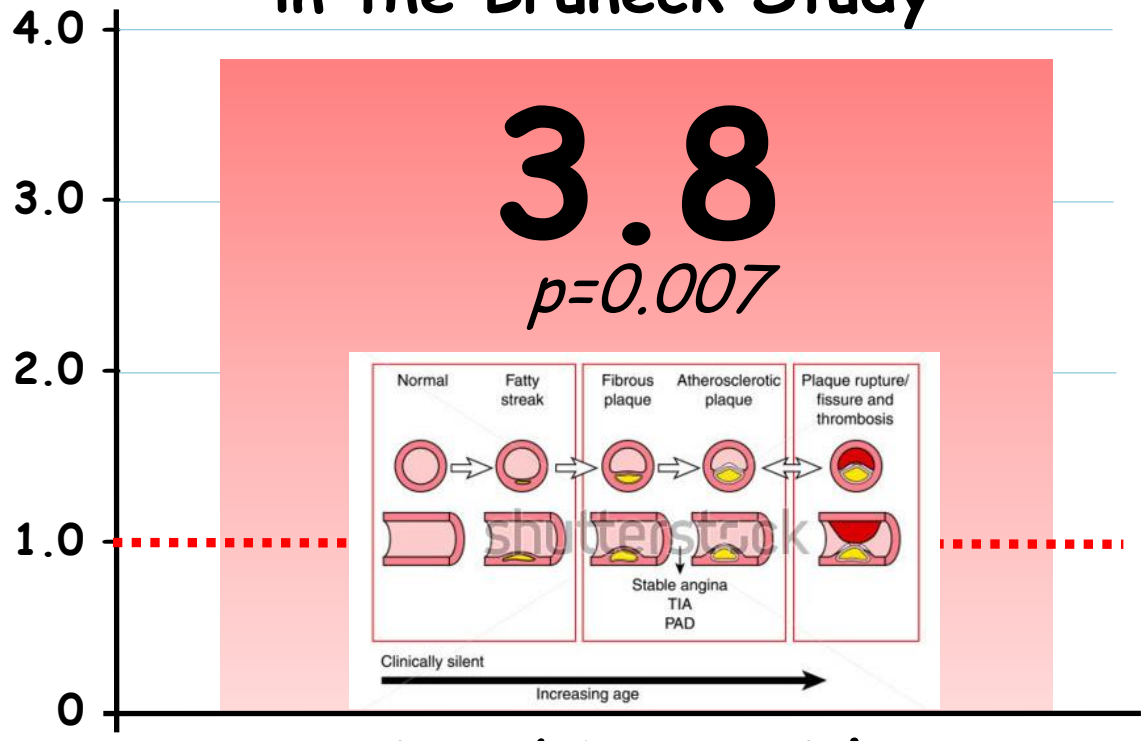
# Allergic rhinitis, asthma, and atherosclerosis in the Bruneck and ARMY studies.

*Knoflach M, Arch Intern Med 2005;165:2521-6.*

- ✓The ARMY study is a cross-sectional evaluation of 141 men aged 17 or 18 years

- ✓The Bruneck Study is a prospective population-based survey of 826 men and women aged 40 to 70 years;

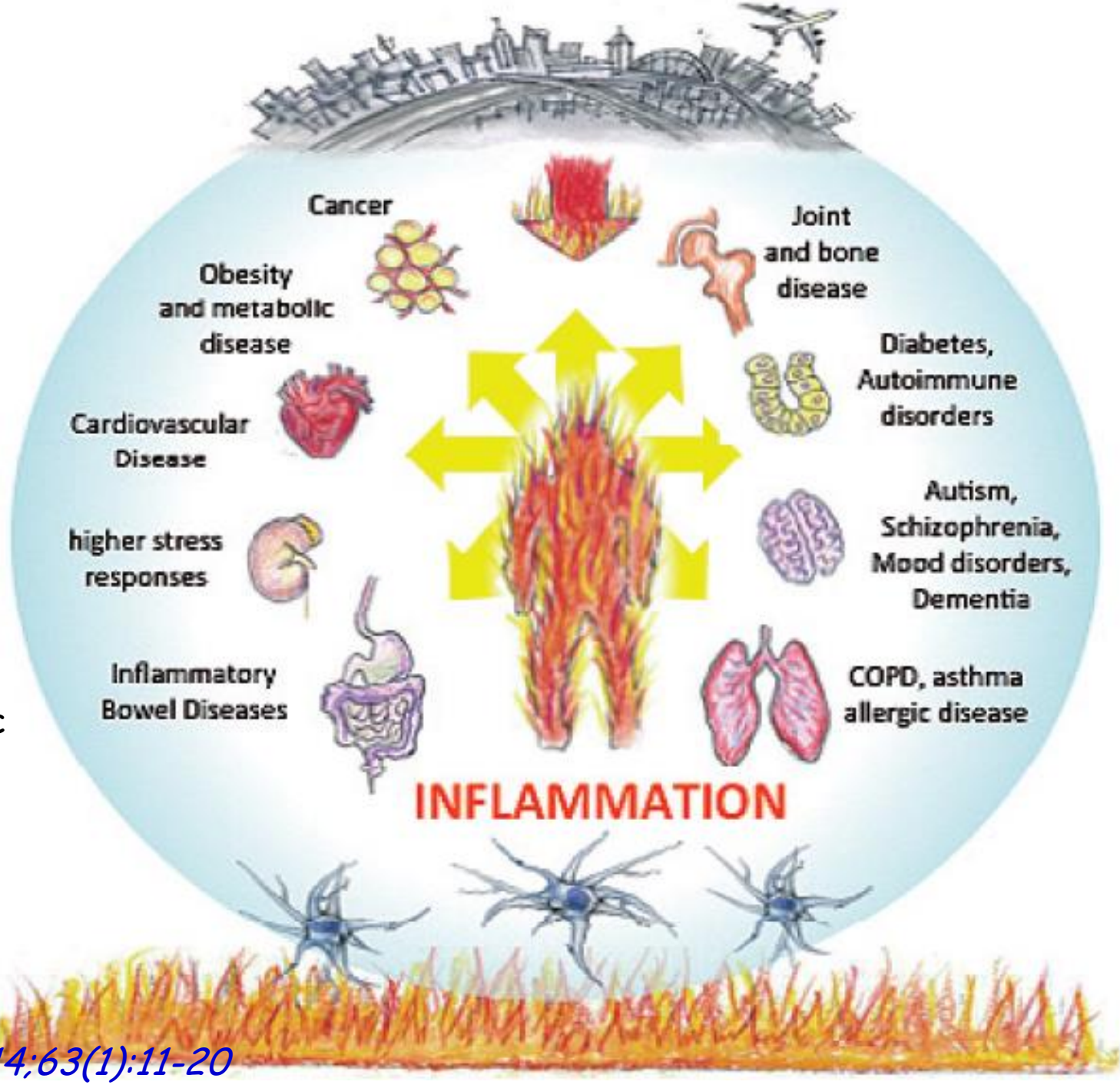
**OR for atherosclerosis development and progression in the Bruneck Study**




**in subjects with allergic disorders**

**A rising propensity for inflammation is implicated in the parallel rise of virtually all NCDs.**

There was little doubt that modern environmental changes promote inflammation and, as a paediatricians, we could already see the first hand effects of this in the first years of life in the epidemic allergic inflammation.




*Prescott S, Allergol Int. 2014;63(1):11-20*

# The allergy epidemic as a canary in the coal mine.

An early indicator of the impact of modern environmental change and specific vulnerability of the immune system.
This early propensity for inflammation and immune dysregulation has implications for rising risk many other later onset non-communicable inflammatory diseases (NCDs).


*Prescott S, Allergol Int. 2014;63(1):11-20*

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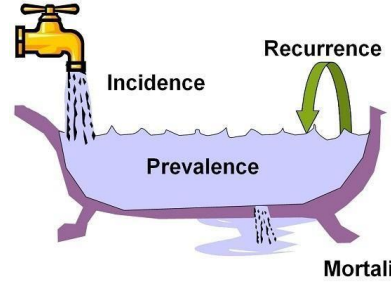
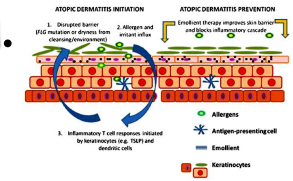
# Summary & Conclusions

Incidence & prevalence of allergic diseases are high and increasing, and climatic changes (us) may have an important etiological role.

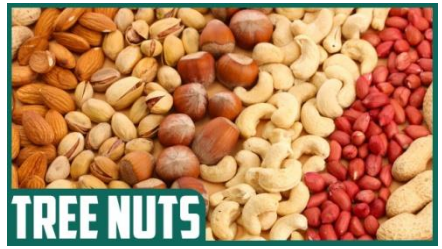



Atopic dermatitis is associated with an increased risk of sensitization but easily implemented strategies may be used for prevention.




Food allergy prevention can be accomplished towards introduction of complementary foods after the 17° week of life while the mother is still breast-feeding

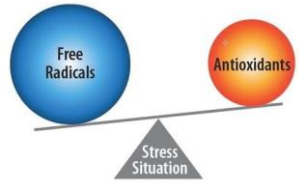

Some food allergies are mediated by pollen sensitization and co-allergy must be distinguished by co-sensitization



# Summary & Conclusions

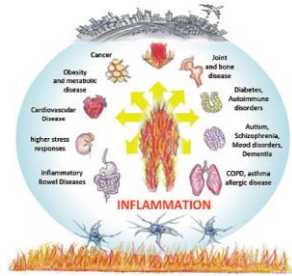
Bronchiolitis is our canary in the mine.

Asthma can be somehow prevented with biological plausible interventions and also enhanching the anti-oxidant defense of the individuals.




In asthma management always consider the correct use of the devices.

Severe allergic rhinitis goes beyond the nose and the burden of allergic diseases may involve the entire organism by mean of inflammation.


Family pediatricians have a central role in the health programming and not only in diseases' management.

fimp
Federazione Italiana Medici Pediatri

*Grazie per*
*la vostra attenzione*
*alla storia che*
*vi ha raccontato*
*mio nonno.*

*Mia Charlize Powell*