
# "Attilio Boner"

# "Le più recenti evidenze scientifiche in Pediatria"

# What is New in General Pediatrics, Allergic & Respiratory Diseases 2019 ?

**Attilio Boner**
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- ✓ **General Pediatrics**
- ✓ Food Allergy
- ✓ Atopic Dermatitis
- ✓ Asthma
- ✓ Anaphylaxis
- ✓ Infectious Respiratory Diseases

# Healthy Child

Healthy Child Programme (HCP)

## Paediatricians parents-child interactions

fimp Federazione Italiana Medici Pediatri

SOCIETÀ ITALIANA DI PEDIATRIA

SIN Società Italiana di Neonatologia

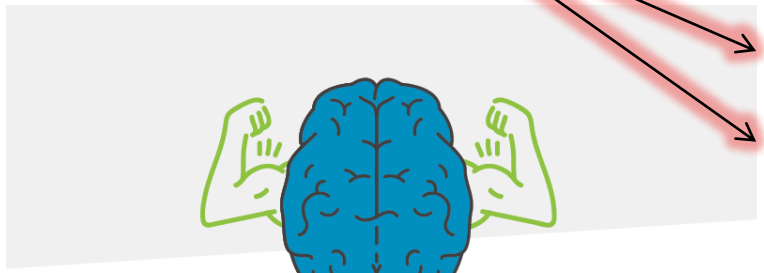
SICuPP Società Italiana delle Cure Primarie Pediatriche

Società Italiana di Pediatria Preventiva e Sociale - SIPPS

# The Impact of Physical Activity on Brain Structure and Function in Youth: A Systematic Review.

*Valkenborghs SR, Pediatrics. 2019 Oct;144(4). pii: e20184032*

Many children and adolescents are not sufficiently active to accrue:



the extensive

- cardiovascular,
- metabolic,


- musculoskeletal,

- mental health

benefits of physical activity.


- *Janssen I, Leblanc AG. Systematic review of the health benefits of physical activity and fitness in school-aged children and youth. Int J Behav Nutr Phys Act. 2010;7(1):40*

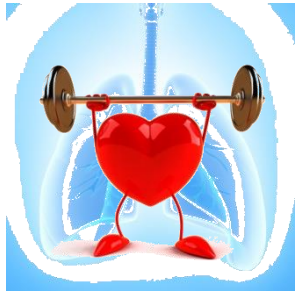
- *Hallal PC, Andersen LB, Bull FC, et al; Lancet Physical Activity Series Working Group. Global physical activity levels: surveillance progress, pitfalls, and prospects. Lancet. 2012;380(9838):247–257*

# The Impact of Physical Activity on Brain Structure and Function in Youth: A Systematic Review.

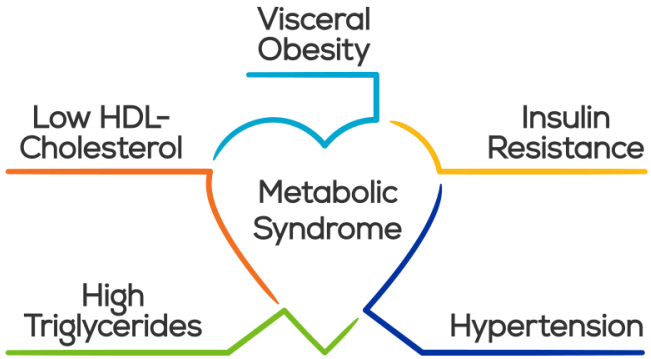
*Valkenborghs SR, Pediatrics. 2019 Oct;144(4). pii: e20184032*

Habitual physical activity is associated with a variety of health-related fitness traits:

- cardiorespiratory,
- morphologic,
- muscular,
- motor,
- metabolic,



- *Lang JJ, Tomkinson GR, Janssen I, et al. Making a case for cardiorespiratory fitness surveillance among children and youth. Exerc Sport Sci Rev. 2018;46(2):66-75*




**Six Components of Fitness Related to Motor Skills**

1. Agility
2. Balance
3. Coordination
4. Power
5. Speed
6. Reaction time

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Habitual physical activity is associated with a variety of health-related fitness traits:

emerging evidence suggests that participation in physical activity and improving physical fitness

may enhance cognitive health across the life span.


- *Biddle SJ, Asare M. Physical activity and mental health in children and adolescents: a review of reviews. Br J Sports Med. 2011;45(11):886–895*
- *Esteban-Cornejo I, Tejero-Gonzalez CM, Sallis JF, Veiga OL. Physical activity and cognition in adolescents: a systematic review. J Sci Med Sport. 2015;18(5):534–539*
- *Donnelly JE, Hillman CH, Castelli D, et al. Physical activity, fitness, cognitive function, and academic achievement in children: a systematic review. Med Sci Sports Exerc. 2016;48(6):1197–1222*
- *Ruiz-Ariza A, Grao-Cruces A, de Loureiro NEM, Martínez-López EJ. Influence of physical fitness on cognitive and academic performance in adolescents:a systematic review from 2005–2015. Int Rev Sport Exerc Psychol. 2017;10(1): 108–133*
- *Costigan SA, Eather N, Plotnikoff RC, Hillman CH, Lubans DR. High-intensity interval training for cognitive and mental health in adolescents. Med Sci Sports Exerc. 2016;48(10):1985–1993*
- *Lubans DR, Smith JJ, Morgan PJ, et al. Mediators of psychological well-being in adolescent boys. J Adolesc Health. 2016;58(2):230–236*

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Physical activity and cognition in adolescents: a systematic


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Specifically,
acute physical activity
can enhance children's

- attention and
- on-task behavior

in the classroom

- *Álvarez-Bueno C, Pesce C, Cavero- Redondo I, et al. Academic achievement and physical activity: a meta-analysis. Pediatrics. 2017;140(6):e20171498*

- *de Greeff JW, Bosker RJ, Oosterlaan J, Visscher C, Hartman E. Effects of physical activity on executive functions, attention and academic performance in preadolescent children: a metaanalysis. J Sci Med Sport. 2018;21(5): 501–507*

- *Daly-Smith AJ, Zwolinsky S, McKenna J, et al. Systematic review of acute physically active learning and classroom movement breaks on children's physical activity, cognition, academic performance and classroom behaviour: understanding critical design features. BMJ Open Sport Exerc Med. 2018;4(1):e000341*

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experimental studies have demonstrated longer-term benefits of physical activity for executive functions:

- attention and
- academic performance




- *de Greeff JW, Bosker RJ, Oosterlaan J, Visscher C, Hartman E. Effects of physical activity on executive functions, attention and academic performance in preadolescent children: a metaanalysis. J Sci Med Sport. 2018;21(5): 501–507.*

- *Marques A, Santos DA, Hillman CH, Sardinha LB. How does academic achievement relate to cardiorespiratory fitness, self-reported physical activity and objectively reported physical activity: a systematic review in children and adolescents aged 6-18 years. Br J Sports Med. 2018; 52(16):1039*

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Higher levels of cardiorespiratory fitness

positively associated with young people's academic achievement.

•*Marques A, Santos DA, Hillman CH, Sardinha LB. How does academic achievement relate to cardiorespiratory fitness, self-reported physical activity and objectively reported physical activity: a systematic review in children and adolescents aged 6-18 years. Br J Sports Med. 2018; 52(16):1039*

awareness of the positive effects of physical activity on cognitive and/or academic outcomes has increased rapidly in the last 5 years,


Mechanisms

*Lubans D, Richards J, Hillman C, et al. Physical activity for cognitive and mental health in youth: a systematic review of mechanisms. Pediatrics. 2016;138(3):e20161642*

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Animal studies have shown molecular effects including:

*Fernandes J, Physical exercise as an epigenetic modulator of brain plasticity and cognition. Neurosci Biobehav Rev. 2017; 80:443–456*

*Lista I, Biological mechanisms of physical activity in preventing cognitive decline. Cell Mol Neurobiol. 2010;30(4):493–503*

*Vaynman S, Hippocampal BDNF mediates the efficacy of exercise on synaptic plasticity and cognition. Eur J Neurosci. 2004;20:2580–2590*

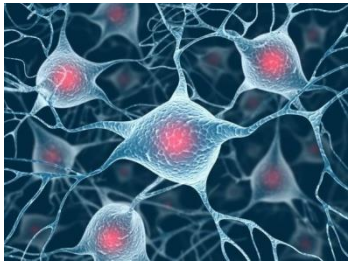
*Rich B, Skeletal myofiber vascular endothelial growth factor is required for the exercise traininginduced increase in dentate gyrus neuronal precursor cells. J Physiol. 2017;595(17):5931–5943*

- epigenetic regulation of gene expression

related changes in concentrations of factors such as brain-derived neurotrophic factor (BDNF) and vascular endothelial growth factor,

**brain plasticity**

- cellular changes such as
  - neurogenesis,
  - synaptogenesis, and
  - angiogenesis.



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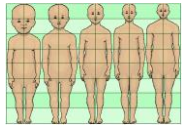
There is now empirical evidence that the same molecular effects exist in humans eg:



- increases in BDNF

and

- vascular endothelial growth factor

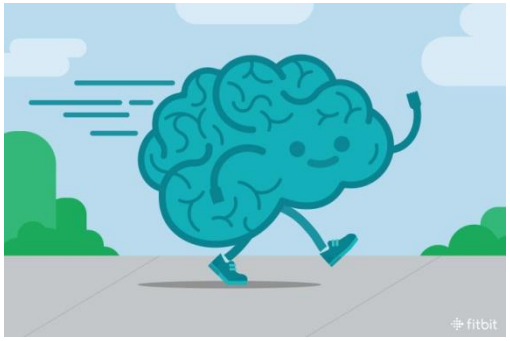
positive effects of physical activity on cognitive health.

- *Hashimoto T, Maintained exercise-enhanced brain executive function related to cerebral lactate metabolism in men. FASEB J. 2018;32(3):1417–1427*

- *Nascimento CM, Physical exercise in MCI elderly promotes reduction of proinflammatory cytokines and improvements on cognition and BDNF peripheral levels. Curr Alzheimer Res. 2014;11(8):799–805*

- *Leckie RL, BDNF mediates improvements in executive function following a 1-year exercise intervention. Front Hum Neurosci. 2014;8:985*

- *Voss MW, Neurobiological markers of exerciserelated brain plasticity in older adults. Brain Behav Immun. 2013;28:90–99*



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In addition,
a randomized controlled trial
in older adults demonstrated that

*Erickson KI, Exercise training increases size of hippocampus and improves memory.Proc Natl Acad Sci USA. 2011;108(7):3017–3022*

12 months of
aerobic exercise

increases in BDNF


- increased hippocampal volume
- improved memory

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studies employing MRI techniques

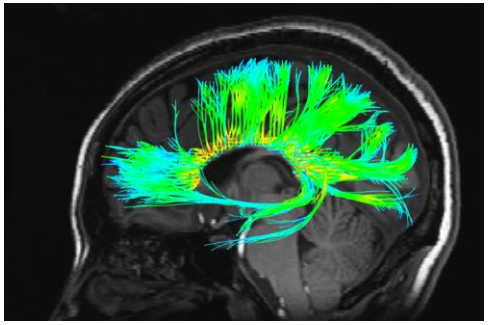
have linked physical activity with brain regions and networks

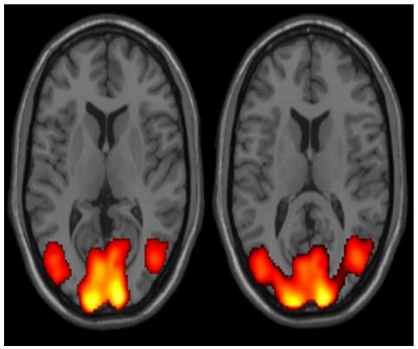
integral to
- cognitive function

and
- scholastic performance

in children and adolescents.

- *Chaddock-Heyman L, Scholastic performance and functional connectivity of brain networks in children. PLoS One. 2018; 13(1):e0190073*
- *Talukdar T, Aerobic fitness explains individual differences in the functional brain connectome of healthy young adults. Cereb Cortex. 2018;28(10):3600–3609*
- *Chaddock L, A neuroimaging investigation of the association between aerobic fitness, hippocampal volume, and memory performance in preadolescent children. Brain Res. 2010;1358:172–183*
- *Bunketorp Käll L, Effects of a curricular physical activity intervention on children's school performance, wellness, and brain development. J Sch Health. 2015;85(10):704–713*





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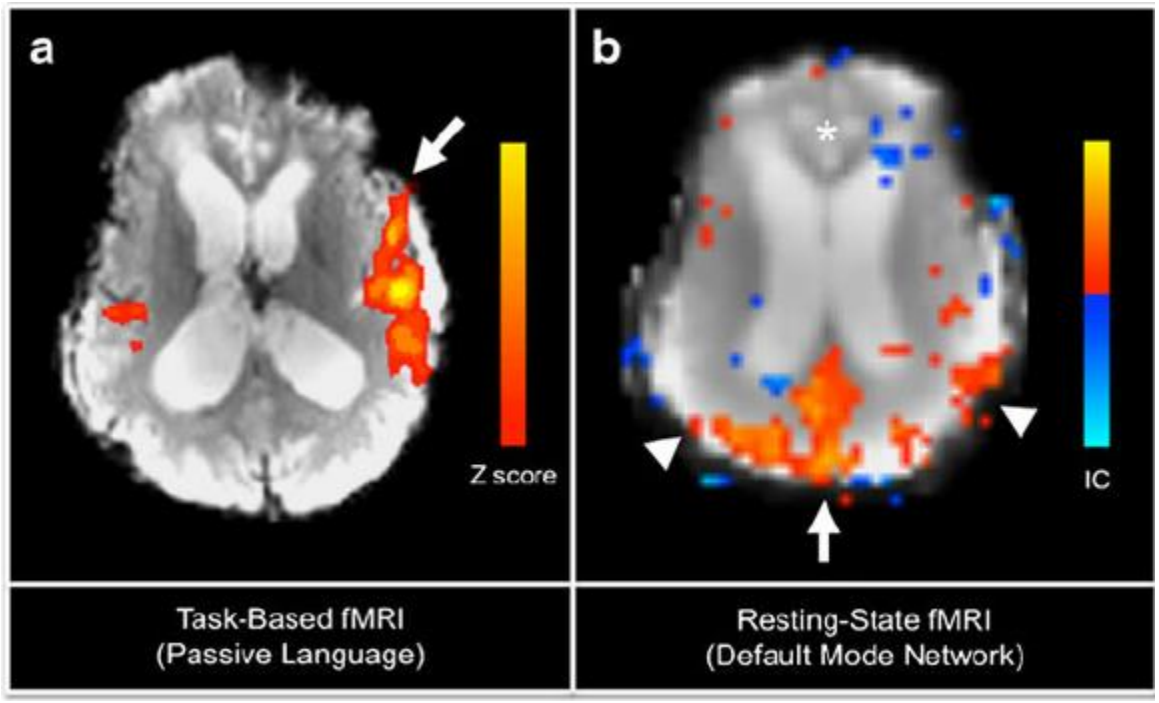
✓9 studies
- task-based functional MRI [*n* = 4],
- diffusion tensor imaging [*n* = 3],
- arterial spin labeling [*n* = 1],
- resting-state functional MRI [*n* = 1]

✓Children aged 8.7 to 10.2 years



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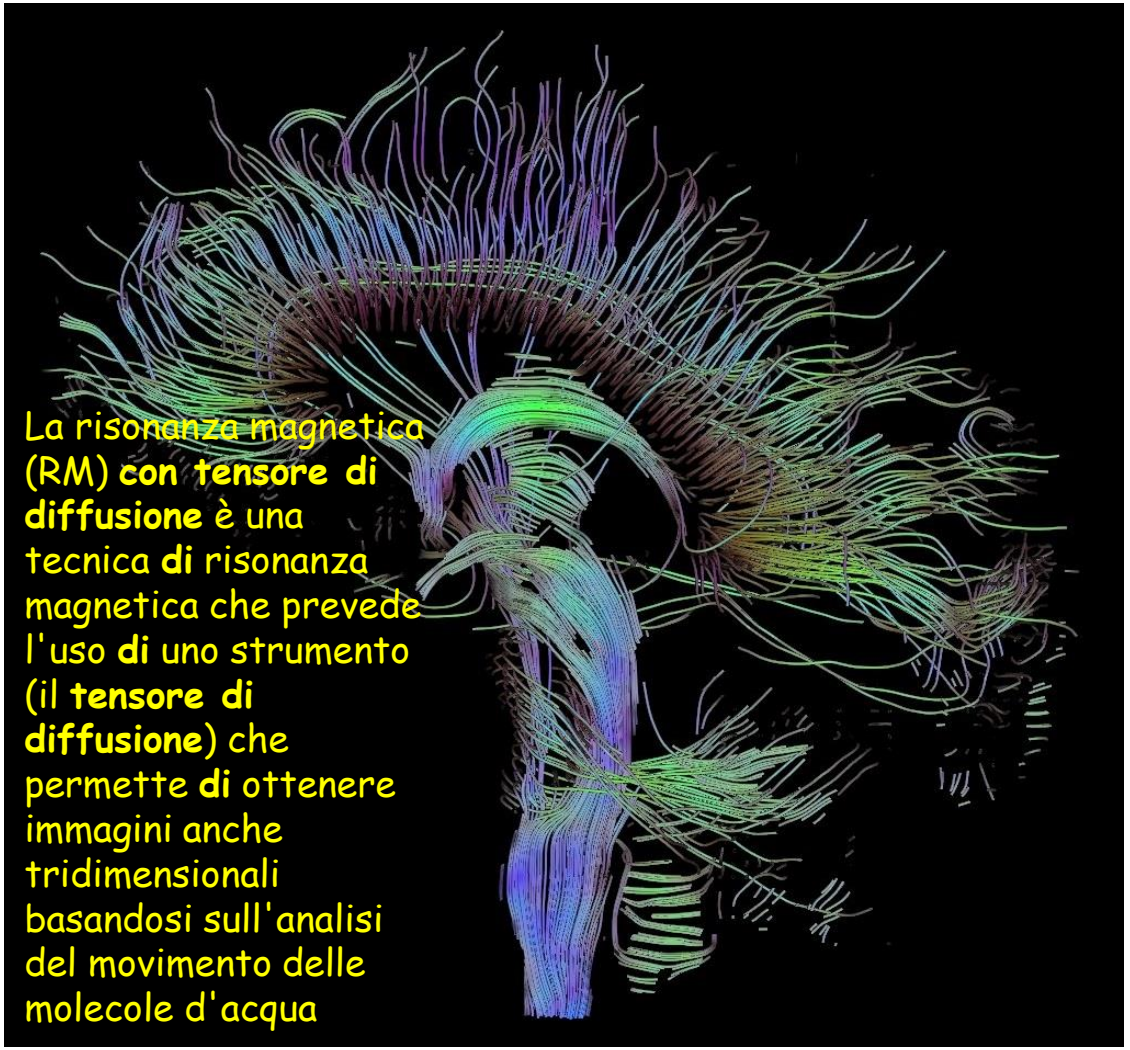

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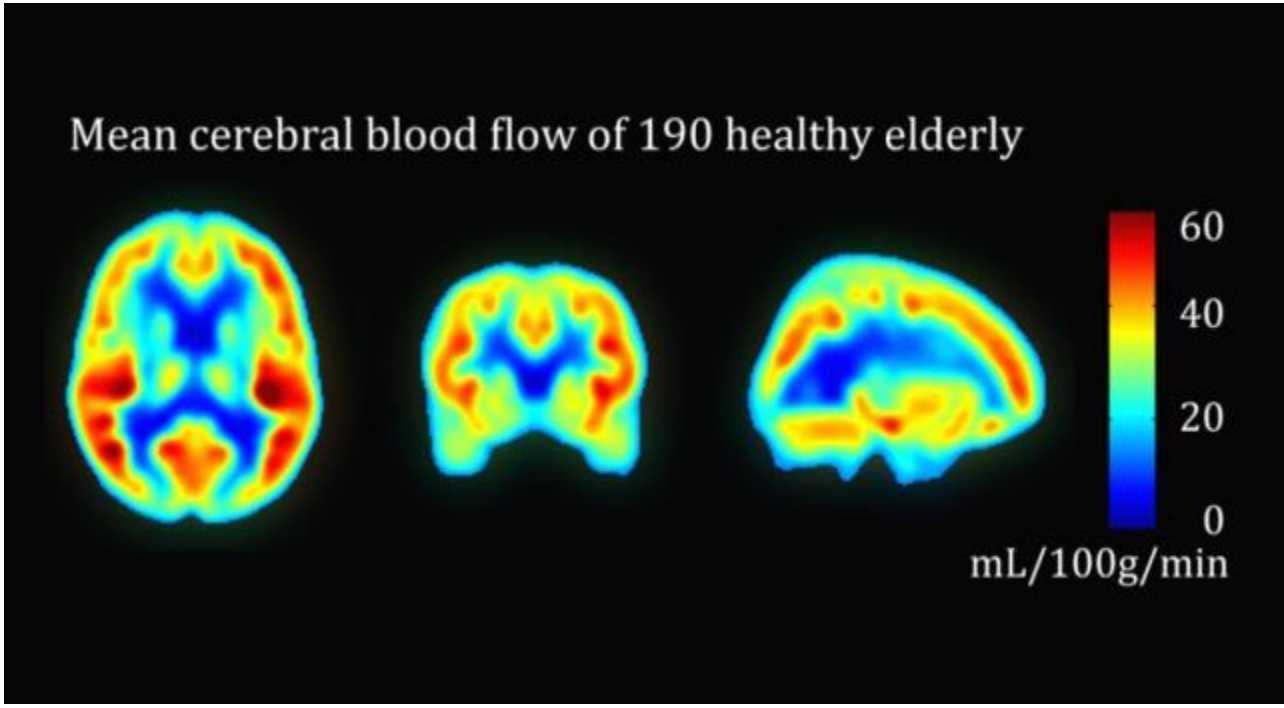


L'etichettatura delle rotazioni arteriose, nota anche come etichettatura degli spin arteriosi, è una tecnica di imaging a risonanza magnetica utilizzata per quantificare la perfusione del sangue cerebrale etichettando l'acqua del sangue mentre scorre attraverso il cervello.

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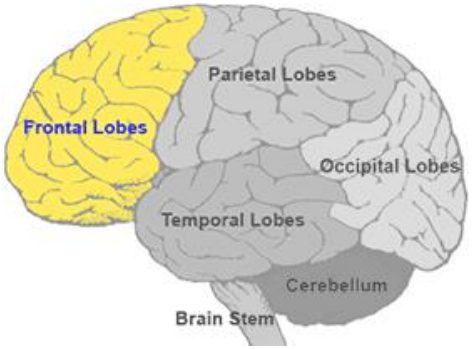
The **frontal lobes** are involved in motor **function**,

- problem solving,
- spontaneity,
- memory,
- language,
- initiation,
- judgement,
- impulse control, and
- social and sexual behavior

Effects were reported for 12 regions, including




- frontal lobe ($n$ = 3),
- parietal lobe ($n$ = 3),
- anterior cingulate cortex ($n$ = 2),
- hippocampus ($n$ = 1), and
- several white matter tracts and functional networks

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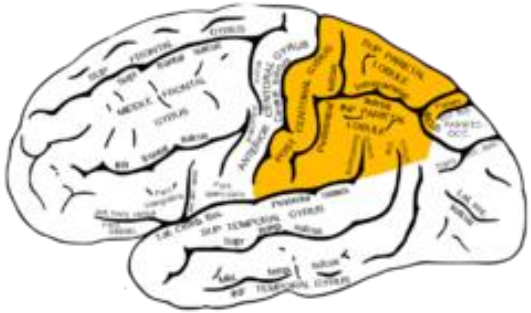
The **parietal lobe functions** in

- processing sensory information regarding the location of parts of the body as well as
- interpreting visual information and
- processing language and mathematics.

Effects were reported for 12 regions, including



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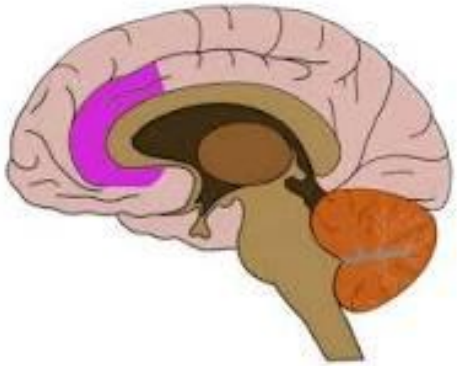
**Anterior cingulate cortex** (ACC) in purple.

front-most portion of the **cingulate cortex**, the **anterior cingulate cortex** (or ACC) has been implicated in several complex cognitive **functions**, such as
empathy,
impulse control,
emotion, and
decision-making.

Effects were reported for 12 regions, including



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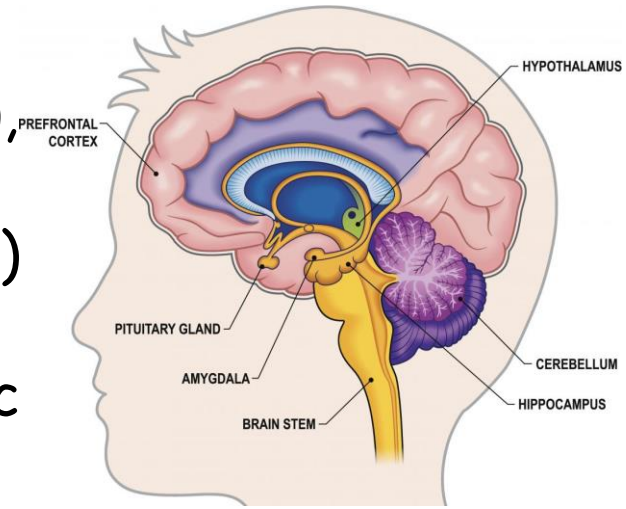
The **hippocampus** is a small, curved formation in the brain that plays an important **role** in the limbic system.

The **hippocampus** is involved in the formation of **new memories** and is also associated with **learning** and **emotions**

Effects were reported for 12 regions, including

- frontal lobe (*n* = 3),
- parietal lobe (*n* = 3)
- anterior cingulate c
- **hippocampus** (*n* = 1), and
- several white matter tracts and functional networks



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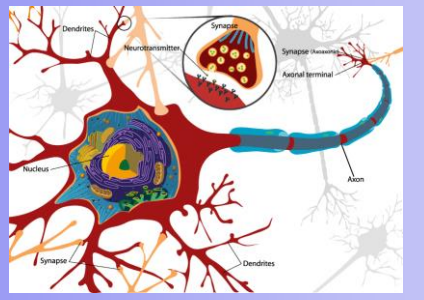
**White matter** is composed of bundles, which **connect various gray matter areas** (the locations of nerve cell bodies) **of the brain to each other**, and carry nerve impulses between neurons.

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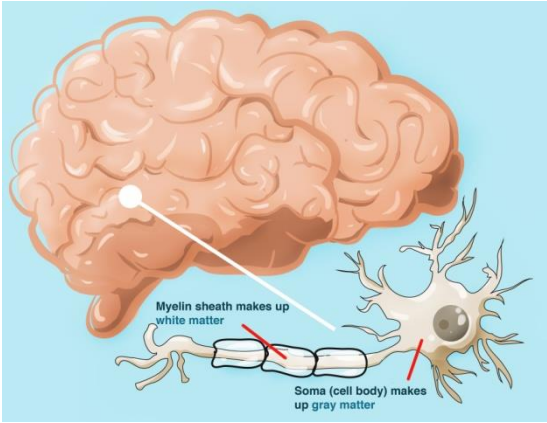


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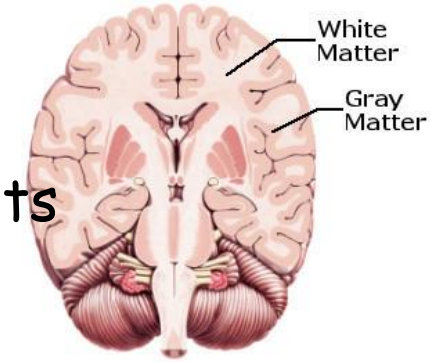
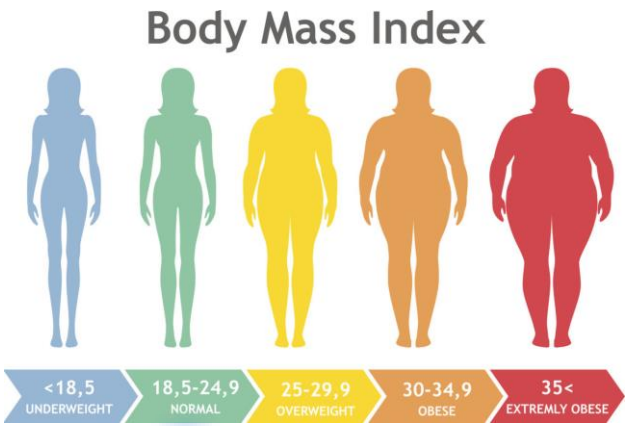
- **several white matter** tracts and functional networks



# General pediatrics
# Obesity

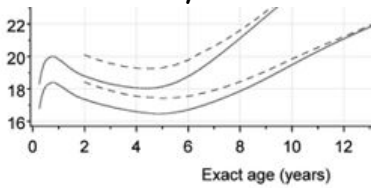


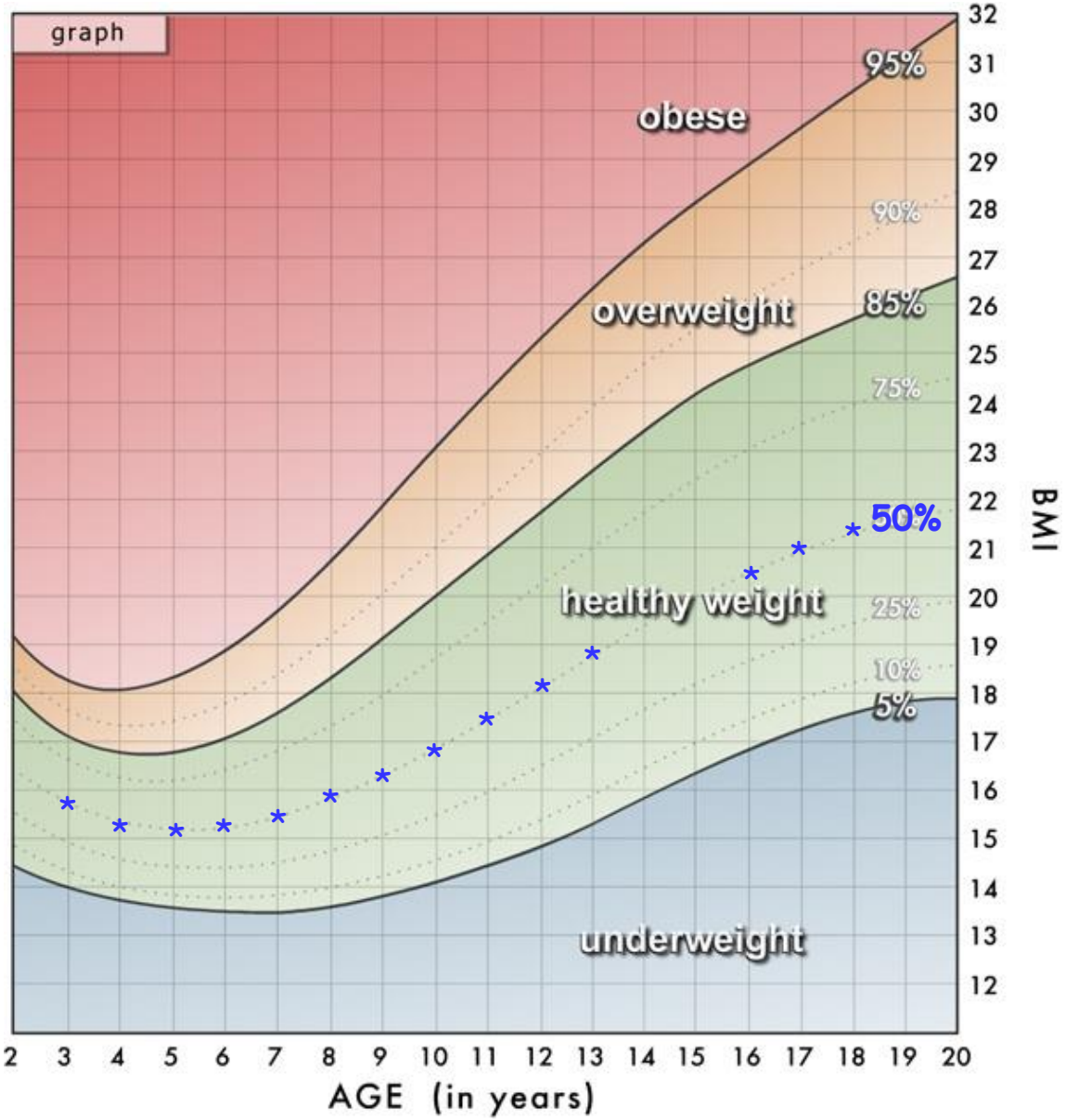

Normal BMI
= 15-20
in children
and adolescents

**Body Mass Index Calculation**

$$BMI = \frac{\text{weight (kg)}}{\text{height (m)}^2}$$

BMI in the first 2 years



# Early excessive growth with distinct seasonality in preschool obesity.

*Isojima T, Arch Dis Child. 2019 Jan;104(1):53-57.*

**OBJECTIVES:**

- Healthy-weight children tend:
  - to gain weight during winter
  - to lose weight during summer.

- However, overweight elementary school children have shown accelerated summertime weight gain.

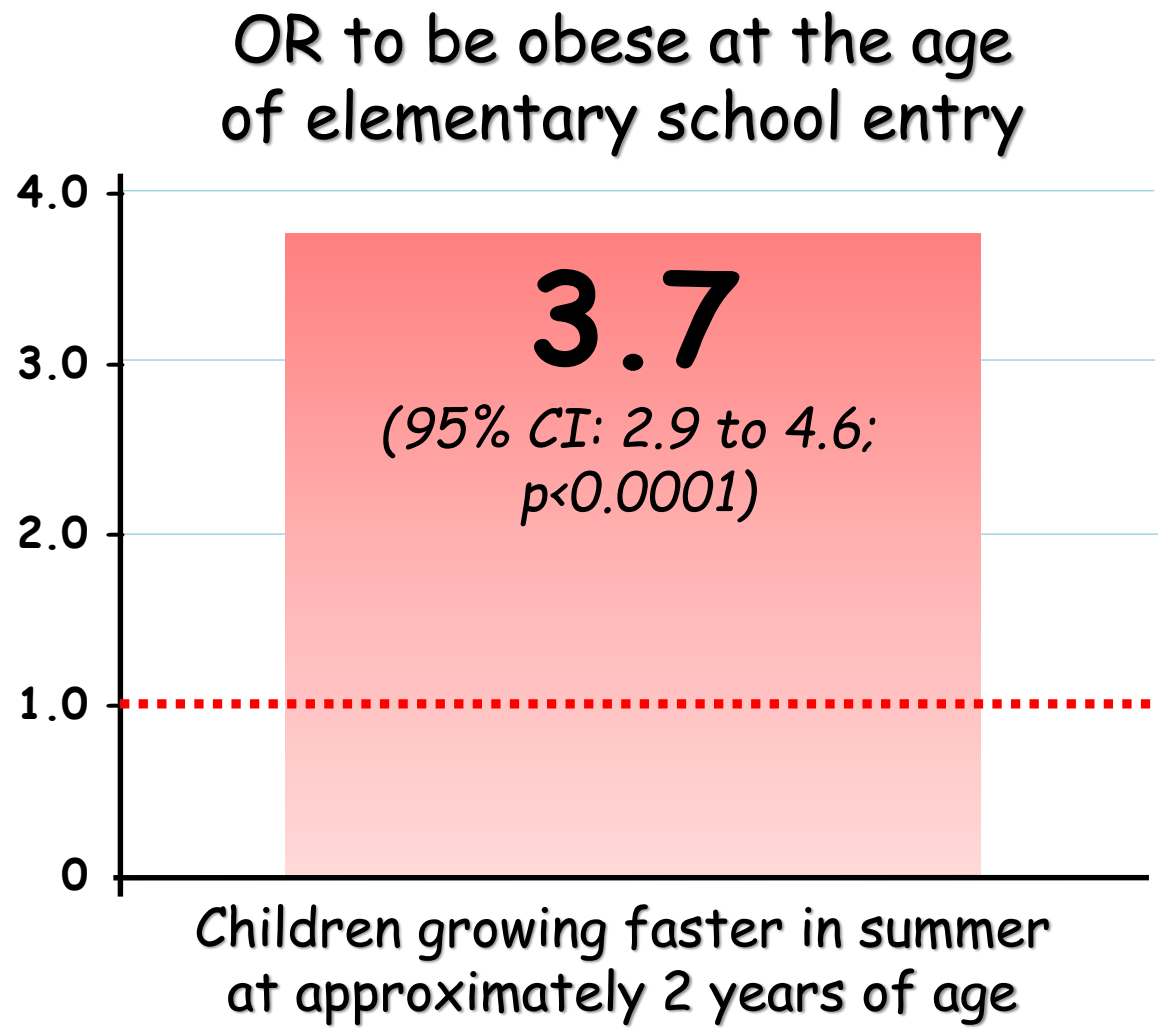

- Whether this seasonal growth variation occurs during preschool period is of substantial interest.

# Early excessive growth with distinct seasonality in preschool obesity.

*Isojima T, Arch Dis Child. 2019 Jan;104(1):53-57.*

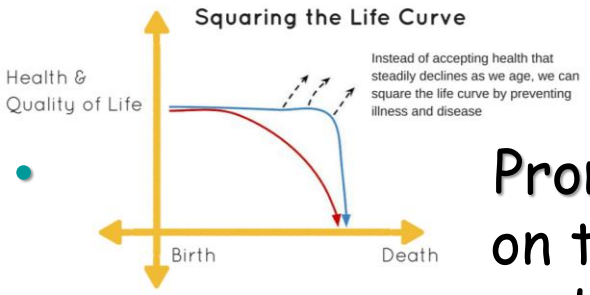
✓retrospective cohort of nursery school children.

✓8 consecutive sets of longitudinal measurements on height and weight obtained from 15 259 preschool children



# Squaring the Curve of Cardiovascular Health From the Beginning of Life.

*Perak AM, Pediatrics. 2018 Apr;141(4). pii: e20172075.*




- Promoting cardiovascular health (CVH) depends on the simultaneous presence of 4 ideal health behaviors and 3 ideal health factors, collectively known as:

"Life's Simple 7":

(1) healthy diet,
(2) optimal physical activity,
(3) nonsmoking,
(4) healthy BMI,


and

➢optimal levels of (5) blood pressure, (6) cholesterol, and (7) glucose.

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ideal CVH is exceedingly rare in adults:
<1% of US adults (age ≥20 years) have all 7 and
just 5% have 6 CVH metrics at ideal levels.

"Life's Simple 7":

(1) healthy diet,
(2) optimal physical activity,
(3) nonsmoking,
(4) healthy BMI,


and

- optimal levels of (5) blood pressure, (6) cholesterol, and (7) glucose.

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- Primordial prevention, or preventing the development of risk factors rather than waiting to prevent clinical events once risk factors develop, is key to to extend the "health span" of the current generation of children by squaring that CVH curve.

- Following beneficial lifestyle patterns is more difficult in adulthood than in childhood, that moving from harmful to protective lifestyle behaviors is harder than maintaining protective patterns.

- To achieve this, we need the 3 M's: we must be able to:
Measure,
Monitor, and
Modify
CVH at the beginning of the life course.

# Squaring the Curve of Cardiovascular Health From the Beginning of Life.

*Perak AM, Pediatrics. 2018 Apr;141(4). pii: e20172075.*

| | Ideal = 2 Points | Intermediate = 1 Point | Poor = 0 Points |
|---|---|---|---|
| Current smoking | Never tried; never smoked whole cigarette | — | Tried in the previous 30 d |
| BMI | <85th percentile (18 - < 20) | 85th–95th percentile | >95th percentile |
| Physical activity | ≥60 min moderate or vigorous intensity each day | >0 and <60 min of moderate or vigorous intensity each day | None |
| Healthy diet* | 4–5 components | 2–3 components | 0–1 components |
| Total cholesterol | <170 mg/dL | 170–199 mg/dL | ≥200 mg/dL |
| Blood pressure | <90th percentile | 90th–95th percentile | >95th percentile |
| Fasting plasma glucose | <100 mg/dL | 100–125 mg/dL | ≥126 mg/dL |

Adapted from Lloyd-Jones DM, Hong Y, Labarthe D, et al; American Heart Association Strategic Planning Task Force and Statistics Committee. Defining and settling national goals for cardiovascular health promotion and disease reduction: the American Heart Association's strategic Impact Goal through 2020 and beyond. Circulation. 2010;121(4):598; and Steinberger J, Daniels SR, Hagberg N, et al; American Heart Association Atherosclerosis, Hypertension, and Obesity in the Young Committee of the Council on Cardiovascular Disease in the Young; Council on Cardiovascular and Stroke Nursing; Council on Epidemiology and Prevention; Council on Functional Genomics and Translational Biology; and Stroke Council. Cardiovascular health promotion in children: challenges and opportunities for 2020 and beyond: a scientific statement from the American Heart Association. *Circulation.* 2016;134(12):e238 where further details can be found. —, not applicable.

*The 5 healthy diet components include the following: adequate daily intakes of (1) fruits and vegetables, (2) fish, and (3) fiber-rich whole grains, and limited intakes of (4) sodium and (5) sugar-sweetened beverages, all scaled for caloric intake.[1]

After infancy, measurement of Life's Simple 7 is generally straightforward and applicable to a broad range of pediatric patients. Each metric can be characterized as poor, intermediate, or ideal on a 0-to-2-point scale to provide a summary score of 0 to 14 points that is readily understood by families.

# General Pediatrics

## Stress

### Stress in Childhood

Stress is a natural & inevitable part of childhood, but the TYPE of stress can make a difference in the impact on a child's brain & body.

"STRESS is a mental, physical or biochemical response to a perceived threat or demand"

**Positive Stress**
Mild stess in the context of good attachment

- Temporary, mild elevation in stress hormones & brief increase in heart rate
- No buffering support necessary
- Increased **RESILIENCE** and confidence
  Development of coping skills

**Tolerable Stress**
Serious, temporary stress, buffeted by supportive relationships

- More severe, continuing cardiovascular and hormonal response
- Presence of buffering caring adult
- Adaption and recovery with some possibility for physical/emotional damage

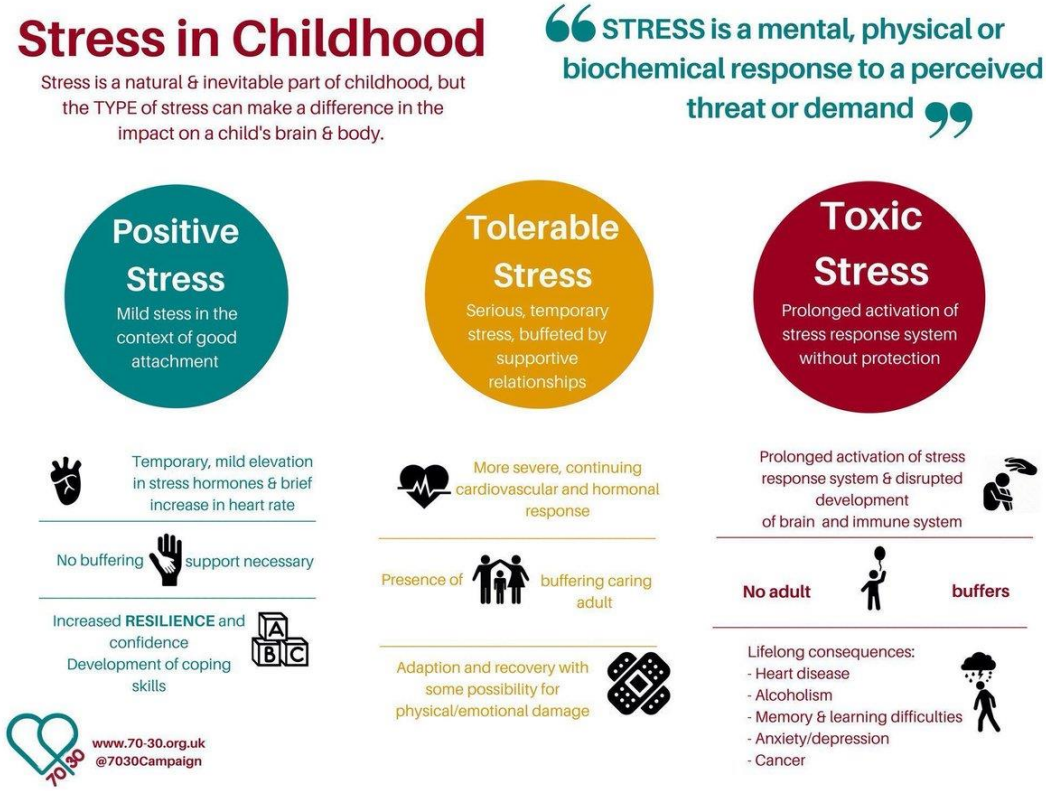
**Toxic Stress**
Prolonged activation of stress response system without protection

- Prolonged activation of stress response system & disrupted development of brain and immune system
- No adult buffers
- Lifelong consequences:
  - Heart disease
  - Alcoholism
  - Memory & learning difficulties
  - Anxiety/depression
  - Cancer

www.70-30.org.uk
@7030Campaign

# Screening for Toxic Stress Risk Factors at Well-Child Visits: The Addressing Social Key Questions for Health Study *Selvaraj K, J Pediatr. 2019 Feb;205:244-249.e4.*

- Toxic stress (TS), is defined as a stress that is strong, frequent, and/or prolonged without sufficient protective factors.




- Both adverse childhood experiences (ACEs), which include abuse, neglect, and household dysfunction, and unmet social needs associated with poverty (eg, food insecurity) increase the chance of developing the long-term biologic effects of TS, thereby making children vulnerable to many negative health outcomes in childhood and adulthood, including mental health disorders, obesity, cardiovascular disease, and early death.

# Screening for Toxic Stress Risk Factors at Well-Child Visits: The Addressing Social Key Questions for Health Study *Selvaraj K, J Pediatr. 2019 Feb;205:244-249.e4.*

- To mitigate these detrimental consequences of **TS**, detection and management of **TS** risk factors are emerging as components of pediatric primary care.

- The American Academy of Pediatrics recommends that medical homes screen for "risk factors within social determinants of health during patient encounters" and "precipitants of TS that are common in their particular practices."

- A significant barrier to screening is the lack of a screening tool for TS risk factors that includes both adverse childhood experiences (ACEs) and unmet social needs.

# Screening for Toxic Stress Risk Factors at Well-Child Visits: The Addressing Social Key Questions for Health Study *Selvaraj K, J Pediatr. 2019 Feb;205:244-249.e4.*

- To mitigate these detrimental consequences of **TS**, detection and management of **TS** risk f
of pedi

To address this gap, our group created the Addressing Social Key Questions for Health Questionnaire (ASK Tool), a 13-item screening tool for ACEs, unmet social needs, and resilience.

- A significant barrier to screening is the lack of a screening tool for TS risk factors that includes both adverse childhood experiences (ACEs) and unmet social needs.

# Screening for Toxic Stress Risk Factors at Well-Child Visits: The Addressing Social Key Questions for Health Study *Selvaraj K, J Pediatr. 2019 Feb;205:244-249.e4.*

**ASK Questions for HEALTH**

We want to make sure that you are connected with all the community services that you need. Most of these services are free. We ask ***all of our families*** to answer the following questions. Only members of our care team will be reviewing the answers to help connect you to the right services.

Passing the General Educational Development (**GED**) tests can result in a credential that's commonly considered **equivalent** to a **high school diploma**.

1. Do you have a high school degree or GED?
   ☐YES
   ☐NO — *Would you like help with this?* — No O — Yes, but not today. O — Yes, ***today.*** O

2. Do you need a job?
   ☐YES — *Would you like help with this?* — No O — Yes, but not today. O — Yes, ***today.*** O
   ☐NO

3. Do you need childcare for your child? (e.g. daycare, afterschool care, etc.)?
   ☐YES — *Would you like help with this?* — No O — Yes, but not today. O — Yes, ***today.*** O
   ☐NO

4. Do you always have enough food for your family?
   ☐YES
   ☐NO — *Would you like help with this?* — No O — Yes, but not today. O — Yes, ***today.*** O

5. In the last 12 months, have you been behind on your electricity, heating, or housing bill?
   ☐YES — *Would you like help with this?* — No O — Yes, but not today. O — Yes, ***today.*** O
   ☐NO

6. Do you need legal advice to help with any problems?
   ☐YES — *Would you like help with this?* — No O — Yes, but not today. O — Yes, ***today.*** O
   ☐NO

Adapted from WE CARE survey (Garg et al, 2007)

Turn page over

*FOR PROVIDER USE ONLY:* *Last updated 07.20.2016*

Person responding to survey (check all that apply):

Mother ☐ Father ☐ Foster parent ☐ Legal Guardian ☐ Patient ☐

Primary Language:

English ☐ Spanish ☐ Other: _____ ☐

Stress in childhood can harm our health. There are ways to stop stress from being so harmful. Our clinic can connect you to services that can help you and your child. You do not have to answer all the questions. **When complete, please hand this questionnaire to your child's doctor.**

**PARENT** Please check box if this happened to ***you*** as a child.

7. Has your child ever lost an important caregiver? (e.g. due to death, divorce, incarceration, deportation, abandonment, etc.)
   ☐YES — *Would you like help with this?* — No O — Yes, but not today. O — Yes, ***today.*** O
   ☐NO — ☐

8. Have you or anyone in your child's home ever felt sad most days or depressed, had mental illness (including drug and alcohol abuse), or attempted suicide?
   ☐YES — *Would you like help with this?* — No O — Yes, but not today. O — Yes, ***today.*** O — ☐
   ☐NO

9. Has your child ever been bullied or bullied someone?
   ☐YES — *Would you like help with this?* — No O — Yes, but not today. O — Yes, ***today.*** O — ☐
   ☐NO

10. Has your child ever seen someone in their home or neighborhood beaten up, shot at, or killed?
    ☐YES — *Would you like help with this?* — No O — Yes, but not today. O — Yes, ***today.*** O — ☐
    ☐NO

11. Do you worry that your child may have been physically abused?
    ☐YES ☐NO — ☐

12. Do you worry that your child may have been sexually abused?
    ☐YES ☐NO — ☐

13. Is there someone who can make your child feel better when they are feeling sad?
    ☐YES ☐NO

*FOR PROVIDER USE ONLY:* *Last updated 07.20.2016*

Please check box for each question for which resources/referrals were given

| 1 | 2 | 3 | 4 | 5 | 6 | 7 | 8 | 9 | 10 | 11 | 12 | 13 |
|---|---|---|---|---|---|---|---|---|---|---|---|---|
| | | | | | | | | | | | | |

MD Initials: x_____ Were symptoms of toxic stress/adverse childhood experiences assessed in this child? [ ] Yes [ ] No [ ] N/A

# Screening for Toxic Stress Risk Factors at Well-Child Visits: The Addressing Social Key Questions for Health Study *Selvaraj K, J Pediatr. 2019 Feb;205:244-249.e4.*

✓Addressing Social Key Questions for Health Questionnaire, a 13-question screen of adverse childhood experiences (ACEs) and unmet social needs.

✓Parents/guardians of children 0-17 years of age received this questionnaire at well-child visits at 4 academic clinics from August 1, 2016 to February 28, 2017. (2569 families in Chicago)


✓Providers reviewed the tool and referred to community resources as needed.

➢Of 2569 families completing the Addressing Social Key Questions for Health Questionnaire,

- 49% reported ≥1 stressor;
- 6% had ≥1 adverse childhood experiences;
- 47% had ≥1 unmet social need.

# Screening for Toxic Stress Risk Factors at Well-Child Visits: The Addressing Social Key Questions for Health Study *Selvaraj K, J Pediatr. 2019 Feb;205:244-249.e4.*

✓Addressing
for H
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✓Prov
referred
as needed.

Universal screening for toxic stress risk factors in pediatric primary care improved identification and management of family needs.

Screening was feasible and acceptable to families.

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Addressin
for Healt

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•6% had ≥
experien

•47% had

# Healthy Child

Healthy Child Programme (HCP)

## Paediatricians & Society interactions

# Association of Reported Concern About Increasing Societal Discrimination With Adverse Behavioral Health Outcomes in Late Adolescence

*Leventhal AM, JAMA Pediatr 2018;172:924-933*

- Public expressions of resentment, discrimination, and hostility toward minority and disadvantaged populations have become increasingly prominent.

- The anti-social climate intensified during 2016 and 2017, when the Trump presidential campaign and administration released several statements and social policy proposals perceived by many as discriminatory.

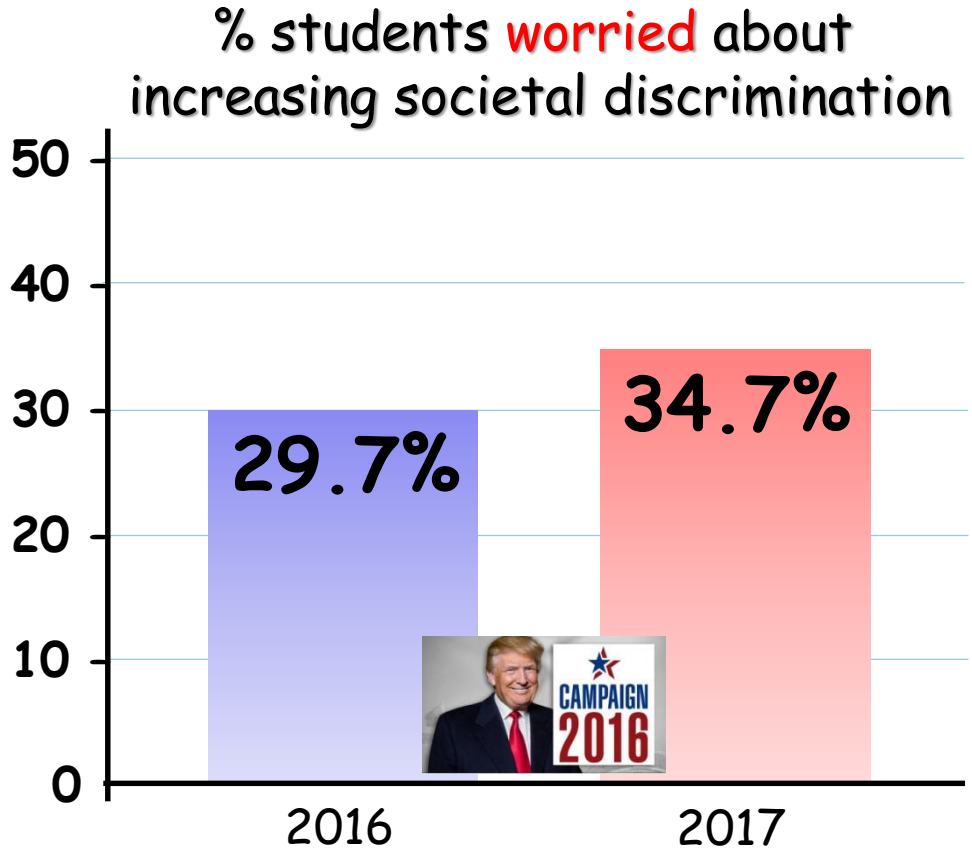

- Because polarizing societal events have historically been linked with stress and behavioral health problems, the ramifications of recent discrimination-associated societal events may be a public health concern, particularly for vulnerable populations, such as adolescents.

# Association of Reported Concern About Increasing Societal Discrimination With Adverse Behavioral Health Outcomes in Late Adolescence

*Leventhal AM, JAMA Pediatr 2018;172:924-933*

✓prospective cohort survey collected data at baseline, 2016 (11th grade), and at follow-up in 2017 (12th grade), at 10 high schools in Los Angeles

✓2572 students completed both surveys



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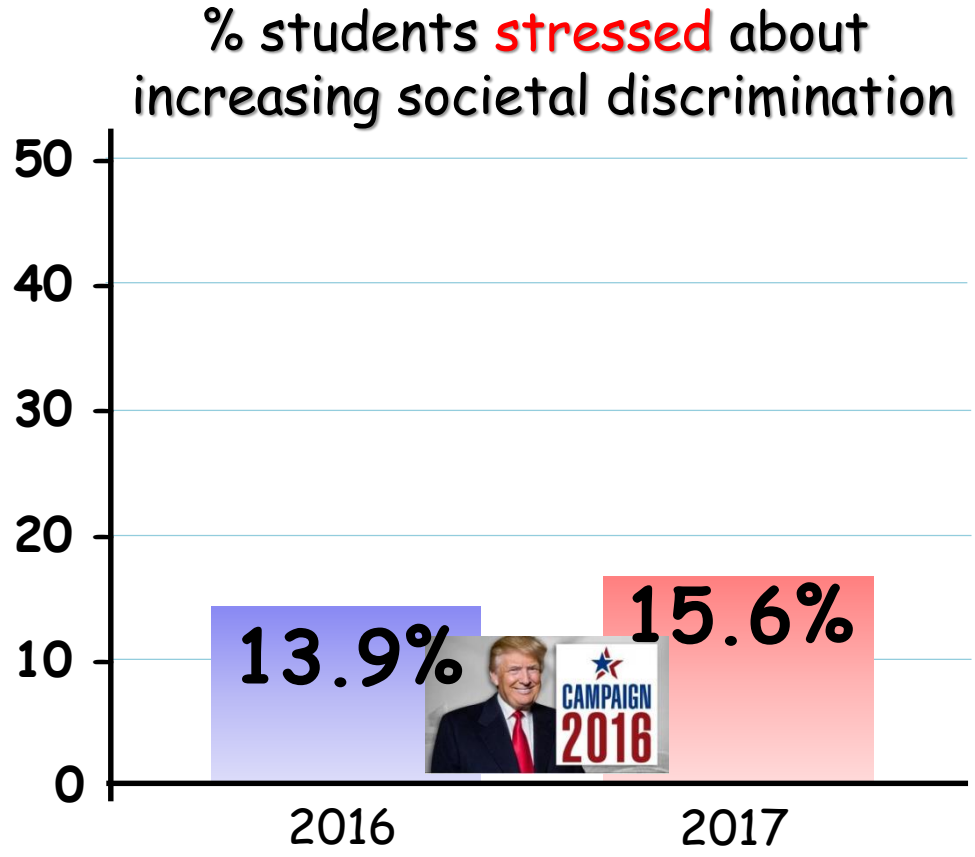


# Association of Reported Concern About Increasing Societal Discrimination With Adverse Behavioral Health Outcomes in Late Adolescence

*Leventhal AM, JAMA Pediatr 2018;172:924-933*

Each 1-SD increase on the societal discrimination concern composite in 2016 was associated with

- more days of past-month cigarette (IRR, 1.77; 95%CI, 1.42-2.20; *P < 0.001*),
- marijuana use (IRR, 1.13; 95%CI, 1.01-1.26; *P = 0.03*),
- alcohol use (IRR, 1.11; 95%CI, 1.02-1.21; *P = 0.01*),
- more substances used (IRR, 1.07; 95%CI, 1.01-1.17; *P = 0.04*),

and greater odds of

- Depression symptoms (OR, 1.11; 95%CI, 1.01-1.23; *P = 0.04*) and
- ADHD symptoms (OR, 1.12; 95%CI, 1.01-1.26; P = *0.04*) in 2017.

# Association of Reported Concern About Increasing Societal Discrimination With Adverse Behavioral Health Outcomes in Late Adolescence

*Leventhal AM, JAMA Pediatr 2018;172:924-933*

## CONCLUSIONS AND RELEVANCE


- Concern over societal discrimination was common among youths in Los Angeles in 2016 and was associated with behavioral health problems 1 year later.

- Adolescents' behavioral responses to recent societal expressions of discrimination may warrant public health attention.

# Doctors Need to Speak Up More.

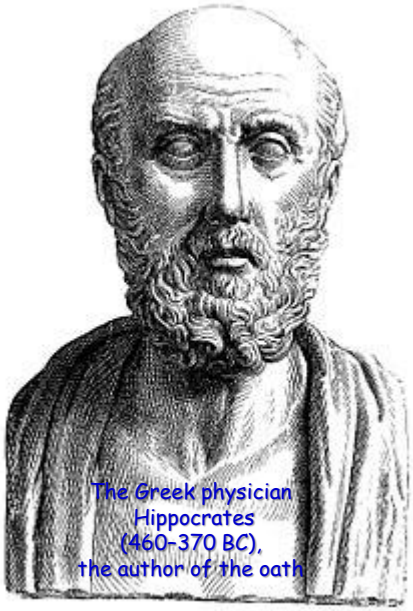
*McLaren JR, Pediatrics. 2019 Jan;143(1). pii: e20182503.*


- A version of the popular "stay in your lane" aproach, is that physicians and medical organizations should not comment on contemporary, hot-button issues such as:
  - immigration
  - nuclear disarmament,

  because these are outside of their fields of expertise and may harm their institutional credibility.


- However, what those advocates neglect to consider is that physicians are bound by an oath to protect the health of all humans, not just those in the examination room.

- It is our adherence to this pledge that opens the door for a broader recognition of the human experience and thus an extension of our "lane".

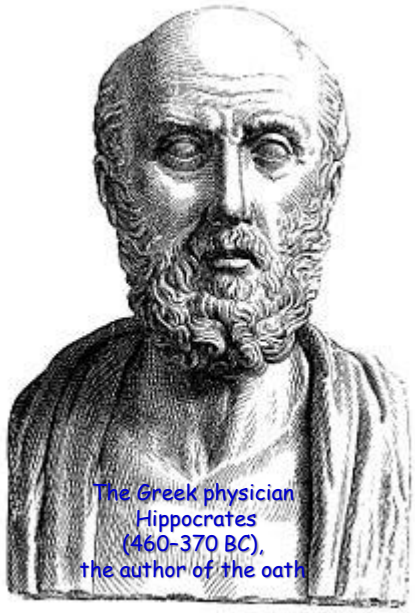


# Doctors Need to Speak Up More.

*McLaren JR, Pediatrics. 2019 Jan;143(1). pii: e20182503.*

*I will remember that I do not treat a fever chart, a cancerous growth, but a sick human being, whose illness may affect the person's family and economic stability.*

*My responsibility includes these related problems, if I am to care adequately for the sick.*




*I will prevent disease whenever I can, for prevention is preferable to cure.*

*I will remember that I remain a member of society, with special obligations to all my fellow human beings, those sound of mind and body as well as the infirm.*

# Doctors Need to Speak Up More.

*McLaren JR, Pediatrics. 2019 Jan;143(1). pii: e20182503.*

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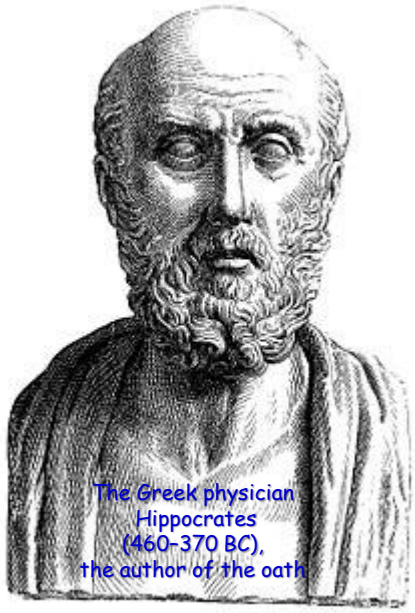



*I will prevent di[illegible] wh[illegible] le to cure.*

*I [illegible] ons to [illegible] inf[illegible]*

These words remind us to not just provide patients with the immediate services they need but to address the root causes of the problems they face.

# Doctors Need to Speak Up More.

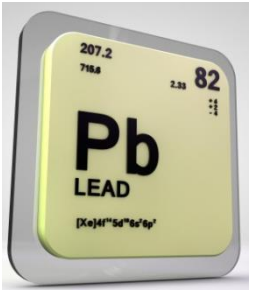
*McLaren JR, Pediatrics. 2019 Jan;143(1). pii: e20182503.*

- **Being on the front lines of patient care**, we are routinely exposed to the faces affected by modern ills, such as:
  - unemployment,
  - food insecurity,
  - drug addiction,
  - gun violence, and
  - racism;

understanding and addressing
these social determinants of health
are also
fundamental components of our vocation.

# Doctors Need to Speak Up More.

*McLaren JR, Pediatrics. 2019 Jan;143(1). pii: e20182503.*

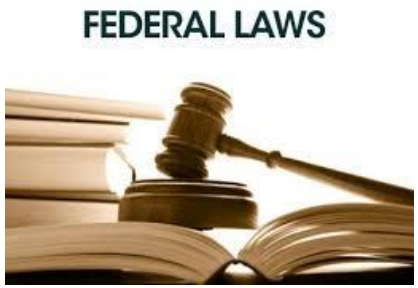



- In the late 1970s, for example, after examining a 3-year-old girl who was nearly comatose in his office, *Needleman and colleagues* made the connection between her illness and toxic levels of **lead** in her blood.

*Needleman HL, et al. Deficits in psychologic and classroom performance of children with elevated dentine lead levels. N Engl J Med. 1979;300(13):689–695*

- **By speaking up and suggesting that even small amounts of the heavy metal could result in chronic learning disabilities**, they brought global awareness to a previously unrecognized problem.

- Their advocacy was instrumental in ushering in a **federal ban on lead** based products, and since it was passed, **lead levels in children have decreased by >90%.**

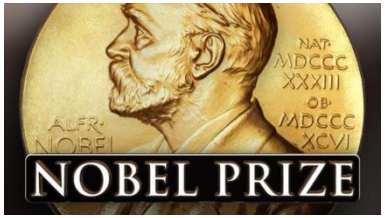


# Doctors Need to Speak Up More.

*McLaren JR, Pediatrics. 2019 Jan;143(1). pii: e20182503.*

- A decade later, during the height of the **Cold War**, the ***physician-led organization International Physicians for the Prevention of Nuclear War*** shared the **Nobel Peace Prize** for "creating an awareness of the catastrophic consequences of atomic warfare."

*Lown B. Nobel peace prize lecture. A prescription for hope. N Engl J Med. 1986;314(15):985–987.*





il cardiologo statunitense Bernard Lown e il cardiologo russo Yevgeniy Chazov.

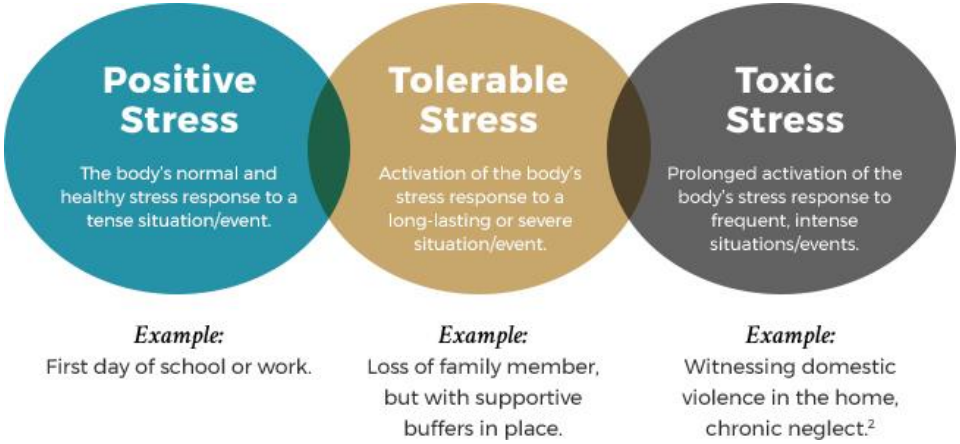
- None of its members were physicists, but these doctors focused the world's attention on the pathologic manifestations of nuclear proliferation and played a meaningful role in the denuclearization talks that followed.

# Doctors Need to Speak Up More.

*McLaren JR, Pediatrics. 2019 Jan;143(1). pii: e20182503.*

- *Danaher,* a pediatrician who is familiar with the physical and psychological effects of toxic stress, **has publicly condemned the current administration's systematic separation of migrant children from their parents.**

*Danaher Fiona. The suffering of children. N Engl J Med. 2018;379(2):e4*




*As physicians, we know that traumatic experiences like the loss of a loving caregiver can inflict **toxic stress on a child**, hindering healthy development and leading to changes in **physiology that promote physical and mental illness throughout the life course**. **Such trauma** can even become epigenetically encoded, thereby passing to future generations.*
*As parents, we can barely begin to imagine the suffering of these families, but like AAP president Colleen Kraft, we might recognize it as* ***"government-sanctioned child abuse,"*** *paid for with millions of taxpayer dollars.*


- Moreover, **speaking up may be good for our psyches, too.** Advocacy for our patients can help to reduce the moral distress that contributes to physician burnout.

*Eisenstein L. To fight burnout, organize. N Engl J Med. 2018;379(6):509–511*

la nostra ignoranza è la LORO forza

*"Il male non è soltanto di chi lo fa: è anche di chi, potendo impedire che lo si faccia, non lo impedisce"*

Tucidide (460 a.C. circa – 399 a.C.-), storico, filosofo, politico e militare greco

# What is New in General Pediatrics, Allergic & Respiratory Diseases 2018 ?


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


- ✓ General Pediatrics
- ✓ **Food Allergy**
- ✓ Atopic Dermatitis
- ✓ Asthma
- ✓ Allergic Rhinitis
- ✓ Anaphylaxis
- ✓ Urticaria & Angioedema
- ✓ Infectious Respiratory Diseases

# Weaning Prevention of food allergy

# Prevention of food allergy: Beyond peanut.

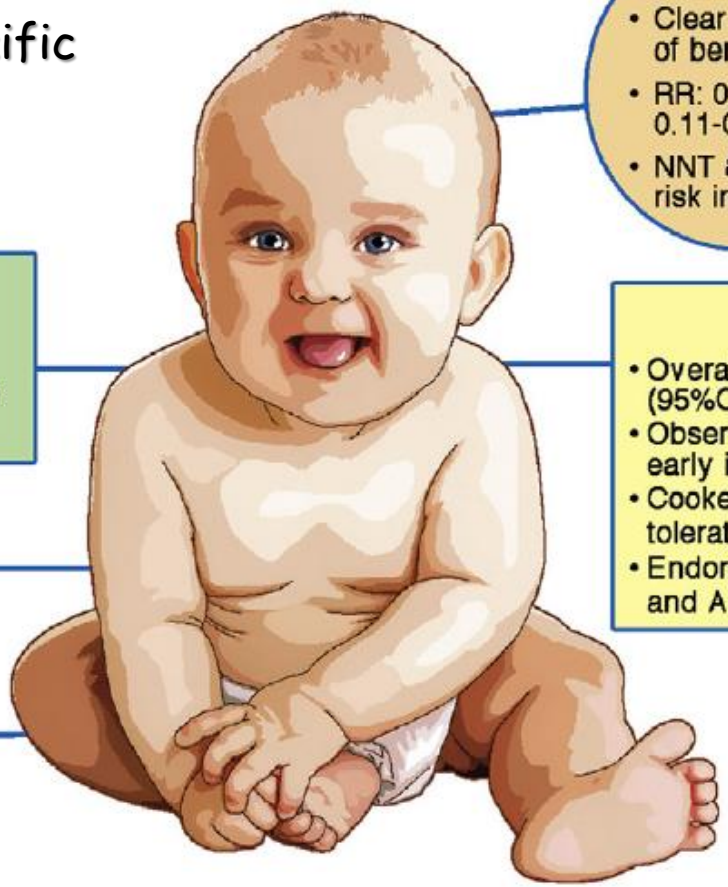
*Bird JA, J Allergy Clin Immunol. 2019 Feb;143(2):545-547.*

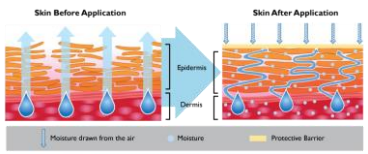
Suitability for the practice of allergen-specific and nonspecific prevention strategies.

**Peanuts**
- Clear evidence of benefit
- RR: 0.29 (95%CI 0.11-0.74)
- NNT 8 in high-risk infants

**Milk, Wheat, Fish, Sesame**
- No specific benefit seen in EAT study

**Egg**
- Overall RR: 0.56 (95%CI 0.36-0.87)
- Observational data favor early intro
- Cooked egg safer & better tolerated
- Endorsed by BSACI and ASCIA






**Soy, Tree Nuts**
- No data from interventional trials

**Skin barrier therapy**
**Pre-/probiotics**
**Vitamin D**

Investigational — No Data — Not Yet Recommended — Recommended

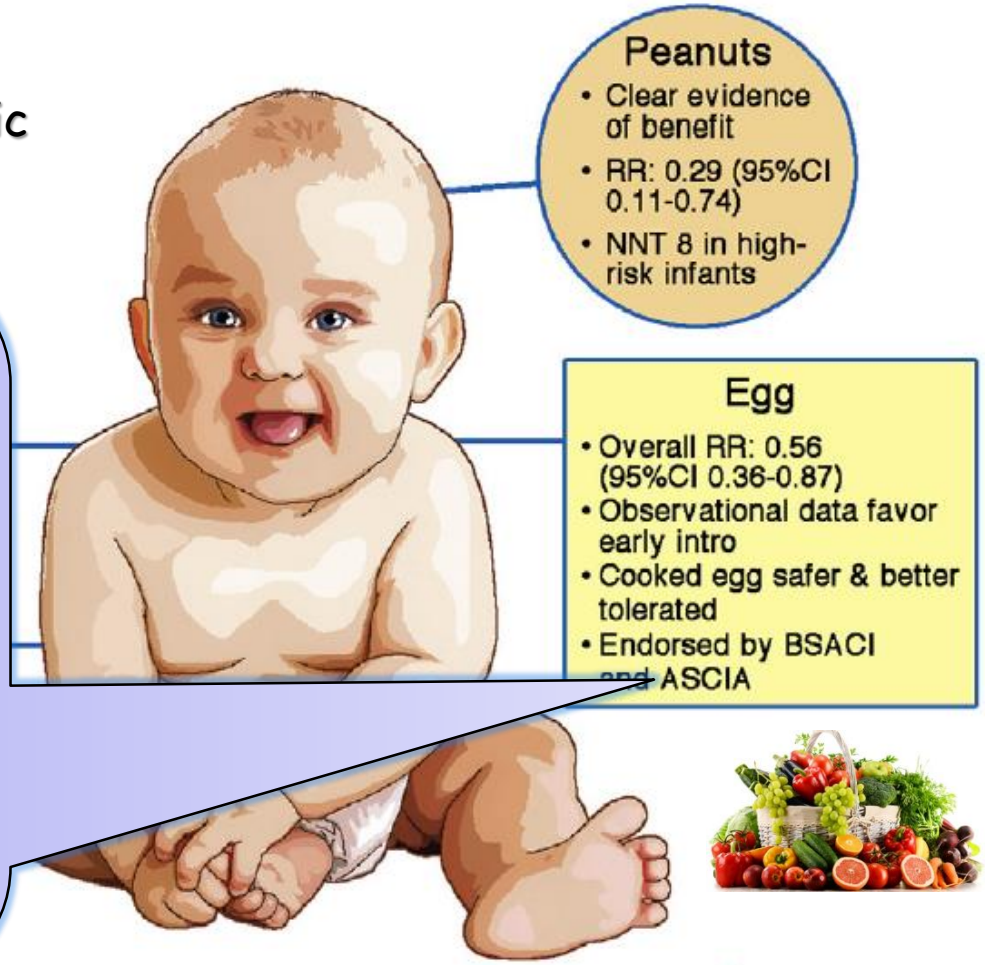
***Suitability for Practice***

# Prevention of food allergy: Beyond peanut.

*Bird JA, J Allergy Clin Immunol. 2019 Feb;143(2):545-547.*

Suitability for the practice of allergen-specific and nonspecific prevention strategies.

the Australasian Society of Clinical Immunology and Allergy states, *"When your infant is ready, introduce foods according to what the family eats, regardless of whether the food is considered to be a common food allergen."*




Investigational | No Data | Not Yet Recommended | Recommended

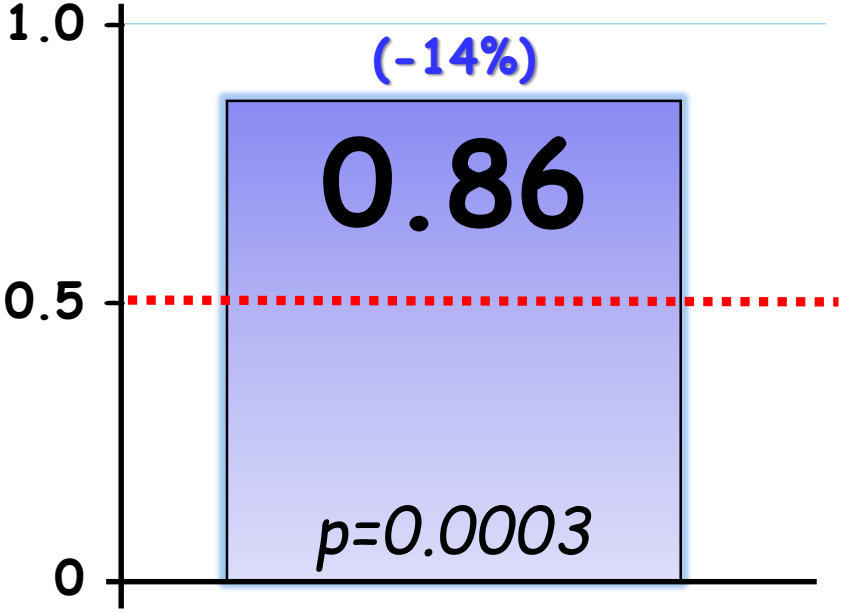
*Suitability for Practice*

# Is yoghurt an acceptable alternative to raw milk for reducing eczema and allergy in infancy?

*Crane J, CEA 2018;48:604-606*


- ✓ Infant eczema at 6 and 12 months.
- ✓ Timing of introduction (0-6 and 6-12 months) and the frequency of consumption of yoghurt.

**HR** of eczema at 12 months




Per category increase: less than once a month, 1-3 times a month, once a week, 2-4 times a week, 5-6 times a week, once a day, and 2 or more times a day

# Food allegy natural history

# A new Luminex-based peptide assay to identify reactivity to baked, fermented, and whole milk.

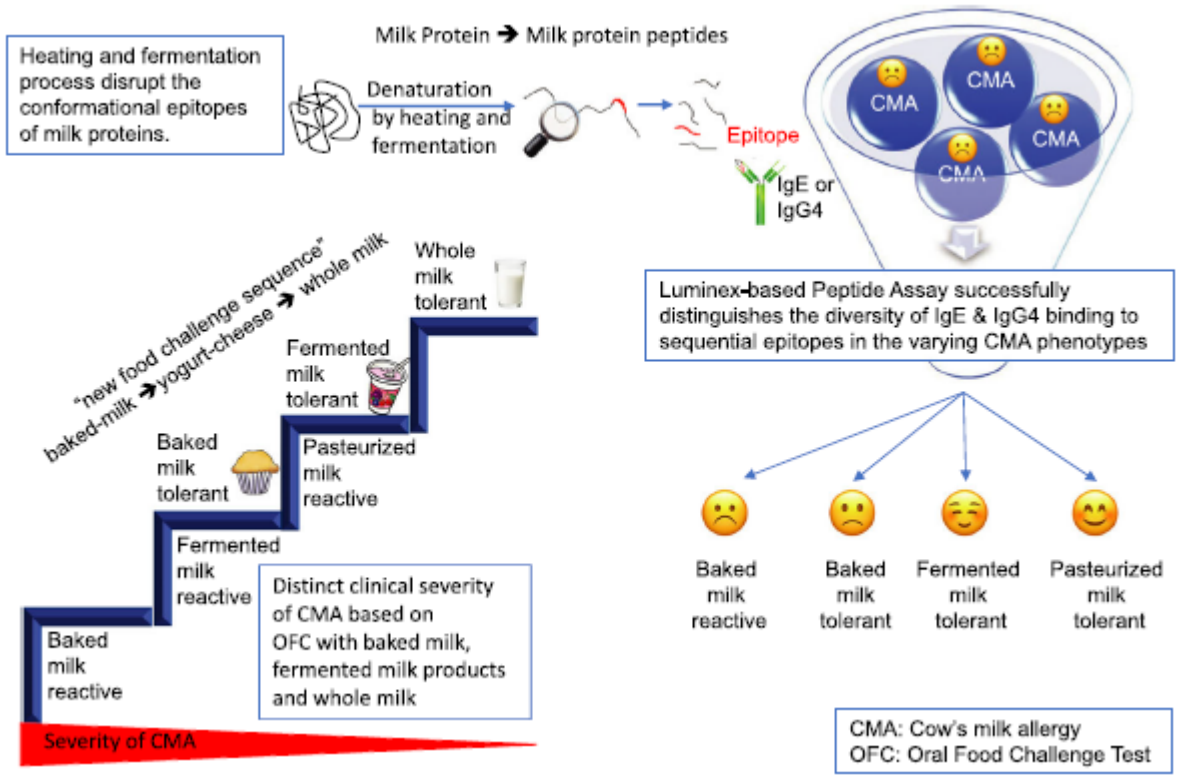
*Sackesen C, Allergy. 2019 Feb;74(2):327-336.*

✓4 groups of reactivity identified by Oral food challenge:
1) baked milk reactive,
2) fermented milk reactive,
3) whole milk reactive, and
4) outgrown.

✓sIgE and sIgG4 binding to milk protein epitopes assessed with a novel Luminex-based peptide assay (LPA).

✓Using machine learning techniques, a model was developed to predict different degrees of CMA.

The new food challenge sequence and Luminex-based peptide assay to identify the clinical phenotypes of reactivity to baked, fermented, and whole cow's milk.



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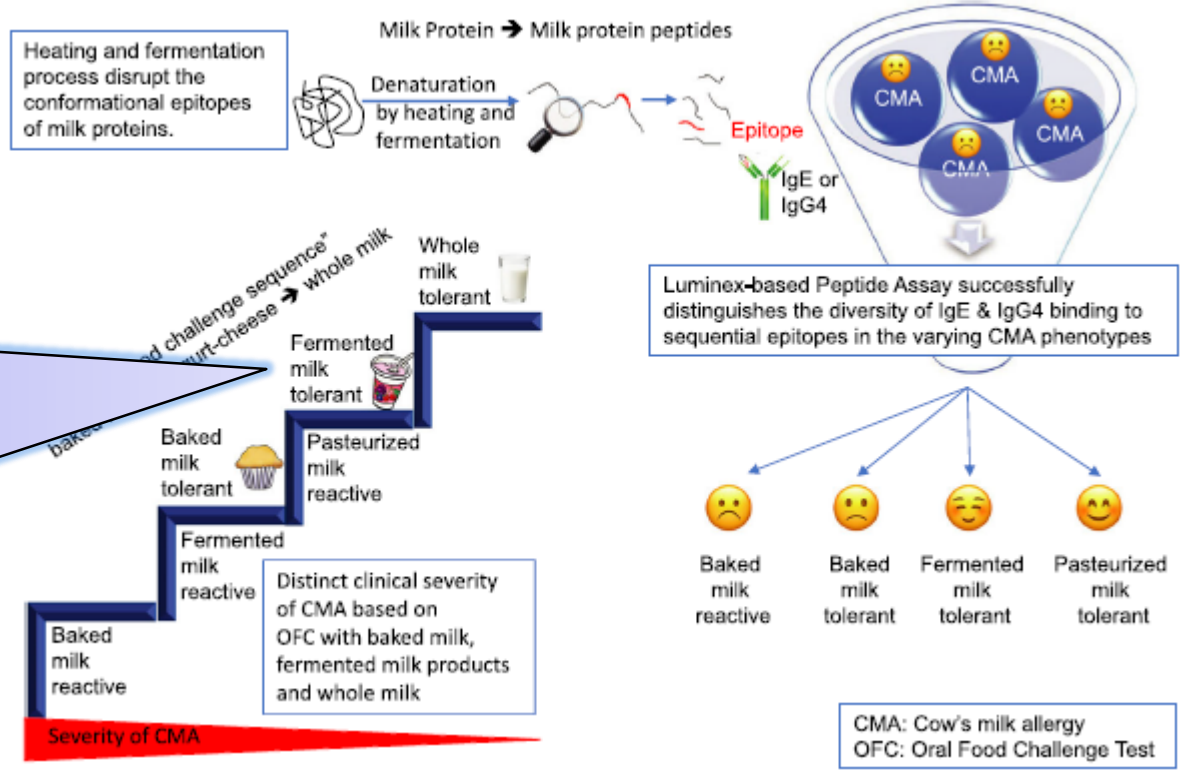
✓4 groups of reactivity identified by Oral food challenge:
1) baked milk reactive,
2) fermented milk reactive,
3) whole milk reactive, and
4) outgrown.

the present study identified a new clinical phenotype of patients with CMA, that is, children tolerant to fermented milk products,

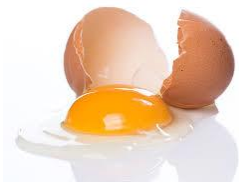

The new food challenge sequence and Luminex-based peptide assay to identify the clinical phenotypes of reactivity to baked, fermented, and whole cow's milk.



# Early life innate immune signatures of persistent food allergy.

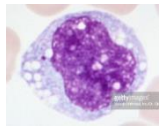
*Neeland MR, J Allergy Clin Immunol. 2018 Sep;142(3):857-864.e3.*

✓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.



✓follow-up egg allergy status at age 2-4 years

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

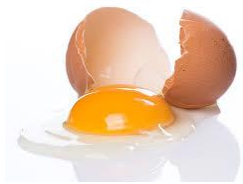


- follow-up analysis revealed that this unique innate immune signature continues into childhood in those with persistent egg allergy and that **increased serum vitamin D levels correlate with** changes in innate immune profiles observed in children who developed **natural tolerance to egg.**

# Early life innate immune signatures of persistent food allergy.

*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.



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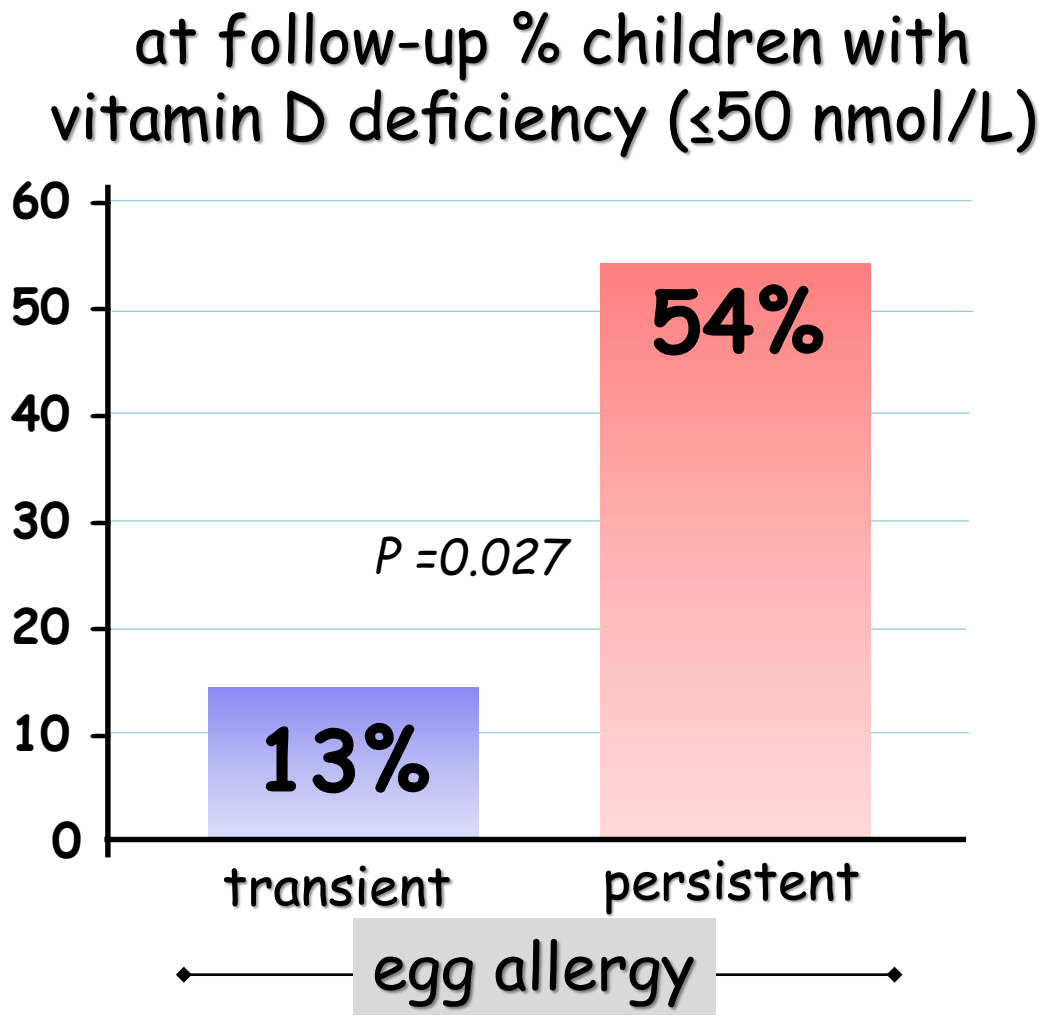

# Challenge

# Review of 400 consecutive oral food challenges to almond.

*Baker MG, Ann Allergy Asthma Immunol. 2019 Feb;122(2):189-192.*

- Almonds are **a healthy source of protein** and can be an important milk product for children with other allergies.

- Allergy to almond is the **third most commonly reported tree nut allergy** in the United States, and the prevalence appears to be increasing in recent years.

- Tree nuts are also one of the most common causes of fatal anaphylaxis, although **the rate of moderate to severe reactions to almond may not be as high as that of other tree nuts**, such as:

cashew, pistachio, pecan, and walnut.

# Review of 400 consecutive oral food challenges to almond.

*Baker MG, Ann Allergy Asthma Immunol. 2019 Feb;122(2):189-192.*


- The diagnosis of **almond allergy** is complicated by **a high rate of false-positive results**.

- The **food-sIgE to almond correlates poorly with oral food challenge** (OFC) outcome.

- A recent study from Israel on tree nut allergy found that among 83 patients recruited because of suspicion of tree nut allergy, only 1 patient was reactive to almond despite 49 (59%) patients demonstrating sensitivity to this food.

*Elizur A, NUT Co Reactivity: ACquiring Knowledge for Elimination Recommendations (NUT CRACKER) study. Allergy. 2017;73(3): 593e601*.

# Review of 400 consecutive oral food challenges to almond.

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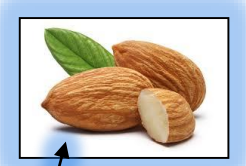


- The diagnosis of almond allergy is complicated by a high rate of false-positive results.
- The food-sIgE to almond correlates poorly with oral food challenge (OFC) outcome.
- A recent
among 8
o
des
Eliz
(NUT CRACKER)

Cross-reactivity between almond and birch appears to make a partial but incomplete contribution to this phenomenon

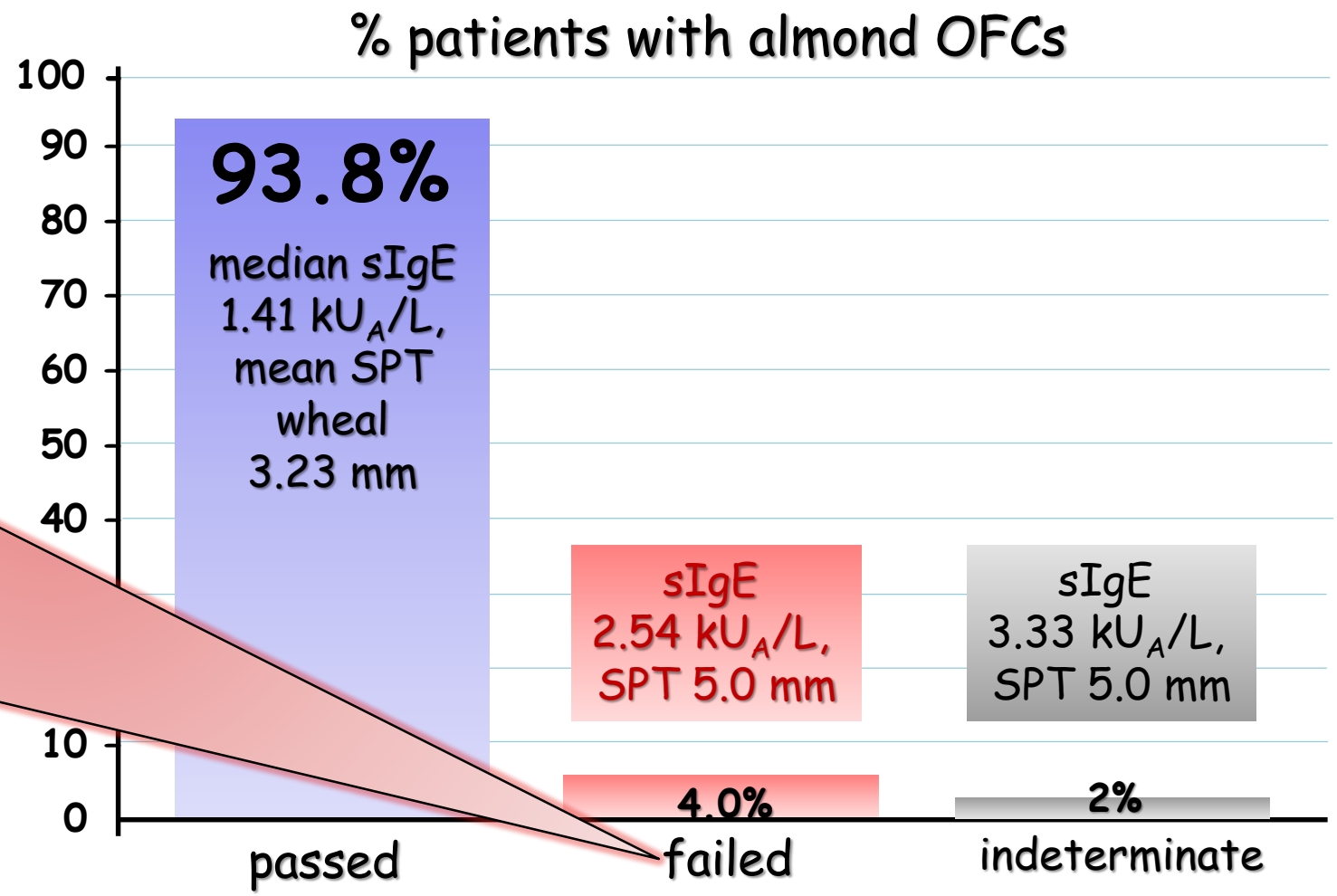
ctions

# Review of 400 consecutive oral food challenges to almond.

*Baker MG, Ann Allergy Asthma Immunol. 2019 Feb;122(2):189-192.*

Among the 16 children who reacted, pruritus was the most common symptom.

Only 2 (12.5%) children had reactions that required epinephrine.



# What is New in General Pediatrics, Allergic & Respiratory Diseases 2019 ?

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

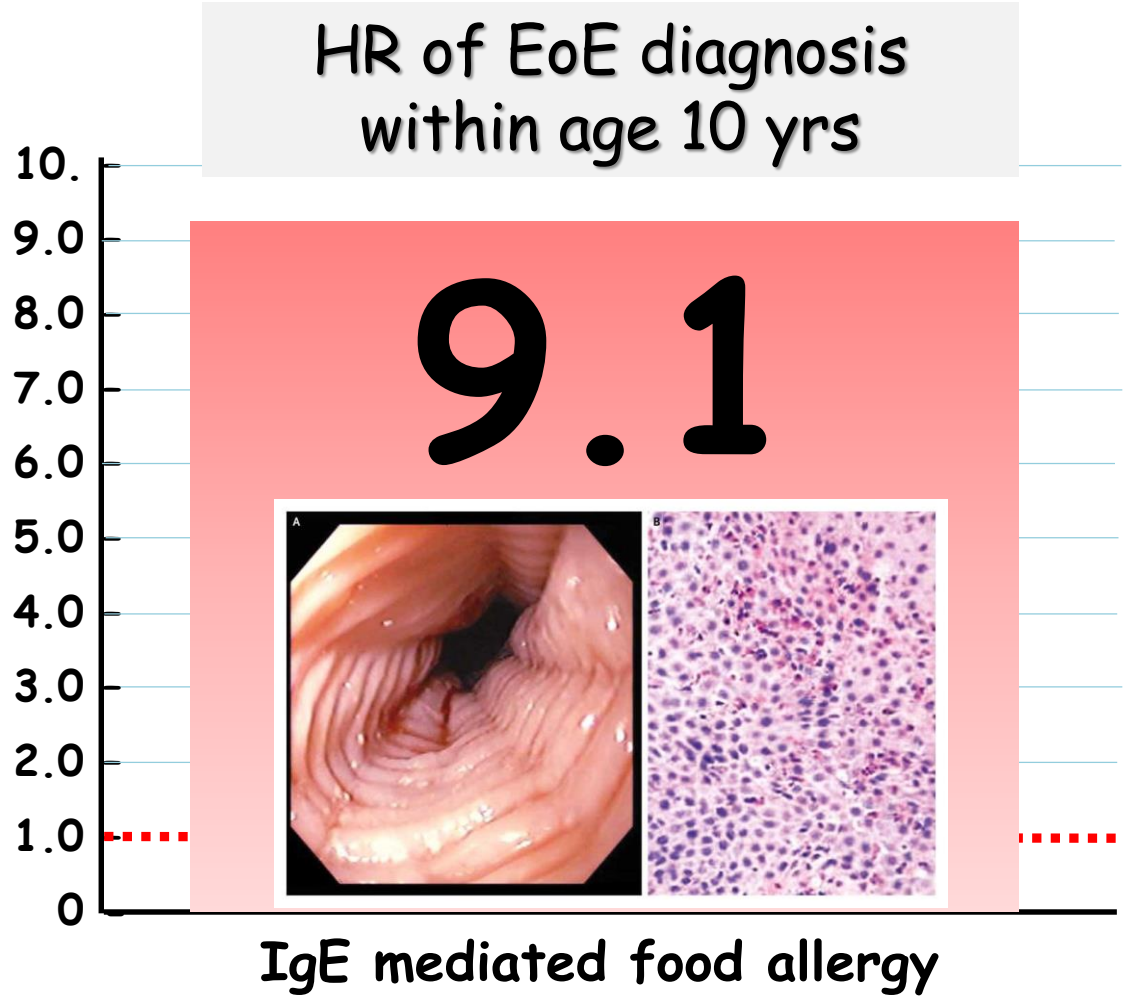
- ✓ General Pediatrics
- ✓ Food Allergy
- ✓ **Atopic Dermatitis**
- ✓ Asthma
- ✓ Allergic Rhinitis
- ✓ Anaphylaxis
- ✓ Urticaria & Angioedema
- ✓ Infectious Respiratory Diseases

# Eosinophilic Esophagitis Is a Late Manifestation of the Allergic March.

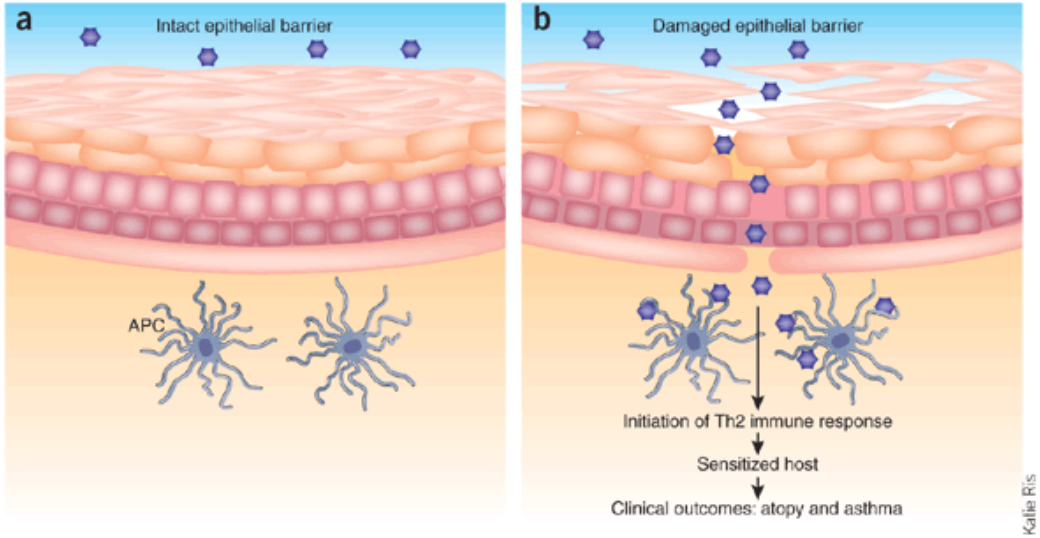
*Hill DA, J Allergy Clin Immunol Pract. 2018 Sep - Oct;6(5):1528-1533.*

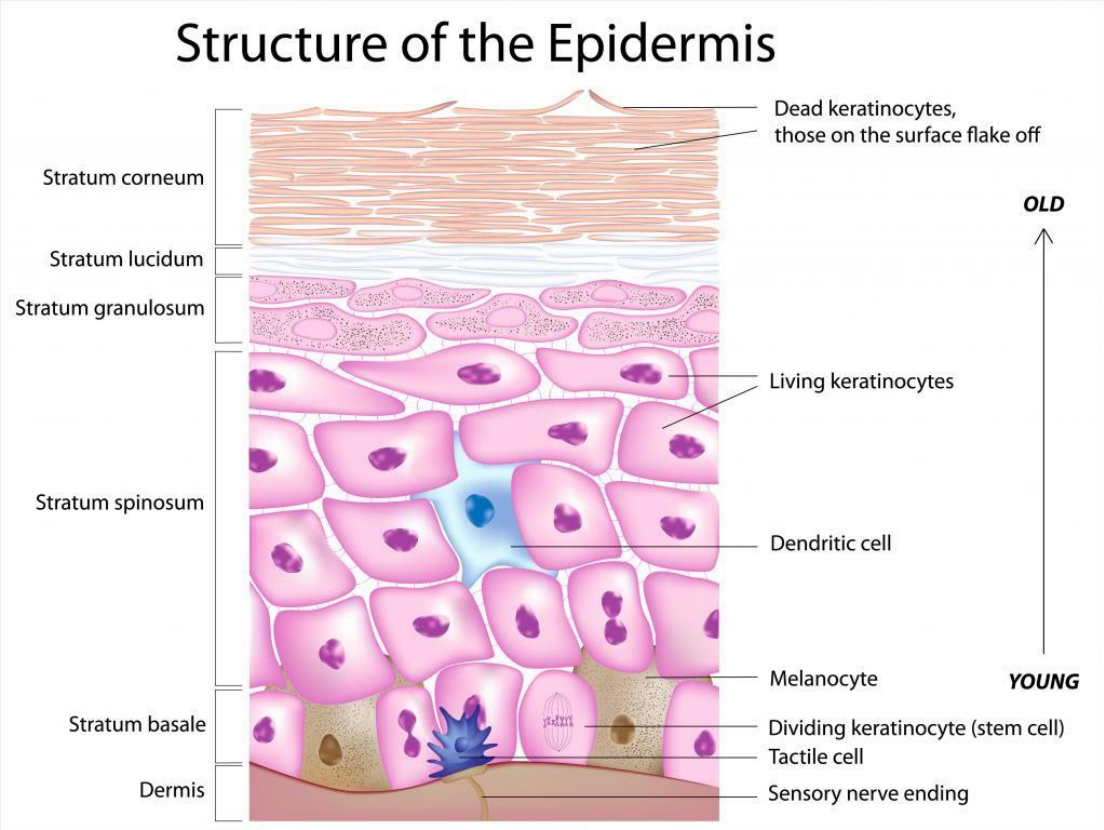
✓a primary care birth cohort of 130,435 children,

✓natural histories of
- atopic dermatitis (AD),
- IgE-mediated food allergy (IgE-FA),
- asthma,
- eosinophilic esophagitis (EoE), and
- allergic rhinitis (AR) in individual patients



# Skin barrier



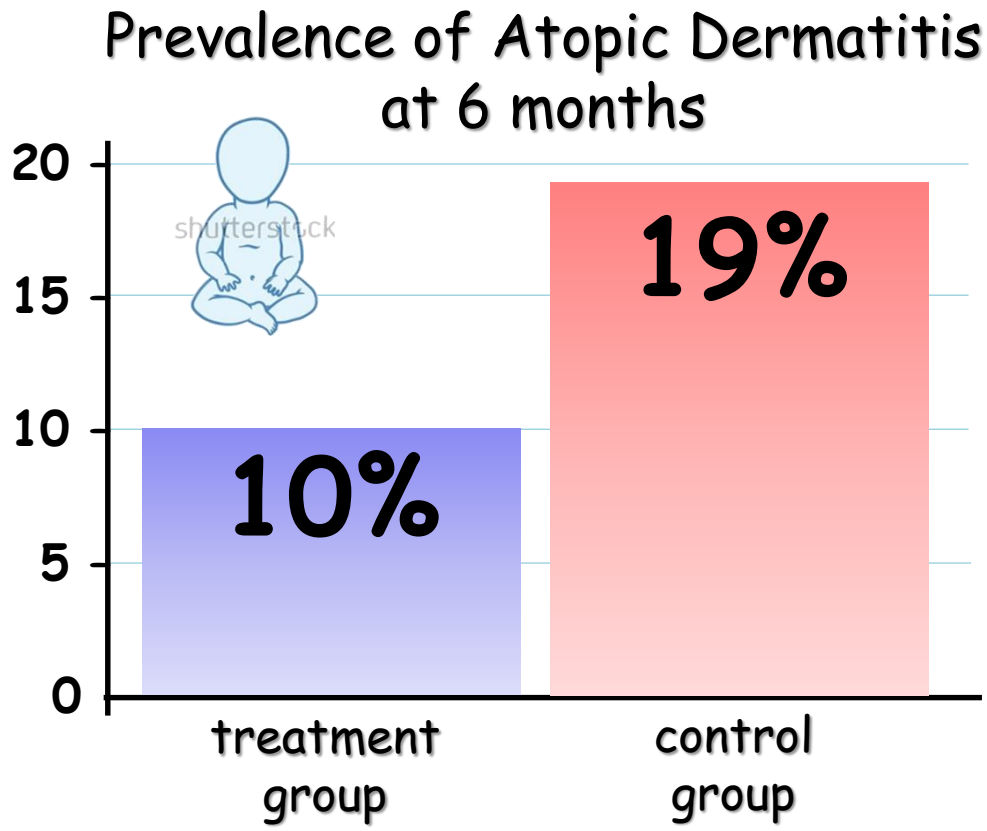
# A randomized trial of a barrier lipid replacement strategy for the prevention of atopic dermatitis and allergic sensitization: the PEBBLES pilot study.

*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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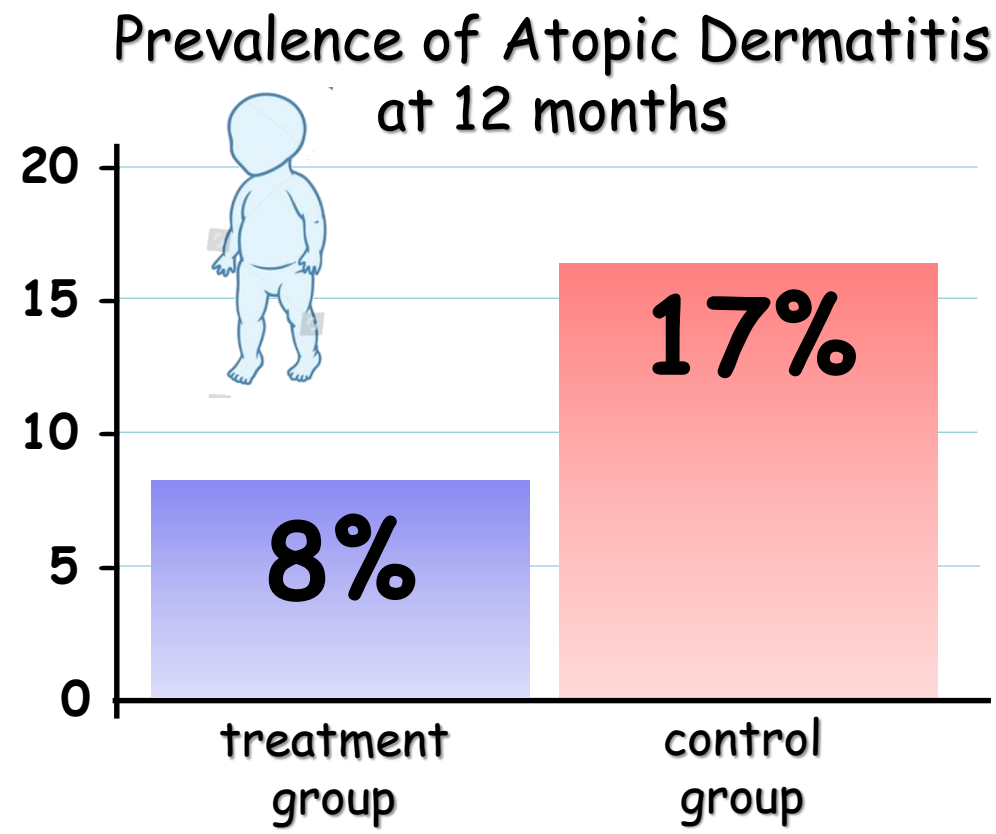

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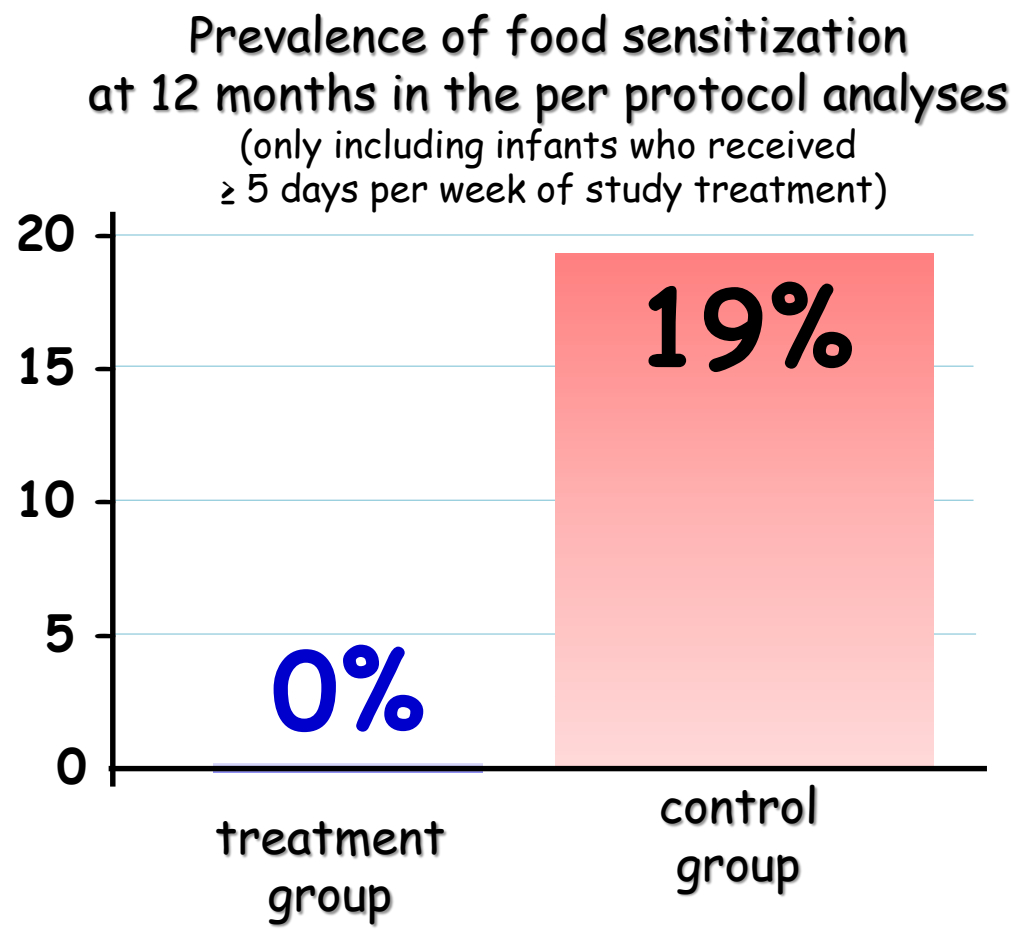
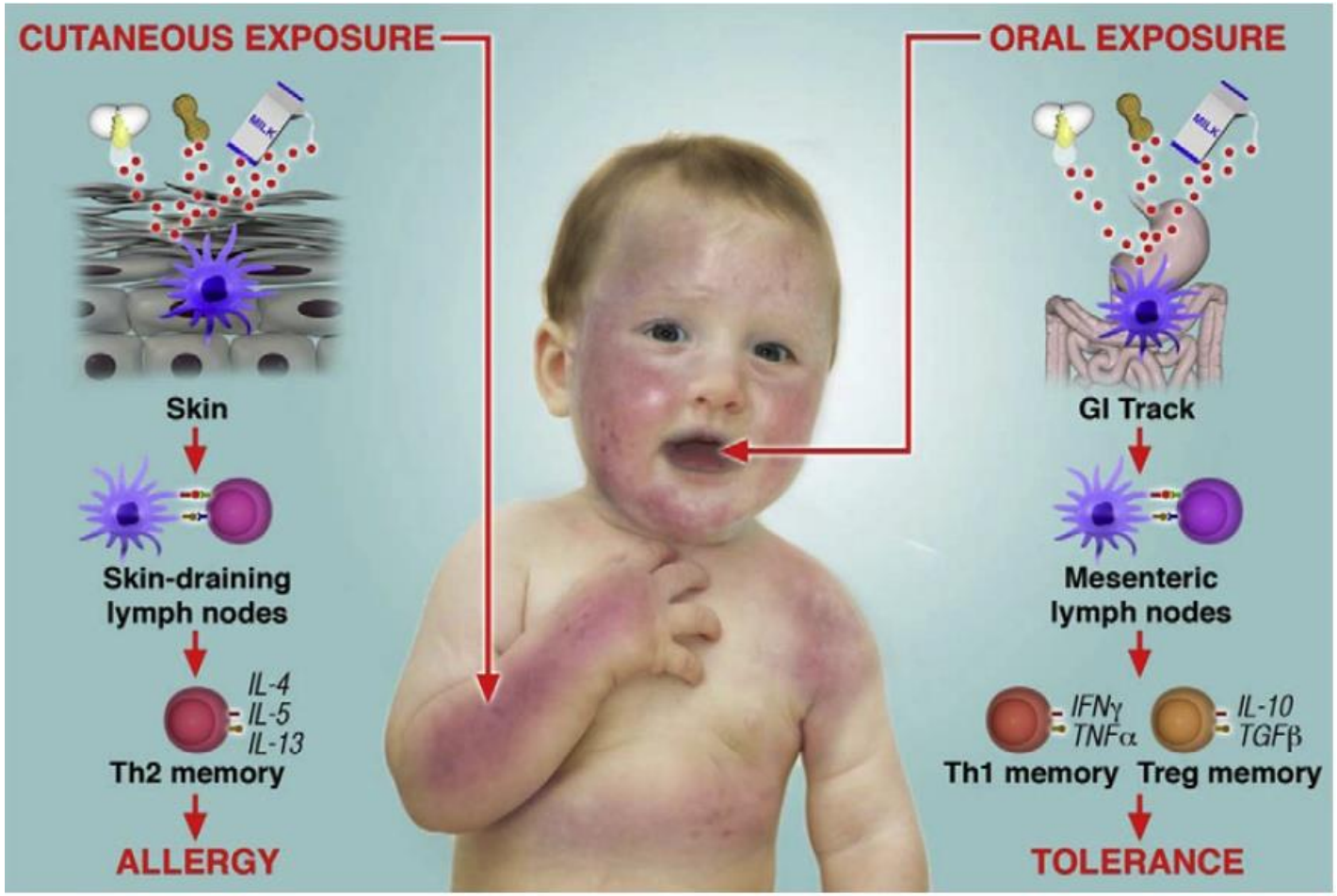


# Environmental Food Exposure: What Is the Risk of Clinical Reactivity From Cross-Contact and What Is the Risk of Sensitization.

*Sheehan WJ, J Allergy Clin Immunol Pract. 2018 Nov-Dec;6:1825-32.*

## THE DUAL-ALLERGEN EXPOSURE HYPOTHESIS

early oral exposure to food protein induces tolerance,
whereas early cutaneous exposure to environmental food allergen results in food sensitization and allergy development




*Lack G. Update on risk factors for food allergy. J Allergy Clin Immunol 2012;129:1187-97.*

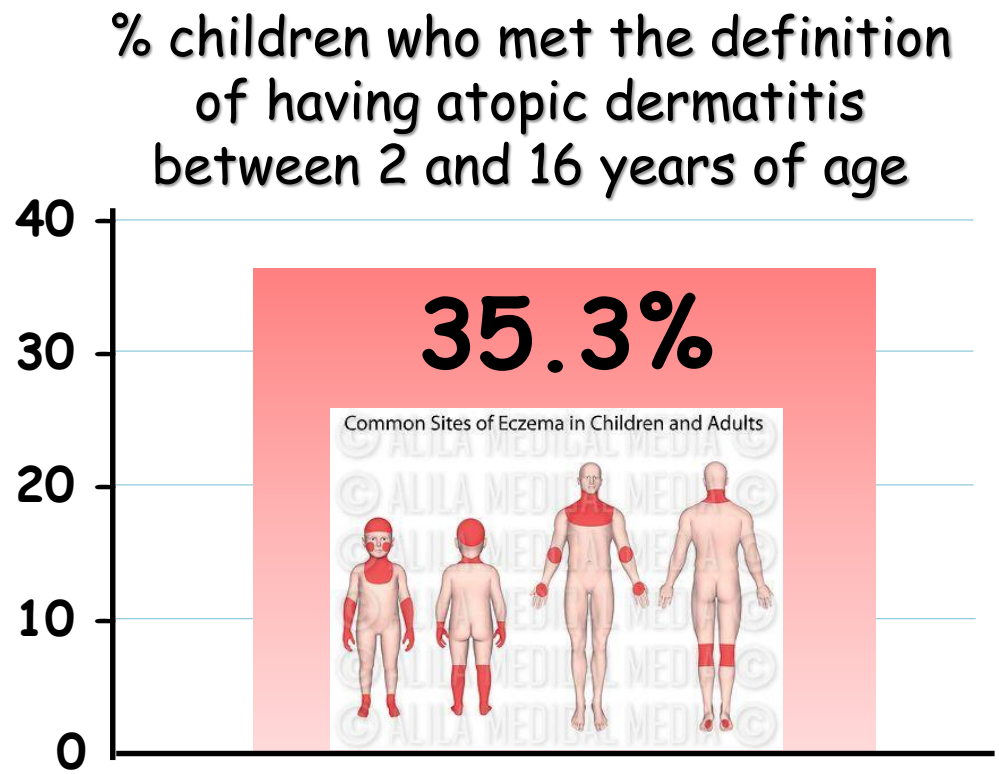
# Atopic dermatitis burden

# Association of Atopic Dermatitis With Sleep Quality in Children.

*Ramirez FD, JAMA Pediatr. 2019 May 1;173(5):e190025.*

✓children enrolled in the Avon Longitudinal Study of Parents and Children, a population-based birth cohort in Avon, United Kingdom. (N = 13 988)

✓followed up with repeated measures of self-reported AD and sleep through 16 years of age.



# Association of Atopic Dermatitis With Sleep Quality in Children.

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% children with active atopic dermatitis reporting each of the 4 sleep-quality disturbances at different child ages.

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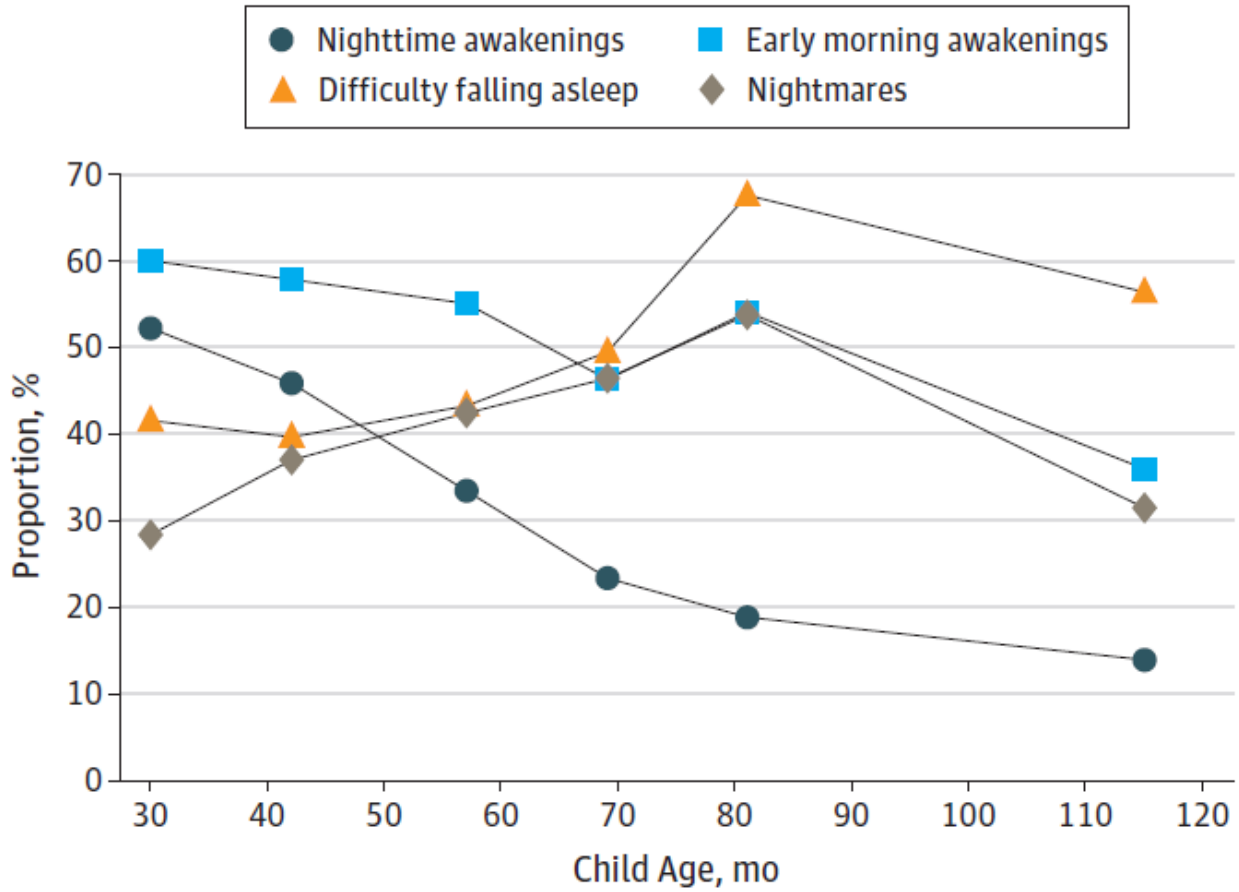

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- ✓ **Asthma**
- ✓ Allergic Rhinitis
- ✓ Anaphylaxis
- ✓ Urticaria & Angioedema
- ✓ Infectious Respiratory Diseases

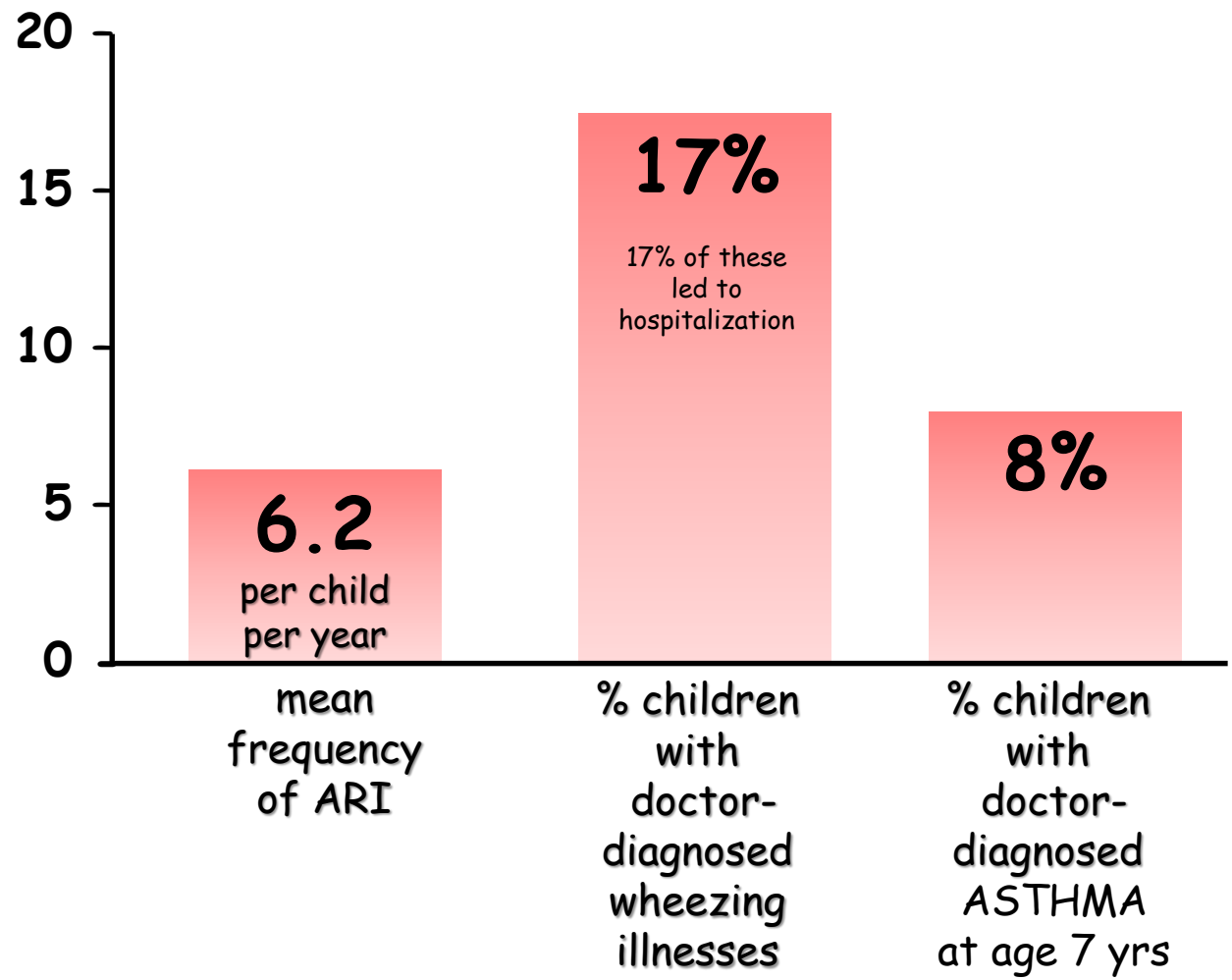
# Risk factors for asthma development

## Early infections

# Acute respiratory infections in early childhood and risk of asthma at age 7 years.

*Toivonen L, Allergy Clin Immunol. 2019 Jan;143(1):407-410.e6.*

✓a prospective, population-based birth cohort study (n= 923) to investigate the association between acute respiratory infections (ARIs) during the first 24 months of life and asthma at age 7 years.



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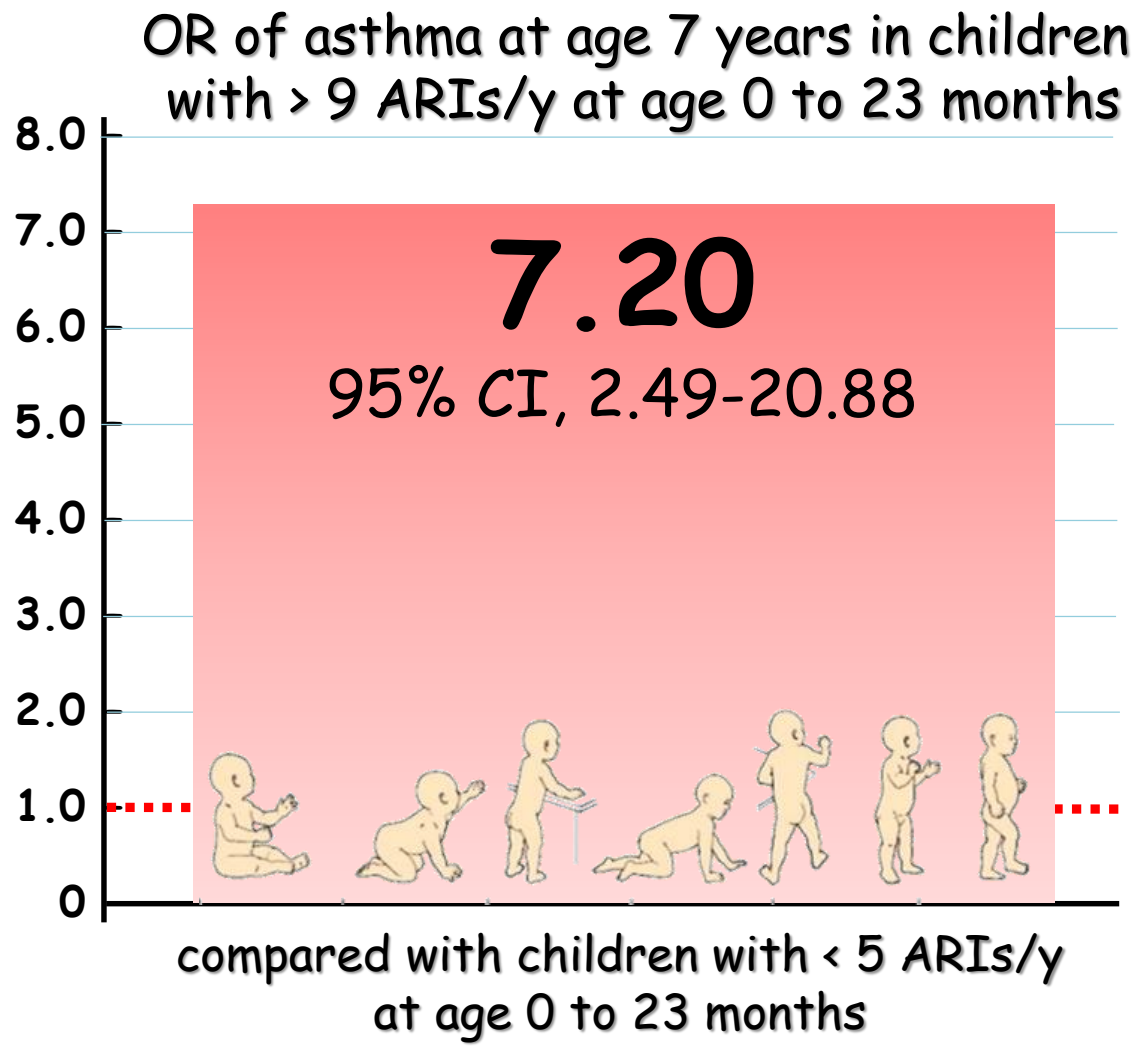
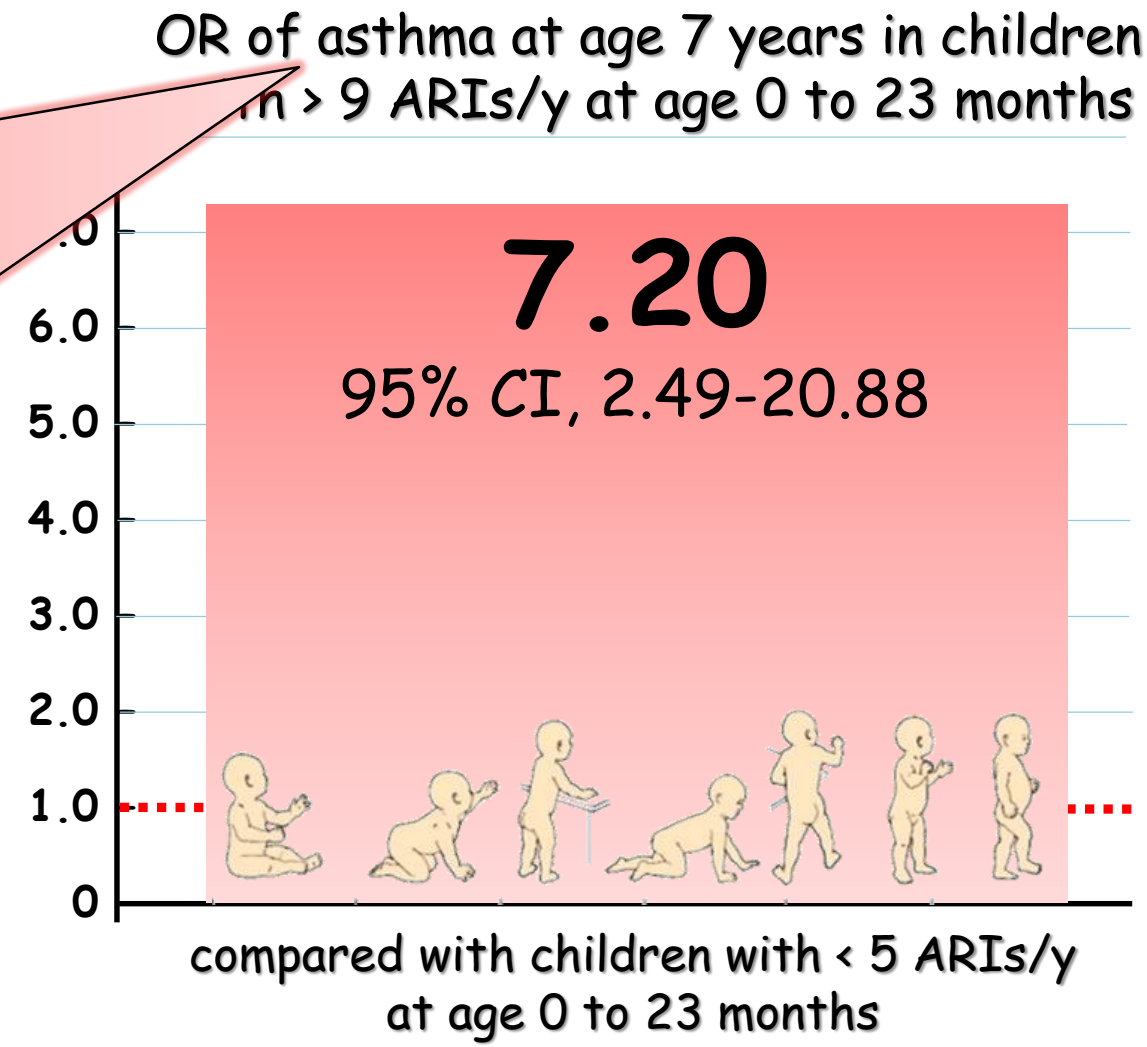


# Acute respiratory infections in early childhood and risk of asthma at age 7 years.

*Toivonen L, Allergy Clin Immunol. 2019 Jan;143(1):407-410.e6.*

The mean duration of ARIs was longer and measures of severity were higher in children with asthma at age 7 years compared with those without asthma.

These findings may reflect poorer immunological responses in children who later develop asthma.

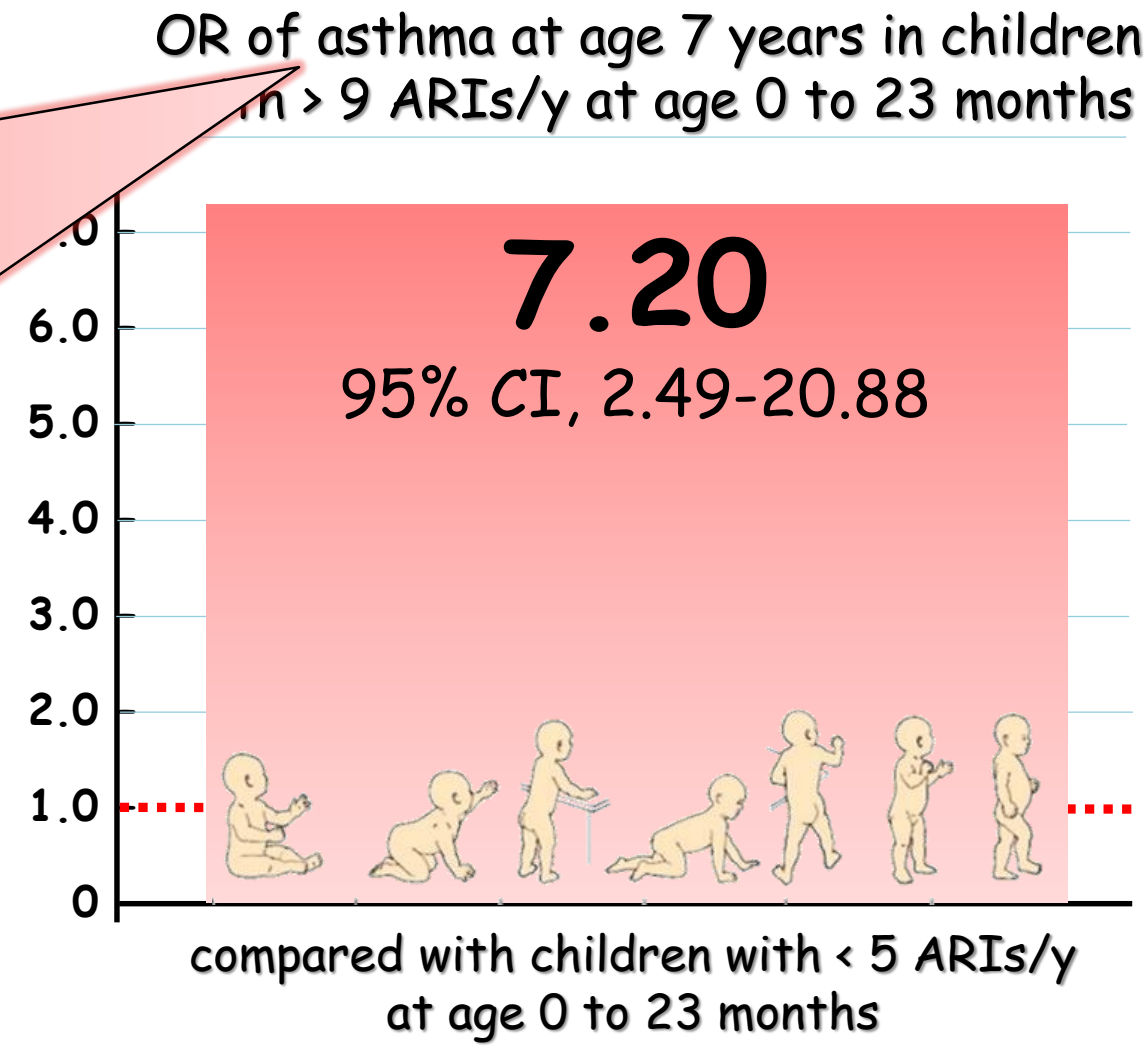


# Acute respiratory infections in early childhood and risk of asthma at age 7 years.

*Toivonen L, Allergy Clin Immunol. 2019 Jan;143(1):407-410.e6.*

*The more the visits* for respiratory problems in the first years of life *the more likely* is the probability of subsequent asthma.

***"To wheeze or not to wheeze": That is not the question.***
*Skytt N, Bisgaard H. J Allergy Clin Immunol. 2012 Aug;130(2): 403-7.e5.*



# Acute respiratory infections in early childhood and risk of asthma at age 7 years.

*Toivonen L, Allergy Clin Immunol. 2019 Jan;143(1):407-410.e6.*

- Our data suggest common mechanisms behind susceptibility to ARIs and asthma:

- **Airway hyperreactivity** in children who later develop asthma may contribute to **prolonging symptoms during ARIs**.

- **Altered cytokine responses/immune responses** to respiratory viruses have been detected in children with asthma and could predispose to ARIs.

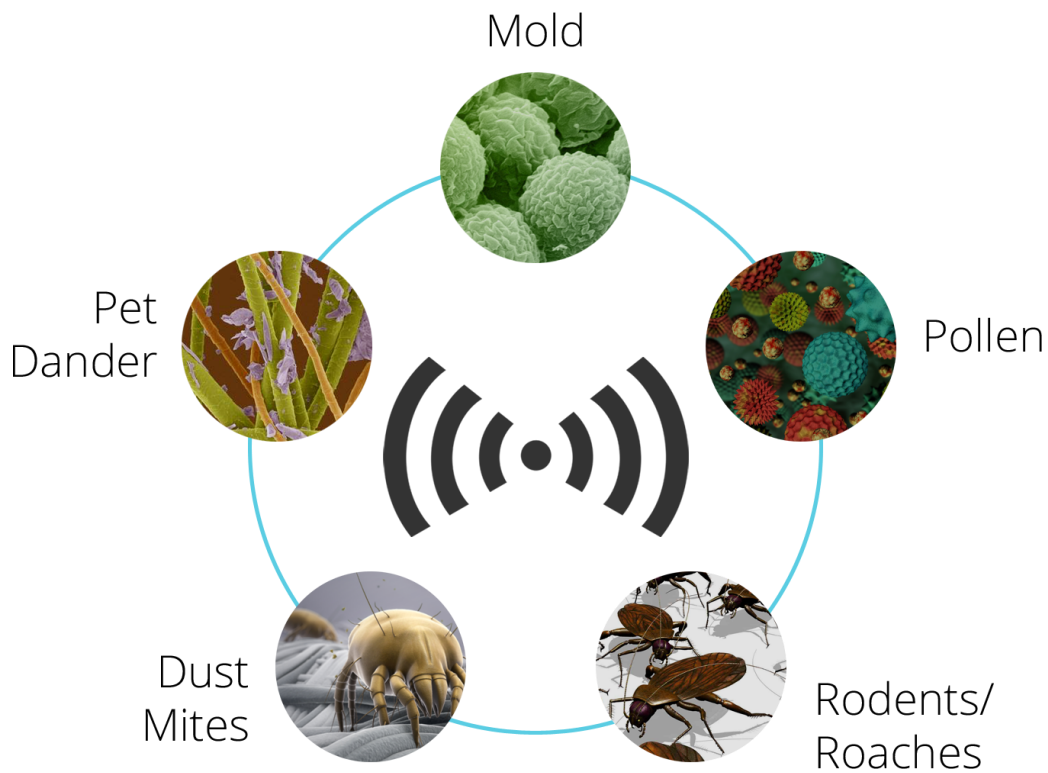
- **Genetic factors** or, as recent data suggest, **airway microbiome** may play a role in susceptibility to ARIs and asthma.

- **Frequent early ARIs may also play a causative role** in the development of asthma by **adversely affecting the developing lungs.**

•*Feldman AS, Toward primary prevention of asthma: reviewing the evidence for early-life respiratory viral infections as modifiable risk factors to prevent childhood asthma. Am J Respir Crit Care Med 2015;191:34-44.*

# Risk factors for asthma development

## Allergen



# Identification of two early life eczema and non-eczema phenotypes with high risk for asthma development.

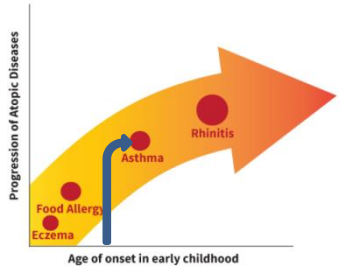
*Johansson E, Clin Exp Allergy. 2019 Jun;49(6):829-837.*

✓505 participants in the Cincinnati Childhood Allergy and Air Pollution Study (CCAAPS), a prospective birth cohort,

✓Longitudinal eczema and asthma outcomes as well as prospective data regarding timing of sensitization to foods and aeroallergens.

✓KIF3A (Kinesin family member 3A) genotypes were available on all children.

➢Two high-risk groups were identified:
one with and
one without early eczema.




•1)the high-risk group with early eczema was more likely to be sensitized to food allergens, while

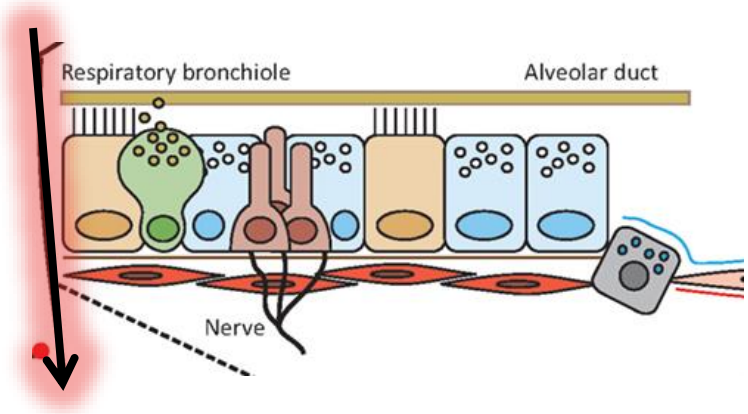
•2)the group without early eczema was more likely to be polysensitized to aeroallergens.

# Identification of two early life eczema and non-eczema phenotypes with high risk for asthma development.

*Johansson E, Clin Exp Allergy. 2019 Jun;49(6):829-837.*

- The second high-risk group characterized by **polysensitization to aeroallergens by age 3 yers** in the absence of early eczema is an important high risk group.

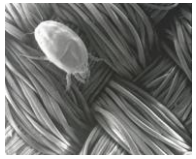
- We hypothesize that while these children do not exhibit eczema, they **may have epithelial barrier defects at** the skin or **lung mucosal surfaces** that do not manifest as clinical eczema.



# Wheeze trajectories are modifiable through early-life intervention and predict asthma in adolescence.

*Owora AH, Pediatr Allergy Immunol. 2018 Sep;29(6):612-621.*

✓Secondary analysis of the **Canadian Asthma Primary Prevention Study (CAPPS)**, a multifaceted prenatal intervention among children at high risk of asthma, followed **from birth to 15 years**.



✓Wheezing trajectories identified by latent class growth analysis.

- Among 525 children, 3 wheeze trajectory groups were identified:
  - **Low-Progressive** (365, 69%),
  - **Early-Transient** (52, 10%), and
  - **Early-Persistent** (108, 21%).

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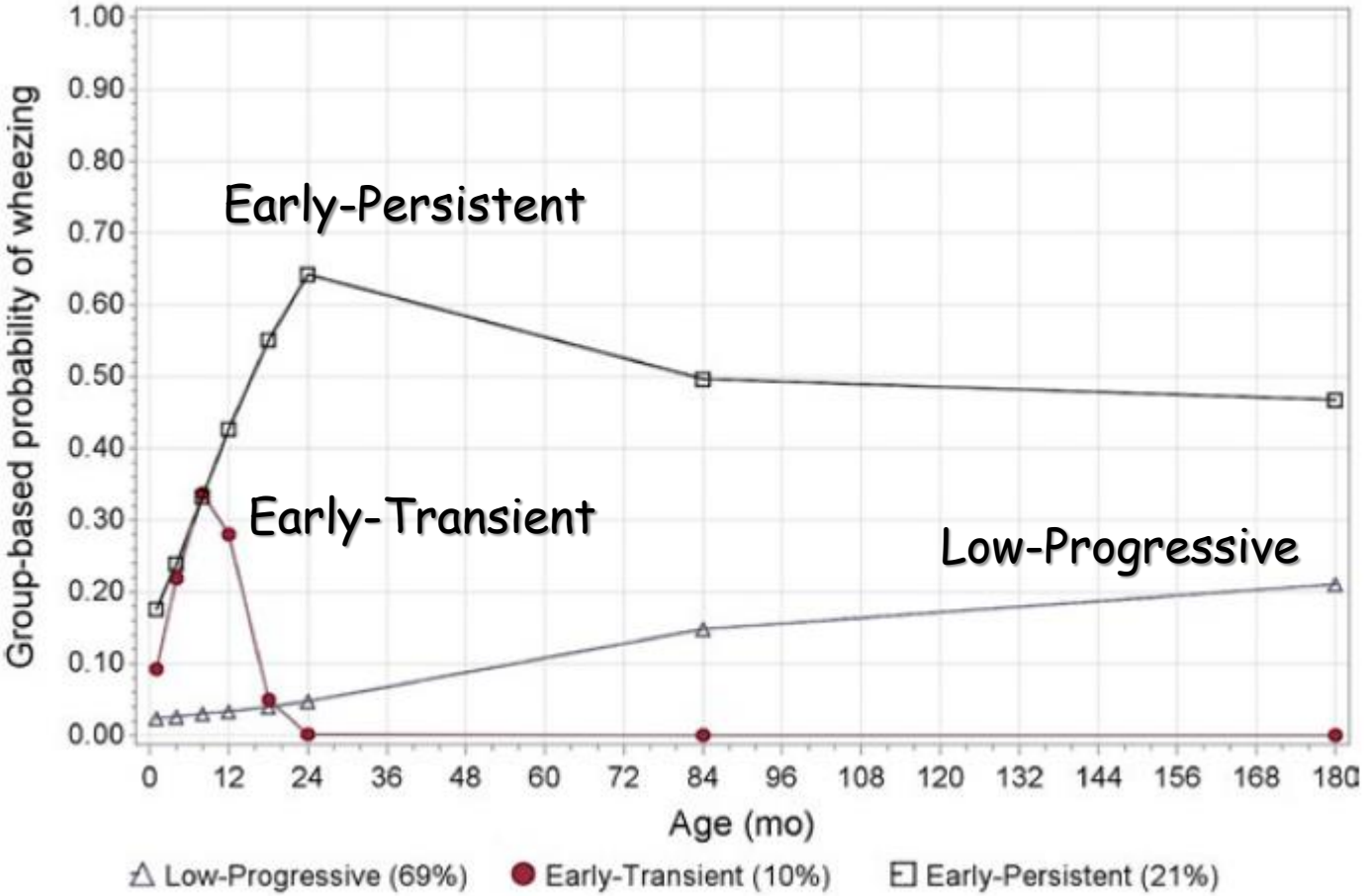
Wheeze trajectories in the CAPPS birth cohort



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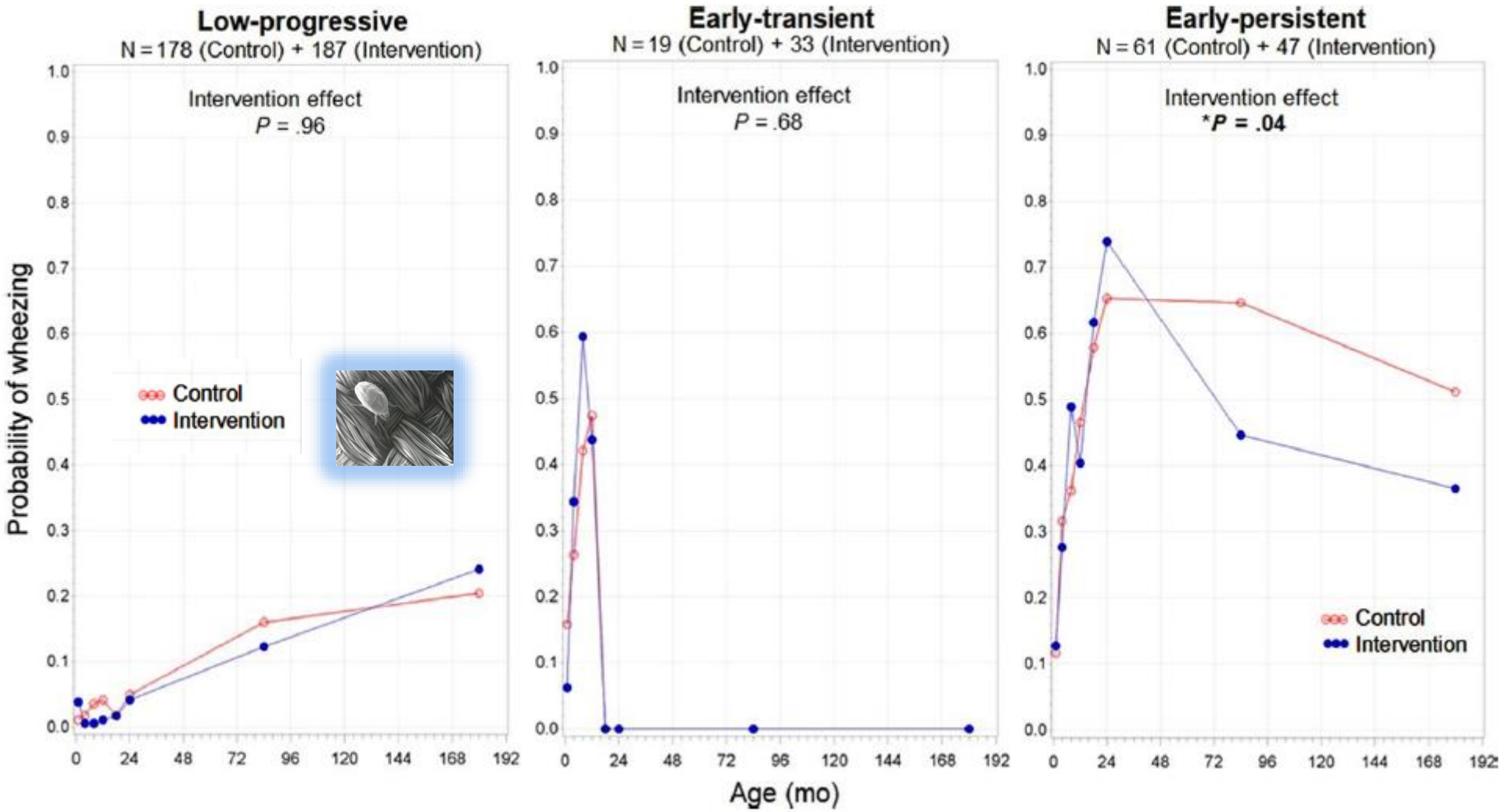


Intervention effect within latent group-based wheeze trajectories in the Canadian Asthma PrimaryPrevention Study

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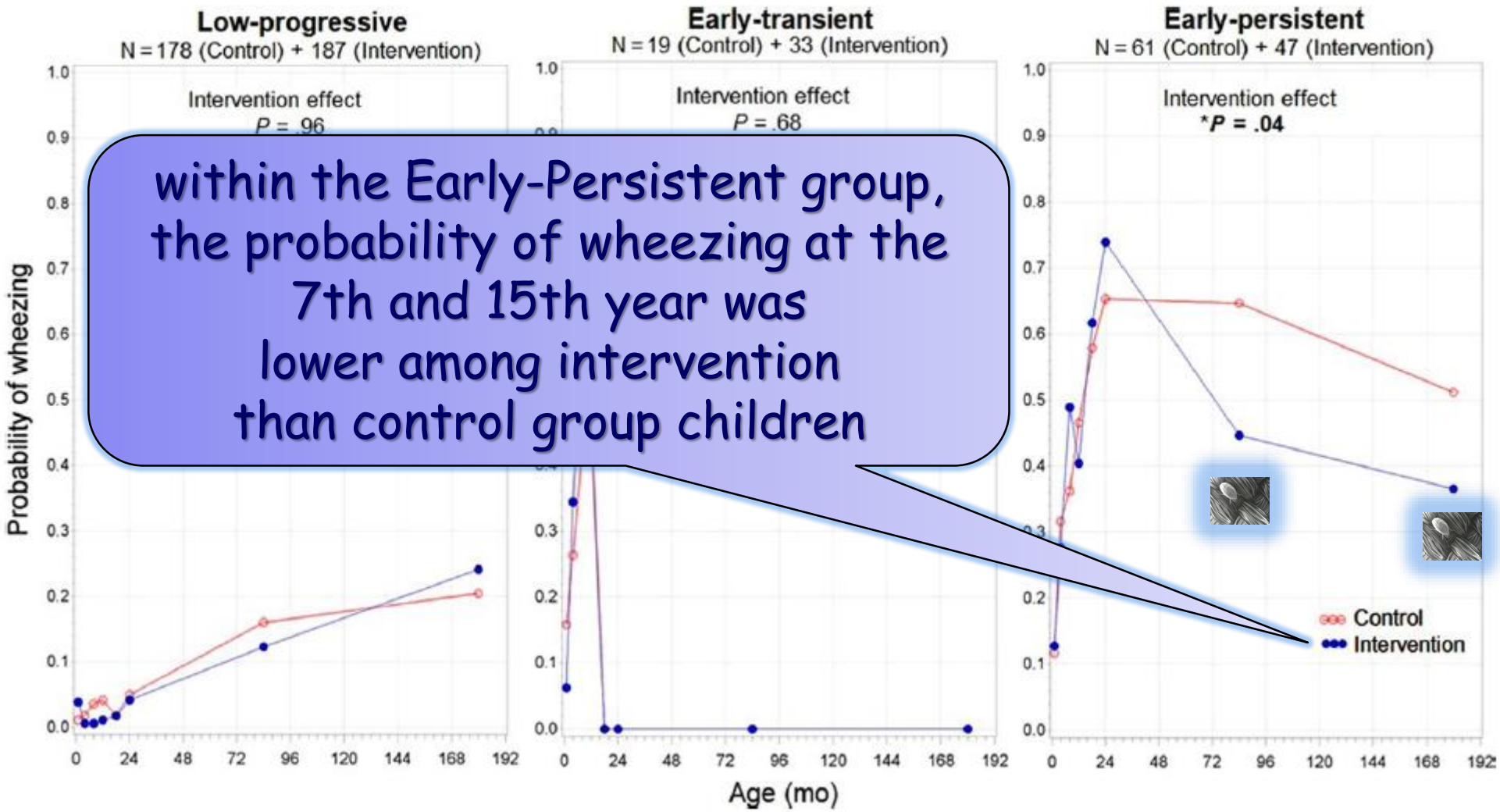


within the Early-Persistent group, the probability of wheezing at the 7th and 15th year was lower among intervention than control group children

Intervention effect within latent group-based wheeze trajectories in the Canadian Asthma PrimaryPrevention Study

# Wheeze trajectories are modifiable through early-life intervention and predict asthma in adolescence.

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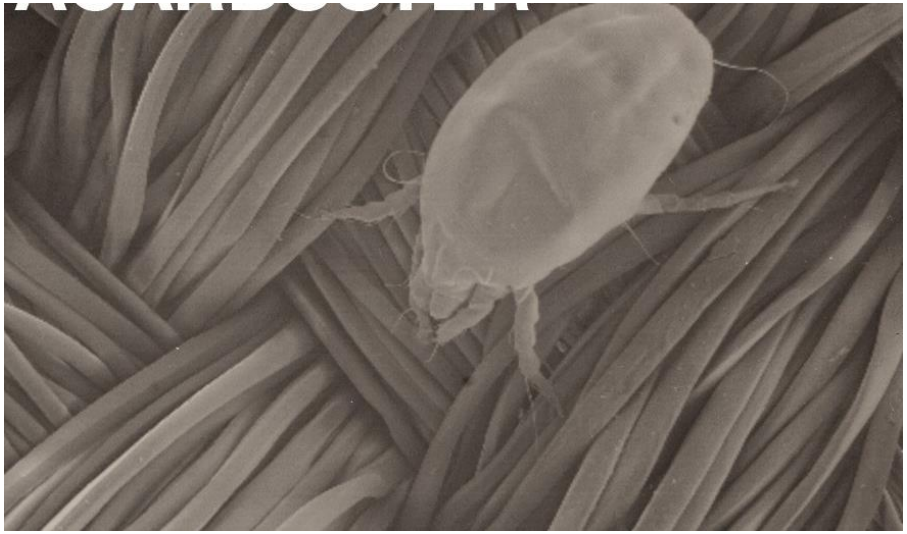
- The CAPPS intervention was effective in decreasing the risk of wheezing during mid-childhood in the Early-Persistent group, but had no effect in the other trajectory groups where wheezing was transient or infrequent.

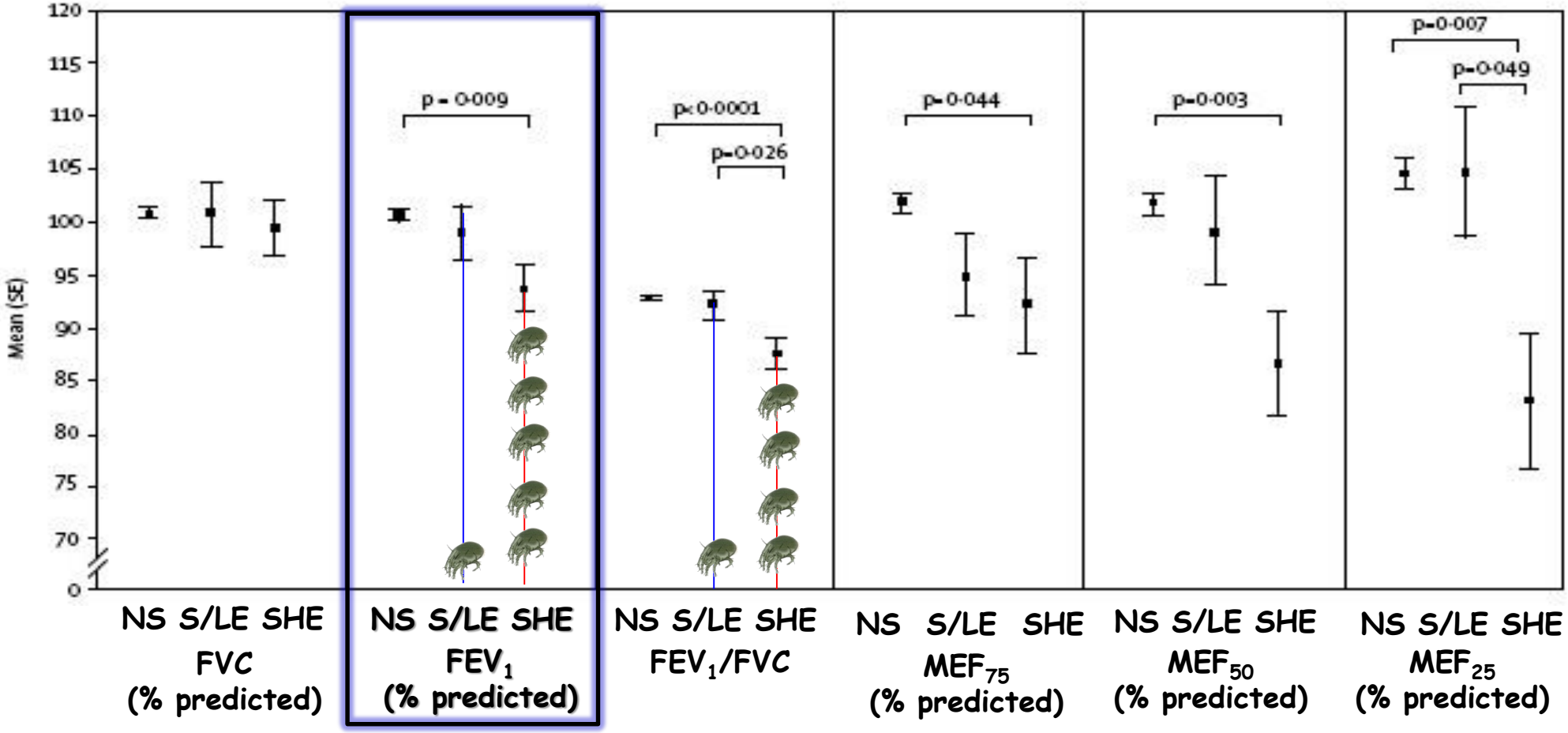


- These results suggest the intervention prevented the pathogenesis of wheezing that occurs later in childhood, which is more likely related to asthma, but did not affect wheezing that occurs during infancy, which is more likely related to respiratory infections.

# Allergy and atopy from infancy to adulthood: Messages from the German birth cohort MAS.

*Lau S, Ann Allergy Asthma Immunol. 2019 Jan;122(1):25-32.*

Effect of allergen sensitisation and exposure at ≤ 3 years on lung function at age 7 years.




NS= Not sensitised to dust mites or cat dander. S/LE= sensitised to dust mites cat dander and low exposure to these allergens. S/HE= Sensitised to dust mites or cat dander and high exposure to these allergen.

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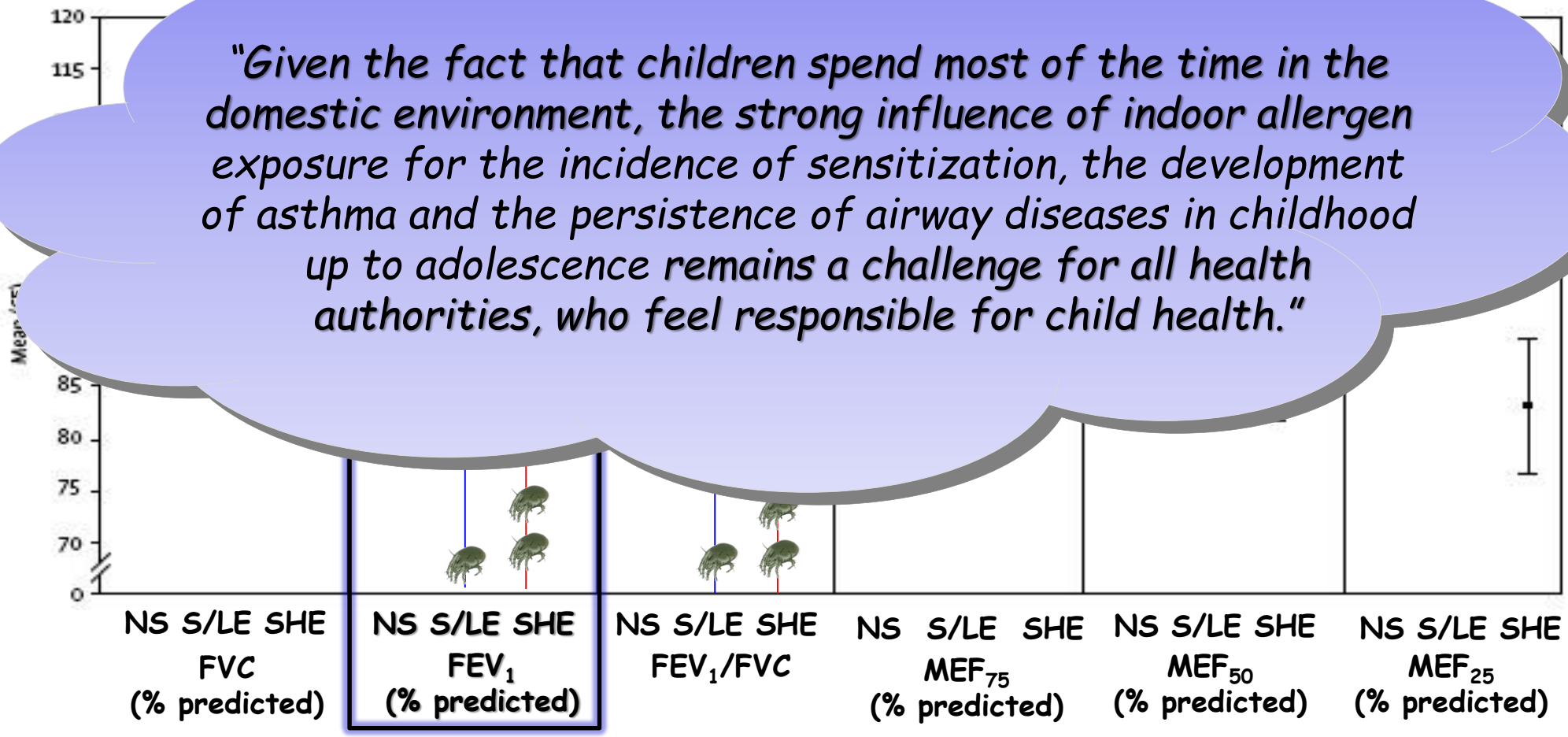


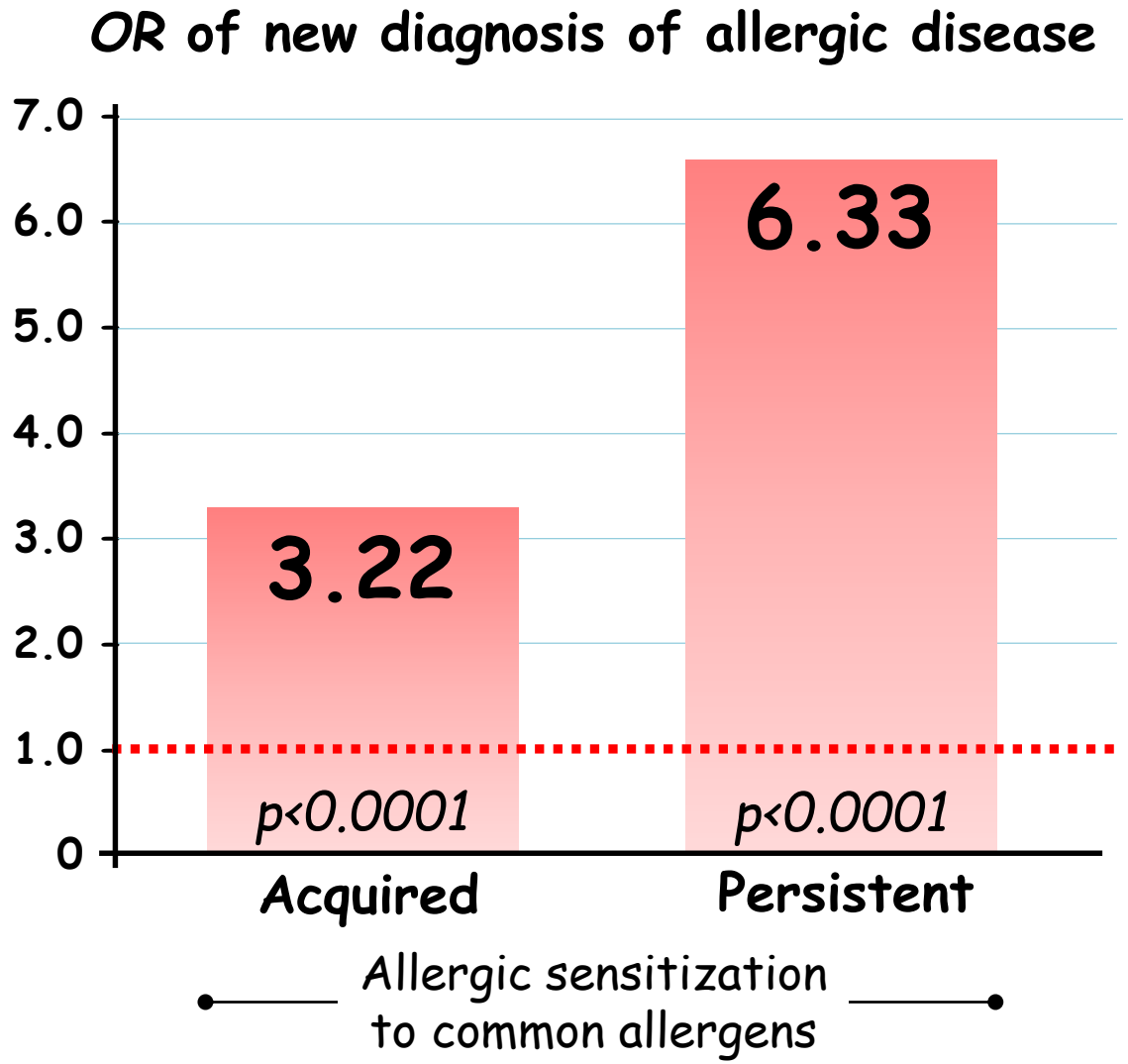

*"Given the fact that children spend most of the time in the domestic environment, the strong influence of indoor allergen exposure for the incidence of sensitization, the development of asthma and the persistence of airway diseases in childhood up to adolescence remains a challenge for all health authorities, who feel responsible for child health."*

NS= Not sensitised to dust mites or cat dander. S/LE= sensitised to dust mites cat dander and low exposure to these allergens. S/HE= Sensitised to dust mites or cat dander and high exposure to these allergen.

# Acquisition, remission, and persistence of eczema, asthma, and rhinitis in children

*Zhang H, CEA 2018;48:568-576*

- ✓ Isle of Wight birth cohort.
- ✓ Allergic sensitization at ages 4, 10, and 18 years.
- ✓ Asthma, rhinitis, and eczema by clinical diagnosis.



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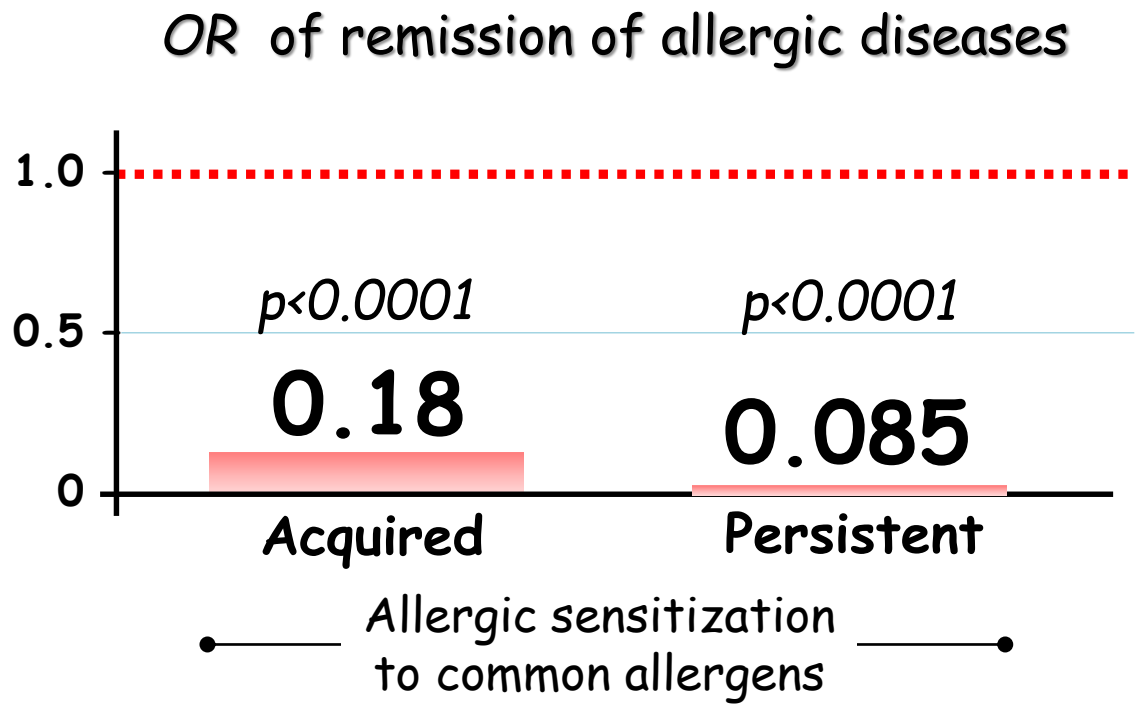


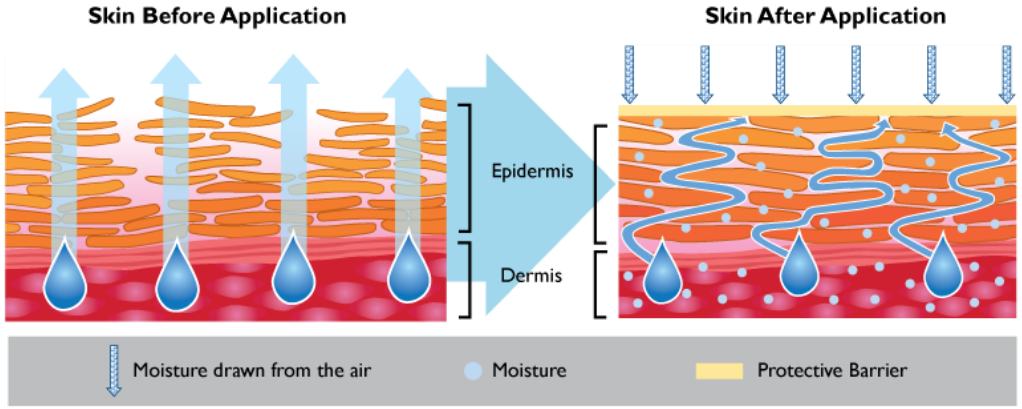
# Acquisition, remission, and persistence of eczema, asthma, and rhinitis in children

*Zhang H, CEA 2018;48:568-576*

***Conclusion:***

- Transition of allergic sensitizations to common allergens is a prognostic factor for subsequent or concurrent transition of eczema, asthma, and rhinitis.

- Prevention or reduction in allergic sensitization has a potential to lead to remission of these conditions.





# Predictive factor for asthma development

# Individual risk assessment tool for school-age asthma prediction in UK birth cohort.

*Wang R, Clin Exp Allergy. 2019 Mar;49(3):292-298.*

**BACKGROUND:**
Current published asthma predictive tools have **moderate positive likelihood ratios (+LR)** but **high negative likelihood ratios (-LR)** based on their recommended cut-offs, which limit their clinical usefulness.

| Positive LR | Negative LR | Interpretation |
|---|---|---|
| > 10 | < 0.1 | Generate large and often conclusive shifts in probability |
| 5 – 10 | 0.1 – 0.2 | Generate moderate shifts in probability |
| 2 – 5 | 0.2 – 0.5 | Generate small but sometimes important shifts in probability |
| 1 – 2 | 0.5 – 1 | Alter probability to a small and rarely important degree |

**OBJECTIVE:**
To develop a simple clinically applicable asthma prediction tool within a population-based birth cohort.

# Individual risk assessment tool for school-age asthma prediction in UK birth cohort.

*Wang R, Clin Exp Allergy. 2019 Mar;49(3):292-298.*

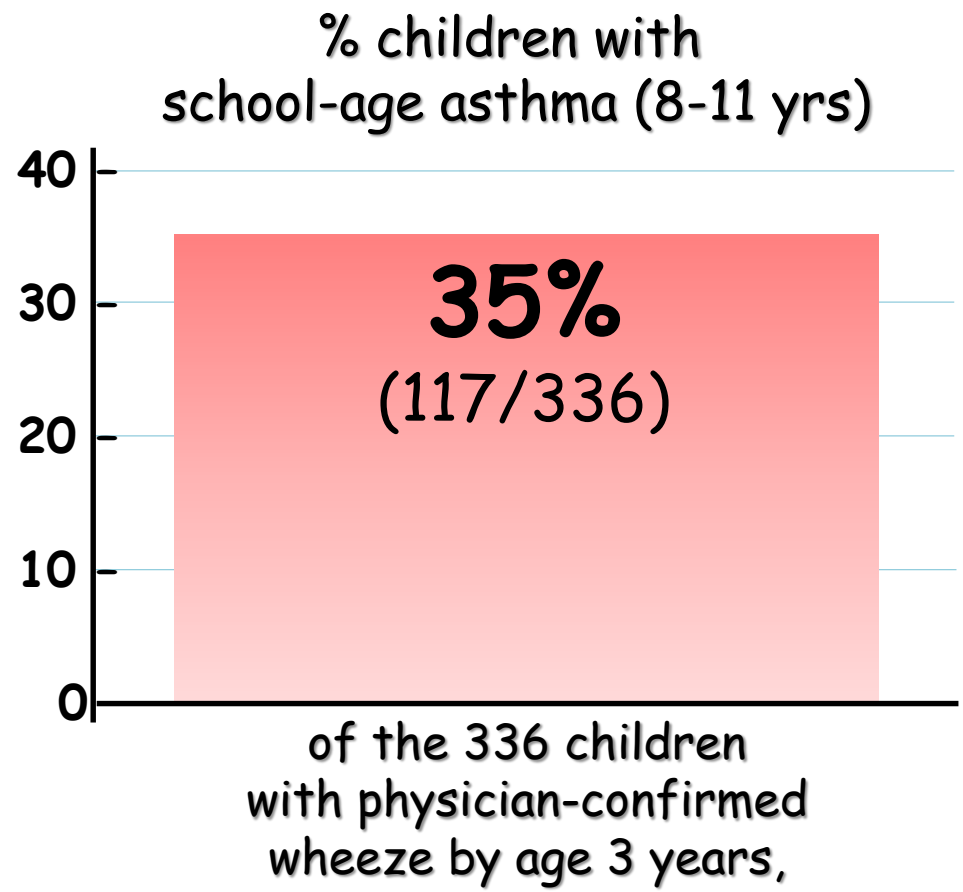
✓Children from the Manchester Asthma and Allergy Study (MAAS)

✓follow-up at ages 3, 8 and 11 years.

✓preschool wheeze extracted from primary-care records.

✓SPTs

✓Asthma at 8/11 years (school-age) defined as parentally reported:
(a) physician-diagnosed asthma and wheeze in the previous 12 months or
(b) ≥3 wheeze attacks in the previous 12 months.



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(a) physician-diagnosed asthma and wheeze in the previous 12 months or
(b) ≥3 wheeze attacks in the previous 12 months.

➢Logistic regression selected 5 significant risk factors which formed the basis of the **MAAS** asthma prediction tool (APT):

- wheeze after exercise;
- wheeze causing breathlessness;
- cough on exertion;
- current eczema
- SPT sensitisation

(maximum score 5).

Responses:
Yes score = 1
No score = 0

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(a) physician-diagnosed asthma and wheeze in the previous 12 months or
(b) ≥3 wheeze attacks in the previous 12 months.

- Children scoring ≥3 at age 3 yrs were at high risk of having asthma at school-age

○PPV > 75%

○+LR 6.3

○-LR 0.6

| Positive LR | Negative LR | Interpretation |
|---|---|---|
| > 10 | < 0.1 | Generate large and often conclusive shifts in probability |
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whereas children who had a score of 0 had very low risk (PPV 9.3%; LR 0.2).

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(a) physician-diagnosed asthma and wheeze in the previous 12 months or
(b) ≥3 wheeze attacks in the previous 12 months.

| MAAS APT score Number N=281 | Number of children within each score developing school-age asthma (% within the score, row%) |
|---|---|
| Score 0 n=86 | 8 (9.3%) |
| Score 1 n=85 | 21 (24.7%) |
| Score 2 n=53 | 20 (37.7%) |
| Score 3 n=43 | 31 (72.1%) |
| Score 4 n=11 | 9 (81.8%) |
| Score 5 n=3 | 3 (100%) |

Risk of asthma at school-age with each score derived at the age of 3 years

# Individual risk assessment tool for school-age asthma prediction in UK birth cohort.

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✓Children fr
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MAAS APT is a simple asthma prediction tool which could easily be applied in clinical and research settings.

- Children scoring ≥3 at age 3 yrs were at high risk of having asthma at school-age
  - PPV > 75%
  - +LR 6.3
  - -LR 0.6

| Positive LR | Negative LR | Interpretation |
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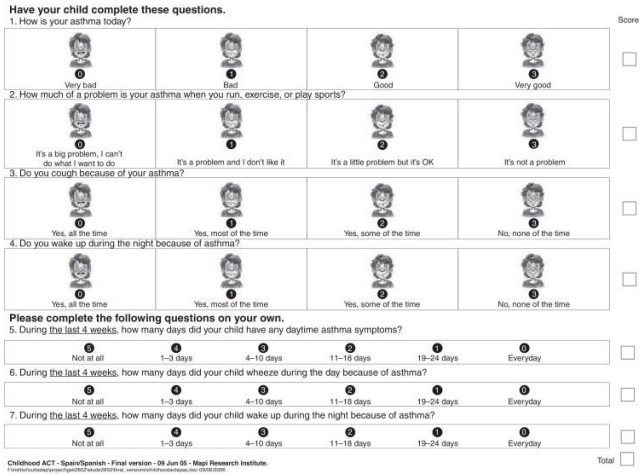
whereas children who had a score of 0 had very low risk (PPV 9.3%; LR 0.2).

# The impact of adenotonsillectomy on pediatric asthma.

*Goldstein NA, Pediatr Pulmonol. 2019 Jan;54(1):20-26.*

- ✓80 children with diagnosed asthma, aged 4-11, undergoing T&A
- ✓62 matched controls by asthma severity classification.
- ✓Follow-up 6 months



**Have your child complete these questions.**

1. How is your asthma today?

| Very bad | Bad | Good | Very good |
|---|---|---|---|
| 0 | 1 | 2 | 3 |

2. How much of a problem is your asthma when you run, exercise, or play sports?

| It's a big problem, I can't do what I want to do | It's a problem and I don't like it | It's a little problem but it's OK | It's not a problem |
|---|---|---|---|
| 0 | 1 | 2 | 3 |

3. Do you cough because of your asthma?

| Yes, all the time | Yes, most of the time | Yes, some of the time | No, none of the time |
|---|---|---|---|
| 0 | 1 | 2 | 3 |

4. Do you wake up during the night because of asthma?

| Yes, all the time | Yes, most of the time | Yes, some of the time | No, none of the time |
|---|---|---|---|
| 0 | 1 | 2 | 3 |

**Please complete the following questions on your own.**

5. During the last 4 weeks, how many days did your child have any daytime asthma symptoms?

| Not at all | 1–3 days | 4–10 days | 11–18 days | 19–24 days | Everyday |
|---|---|---|---|---|---|
| 5 | 4 | 3 | 2 | 1 | 0 |

6. During the last 4 weeks, how many days did your child wheeze during the day because of asthma?

| Not at all | 1–3 days | 4–10 days | 11–18 days | 19–24 days | Everyday |
|---|---|---|---|---|---|
| 5 | 4 | 3 | 2 | 1 | 0 |

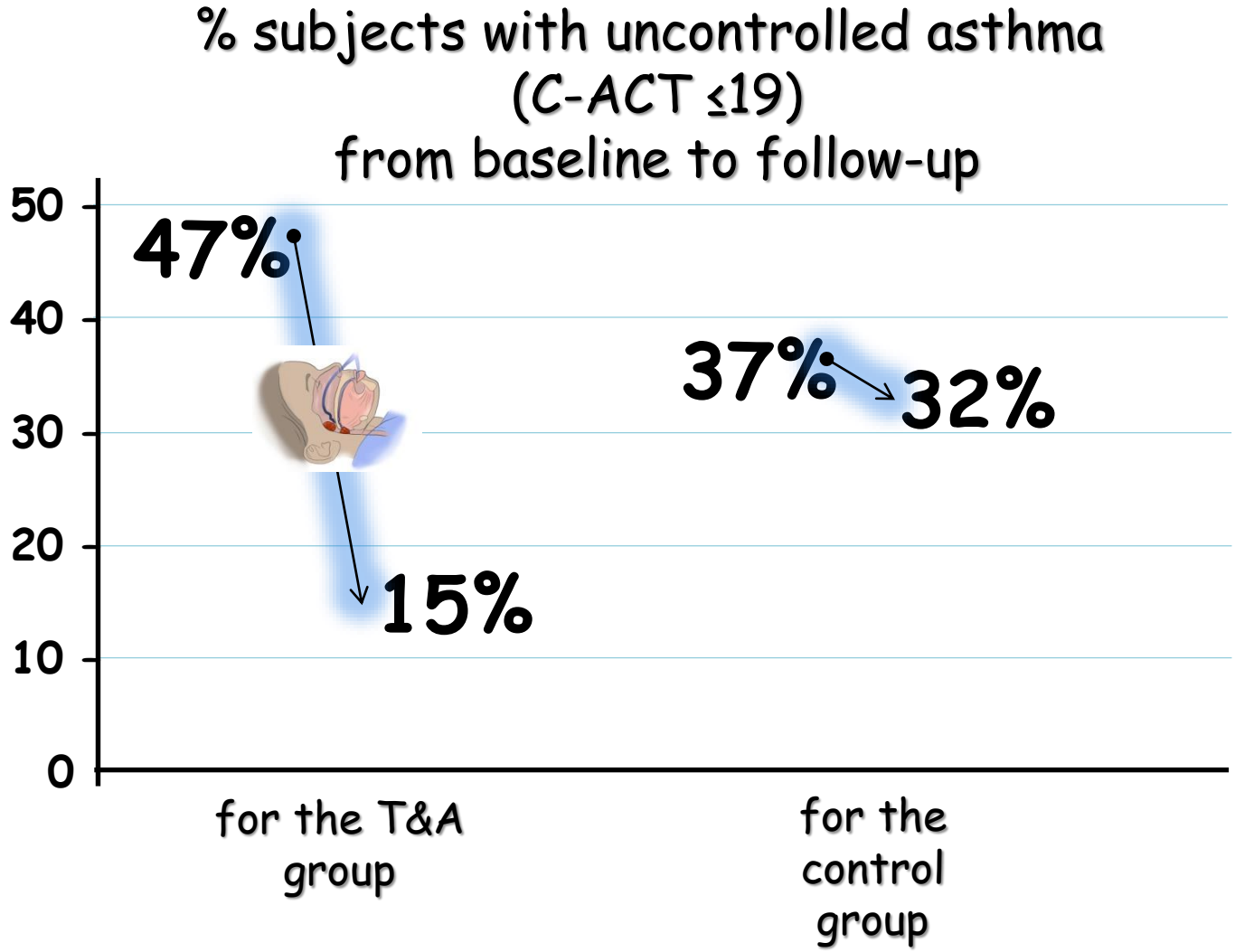
7. During the last 4 weeks, how many days did your child wake up during the night because of asthma?

| Not at all | 1–3 days | 4–10 days | 11–18 days | 19–24 days | Everyday |
|---|---|---|---|---|---|
| 5 | 4 | 3 | 2 | 1 | 0 |

Score

Total

**Childhood ACT - Spain/Spanish - Final version - 09 Jun 05 - Mapi Research Institute.**



# Asthma
# Indication
# for Hospital admission

# Development of a pediatric asthma predictive index for hospitalization.

*Jean T. Ann Allergy Asthma Immunol. 2019 Mar;122(3):283-288.*

**BACKGROUND:**


- Variation in emergency department (ED) management for asthma exacerbation leads to disparities in care.
- Current asthma severity scores are insufficient to be used for hospitalization decisions.

**OBJECTIVE:**

- To develop and internally validate an asthma predictive index for hospitalization (APIH) to guide practitioners in their admission decision for children with asthma exacerbations.

# Development of a pediatric asthma predictive index for hospitalization.

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✓12,066 children
5-18 years old
diagnosed with
asthma
exacerbation
in the ED

Table 1. Range of respiration rates[2]

| Group | Age | Breaths/min |
|---|---|---|
| Newborn to 6 weeks | Newborn to 6 weeks | 30 - 60 |
| Infant | 6 weeks to 6 months | 25 - 40 |
| Toddler | 1 to 3 years | 20 - 30 |
| Young Children | 3 to 6 years | 20 - 25 |
| Older Children | 10 to 14 years | 15 - 20 |
| Adults | Adults | 12 - 20 |

The highest risk factors associated with asthma hospitalization from the ED are:

1. oxygen saturation less than 94%,
2. respiratory rate greater than 31/min,
3. history of pneumonia, and
4. asthma ED visits in past 12 months.

with a predictive model that **combined** these risk factors, the **OR** was **44.9**

# Development of a pediatric asthma predictive index for hospitalization.

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Final Reduced Asthma Prediction Model Using Entire Cohort Population

| Predictor | OR (95% CI) |
|---|---|
| Oxygen saturation <94% | 3.3 (2.8-4.0) |
| Respiration rate >31/min | 3.1 (2.6-3.7) |
| Pneumonia history | 2.7 (2.2-3.2) |
| Asthma ED visit in 12 mo | 1.6 (1.4-2.0) |
| All 4 risk factors vs no risk factors | 44.9 (32.8-61.4) |

Abbreviations: ED, emergency department; OR, odds ratio.

**CONCLUSION:**

We have developed and internally validated a pediatric hospitalization prediction index for acute asthma exacerbation in the ED.

**Development of a pediatric asthma predictive index for hospitalization.**

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# Is My Child Breathing **Too Fast?**

| | |
|---|---|
| **Up to 6 months:** | 30-60 BREATHS PER MINUTE |
| **6-12 months:** | 24-30 BREATHS PER MINUTE |
| **1-5 years:** | 20-30 BREATHS PER MINUTE |
| **6-12 years:** | 12-20 BREATHS PER MINUTE |
| **12 years and up** | 12-20 BREATHS PER MINUTE |

# Asthma treatment

## Wheezing infants

# Asthma treatment

## bronchodilators

# Salbutamol and ipratropium by inhaler is superior to nebulizer in children with severe acute asthma exacerbation: Randomized clinical trial.

*Iramain R, Pediatr Pulmonol. 2019 Apr;54(4):372-377.*


- In the United States, 2.1 and 10.7% of children with asthma (ages 0-17 years) have been reported **at least one hospitalization** and **at least one emergency room (ER) visit** in the previous year, respectively.


- In 2008, there were 10.5 million missed school days due to asthma among American schoolchildren.


- Moreover, severe exacerbations are risk markers of both subsequent exacerbations and mortality from asthma.

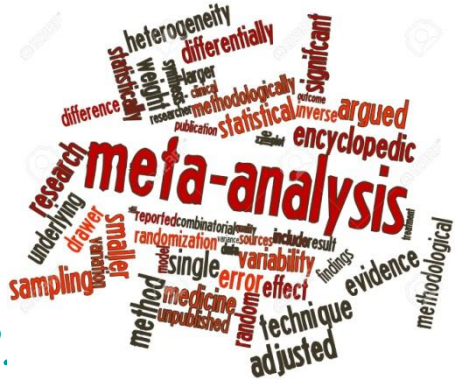
# Salbutamol and ipratropium by inhaler is superior to nebulizer in children with severe acute asthma exacerbation: Randomized clinical trial.

*Iramain R, Pediatr Pulmonol. 2019 Apr;54(4):372-377.*


- **Meta-analysis** showed that using salbutamol (or albuterol) by meter doses inhaler (MDI) with a valved holding chamber (VHC) In children with moderate-severe acute asthma exacerbation was more effective, that is, **fewer hospital admissions, more clinical improvement, and had fewer adverse effects** (tremor and tachycardia) **than salbutamol by nebulizer.**


- *Castro-Rodriguez JA, Agonists through metered-dose inhaler with valved holding chamber versus nebulizer for acute exacerbation of wheezing or asthma in children under 5 years of age: a systematic review with meta-analysis. J Pediatr. 2004;145: 172–177.*

- *Cates CJ, Holding chambers (spacers) versus nebulisers for beta-agonist treatment of acute asthma. Cochrane Database Syst Rev. 2006;CD000052.*



# Salbutamol and ipratropium by inhaler is superior to nebulizer in children with severe acute asthma exacerbation: Randomized clinical trial.

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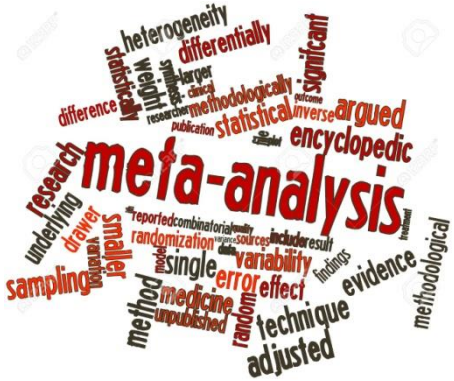
- For children with more severe asthma exacerbation adding ipratropium bromide to salbutamol results in a better response (less hospital admission, improvement in lung function, and clinical score) with less adverse effects (less nausea and tremor) than salbutamol alone.


- *Rodrigo G, Castro-Rodriguez JA. Anticholinergics in the treatment of children and adults with acute asthma: a systematic review with metaanalysis. Thorax. 2005;60:740–746.*

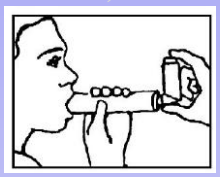
- *Griffiths B, Ducharme FM. Combined inhaled anticholinergics And short-acting beta2-agonists for initial treatment of acute asthma in children. Cochrane Database Syst Rev. 2013; Article no. CD000060.*



# Salbutamol and ipratropium by inhaler is superior to nebulizer in children with severe acute asthma exacerbatio

Therefore, several international guidelines recommend the use of salbutamol by MDI rather than by nebulizer for moderate-severe asthma exacerbations.


- *Global Initiative for Asthma. Global strategy for asthma management and prevention. 2017. Available from: http://www.ginasthma.org. Accessed March 2017.*
- *National Asthma Education and Prevention Program. Expert Panel Report 3: Guidelines for the Diagnosis and Management of Asthma, 2007. Bethesda, MD: National Institutes of Health, National Heart, Lung, and Blood Institute. Available from: http://www.nhlbi.nih.gov/guidelines/asthma/asthgdln.pdf.*
- *British Thoracic Society; Scottish Intercollegiate Guidelines Network. British guideline on the management of asthma. Thorax. 2014;69:1–192.*

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# Salbutamol and ipratropium by inhaler is superior to nebulizer in children with severe acute asthma exacerbation: Randomized clinical trial.

*Iramain R, Pediatr Pulmonol. 2019 Apr;54(4):372-377.*

**INTRODUCTION:**

In moderate-severe asthma exacerbation, salbutamol by inhaler (MDI) is superior to salbutamol delivered by nebulizer (NEB); however, to our knowledge, no studies in children with exclusively severe exacerbations were performed.

**OBJECTIVE:**

To compare the efficacy of salbutamol and ipratropium bromide by MDI versus by NEB in severe asthma exacerbations

# Salbutamol and ipratropium by inhaler is superior to nebulizer in children with severe acute asthma exacerbation: Randomized clinical trial.

*Iramain R, Pediatr Pulmonol. 2019 Apr;54(4):372-377.*

✓103 children (2-14 years of age) with severe asthma exacerbations (defined by the Pulmonary Score ≥ 7) seen at the emergency room

✓One group received salbutamol and ipratropium (two puff every 10 min for 2 h and then every 30 min for 2 h more) by MDI with a valved-holding chamber and mask along with oxygen by a cannula separately (MDI-SIB);

the other received nebulization with oxygen by nasal cannula (NEB-SIB) of salbutamol and ipratropium (1 every 20 min for 2 h and then every 30 min for 2 h more).

**TABLE 1** Pulmonary score[12]

| | Respiratory rate (breaths/min) | | | |
|---|---|---|---|---|
| Score | <6 yrs | ≥6 yrs | Wheezing | Accessory muscle use-sternocleidomastoid |
| 0 | <30 | <20 | None | No apparent increase |
| 1 | 31-45 | 21-35 | Terminal expiration with stethoscope | Mild increase |
| 2 | 46-60 | 36-50 | Entire expiration with stethoscope | Increase |
| 3 | >60 | >50 | Inspiration & expiration without stethoscope | Maximal activity |

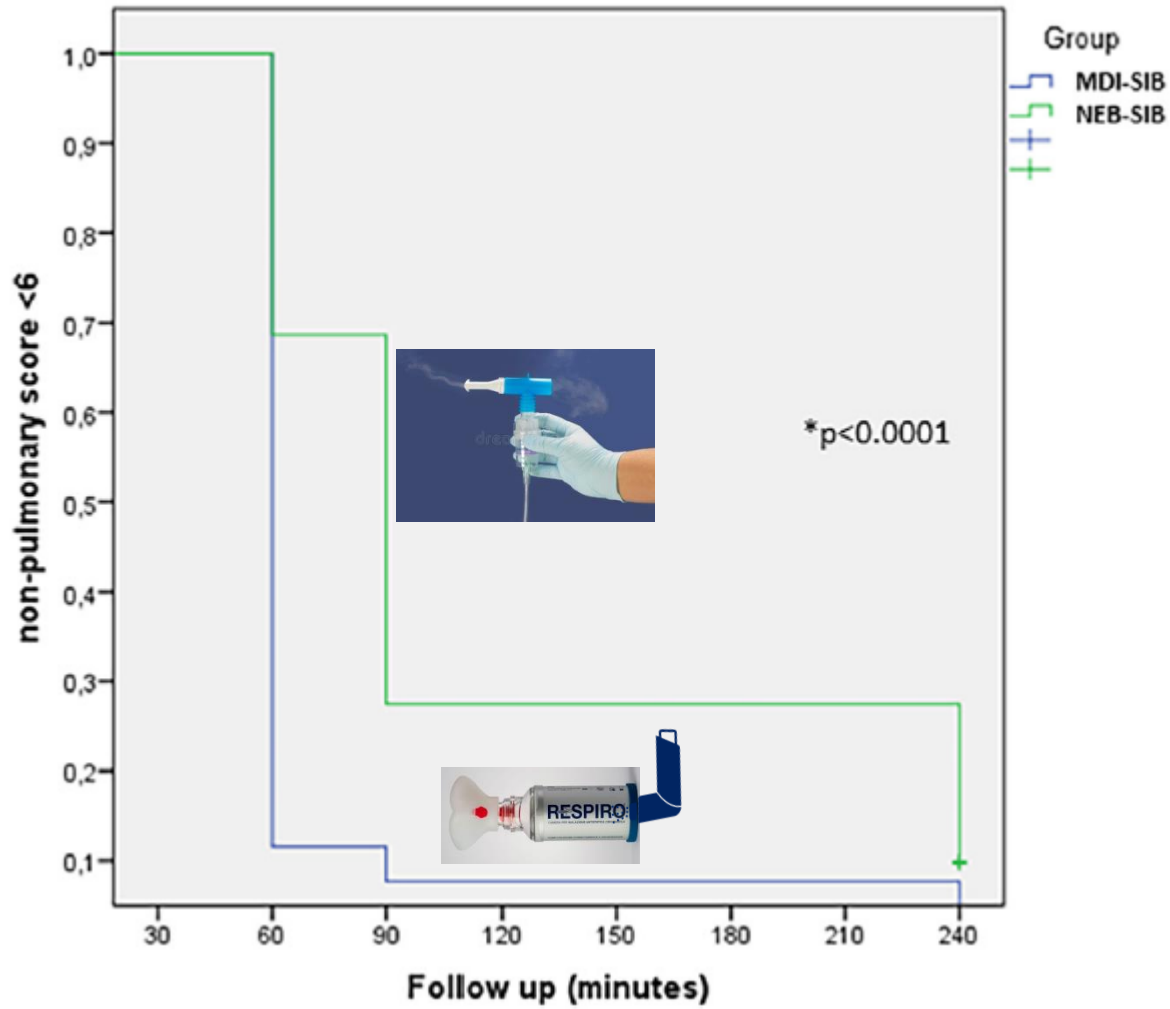
The Pulmonary Score ranges from 0 (no or very mild exacerbation) to 9 (severe exacerbation).

# Salbutamol and ipratropium by inhaler is superior to nebulizer in children with severe acute asthma exacerbation: Randomized clinical trial.

*Iramain R, Pediatr Pulmonol. 2019 Apr;54(4):372-377.*

Primary outcome was the rate of hospitalization (Pulmonary Score ≥ 7) after 4 h and secondary outcome was oxygen saturation.

Survival analysis for non-pulmonary score <6 during the treatment between groups



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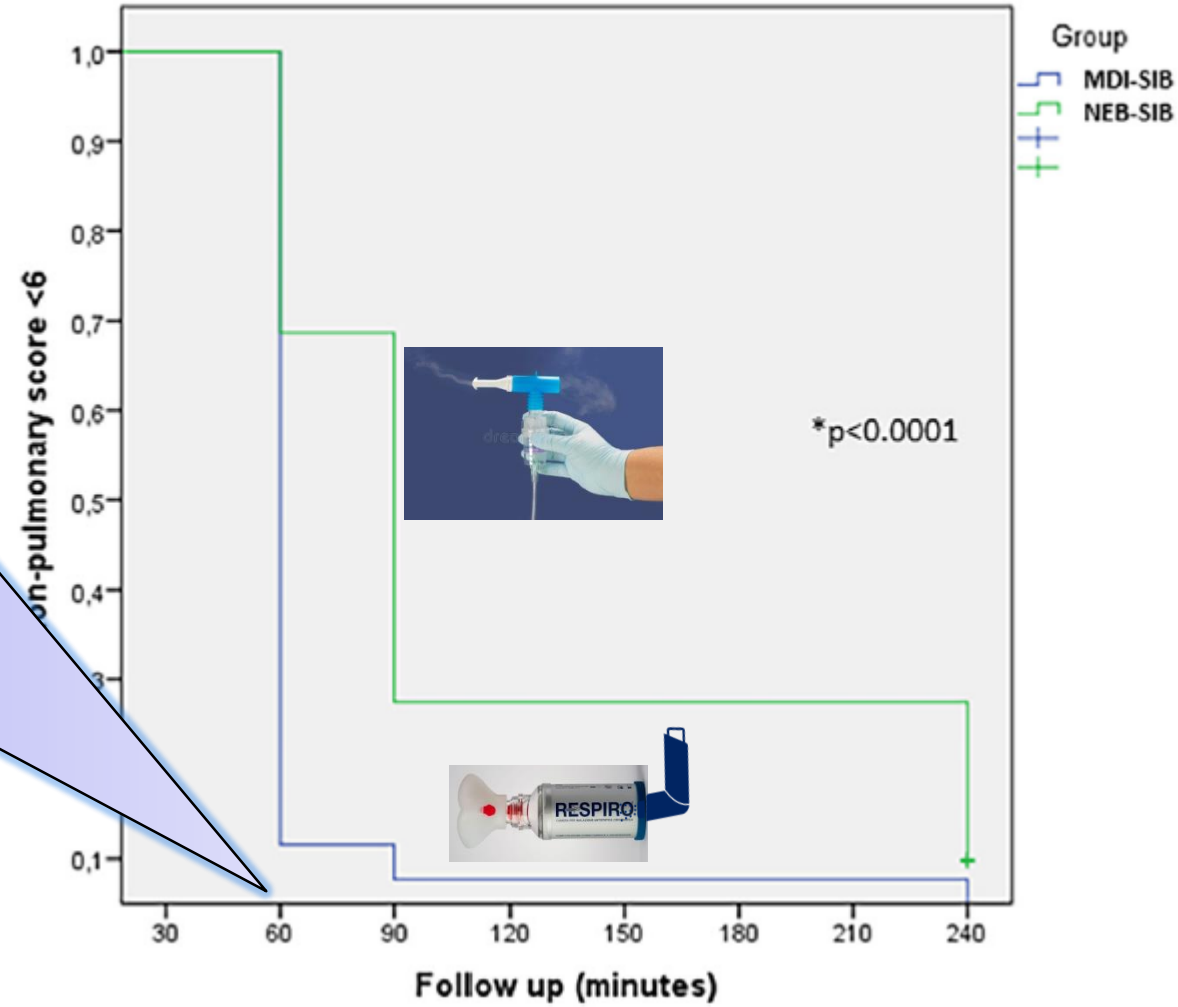
*Iramain R, Pediatr Pulmonol. 2019 Apr;54(4):372-377.*

We found no improvement in clinical score at 30 min nor saturation at 60 min.

These results are in accordance with systematic reviews showing that **only after repeated doses of salbutamol and ipratropium bromide a clinical effect is reached.**



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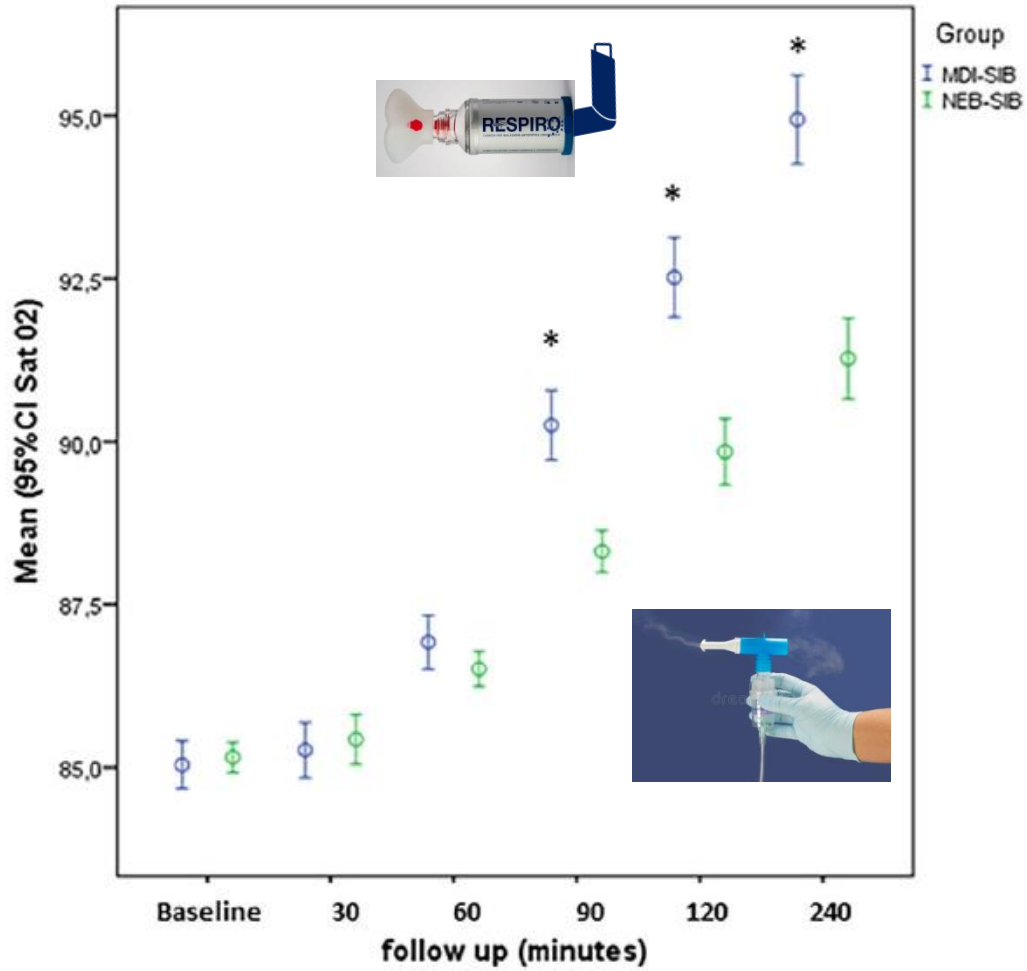
Oxygen saturation (mean and 95%CI) during the treatment between groups
*(*P < 0.0001)*



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nebulizers use higher doses of drugs, higher oral pharyngeal deposit, and more systemic absorption of the drug compared to MDI

**TABLE 3** Comparison of treatment between the two study groups

| | MDI-SIB (*n* = 52) | NEB-SIB (*n* = 51) | *P*-value |
|---|---|---|---|
| Heart rate (beat/min) | | | |
| Basal | 156.63 ± 1.84 | 156.54 ± 1.77 | 0.8 |
| 30 min | 156.76 ± 4.88 | 160.17 ± 4.77 | 0.003 |
| 60 min | 159.67 ± 7.29 | 166.84 ± 6.67 | <0.00001 |
| 90 min | 158.46 ± 8.24 | 166.84 ± 6.67 | <0.00001 |
| 120 min | 158.34 ± 5.10 | 173.05 ± 8.58 | <0.00001 |
| 4 h | 144.7692 ± 6.50 | 172.20 ± 9.52 | <0.00001 |
| Hospital admission at 4 h[a] | 3 (5.76%) | 14 (27.45%) | 0.003 |

hospital admission (~80% decrease),

# Let Them Breathe: A Plea to Pediatricians to Advocate for Stock Inhaler Policies at School.

*Pappalardo AA, Pediatrics. 2019 Jul;144(1). pii: e20182857.*

- In a study of asthma-related deaths in the school setting **between 1990 and 2003, authors cited 38 reported asthma school deaths**, which the authors believe was an underestimate.

*Greiling AK, A preliminary investigation of asthma mortality in schools. J Sch Health. 2005; 75(8):286-290*

- **31%** of these children died while waiting for medical intervention.

➢ These adverse events are likely **avoidable with stock inhalers** because access to rescue medications is a key component of guideline-based response in asthma emergencies

# Let Them Breathe: A Plea to Pediatricians to Advocate for Stock Inhaler Policies at School.

*Pappalardo AA, Pediatrics. 2019 Jul;144(1). pii: e20182857.*

- Schools can purchase a single inhaler containing albuterol to administer to anyone who experiences:
  - the sudden onset of cough,
  - shortness of breath, and
  - chest tightness

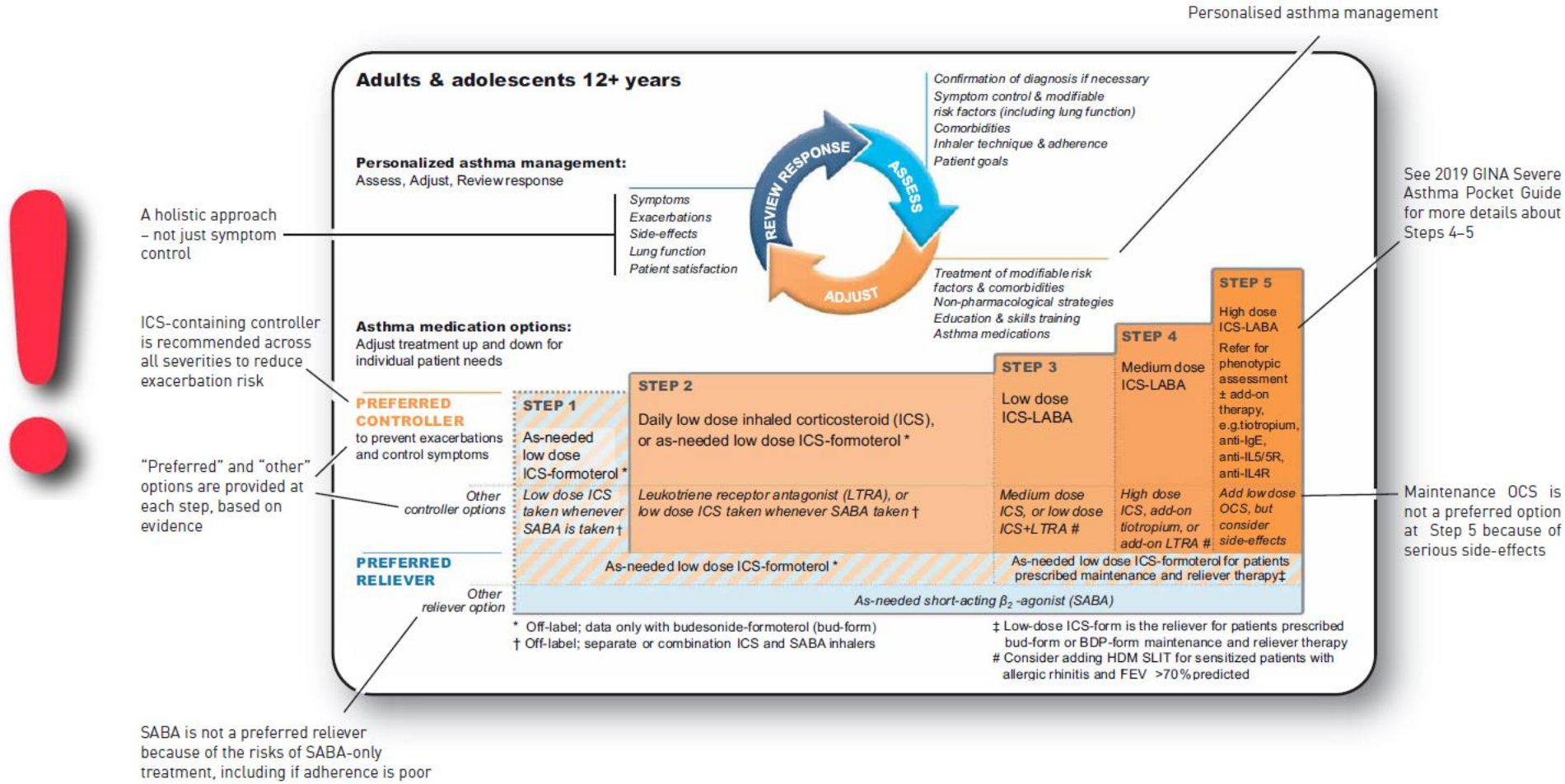
that signals an asthma attack.

# Asthma treatment

## ICS

# GINA 2019: a fundamental change in asthma management: Treatment of asthma with short-acting bronchodilators alone is no longer recommended for adults and adolescents.

*Reddel HK, Eur Respir J. 2019 Jun 27;53(6). pii: 1901046.*



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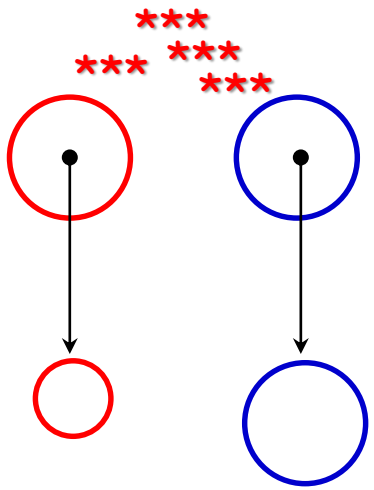
- In April 2019, the Global Initiative for Asthma (GINA) published new recommendations that might be considered the most fundamental change in asthma management in 30 years.

- *For safety, GINA no longer recommends treatment of asthma in adolescents and adults with SABA alone.*

- *Instead, to reduce their risk of serious exacerbations, all adults and adolescents with asthma should receive either symptom-driven (in mild asthma) or daily inhaled corticosteroid (ICS)-containing treatment.*



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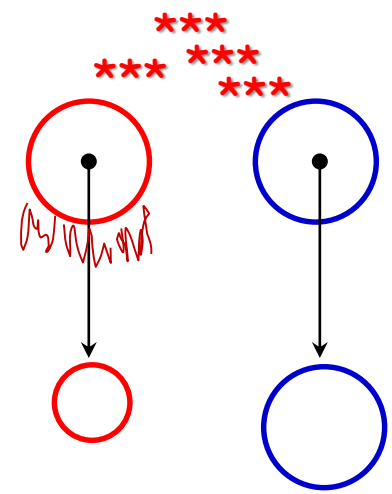

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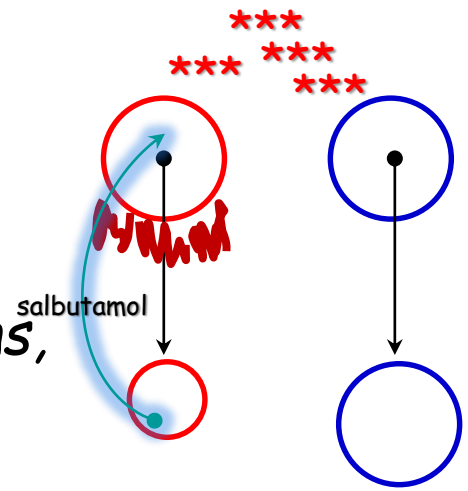


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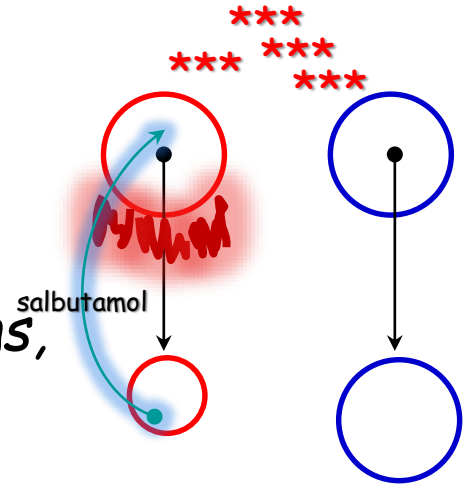

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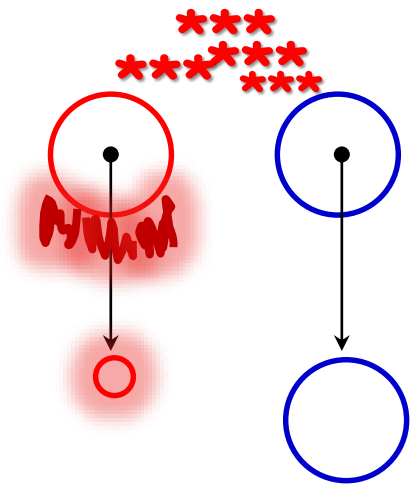


- *Instead, to reduce their risk of serious exacerbations, all adults and adolescents with asthma should receive either symptom-driven (in mild asthma) or daily inhaled corticosteroid (ICS)-containing treatment.*

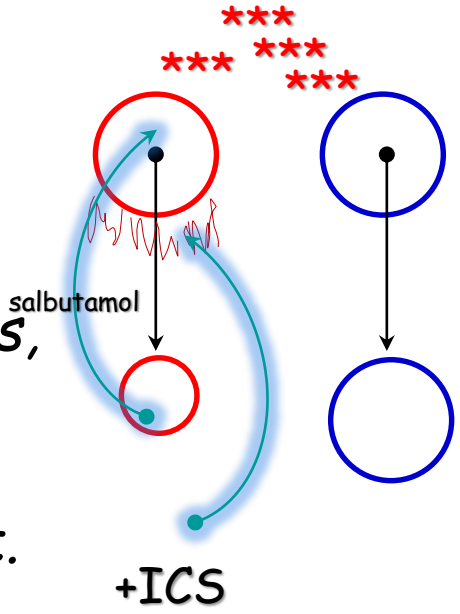
# GINA 2019: a fundamental change in asthma management: Treatment of asthma with short-acting bronchodilators alone is no longer recommended for adults and adolescents.

*Reddel HK, Eur Respir J. 2019 Jun 27;53(6). pii: 1901046.*

- In April 2019, the Global Initiative for Asthma (GINA) published new recommendations that might be considered the most fundamental change in asthma management in 30 years.

- *For safety, GINA no longer recommends treatment of asthma in adolescents and adults with SABA alone.*

- *Instead, to reduce their risk of serious exacerbations, all adults and adolescents with asthma should receive either symptom-driven (in mild asthma) or daily inhaled corticosteroid (ICS)-containing treatment.*



# What is New in General Pediatrics, Allergic & Respiratory Diseases 2019 ?


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


- ✓ General Pediatrics
- ✓ Food Allergy
- ✓ Atopic Dermatitis
- ✓ Asthma
- ✓ **Anaphylaxis**
- ✓ Urticaria & Angioedema
- ✓ Infectious Respiratory Diseases

# A longitudinal study of hymenoptera stings in preschool children.

*Clifford D, Pediatr Allergy Immunol. 2019 Feb;30(1):93-98.*

- The number of **systemic reactions** reported in our study was low throughout our follow-up to 5 years, only eight children in total or **2% of those that were stung**.

- **Skin prick testing was positive in 0.9% at 2 years and 0.4% at 5 years**, with only one child sensitized to both bee and wasp at 2 years.

- **Five of those who had a positive SPT at 2 years had not been stung**, implying that cross-reactivity from IgE antibodies for different venoms or bites can take place.

- **No child was sensitized at both 2 and 5 years**, indicating that this non-specific venom sensitization can wane, and three were subsequently stung, with no systemic reaction.

- This confirms the **low specificity of skin prick testing in a general population**

# What is New in General Pediatrics, Allergic & Respiratory Diseases 2019 ?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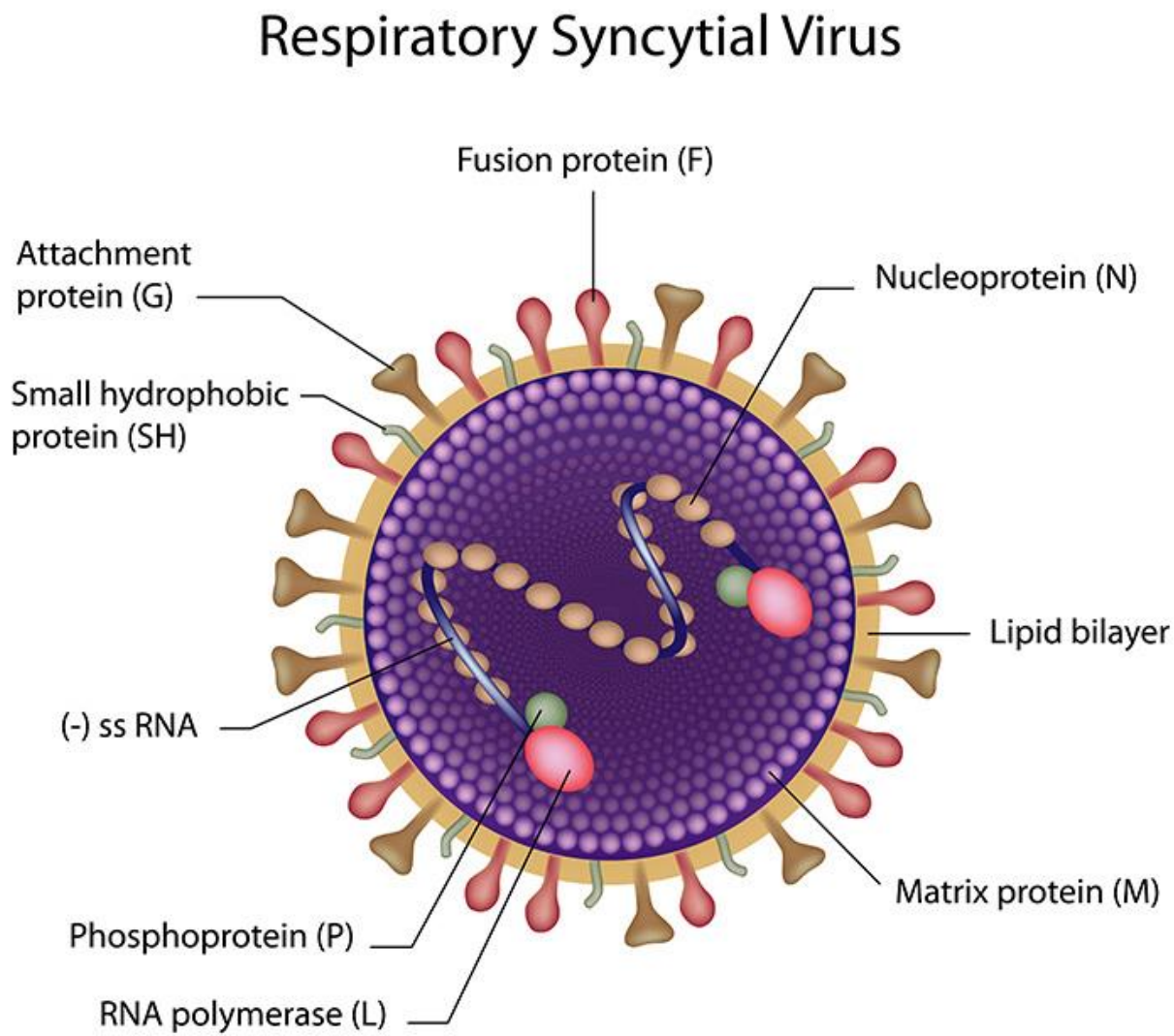
- ✓ **Infectious Respiratory Diseases**

# bronchiolitis



# Modified Tal Score:
# Validated score for prediction of bronchiolitis severity.

*Golan-Tripto I, Pediatr Pulmonol. 2018 Jun;53(6):796-801.*

- It is difficult to assess the **severity of acute bronchiolitis** using laboratory tests or pulmonary function testing in the pediatric population, thus, several different scoring systems are being used, including the **Tal score,**[1] **Modified Tal score (MTS)**[2] **Lowell score,**[3] **Wang score,**[4] **and Liu score.**[5]


*1. Tal A, Dexamethasone and salbutamol in the treatment of acute wheezing in infants. Pediatrics. 1983;71:13–18.*

*2. McCallum GB, Severity scoring systems: are they internally valid, reliable and predictive of oxygen use in children with acute bronchiolitis? Pediatr Pulmonol. 2013;48:797–803.*

*3. Lowell DI, Wheezing in infants: the response to epinephrine. Pediatrics. 1987;79:939–945.*

*4. Wang, Observer agreement for respiratory signs and oximetry in infants hospitalized with lower respiratory infections. Am Rev Respir Dis. 1992;145:106–109.*

*5. Liu LL. Use of a respiratory clinical score among different providers. Pediatr Pulmonol. 2004;37:243–248.*

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2. McCal ... of a

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Many different scoring systems causes inhomogeneity in clinical researches and practical clinics, therefore, **there exists a need for a unique and uniform clinical scoring system.**

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*4. Wa… 1*

*5. … Pulmonol. 2004;37:2 15…*


**McCallum et al**[2] reviewed the available scoring systems and identified the **MTS as the most clinically appropriate and easy to use.**
They concluded that the MTS is repeatable and can be reliably used in research and clinical practice

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## Modified Tal score *7,8*

| | Modified Tal score | | | | |
|---|---|---|---|---|---|
| | Respiratory rate (breaths/min) | | | | |
| Score | Age <6 months | Age ≥6 months | Wheezing/Crackles | $O_2$ Saturation (room air) | Accessory respiratory muscle utilization |
| 0 | ≤40 | ≤30 | None | ≥95 | None (no chest in-drawing) |
| 1 | 41-55 | 31-45 | Expiration only | 92-94 | + Presence of mild intercostal in-drawing |
| 2 | 56-70 | 46-60 | Expiration and inspiration with stethoscope only | 90-91 | ++ Moderate amount of intercostal in-drawing |
| 3 | ≥71 | ≥61 | Expiration and inspiration without stethoscope | ≤89 | +++ Moderate or marked intercostal in-drawing, with present of head bobbing or tracheal tug |


*7. Tal A, Dexamethasone and salbutamol in the treatment of acute wheezing in infants. Pediatrics. 1983;71:13–18.*

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# Modified Tal Score:
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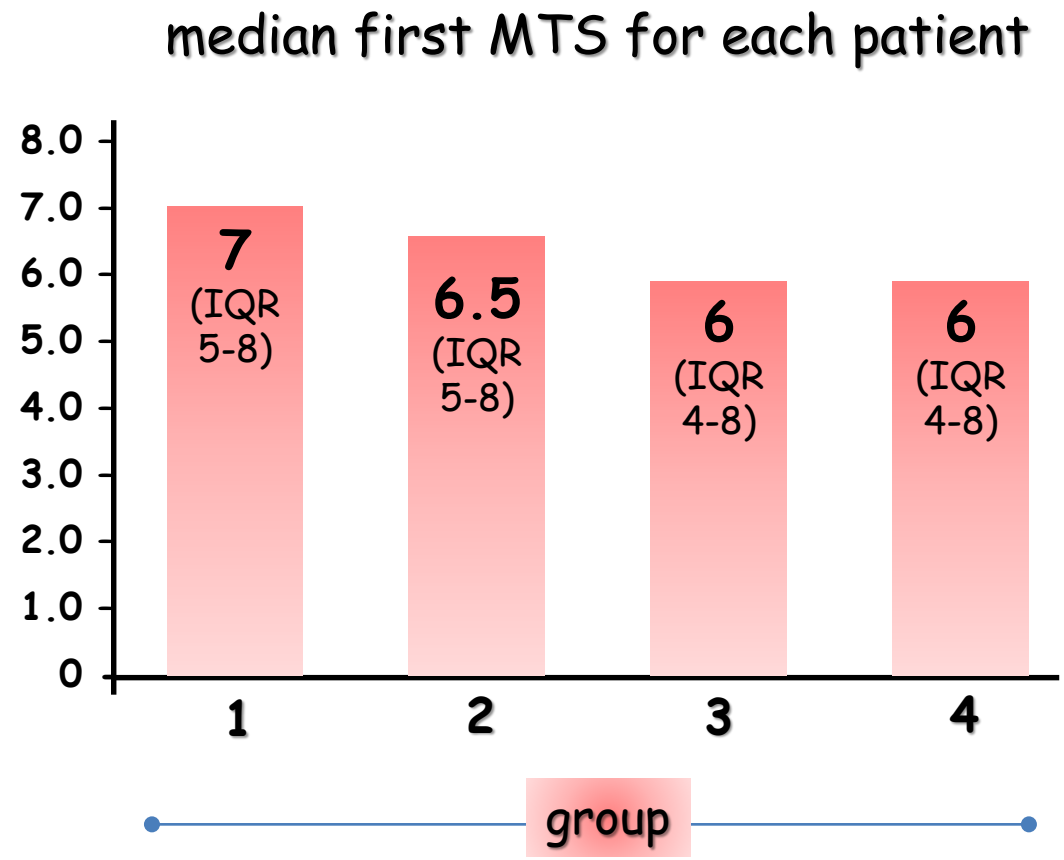
*Golan-Tripto I, Pediatr Pulmonol. 2018 Jun;53(6):796-801.*

✓prospective cohort study included 50 infants of <12 months of age diagnosed with bronchiolitis and assessed via **Modified Tal Score (MTS).**

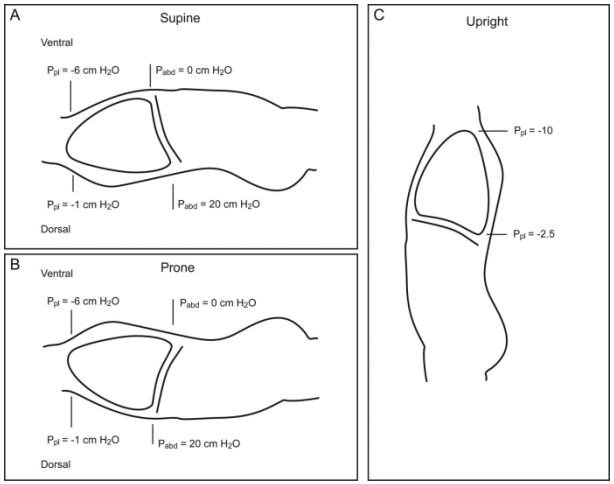
✓intra-class correlation coefficient (ICC) among four groups of raters:
group 1, **board-certified pediatric pulmonologists;**
group 2, **board-certified pediatricians;**
group 3, **senior pediatric residents;** and
group 4, **junior pediatric residents.**

✓24 physicians recorded a total of 600 scores



# Physiological Effect of Prone Position in Children with Severe Bronchiolitis: A Randomized Cross-Over Study (BRONCHIO-DV)

*Baudin F, J Pediatr. 2019 Feb;205:112-119.e4.*




- Prone positioning has been proposed in children with severe bronchiolitis.

- The prone position is easy to perform in small children and is commonly used in neonatal and pediatric intensive care.

- In adults, the prone position significantly decreases mortality in patients with severe acute respiratory distress syndrome and improves oxygenation.

- Moreover, the prone position may improve respiratory mechanics and gas exchange in adults with chronic bronchitis as in neonates.

# Physiological Effect of Prone Position in Children with Severe Bronchiolitis: A Randomized Cross-Over Study (BRONCHIO-DV)

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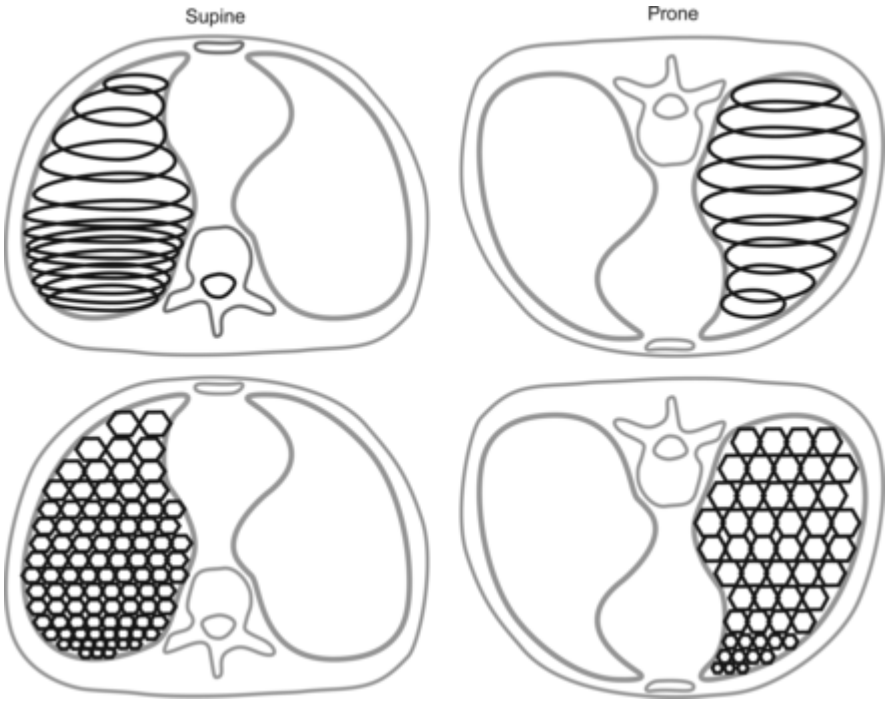
- The prone position is also able to decrease airway resistance in children invasively ventilated for severe viral bronchiolitis and to decrease apnea occurrence in children with mild bronchiolitis.

- Therefore, we hypothesized that the prone position may improve respiratory mechanics in children with severe bronchiolitis requiring nasal continuous positive airway pressure (nCPAP).




supine position causes higher strain (sforzo) and larger variation in the distribution of alveolar sizes due to the effects of gravity and a steeper stress production during mechanical inspiration in the upper lung regions. In contrast, prone position produces a more even strain and more homogeneous distribution of alveolar size that lessens inhomogeneity in stress development throughout the lungs during mechanical inspiration.

# Physiological Effect of Prone Position in Children with Severe Bronchiolitis: A Randomized Cross-Over Study (BRONCHIO-DV)

*Baudin F, J Pediatr. 2019 Feb;205:112-119.e4.*

✓14 infants, median age 33 days

✓randomized to 7 $cmH_2O$ continuous positive airway pressure for 1 hour in the prone position or in the supine position, followed by cross-over.

✓Flow, esophageal, airway, gastric, and transdiaphragmatic pressures, as well as electrical activity of the diaphragm were simultaneously recorded.

✓modified Wood clinical asthma score

➢in the prone position than in the supine position were significantly lower:

•the median esophageal pressure-time product per minute (227 $cmH_2O$*s/minute vs 353 $cmH_2O$*s/minute; $P = 0.048$),

•the modified Wood clinical asthma score ($P = 0.033$) and

•the electrical activity of the diaphragm ($P = 0.006$).

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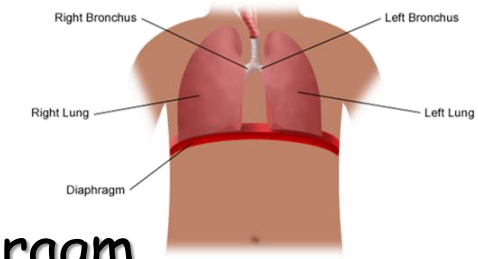


•the neuromechanical efficiency of the diaphragm, as assessed by transdiaphramagtic pressure to electrical activity of the diaphragm swing ratio.

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This study suggests a benefit of the prone position for infants with severe bronchiolitis requiring non-invasive ventilation by significantly decreasing the inspiratory effort and the metabolic cost of breathing.

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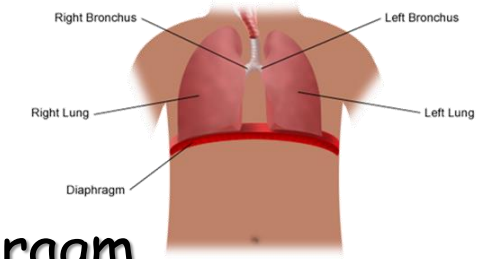


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# Chronic Cough Related to Acute Viral Bronchiolitis in Children: CHEST Expert Panel Report.

*Chang AB, Chest. 2018 Aug;154(2):378-382.*

**1. For children with chronic cough (> 4 weeks) after acute viral bronchiolitis, we suggest that the cough be managed according to the CHEST pediatric chronic cough guidelines**

*Remark:* These include the evaluation for the presence of cough pointers and the use of 2 weeks of antibiotics targeted to common respiratory bacteria (*Streptococcus pneumoniae, Haemophilus influenzae, Moraxella catarrhalis*) and local antibiotic sensitivities managing in children with wet or productive cough unrelated to an underlying disease and without any specific cough pointers (eg, coughing with feeding, digital clubbing).

# Chronic Cough Related to Acute Viral Bronchiolitis in Children: CHEST Expert Panel Report.

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**2. For children with chronic cough (> 4 weeks) after acute viral bronchiolitis, we suggest that asthma medications not be used for the cough unless other evidence of asthma is present.**

*Remark:* Symptoms of asthma include the presence of recurrent wheeze, and/or dyspnea, Rint reversibility.


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If present think of the opportunity for a treatment with azithromycin


# 22° FORMAT Verona 08-09/05/2020