

WHEEZING IN ETÀ PRESCOLARE: DALLA TEORIA ALLA PRATICA

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1594

SIPPS
Siena 2009

WHEEZING DISORDERS IN PRESCHOOL CHILDREN

Wheezing illnesses are common and may affect as many as **50%** of preschool children, resulting in substantial impact on the children, their families and the health care system

Martinez NEJM 1995



Pre-school Wheeze: More Questions Than Answers

Monika Gappa, MD^{1*} and Andrew Bush, MD²

Practice Imperfect — Treatment for Wheezing in Preschoolers

Andrew Bush, M.D.

The Challenge of Managing Wheezing in Infants

Urs Frey, M.D., Ph.D., and Erika von Mutius, M.D., M.Sc.

The NEW ENGLAND
JOURNAL *of* MEDICINE

ESTABLISHED IN 1812

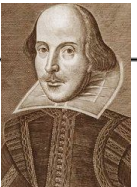
MAY 11, 2006


VOL. 354 NO. 19



Asthma in the preschool child: Still a rose by any other name?

Allan B. Becker,





Uno dei piu' importanti progressi degli ultimi anni è aver capito che il wheezing del bambini in età prescolare **non è una singola malattia ma uno spettro di fenotipi** sostenuti da differenti meccanismi e patterns infiammatori

AIRWAY INFLAMMATION IS HETEROGENEOUS

Traditional
strategy

One therapy
fits all



Personalized
strategy

One fits one

WHEEZING PHENOTYPES

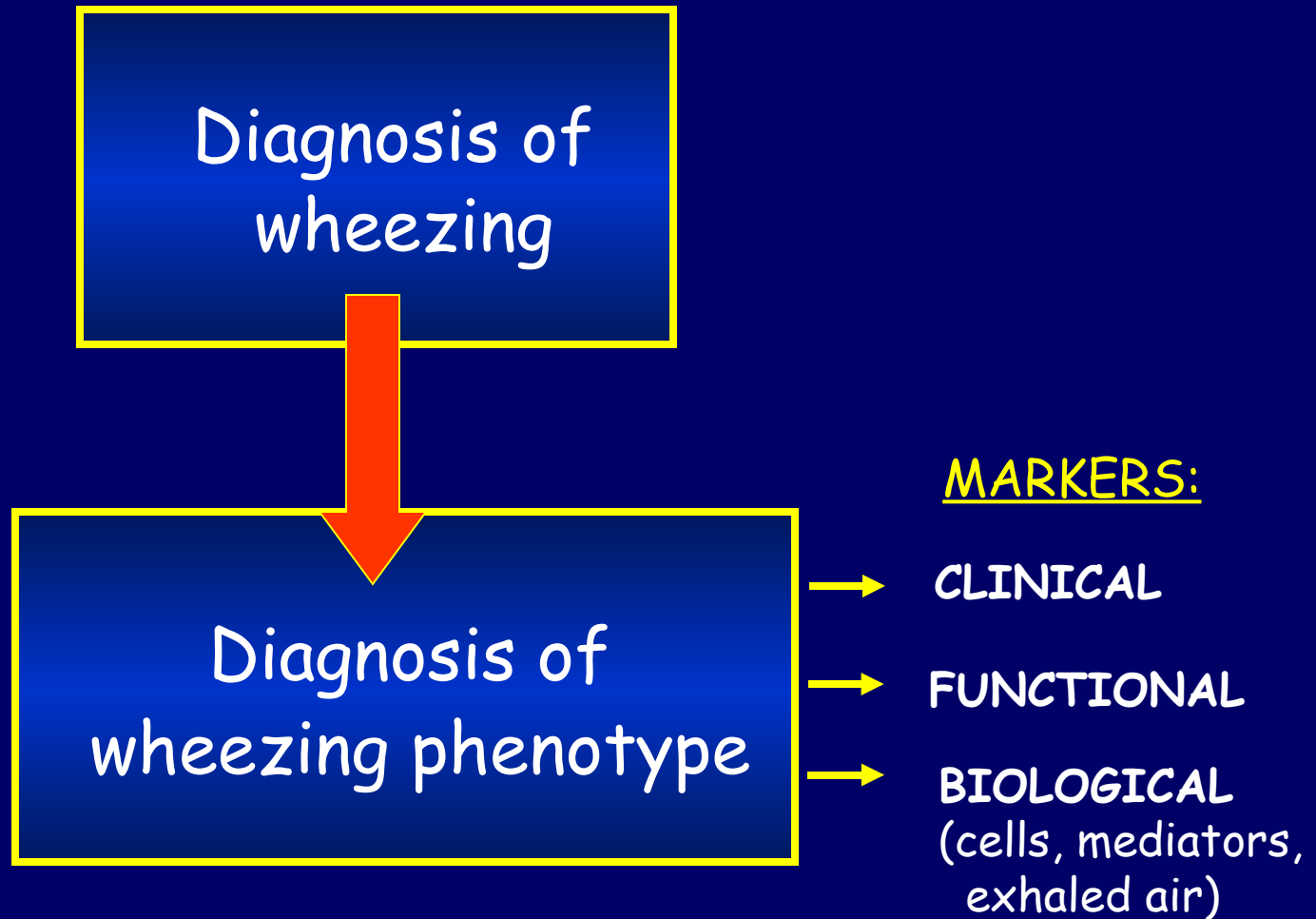
Diagnosis of
wheezing



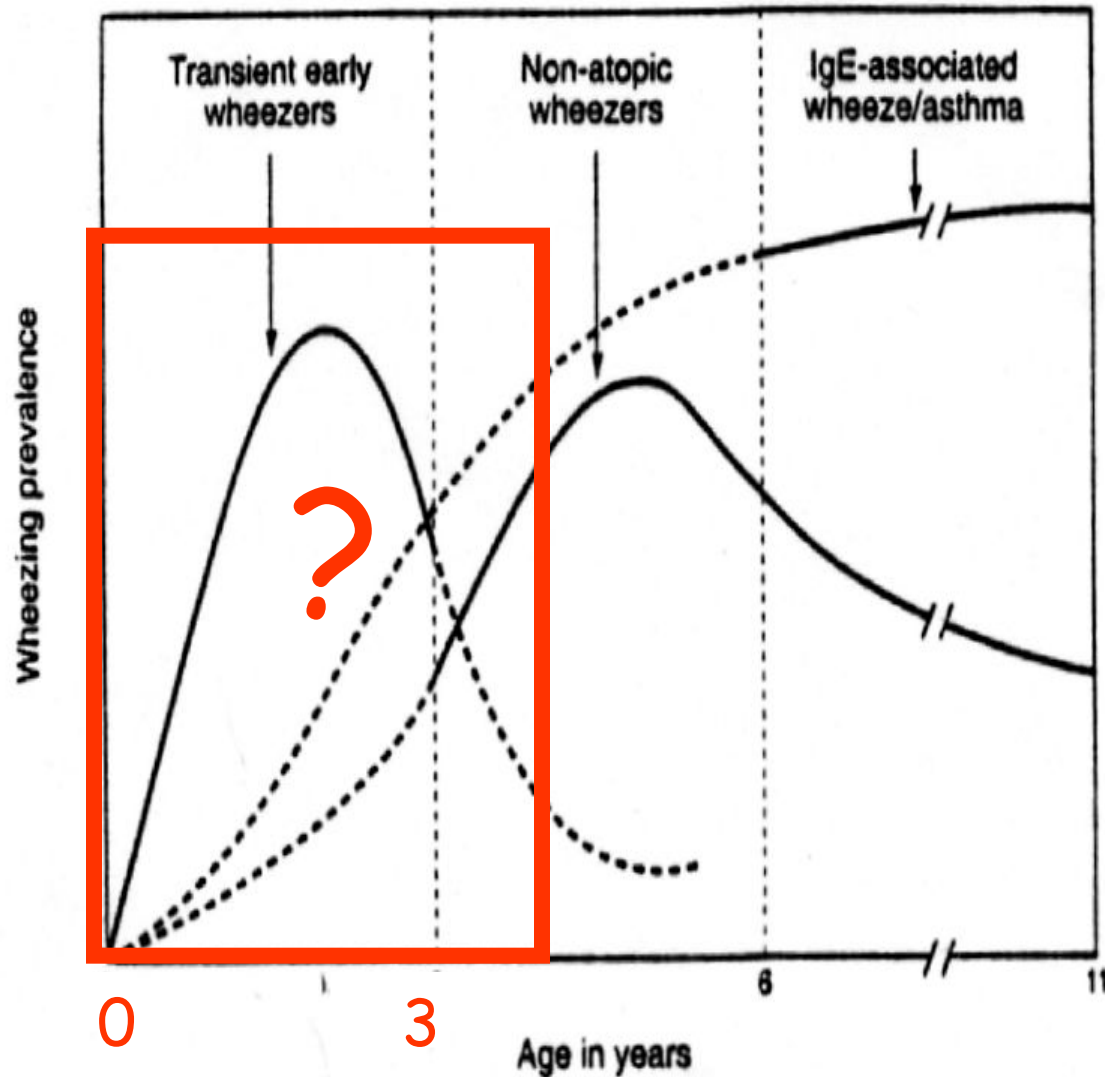
Diagnosis of
wheezing phenotype



MOVING TOWARD PERSONALIZED MEDICINE

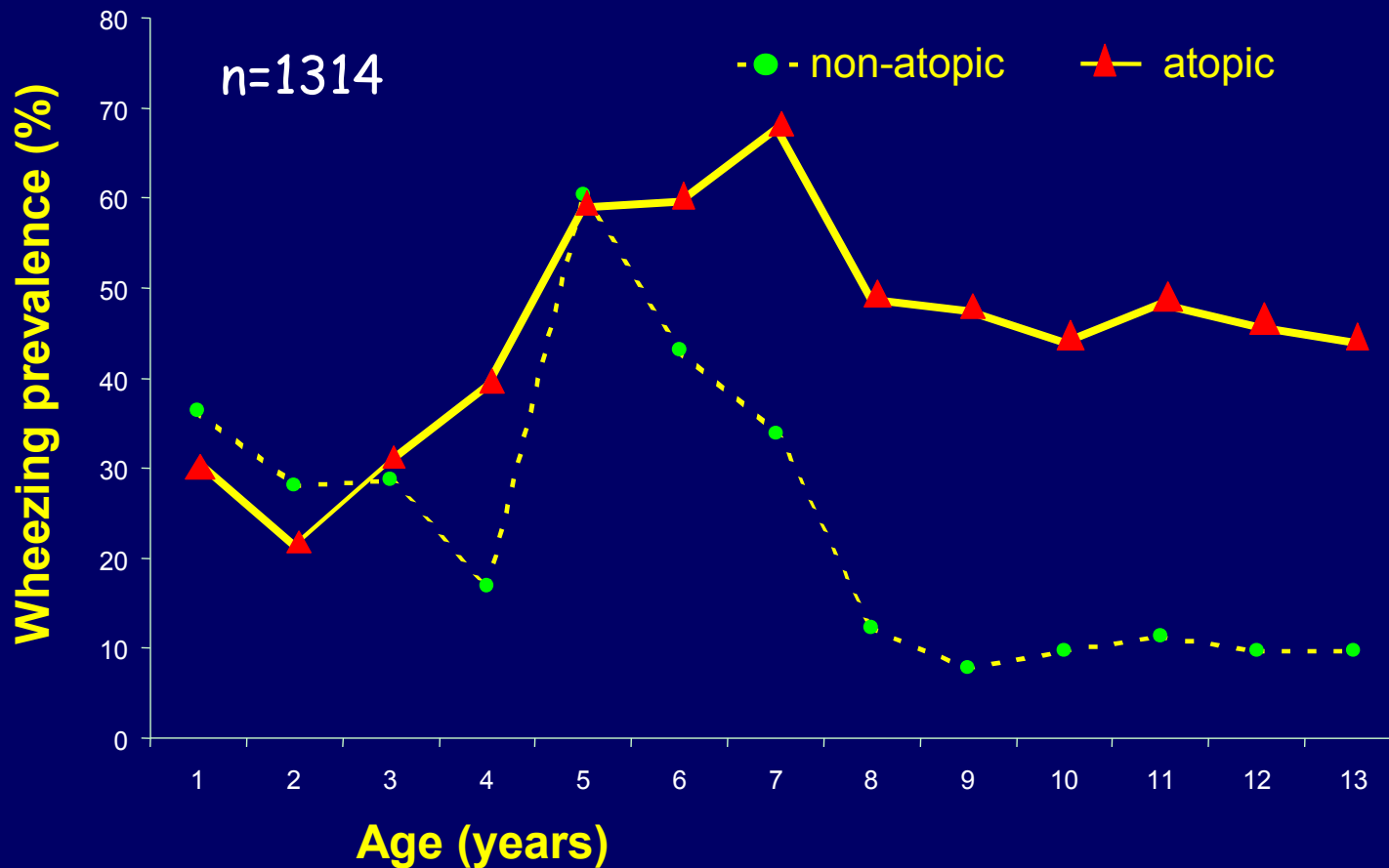


Wheezing phenotypes in preschool children based on "duration of symptoms"



F. Martinez

Atopic children (▲) are more likely to continue wheezing by the time they reach adolescence



MAS study - Illi et al Lancet 2006



Però.....

I fenotipi descritti negli studi epidemiologici
"Transient " vs "Persistent" wheezing
sono stati individuati retrospettivamente (a
6 anni) e sono di scarso valore nella pratica
clinica di fronte ad un bambino di 2-3 anni

Saglani Curr Op ACI 2009

Eur Respir J 2008; 32: 1096–1110
DOI: 10.1183/09031936.00002108
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ERS TASK FORCE

Definition, assessment and treatment of wheezing disorders in preschool children: an evidence-based approach

P.L.P. Brand, E. Baraldi, H. Bisgaard, A.L. Boner, J.A. Castro-Rodriguez, A. Custovic, J. de Blic, J.C. de Jongste, E. Eber, M.L. Everard, U. Frey, M. Gappa, L. Garcia-Marcos, J. Grigg, W. Lenney, P. Le Souëf, S. McKenzie, P.J.F.M. Merkus, F. Midulla, J.Y. Paton, G. Piacentini, P. Pohunek, G.A. Rossi, P. Seddon, M. Silverman, P.D. Sly, S. Stick, A. Valiulis, W.M.C. van Aalderen, J.H. Wildhaber, G. Wennergren, N. Wilson, Z. Zivkovic and A. Bush



Brand Eur Resp J 2008;32:1096

Grading quality of evidence and strength of recommendations

GRADE Working Group

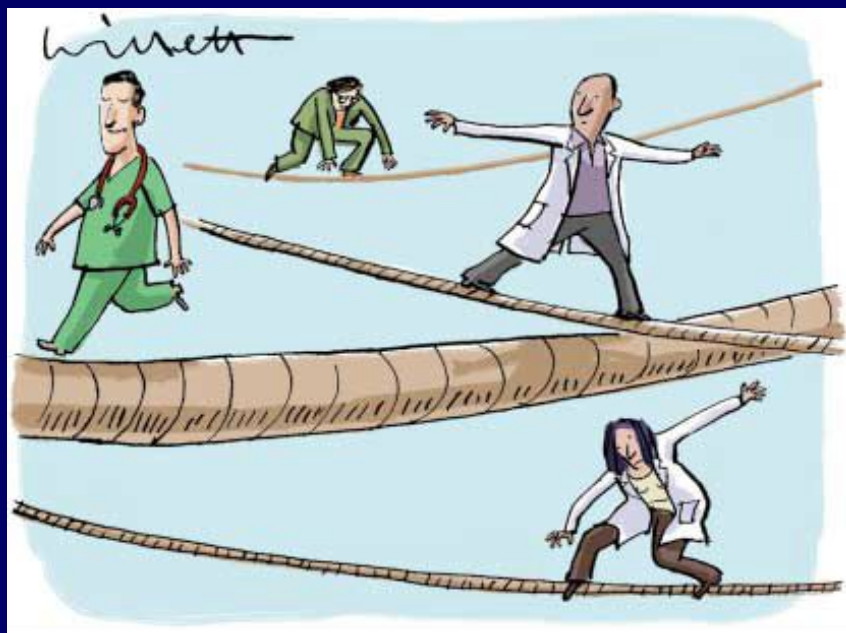
BMJ 2004;328:1490

RATING QUALITY OF EVIDENCE AND STRENGTH OF RECOMMENDATIONS

GRADE: going from evidence to recommendations

The GRADE system classifies recommendations made in guidelines as either strong or weak. This article explores the meaning of these descriptions and their implications for patients, clinicians, and policy makers

BMJ 2008;336:1049



Quality of evidence

High quality	⊕⊕⊕⊕ or A
Moderate quality	⊕⊕⊕○ or B
Low quality	⊕⊕○○ or C
Very low quality	⊕○○○ or D

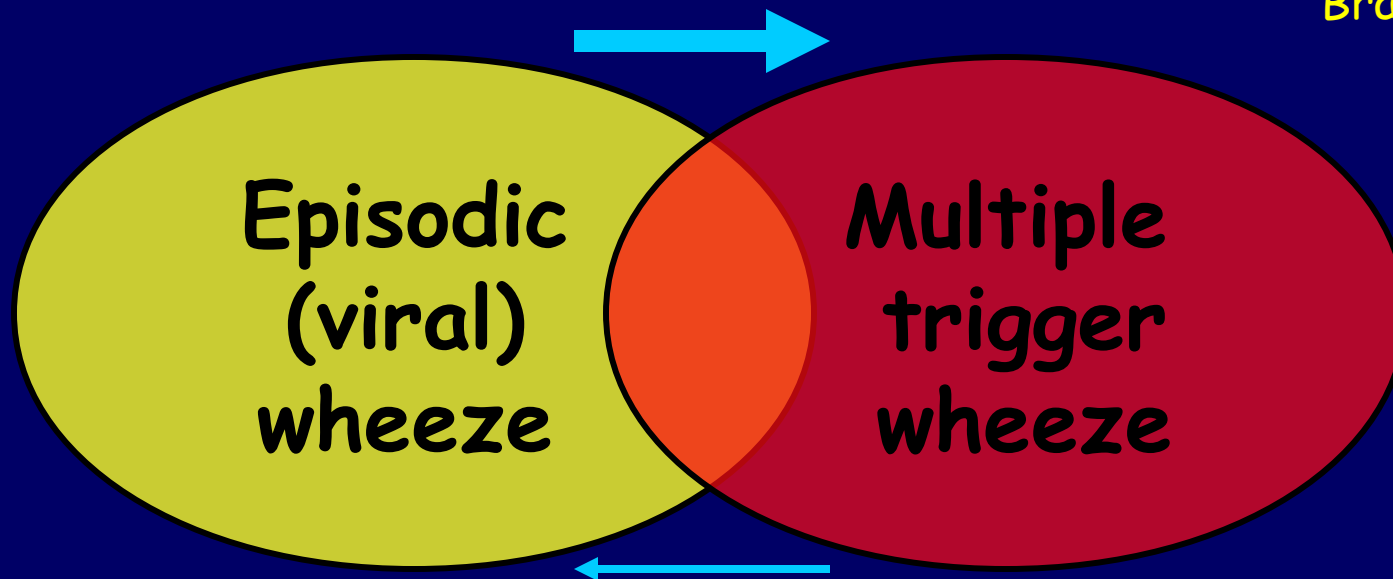
Strength of recommendation

Strong recommendation for using an intervention	↑↑ or 1
Weak recommendation for using an intervention	↑? or 2
Weak recommendation against using an intervention	↓? or 2
Strong recommendation against using an intervention	↓↓ or 1



WHEEZING PHENOTYPES based on "temporal pattern"

Brand ERJ 2008



Children who wheeze
intermittently and are
well between episodes

Triggers: viruses

Wheeze both during and
between exacerbations

Triggers: virus, smoke,
allergens, exercise

Episodic
(viral)
wheeze

Early rhinovirus



asthma

PRESCHOOL-AGE CHILDREN HAVE

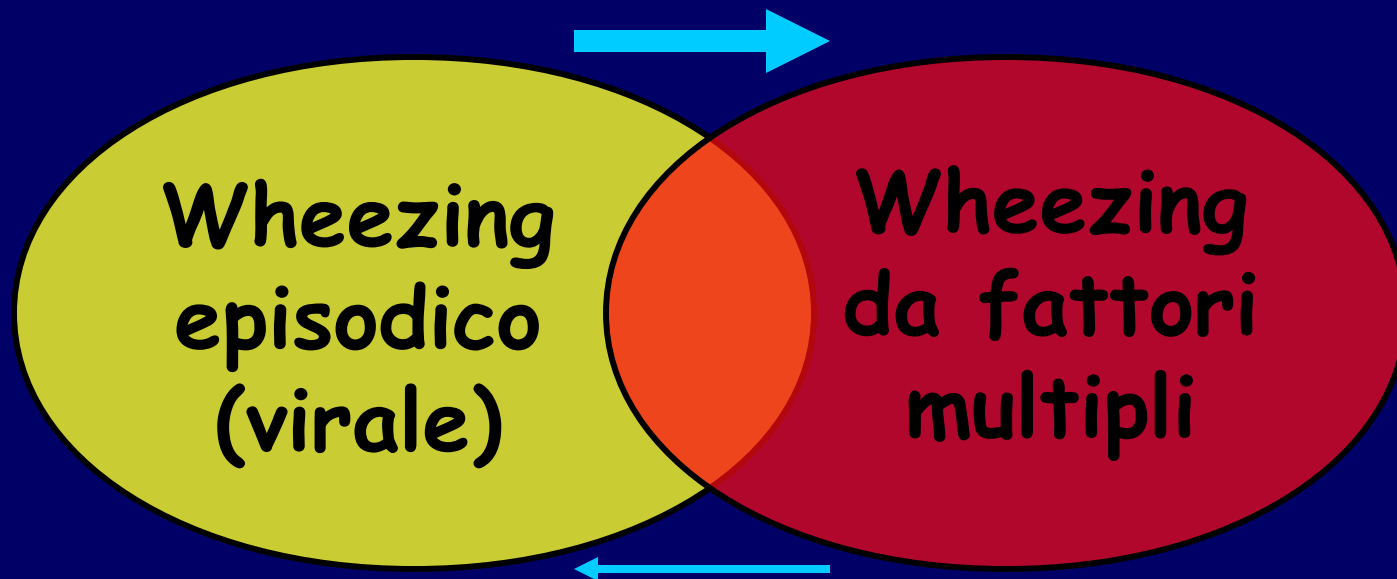
6 to 10

UPPER RESPIRATORY TRACT
INFECTIONS EACH YEAR

Ducharme NEJM 2009
Wald J Pediatr 1991



WHEEZING PHENOTYPES based on "temporal pattern"



Children who wheeze intermittently and are well between episodes

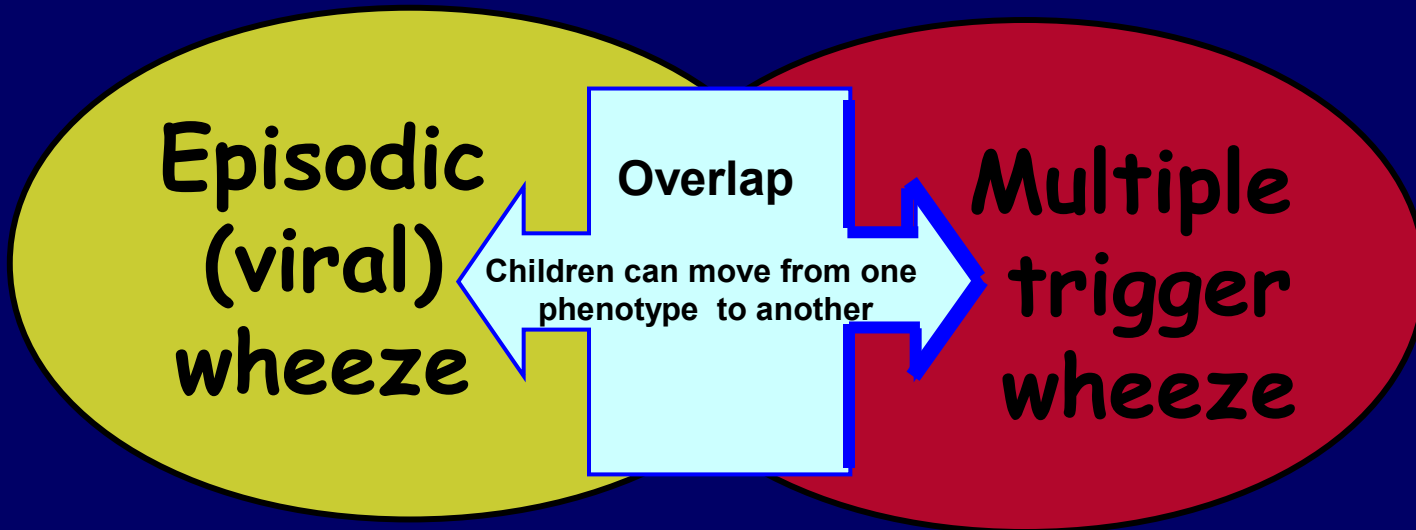
Triggers: viruses

Wheeze both during and between exacerbations

Triggers: virus, smoke, allergenes, exercise



WHEEZING IN PRE-SCHOOL CHILDREN



Children who wheeze intermittently and are well between episodes

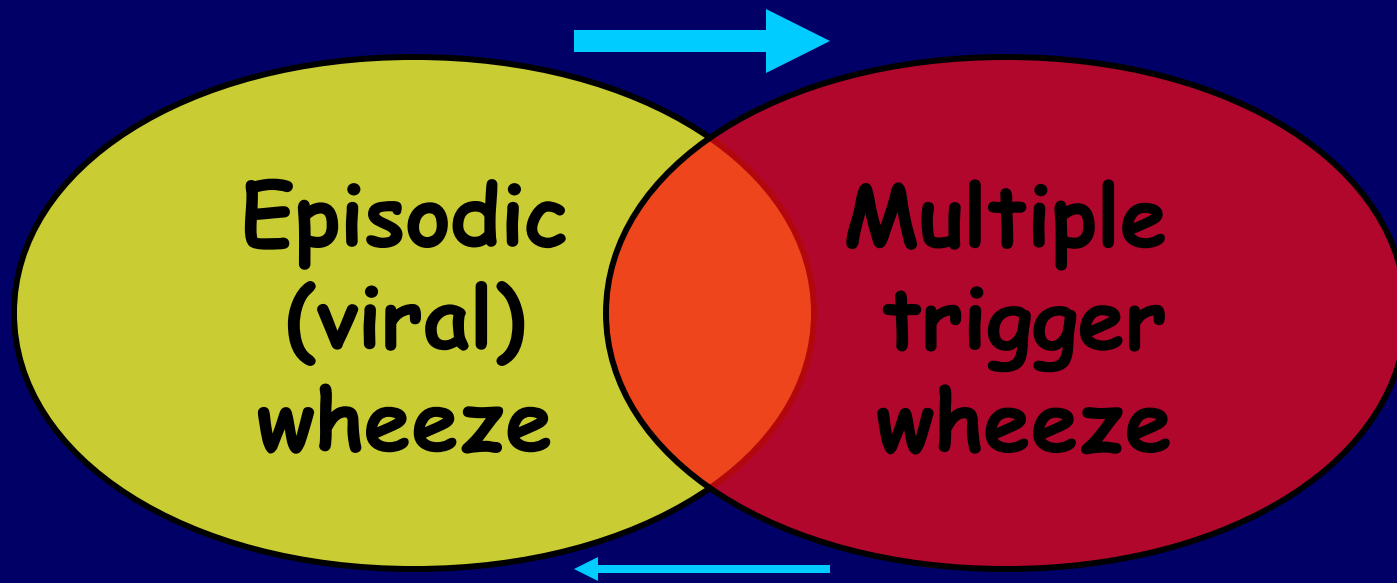
Triggers: viruses

Wheeze both during and between exacerbations

Triggers: virus, smoke, allergenes, exercise



WHEEZING PHENOTYPES based on "temporal pattern"



This classification has the merit of being able to be used at the time the child is seen and it has relevance to treatment



WHEEZING DISORDERS IN PRESCHOOL CHILDREN

RECOMMENDATIONS:

DEFINITIONS OF PHENOTYPES (based on low-level evidence)

- 1) For clinical purposes, wheeze should be classified as episodic (viral) or multiple-trigger wheeze.
- 2) Use of the terms “transient”, “persistent” wheeze should be limited to population-based cohort studies and should not be used clinically.
- 3) The term asthma should probably not be used in preschool children (lack of data regarding underlying inflammation).



Wheezing

is a symptom and not a diagnosis !

Many disorders can cause wheezing and it cannot be managed appropriately in the basis of a presumptive diagnosis

Differential diagnosis of recurrent wheezing in infancy

- Multiple trigger vs. “viral wheeze”
- Tracheobronchomalacia
- Persistent infections (Mycoplasma, Chlamydia)
- GER, foreign body
- Tracheal/bronchial compression
- Prematurity and BPD
- TBC, CF, cilia dysfunction



WHEEZING DISORDERS IN PRESCHOOL CHILDREN

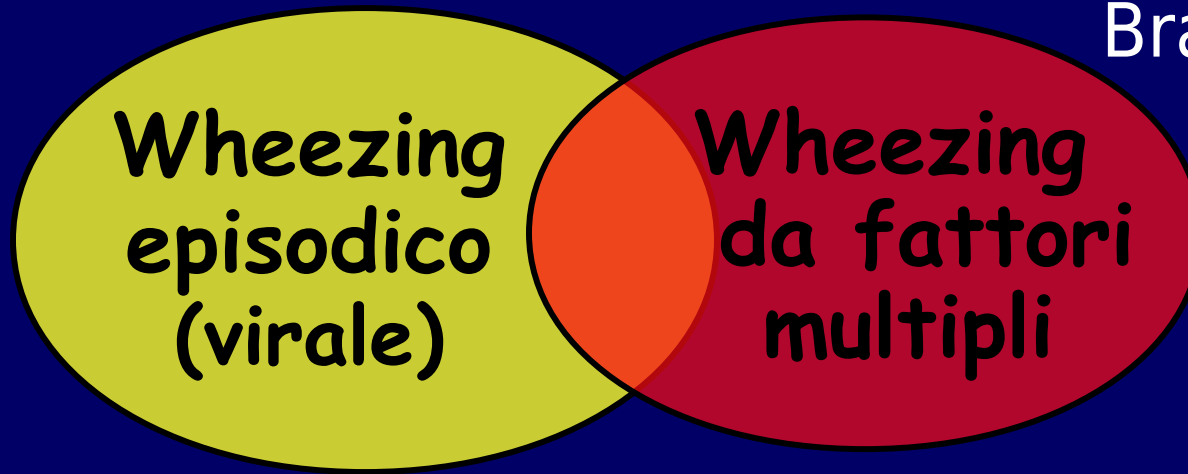
RECOMMENDATIONS:

ASSESSMENT (based on low-level evidence)

- 1) Parentally reported wheeze should be confirmed by a health professional.
- 2) Tests of allergic sensitisation should be performed in patients requiring long-term treatment.
- 3) Other investigations: wheeze is unusually severe, therapy-resistant or accompanied by unusual clinical features

Definition, assessment and treatment of wheezing disorders in preschool children: an evidence-based approach

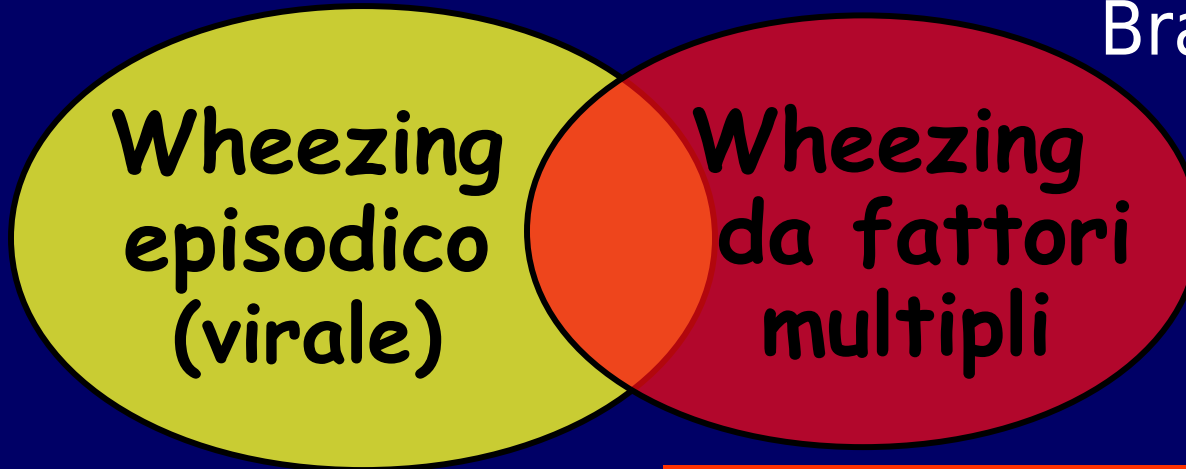
Brand ERJ al 2008



- Maintenance therapy
- Treatment of acute wheezing episodes

Definition, assessment and treatment of wheezing disorders in preschool children: an evidence-based approach

Brand ERJ al 2008



Therapy:

- 1) MONTELUKAST
(maintenance or starting with viral cold)
- 2) Consider ICS

Therapy:

- 1) INHALED STEROIDS
(maintenance up to 400 mcg BDP)
- 2) Consider Montelukast

LOW-LEVEL EVIDENCE !

WHEN STARTING MAINTENANCE THERAPY ?

Regular controller treatment is suggested:

- The disease is not controlled
- Viral-induced episodes > 6 weeks
- Severe episodes
- Presence of risk factors ?

Treatment duration

- Periods of 3 months

GINA 2009

ERS 2008

NAEPP 2007

LA TERAPIA
DEL BAMBINO CON WHEEZING
IN ETA' PRESCOLARE

ovvero l'argomento dei MA.....



The NEW ENGLAND
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VOL. 354 NO. 19

PEAK study
Ducharme study
Leicester study

THE LANCET

IFWIN study



PRE-EMPT study

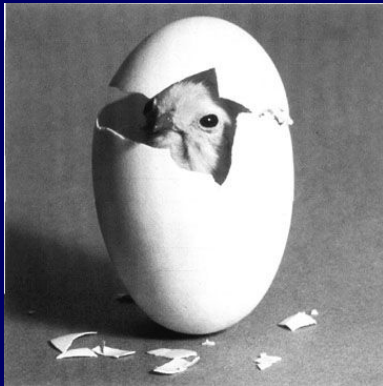
PEDIATRICS®

September study



TRATTAMENTO CONTINUO
CON STEROIDI

Se trattiamo precocemente bambini con wheezing e alto rischio di asma riusciremo a cambiare la storia naturale della malattia ?



F.D. Martinez NEJM 2003

FATTORI DI RISCHIO PER LO SVILUPPO DI ASMA (API)

≥3-4 episodi di wheezing
nell'ultimo anno

associati a

Un criterio maggiore:

- Un genitore con asma
- Dermatite atopica
- Sensibilizzazione ad inalanti

Oppure

Due criteri minori:

- Sensibilizzazione ad alimenti
- Wheezing al di fuori degli episodi infettivi
- Eosinofilia (>4%)

Quando un bambino presenta un indice API positivo ha una probabilità di sviluppare asma tra i 6 e i 13 anni aumentata da 4 a 10 volte.

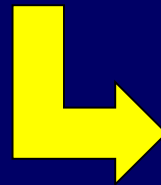
Più del 95% dei bambini con API negativo nei primi 3 anni di vita non sviluppa asma tra i 6 e i 13 anni



PEAK STUDY

Early intervention with 2 years of fluticasone in young children (n=285) with 3 previous episodes of wheezing and **HIGH RISK FOR ASTHMA**

Age: 2-3 years old



- Parental history of asthma
- Atopic dermatitis
- Sensitization to 1 aeroallergen.

RDB placebo controlled:

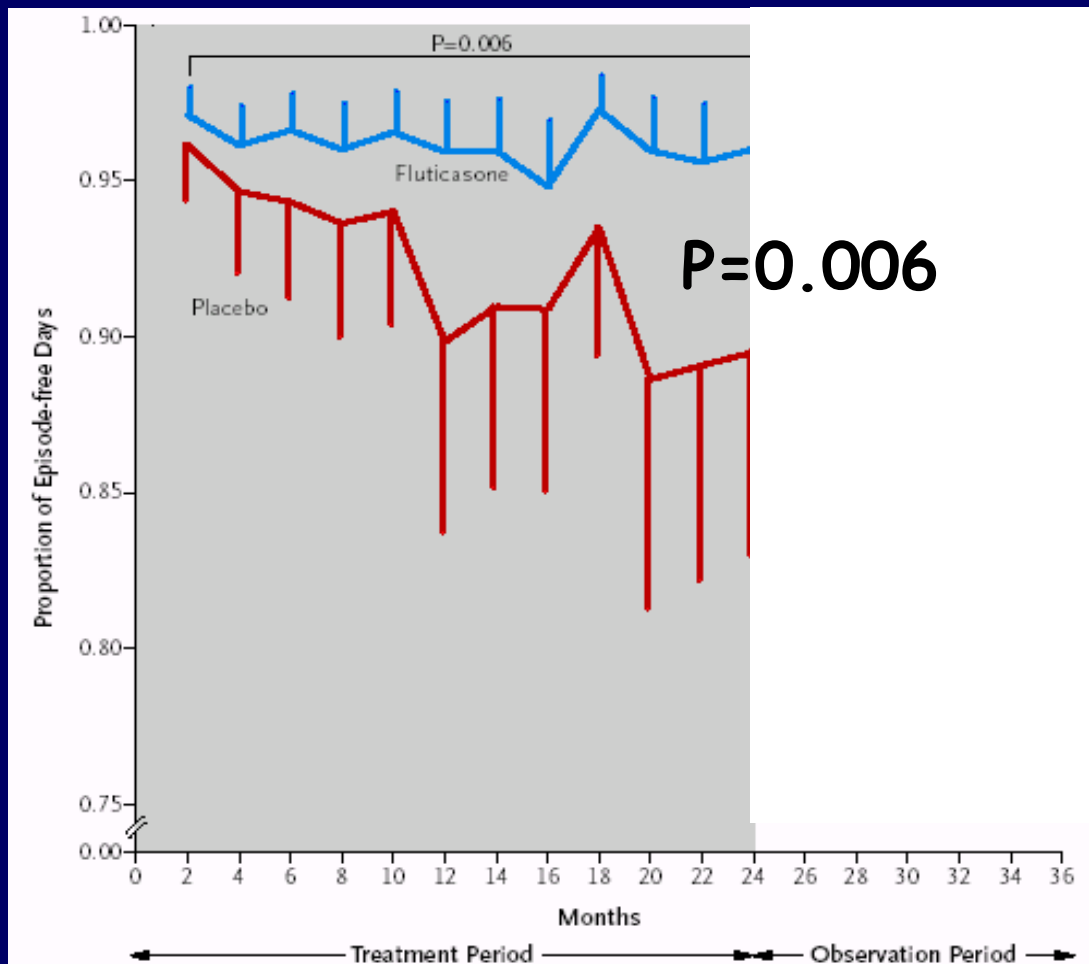
→ Fluticasone
(88 mcg x 2)

→ placebo

} for 2 years → 1 year observation

PEAK STUDY

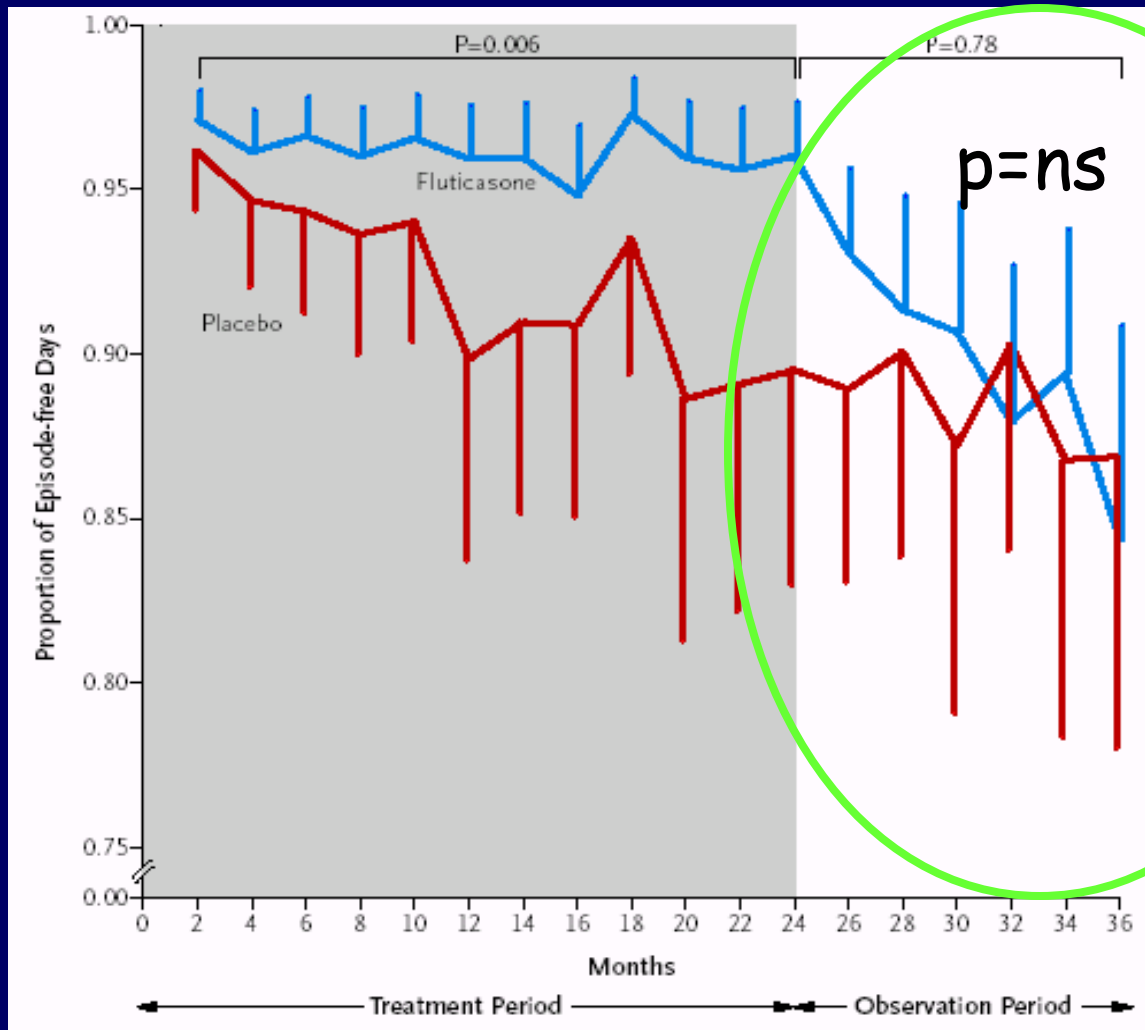
2 years of ICS in children at high risk for asthma reduced symptoms and exacerbations **but.....**



Guilbert NEJM 2006

PEAK STUDY

but cannot modify the natural history of asthma!



Guilbert NEJM 2006

ICS therapy



should not be used to prevent disease progression in children



but rather to achieve symptom control and to reduce the risk of exacerbations



I fattori di rischio per lo
sviluppo di asma
(familiarità per asma, eczema,
sensibilizzazione allergica.....)

NON sono markers predittivi di
responsività agli steroidi !

Patient characteristics associated with improved outcomes with use of an inhaled corticosteroid in preschool children at risk for asthma

PEAK STUDY

Bacharier JACI 2009

Patient characteristics associated with favorable response to ICS therapy:

- Male sex
- Aeroallergen sensitization
- ED visit or hospitalization

Patient characteristics associated with improved outcomes with use of an inhaled corticosteroid in preschool children at risk for asthma

PEAK STUDY

Bacharier JACI 2009

Patient characteristics NOT influencing ICS responsivity:

- Age
- Parental asthma
- Duration of asthma
- Eczema
- Eosinophilia
- Total IgE



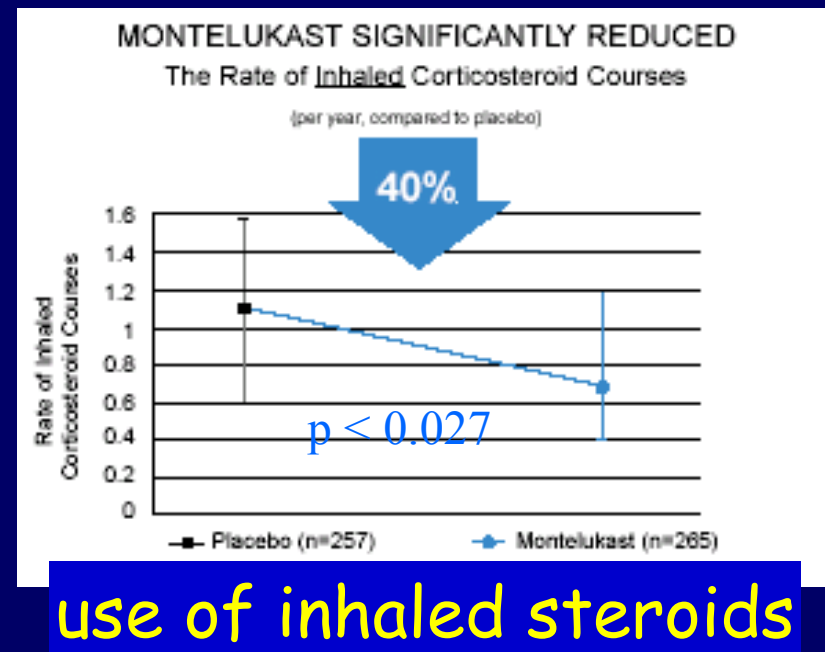
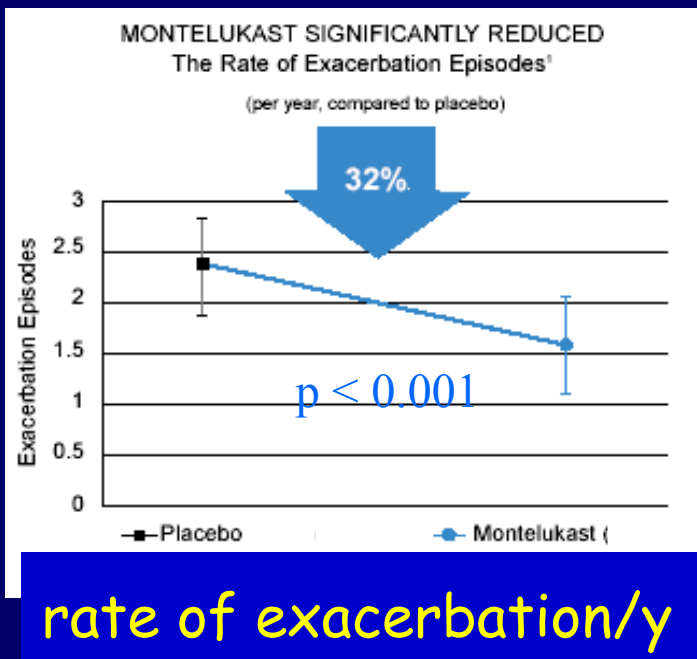
quello che pensavamo di sapere e che
invece dobbiamo ripensare.....



Trattamento continuo
con montelukast

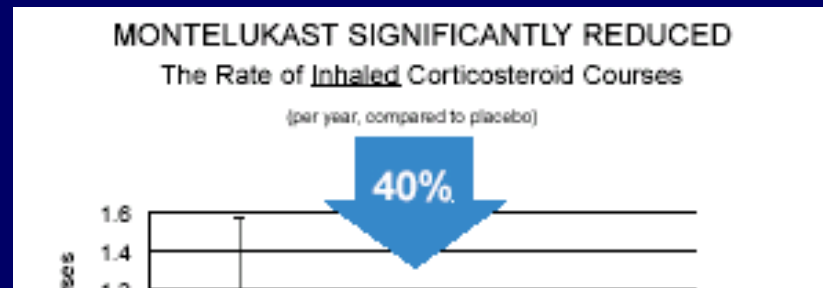
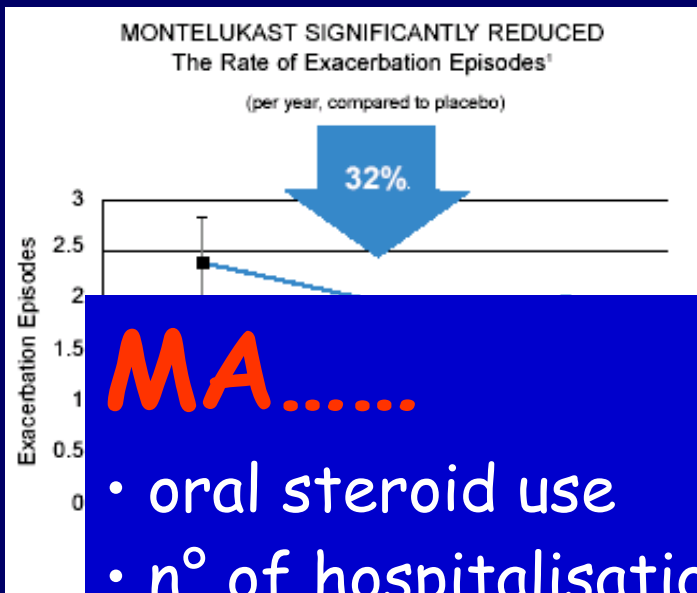
PREVIA "Prevention of Viral-Induced Asthma

- 549 children 2-5 years with recurrent wheezing
- placebo or montelukast (4 mg) for 1 year



PREVIA "Prevention of Viral-Induced Asthma

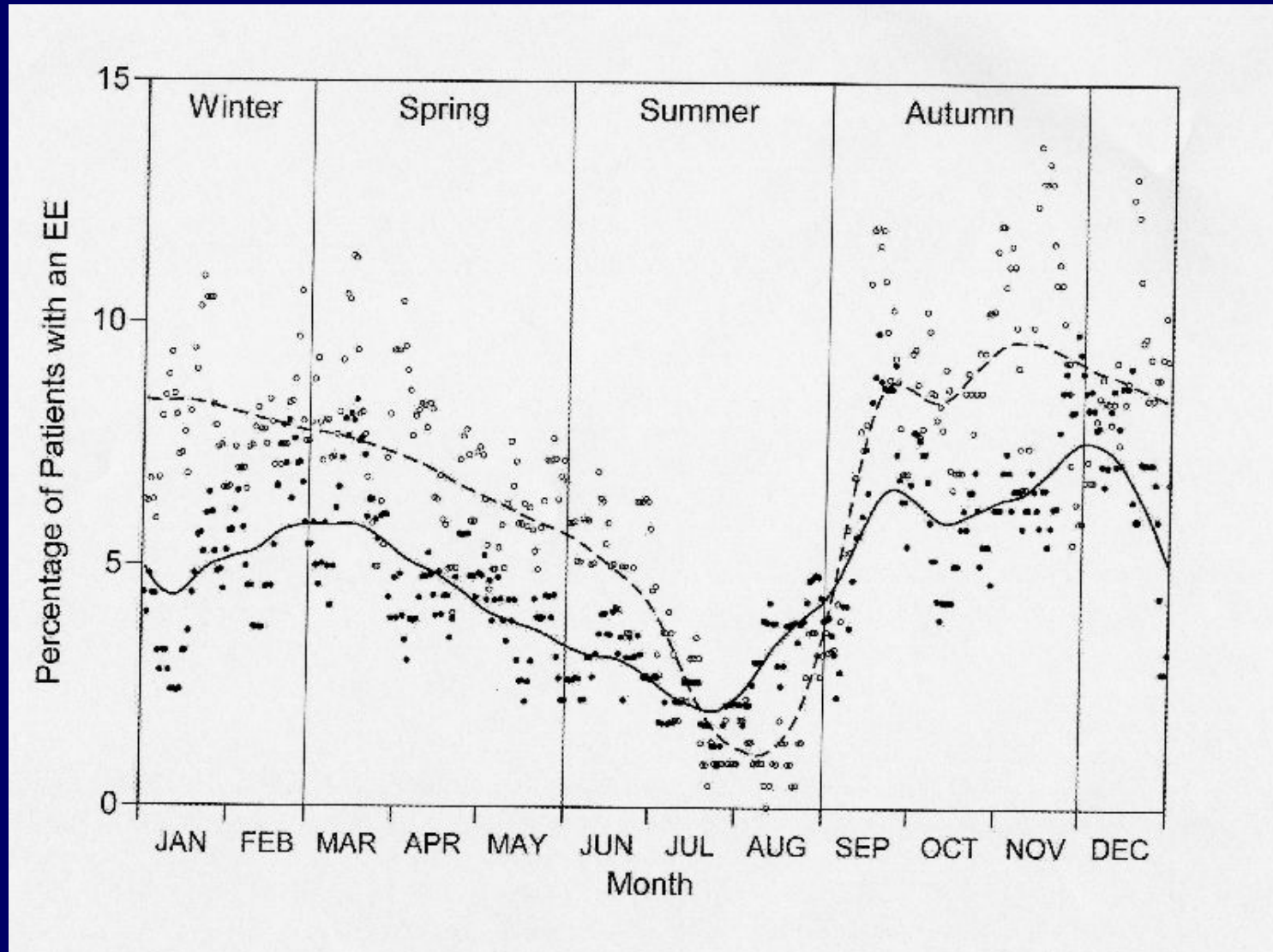
- 549 children 2-5 years with recurrent wheezing
- placebo or montelukast (4 mg) for 1 year



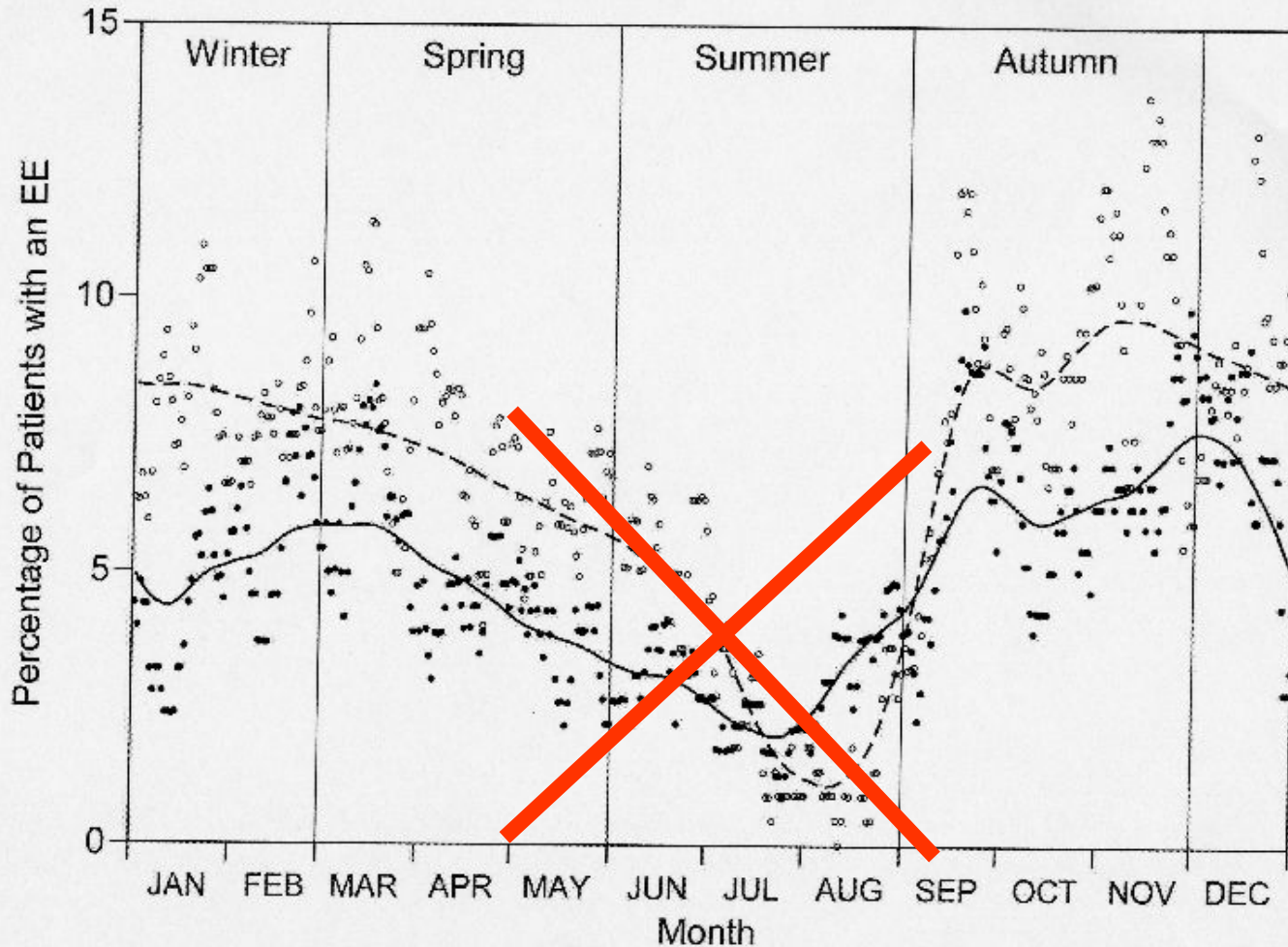
MA.....

- oral steroid use
 - n° of hospitalisations
- } were similar among the 2 groups

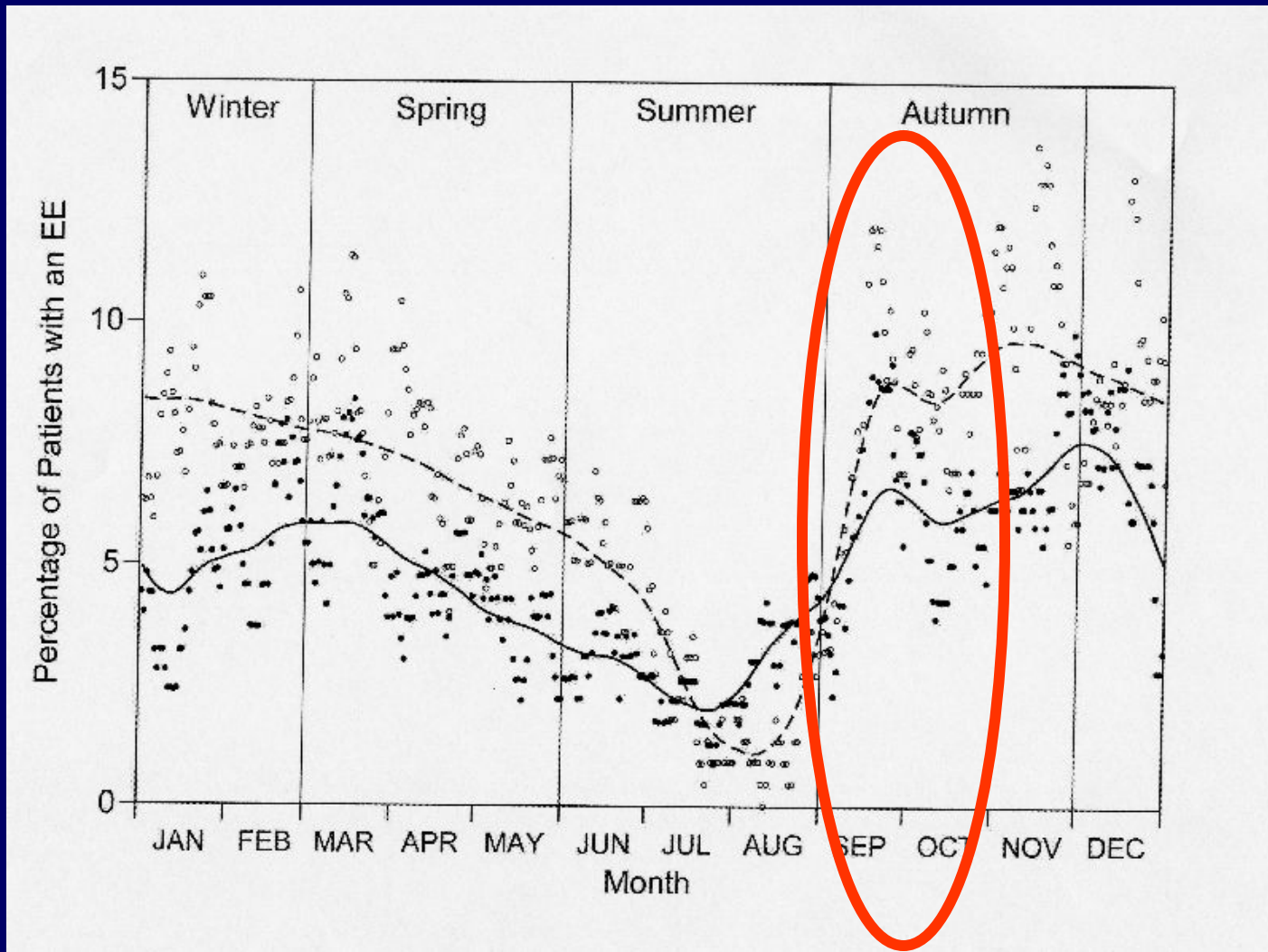
Daily % of children with an exacerbation episode



Daily % of children with an exacerbation episode



The September Epidemic of Asthma Exacerbation





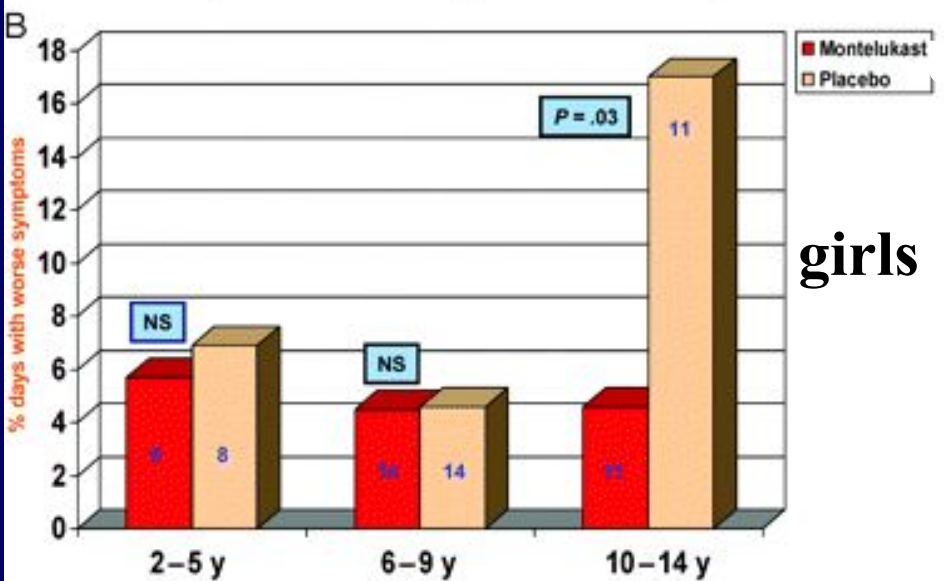
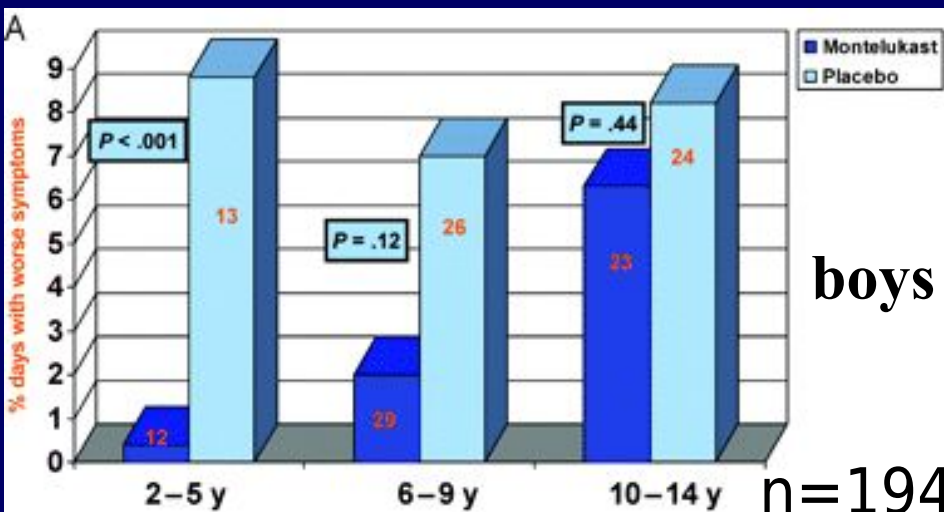
Perspectives in asthma

Understanding the **September** asthma epidemic

Malcolm R. Sears, FRACP,^{a,b} and Neil W. Johnston, MSc^b *Hamilton, Ontario, Canada*

- Dal 20 al 25% dei ricoveri per riacutizzazioni asmatiche avvengono in Settembre
- Le riacutizzazioni di Settembre si associano, in circa l'80% dei casi, ad infezioni virali in prevalenza da rinovirus
- Un inadeguato trattamento con farmaci anti-asmatici di controllo in Settembre favorisce le riacutizzazioni

Attenuation of the September epidemic of asthma exacerbations: montelukast added to usual therapy



September 1 - October 15

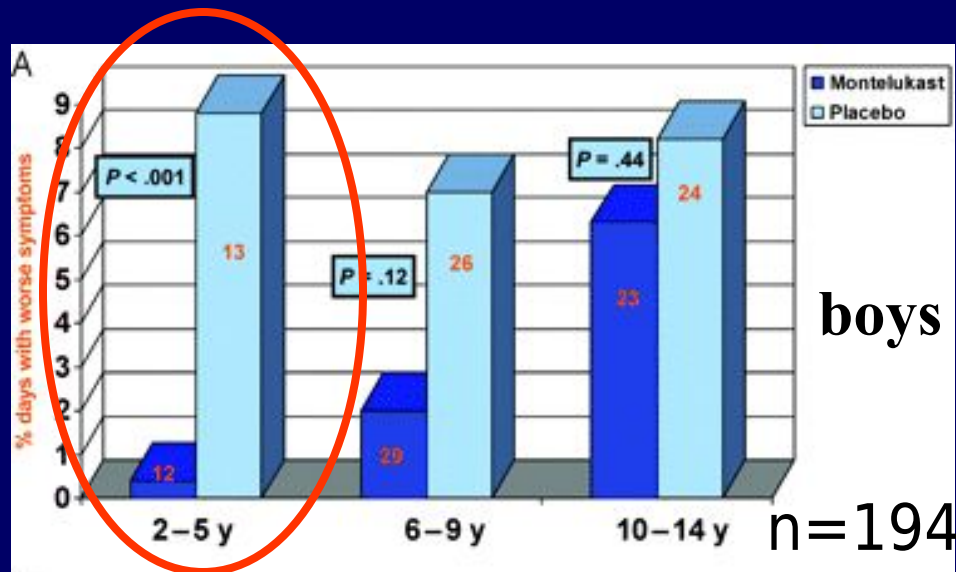
boys

reduction on:

asthma symptoms (- 53%)

unscheduled visits (4 x)

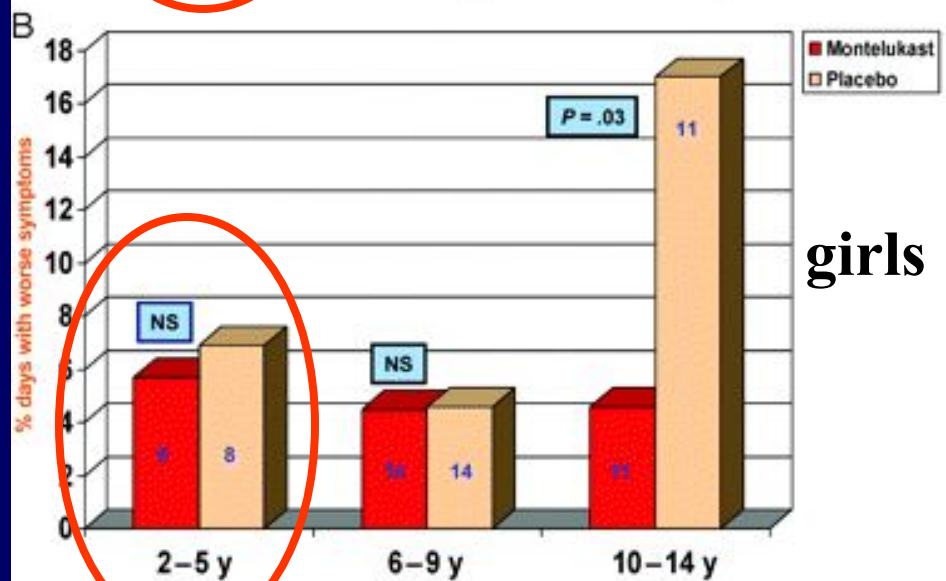
Attenuation of the September epidemic of asthma exacerbations: montelukast added to usual therapy



boys

MA

**Boys 2-5 yrs
greater benefit !**



girls



TREATMENT RECOMMENDATIONS

(based on low-level evidence)

DELIVERY DEVICES

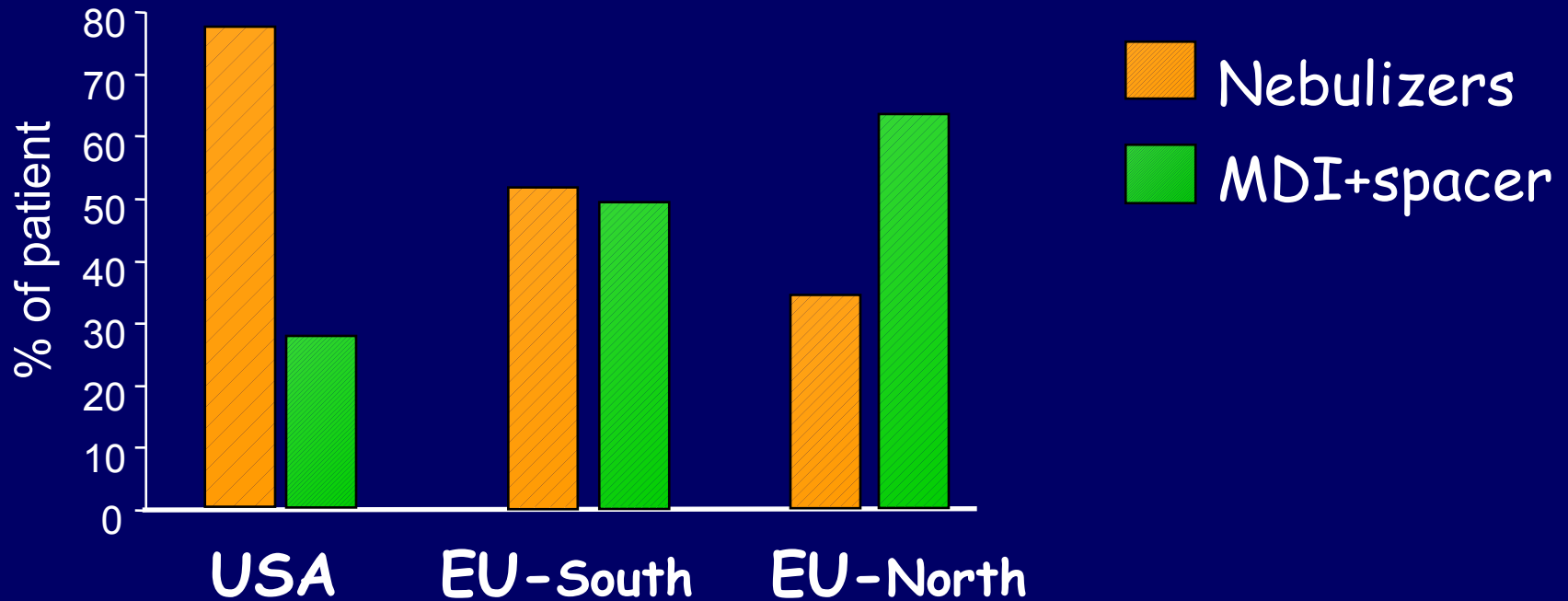
- 1) A pMDI-spacer combination is the preferred device (face mask or mouthpiece) →

Prevalence of Asthma-Like Symptoms in Young Children

Hans Bisgaard, MD^{1*} and Stanley Szefer, MD²

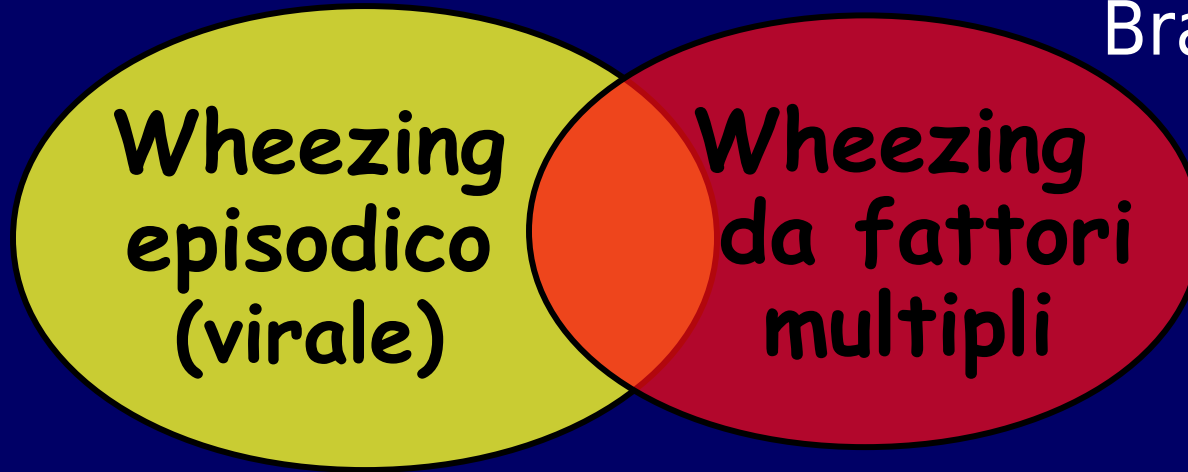
Ped Pulm 2007

Objective: prevalence and treatment of asthma-like symptoms in **pre-school children** in USA and Europe (n=2700 mothers)



Definition, assessment and treatment of wheezing disorders in preschool children: an evidence-based approach

Brand ERJ al 2008



- Maintenance therapy
- Treatment of acute wheezing episodes



TREATMENT RECOMMENDATIONS

(based on low-level evidence)

ACUTE WHEEZING EPISODE

- 1) Inhaled short-acting b2-agonists (with addition of ipratropium if severe wheeze)
- 2) A trial of oral corticosteroids should probably be given if severity that they need to be admitted to hospital.
- 3) High-dose ICS therapy is not recommended.

Oral Prednisolone for Preschool Children with Acute Virus-Induced Wheezing

The NEW ENGLAND
JOURNAL of MEDICINE

virus-induced wheezing attack – hospital (age 10m-6 y)
day oral prednisolone vs. placebo

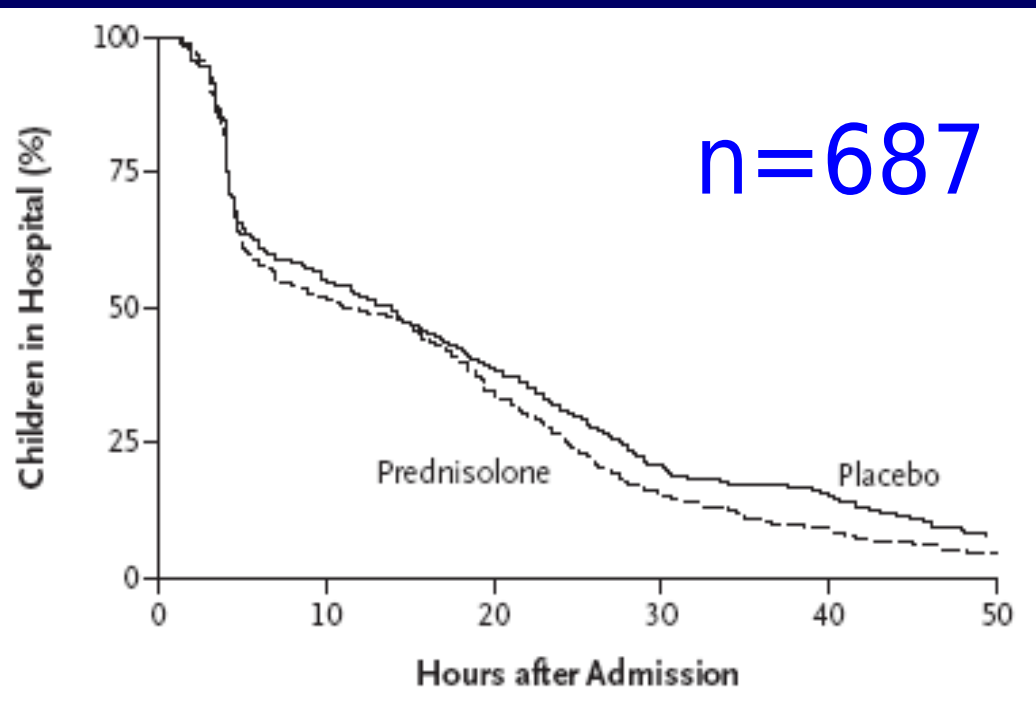


Figure 2. Kaplan–Meier Estimates of the Proportion of Children Remaining in the Hospital.

Secondary outcomes

- symptoms score : NS
- salbutamol score : NS
- subgroup with risk factor for asthma : NS (n=124)

EDITORIALS



Practice Imperfect — Treatment for Wheezing in Preschoolers

Andrew Bush, M.D.

It is disturbing to contemplate how many unnecessary courses of prednisolone have been given over the years, in good faith, because we all assumed that preschool children are little adults. There is certainly a lesson there for the use of other medications.

EDITORIALS



Practice Imperfect — Treatment for Wheezing in Preschoolers

Andrew Bush, M.D.

prednisolone may have a role in the treatment of preschool children with atopy who have acute exacerbations, particularly in patients with multitrigger wheezing. It is also possible that episodic wheezing that is severe enough to warrant admission to an intensive care unit should be treated with prednisolone. How-

WHEEZING PHENOTYPES MOVING TOWARD PERSONALIZED MEDICINE

Diagnosis of
wheezing



Diagnosis of
wheezing phenotype



Come sarebbe a dire "...Troppi caffè" ?



www.carloneworld.it

Grazie per
l'attenzione