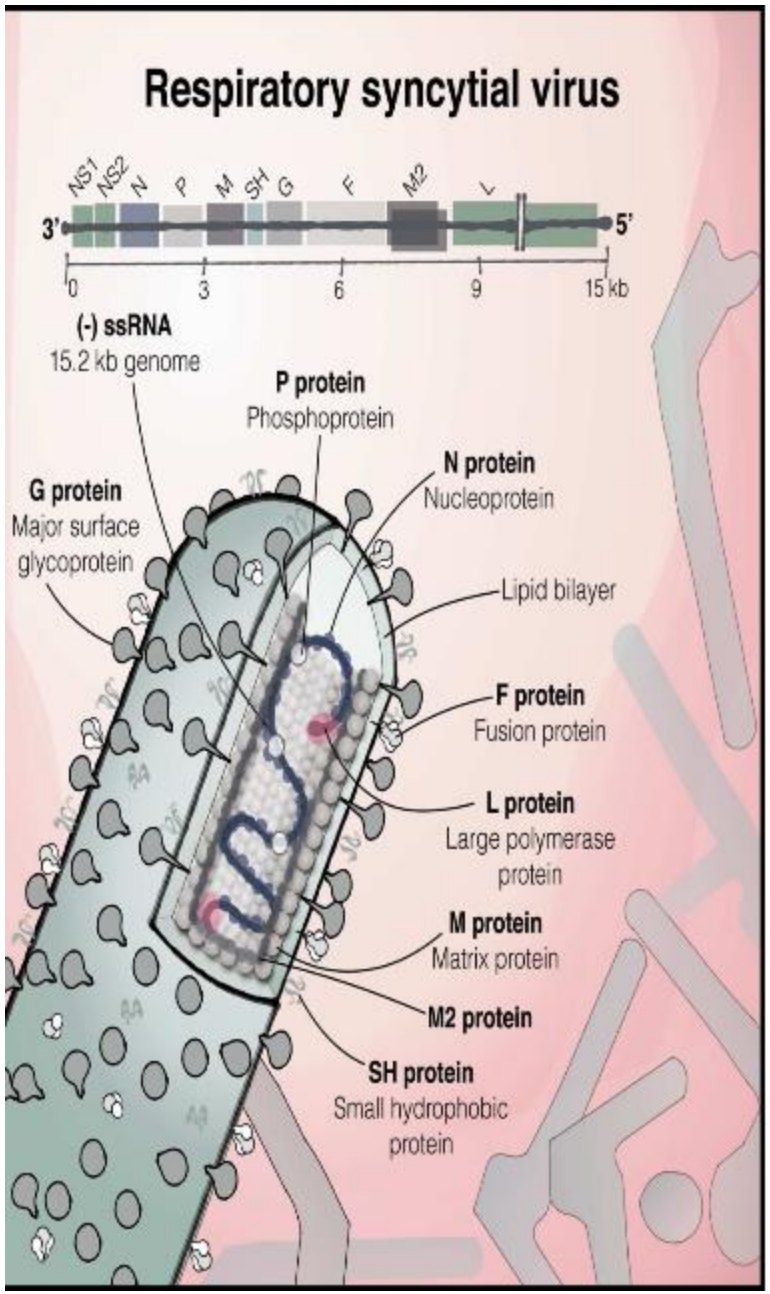
7th
JOINT MEETING
In pediatria e medicina dell'adolescenza
Sobre pediatría y medicina de la adolescencia
21-22-23-24 OTTOBRE 2015 CATANZARO ITALIA

# Nuove evidenze nella gestione della Bronchiolite

***Nueva evidencia en el tratamiento de la bronquiolitis***

**Domenico Minasi**

UOC Pediatria ASP di Reggio Calabria




# Respiratory Syncytial Virus (RSV) is the commonest cause of severe respiratory infection in infants

**Leading cause of hospitalization in infants** ( over 3 million hospitalizations and around 66,000 deaths world wide each year)

- Up to 3% of all children in first year of life are hospitalized with bronchiolitis (18% of all hospitalizations in US)

- 10-12% need intensive care

**Previous infection does not transmit persistent immunity and reinfection is common and can recur in the same RSV season**

Nair H, *Lancet (2010)*
HallCB, *N Engl J Med (2009)*

# BRONCHIOLITIS

**In North America, bronchiolitis commonly is applied more broadly but is linked to the specific finding of wheeze:**

*"a constellation of clinical symptoms and signs including a viral upper respiratory prodrome followed by increased respiratory effort and wheezing in children less than 2 years of age."*

**In the United Kingdom, the term tends to be used more specifically**:

*"a seasonal viral illness characterized by fever, nasal discharge, and dry, wheezy cough. On examination there are fine inspiratory crackles and/or high pitched expiratory wheeze."*


- Bush A, et al. Managing wheeze in preschool children. BMJ 2014;348
- Scottish Intercollegiate Guidelines Network.Bronchiolitis in children November 2006
- American Academy of Pediatrics. Clinical Practice Guideline: The Diagnosis, Management, and Prevention of Bronchiolitis. Pediatrics 2014;134;e1474
- Cincinnati Children's Hospital Medical Center; 2006 May
- Zorc JJ, Hall CB Bronchiolitis: Recent Evidence on Diagnosis and Management. Pediatrics 2010;125;342

ITALIAN JOURNAL OF PEDIATRICS

# Diagnosis of bronchiolitis

*Diagnosis of bronchiolitisis divided into two main phases: clinical diagnosis and etiological diagnosis*

## Clinical diagnosis

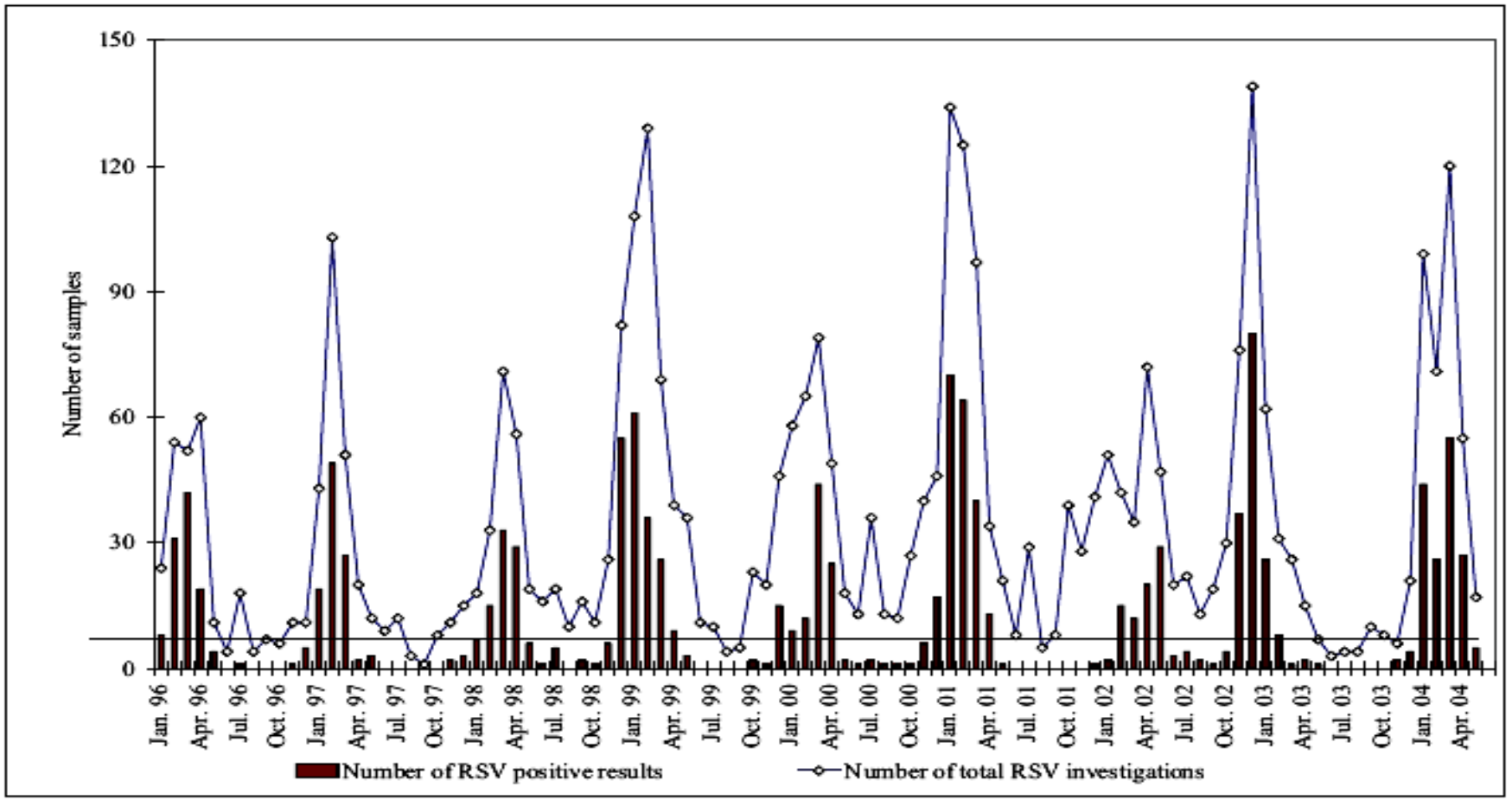
of disease and its severity is rooted in **the clinician's interpretation of the constellation of characteristic findings,** and is independent from any specific clinical features and diagnostic tests**.**

## Etiological diagnosis

The virus may be isolated by the following methods, which aim at identifying either the virus (through genome detection) or its antigens:

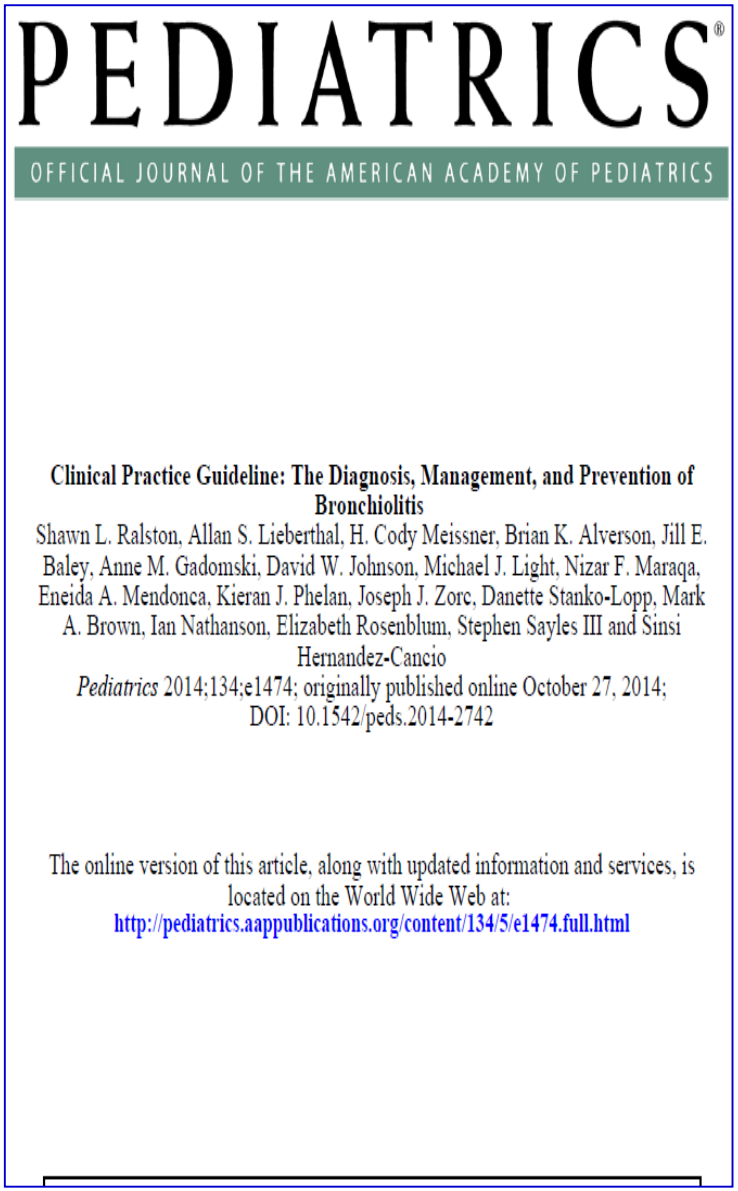
- **Antigen detection** (immunofluorescence, enzyme immunoassay). *These are the so-called "Rapid ntigen-detection tests" with an 80–90% sensitivity which might yield false negatives in infants younger than 3 months of age.*
- **Genome detection** - *PCR is the gold standard diagnostic test in consideration of its 93-100% sensitivity and its 64-100% specificity.*

# DEFINING THE TIMING OF RESPIRATORY SYNCYTIAL VIRUS (RSV) OUTBREAKS: AN EPIDEMIOLOGICAL STUDY




**Timing : start** Nov-Dic,***peak*** Gen.-Feb., ***end*** Mar.-Apr

Ladwig BMC Infectious Diseases 2006



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OFFICIAL JOURNAL OF THE AMERICAN ACADEMY OF PEDIATRICS

**Clinical Practice Guideline: The Diagnosis, Management, and Prevention of Bronchiolitis**

Shawn L. Ralston, Allan S. Lieberthal, H. Cody Meissner, Brian K. Alverson, Jill E. Baley, Anne M. Gadomski, David W. Johnson, Michael J. Light, Nizar F. Maraqa, Eneida A. Mendonca, Kieran J. Phelan, Joseph J. Zorc, Danette Stanko-Lopp, Mark A. Brown, Ian Nathanson, Elizabeth Rosenblum, Stephen Sayles III and Sinsi Hernandez-Cancio

*Pediatrics* 2014;134;e1474; originally published online October 27, 2014; DOI: 10.1542/peds.2014-2742

The online version of this article, along with updated information and services, is located on the World Wide Web at: http://pediatrics.aappublications.org/content/134/5/e1474.full.html

# RISK FACTORS FOR SEVERE BRONCHIOLITIS

**Prematurity and BPD**

**Age less than 12 weeks**

**Congenital cardiac illness**

*other diseases which might complicate the presentation of acute respiratory infections include*

**Immunodeficiency**

**severe neurological deficit**

**airway malformation,**

Baraldi *et al. Italian Journal of Pediatrics* 2014, **40**:65
http://www.ijponline.net/content/40/1/65

ITALIAN JOURNAL
OF PEDIATRICS

REVIEW

# Inter-society consensus document on treatment and prevention of bronchiolitis in newborns and infants

## Pediatric primary health care assistance

It is important to point out that the milder forms of bronchiolitis may be adequately managed in the outpatient setting by primary care pediatricians, thus limiting hospital admissions. In the outpatient setting the

## Indications to hospitalization

The admission status must be assessed on a case-by-case basis, as there have been no findings from physical examination consistently associated with outcomes of bronchiolitis [13].

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# Indications to hospitalization

*Hospitalization is warranted based on the following conditions:*

- **$O_2$ saturation persistently lower than 90-92%**
- **Entity of respiratory distress**
- **Presence of apnea** (5-10% RSV, HRV)
- **Dehydration** (<50% of usual fluid intake in preceding 24 h)
- **Pre-existing risk factors** (prematurity, BPD,CHD, immunodeficiency, airway malformation,severe neurological deficit, cystic fibrosis,Social factors: *distance from the hospital, access to means of transportation or communication, parents*)

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**Diagnosis and Management of Bronchiolitis**
Subcommittee on Diagnosis and Management of Bronchiolitis
*Pediatrics* 2006;118;1774
DOI: 10.1542/peds.2006-2223



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National Guideline Clearinghouse
www.guideline.gov
AHRQ

## Complete Summary

### GUIDELINE TITLE

Evidence-based clinical practice guideline for medical management of bronchiolitis in infants less than 1 year of age presenting with a first time episode.

Baraldi *et al. Italian Journal of Pediatrics* 2014, **40**:65
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REVIEW Open Access

# Inter-society consensus document on treatment and prevention of bronchiolitis in newborns and infants

2014

PEDIATRICS
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2014

SIGN
Scottish Intercollegiate Guidelines Network

NHS
Quality Improvement Scotland

91 **Bronchiolitis in children**
A national clinical guideline

**Clinical Practice Guideline: The Diagnosis, Management, and Prevention of Bronchiolitis**
Shawn L. Ralston, Allan S. Lieberthal, H. Cody Meissner, Brian K. Alverson, Jill E. Baley, Anne M. Gadomski, David W. Johnson, Michael J. Light, Nizar F. Maraqa, Eneida A. Mendonca, Kieran J. Phelan, Joseph J. Zorc, Danielle Stanko-Lopp, Mark A. Brown, Ian Nathanson, Elizabeth Rosenblum, Stephen Sayles III and Sinsi Hernández-Cancio
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# Treatment of bronchiolitis

**(outpatients setting/ emergency room/hospital)**

The basic management of bronchiolitis is based on treatments that assure the patient is clinically stable, well oxygenated and well hydrated , with repeated clinical assessment.

Lacking a specific etiological treatment, therapy for bronchiolitis includes supportive and pharmacological therapies to control respiratory and systemic symptoms .

Scottish

91 Bronchiolitis in children
A national clinical guideline

located on the World Wide Web at:
http://pediatrics.aappublications.org/content/134/5/e1474.full.html

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Cincinnati Children's Hospital Medical Center

**Hydration**

and

**Oxygen**

**Supplementation**

are the mainstay of

bronchiolitis treatment

# When supplemental $O_2$ is indicated?

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Supplemental $O_2$ is indicated when SatO2 falls persistently **< 90%**

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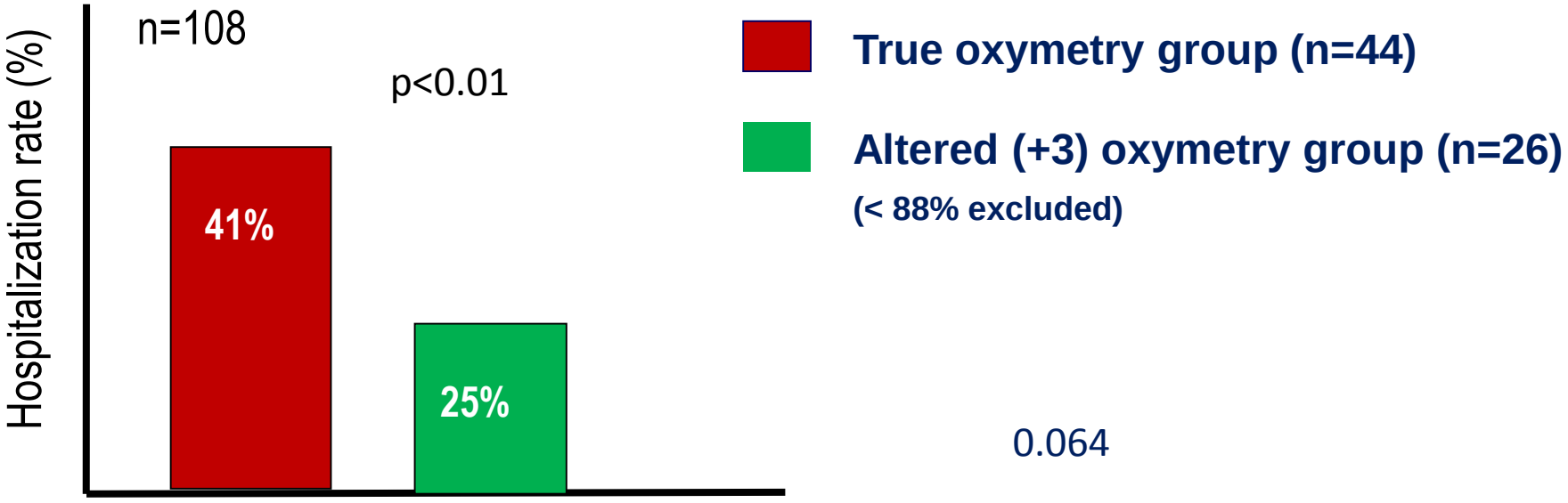
Infants with $O_2$ saturation levels **< 92%** should receive supplemental oxygen by nasal cannulae or facemask

**HOW TO OBTAIN A GOOD MEASUREMENT OF $O_2$ SATURATION ?**

**proper probe and appropriate place**
**avoid movement**
**stability of readings pulse amplitude**
**vasoconstriction and hypothermia**

# Effect of Oximetry on Hospitalization in Bronchiolitis: A Randomized Clinical Trial

JAMA. 2014;312(7):712-718.




**Conclusions and Relevance** Among infants presenting to an emergency department with mild to moderate bronchiolitis, those with an artificially elevated pulse oximetry reading **were less likely to be hospitalized** within 72 hours or to receive active hospital care for more than 6 hours than those with unaltered oximetry readings.

**This suggests that oxygen should not be the only factor in the decision to admit**

# Nasogastric hydration versus intravenous hydration for infants with bronchiolitis: a randomised trial

THE LANCET Respiratory Medicine

**Hydration is the mainstay of bronchiolitis treatment**

*Multicenter randomized trial, infants 2-12 months admitted to hospitals in Australia and NZ*

*Randomly allocated to - nasogastric hydration (n=323)*
*- intravenous hydration (n=294)*

**Results:** No differences in length of hospital stay, rate of admission to ICU, adverse events.

**Conclusion**: Both I.V. and nasogastric hydration are appropriate.

Oakley Lancet Resp Med 2013

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# Inter–society consensus document on treatment and prevention of bronchiolitis in newborns and infants

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| **Nebulized 3% hypertonic saline** | Safe and effective<br>Recommended |
| **Respiratory physical therapy during acute phase of disease** | Not effective |
| **Environment humidification** | Insufficient evidence |
| **Pharmacological therapy** | |
| **Nebulized Beta 2-agonists** | Not effective (the possibility of a therapeutic trial of salbutamol is contemplated) |
| **Nebulized adrenaline** | Decreases hospitalizations in patients presenting to ER |
| **Nebulized and systemic steroids** | Not effective |
| **Antibiotics** | Only in selected cases (bacterial co-infection/pre-existing diseases) |
| **Ribavirin** | Only in selected cases (severe forms/pre-existing diseases) |
| **Nebulized DNase** | Not effective |
| **Montelukast** | Apparently not effective |

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# Nebulized hypertonic saline (HS) solution for bronchiolitis in infants

- improves mucociliary clearance through rehydration of airway surface liquid
- HS reduces edema of the airways by absorbing water from the mucosa
- HS breaks the ionic bonds within the mucus gel
- HS increases the ciliary beat frequency

Mandelberg Pediatr Pulm 2010

# Nebulized hypertonic saline solution for acute bronchiolitis in infants

Zhang – Cochrane 2013 Jul

11 trials involving 1090 infants with mild to moderate acute viral bronchiolitis 4 trials

Current evidence suggests nebulised 3% saline:

- reduces the length of hospital stay among infants hospitalised with non-severe acute viral bronchiolitis

- improves the clinical severity score in both outpatient and inpatient populations.

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# Nebulized hypertonic saline solution

## Key Action Statement 4b

Clinicians may administer nebulized hypertonic saline to infants and children hospitalized for bronchiolitis.

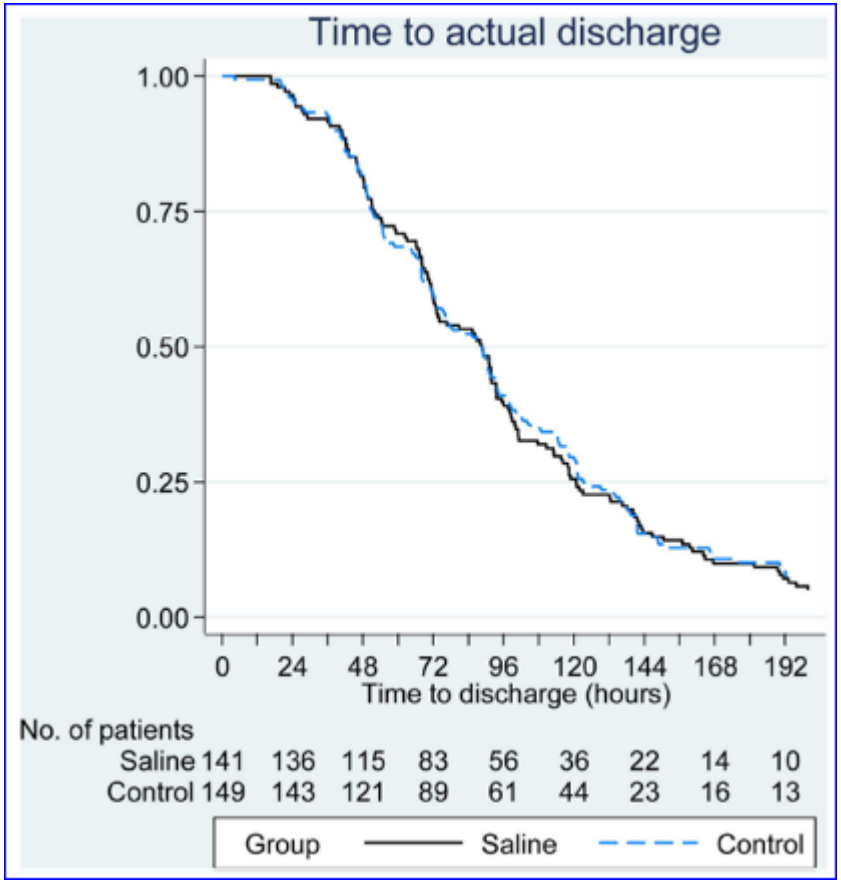
(Evidence Quality: B; Recommendation Strength: Weak)

***American Academy of Pediatrics.***
***Clinical Practice Guideline: The Diagnosis, Management, and Prevention of Bronchiolitis.***
***Pediatrics 2014;134;e1474***

# SABRE: a multicentre randomised control trial of nebulised hypertonic saline in infants hospitalised with acute bronchiolitis

Mark L Everard,[1] Daniel Hind,[2] Kelechi Ugonna,[3] Jennifer Freeman,[4] Mike Bradburn,[2]

**Thorax 2014;69:1105–1112**




Results A total of 317 infants were recruited to the study. 158 infants were randomised to HS and 159 to standard care .

There was no difference between the two arms in time to being declared fit for discharge nor to actual discharge

**Nebulised hypertonic saline does not reduce the length of stay in infants hospitalised with acute bronchiolitis**

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inhaled beta agonists are not effective for bronchiolitis, in that they do not improve oxygen saturation, do not decrease need for and length of hospital stay nor reduce overall duration of symptoms.

However, as a favourable response may be observed in a number of cases, a single therapeutic trial with salbutamol by aerosol may be considered, in particular in children with a family history of allergy, asthma and/oratopy.

ITALIAN JOURNAL OF PEDIATRICS

# Inter–society consensus document on treatment and prevention of bronchiolitis in newborns and infants

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| Nebulized adrenaline | Decreases hospitalizations in patients |

However, given the greater strength of the evidence demonstrating no benefit, and that there is no well-established way to determine an "objective method of response" to bronchodilators in bronchiolitis, this option has been removed. (AAP 2014)

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# Epinephrine for bronchiolitis (Review)

Hartling L, Bialy LM, Vandermeer B, Tjosvold L, Johnson DW, Plint AC, Klassen TP, Patel H, Fernandes RM

THE COCHRANE COLLABORATION®

might be effective in decreasing need for hospitalization in children presenting to the emergency but there are **insufficient evidence to support the prolonged use of epinephrine for the treatment of bronchiolitis** among inpatients

**The Cochrane Library 2011, Issue 6**

The NEW ENGLAND JOURNAL of MEDICINE

ORIGINAL ARTICLE

# Racemic Adrenaline and Inhalation Strategies in Acute Bronchiolitis

Håvard Ove Skjerven, M.D., Jon Olav Gjengstø Hunderi, M.D., Sabine Kristin Brügmann-Pieper, M.D., Anne Charlotte Brun, M.D., Hanne Engen, M.D., Leif Eskedal, M.D., Ph.D., Marius Haavaldsen, M.D., Bente Kvenshagen, M.D., Ph.D., Jon Lunde, M.D., Leif Bjarte Rolfsjord, M.D., Christian Siva, M.D., Truls Vikin, M.D., Petter Mowinckel, M.Sc., Kai-Håkon Carlsen, M.D., Ph.D., and Karin C. Lødrup Carlsen, M.D., Ph.D.

**N Engl J Med 2013;368:2286-93**.

METHODS

In this eight-center, randomized, double-blind trial with a 2-by-2 factorial design, we compared inhaled racemic adrenaline with inhaled saline and on-demand inhalation with fixed-schedule inhalation (up to every 2 hours) in infants (<12 months of age) with moderate-to-severe acute bronchiolitis. An overall clinical score of 4 or higher (on a scale of 0 to 10, with higher scores indicating more severe illness) was required for study inclusion. Any use of oxygen therapy, nasogastric-tube feeding, or ventilatory support was recorded. The primary outcome was the length of the hospital stay, with analyses conducted according to the intention-to-treat principle.

404 infants

The NEW ENGLAND JOURNAL of MEDICINE

ORIGINAL ARTICLE

# Racemic Adrenaline and Inhalation Strategies in Acute Bronchiolitis

Håvard Ove Skjerven, M.D., Jon Olav Gjengstø Hunderi, M.D., Sabine Kristin Brügmann-Pieper, M.D., Anne Charlotte Brun, M.D., Hanne Engen, M.D., Leif Eskedal, M.D., Ph.D., Marius Haavaldsen, M.D., Bente Kvenshagen, M.D., Ph.D., Jon Lunde, M.D., Leif Bjarte Rolfsjord, M.D., Christian Siva, M.D., Truls Vikin, M.D., Petter Mowinckel, M.Sc., Kai-Håkon Carlsen, M.D., Ph.D., and Karin C. Lødrup Carlsen, M.D., Ph.D.

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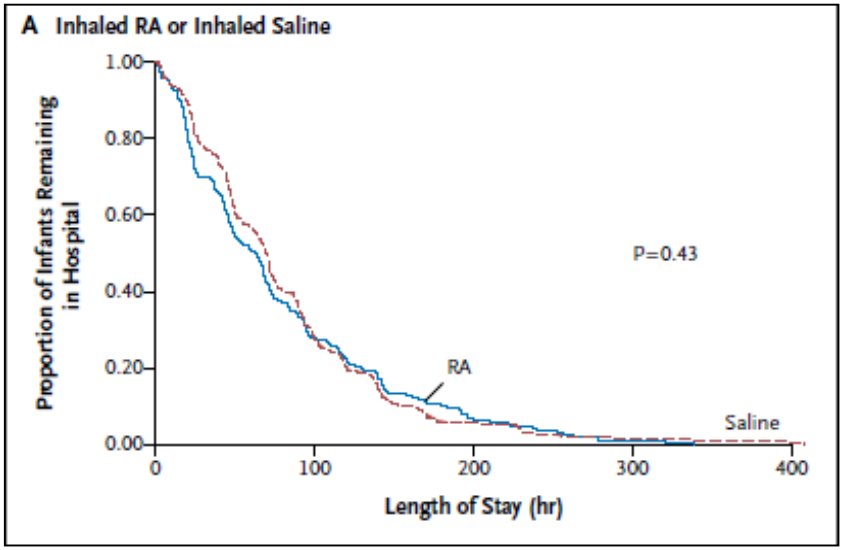
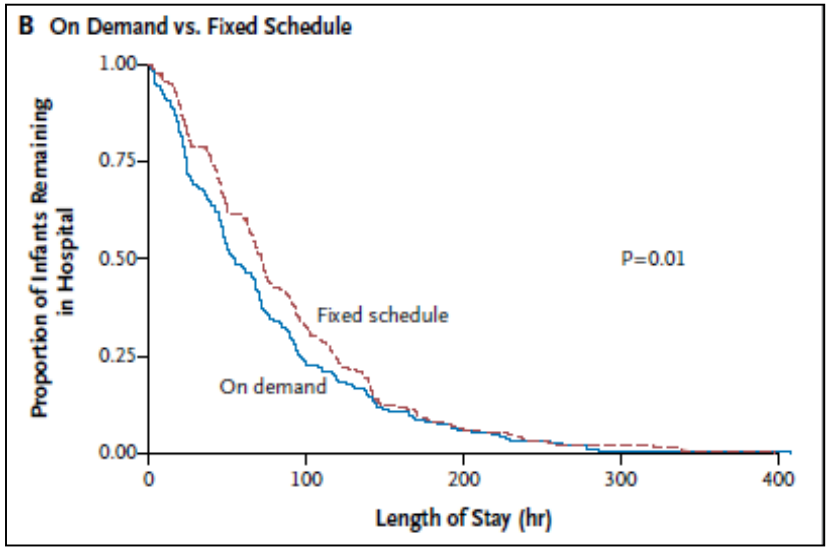


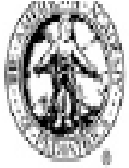




**In the treatment of acute bronchiolitis in infants, inhaled racemic adrenaline is not more effective than inhaled saline. However, the strategy of inhalation on demand appears to be superior to that of inhalation on a fixed schedule**

CLINICAL PRACTICE GUIDELINE

# Clinical Practice Guideline: The Diagnosis, Management, and Prevention of Bronchiolitis

American Academy of Pediatrics



**2014**

## EPINEPHRINE

### Key Action Statement 3

**Clinicians should not administer epinephrine to infants and children with a diagnosis of bronchiolitis (Evidence Quality: B; Recommendation Strength: Strong Recommendation).**

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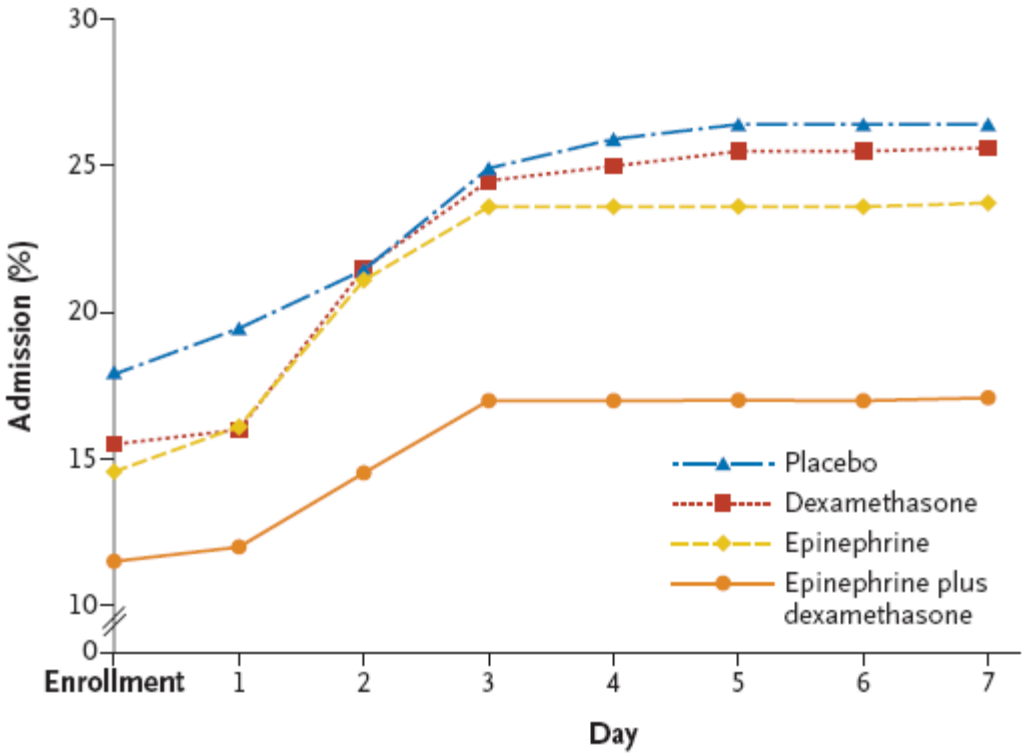
**Because of the lack of studies and potential adverse effects nebulised <u>adrenaline is NOT recommended in the home setting</u>**

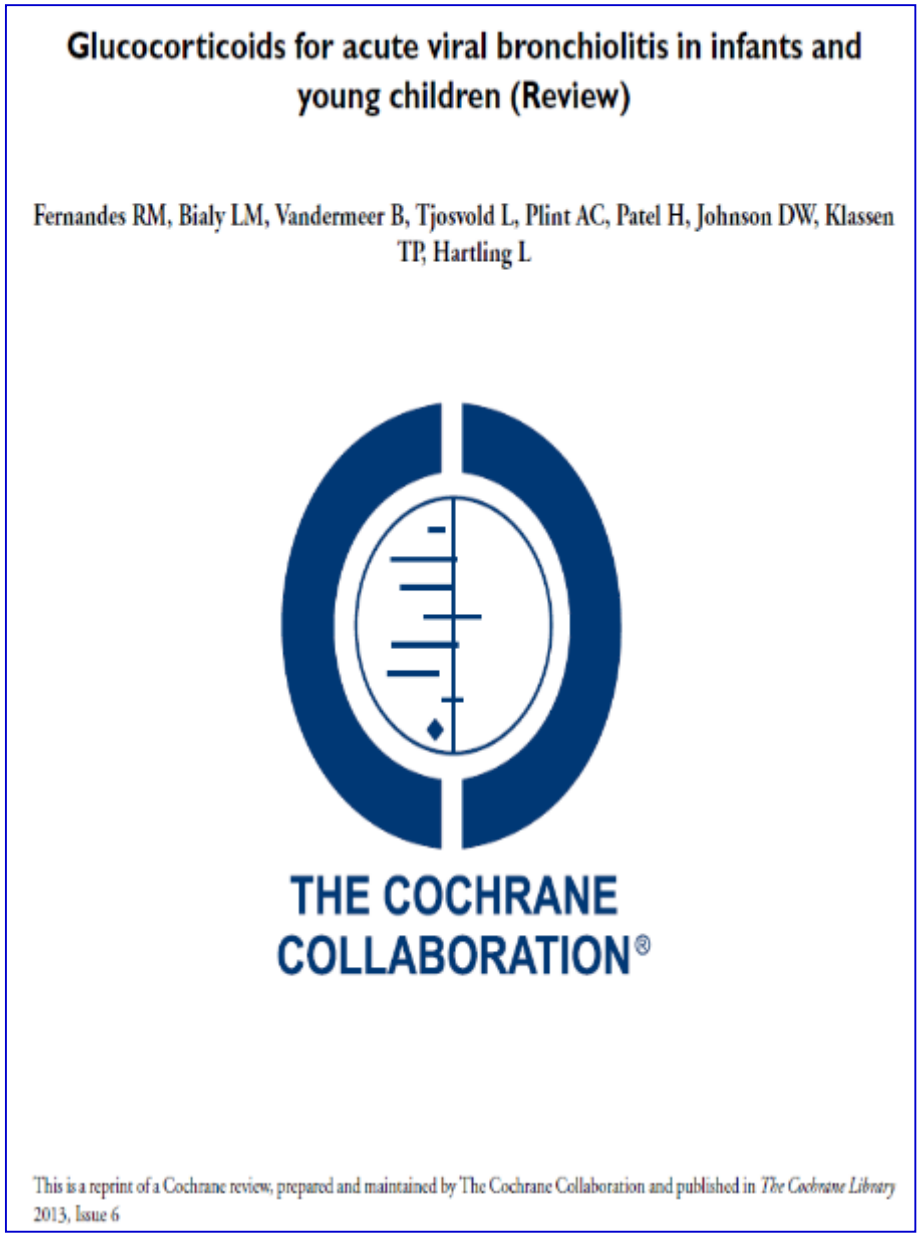
# Epinephrine and Dexamethasone in Children with Bronchiolitis

Amy C. Plint, M.Sc. David W. Johnson, Hema Patelfor Pediatric Emergency Research Canada (PERC)

N Engl J Med 2009;360:2079-89.




**Cumulative Admissions during the First 7 Days after the Initial Emergency Department Visit, According to Study Group**




# Corticosteroids

*17 trials - 2596 participants*

**Current evidence does not support a clinically relevant effect of systemic or inhaled glucocorticoids on admissions or length of hospitalisation**

Glucocorticoids for acute viral bronchiolitis in infants and

Fernan

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# Corticosteroids are NOT recommended for the treatment of acute bronchiolitis

**sistemic corticosteroids:** no benefits were found in length of stay, clinical score or outcomes

**inhaled corticosteroids:** no benefits in the course of acute disease - no benefits in the prevention of post-bronchiolitic wheeze

60% hospitalized children with brochiolitis receive corticosteroids

This is a r
2013, Issu

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NOT EFFECTIVE

# …AND IN THE CASE OF BRONCHIOLITIS DETERIORATION?

# HFNC Oxygen delivery

**H** ***H****igh* ***H****eated* ***H****umidified*

**F** *Flow*

**N** *Nasal*

**C** *Cannula*

# Come agiscono gli alti flussi?

-wash-out dello spazio morto naso-faringeo

- riducono la resistenza al flusso aereo

- forniscono pressione positiva che:

•*riduce il carico dei muscoli respiratori*
• *mantiene pervi gli alveoli e previene le microatelettasie*

# High Flow Nasal Cannulae Therapy in Infants with Bronchiolitis

Christine McKiernan, MD, Lee Chadrick Chua, MD, Paul F. Visintainer, PhD, and Holley Allen, MD

**J Pediatr 2010;156:634-8**

*Results:*

In the season after the introduction of HFNC, only 9% of infants admitted to the PICU with bronchiolitis required intubation, compared with 23% in the prior season (P= .043).

Median PICU length of stay for children with bronchiolitis decreased from 6 to 4 days after the introduction of HFNC.

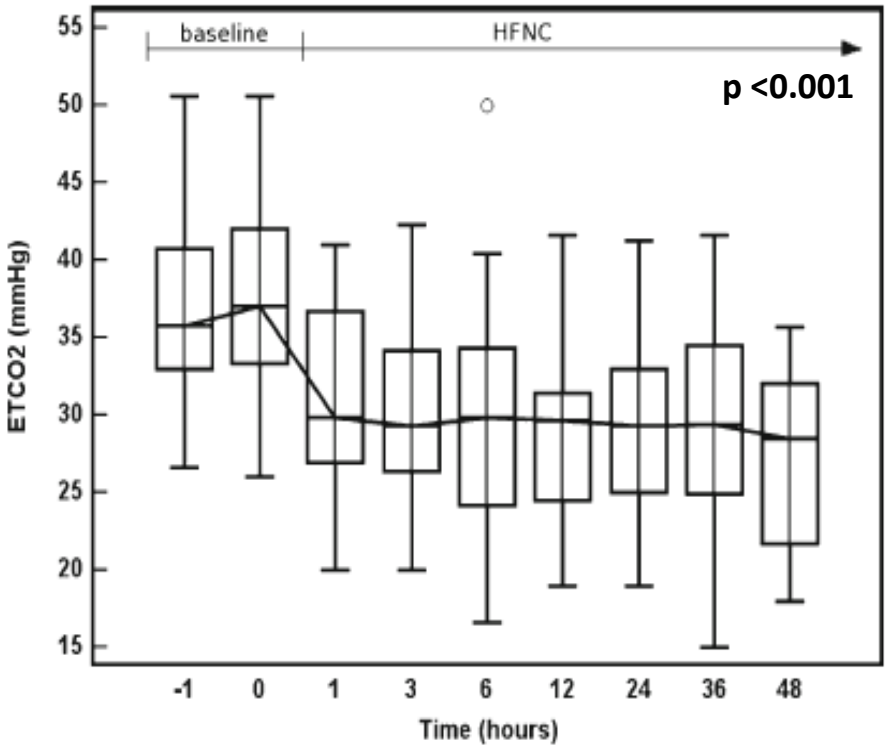
*Discussion:*

Heated humidified high-flow nasal cannulae (HFNC) **decreases** rates of intubation in infants with bronchiolitis by decreasing the respiratory rate and work of breathing by providing a comfortable and well-tolerated means of noninvasive ventilatory support.

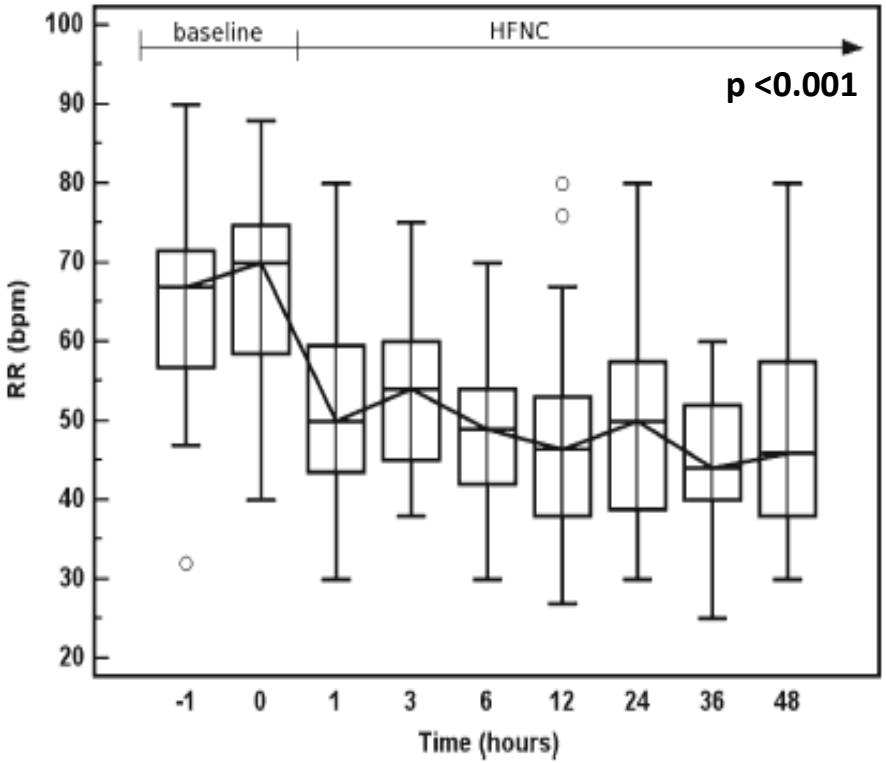
# High-flow nasal cannula oxygen for bronchiolitis in a pediatric ward: a pilot study

Silvia Bressan · Marco Balzani · Baruch Krauss · Andrea Pettenazzo · Stefania Zanconato · Eugenio Baraldi

Eur J Pediatr (2013) 172:1649–1656




ETCO2 values distribution over time pre and during HFNC therapy




RR values distribution over time pre and during HFNC therapy.

# High-flow nasal cannula oxygen therapy for infants with bronchiolitis: Pilot study

Mayfield et al **J Paed Child Health 2014**

**Patients:** 61 HFNC vs. 33 standard treatment (previous year)

**Aim:** to investigate the safety of HFNC treatment in a **pediatric ward setting**

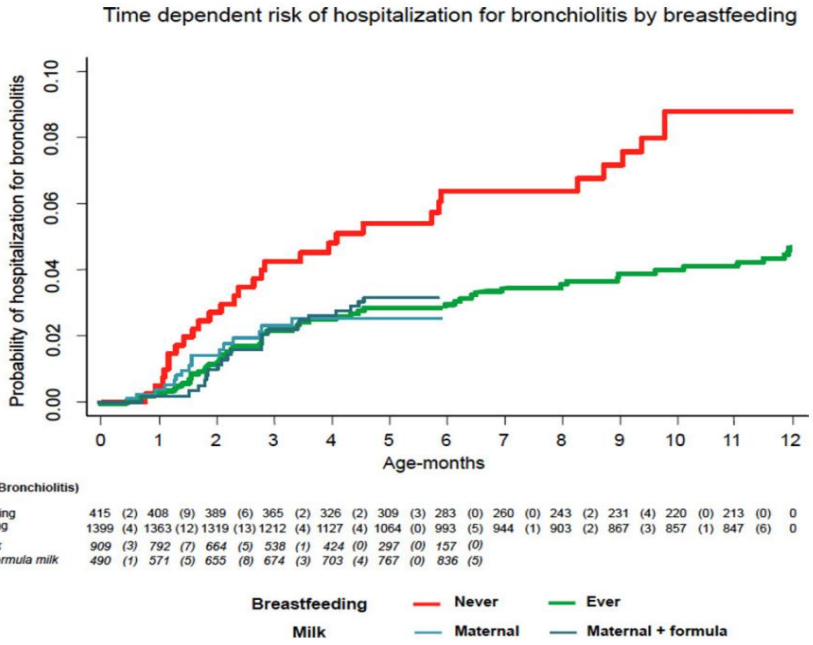
**Flow rate: 2 L/kg/min** (max flow 10 L/min)

**Results:**
feasible in a pediatric ward setting reduced admission to PICU
no adverse effects

# Maternal milk protects infants against bronchiolitis during the first year of life. Results from an Italian cohort of newborns

**Lanari M EHD 2013**

PREVENTION




# Updated Guidance for Palivizumab Prophylaxis Among Infants and Young Children at Increased Risk of Hospitalization for Respiratory Syncytial Virus Infection

American Academy of Pediatrics

DEDICATED TO THE HEALTH OF ALL CHILDREN™

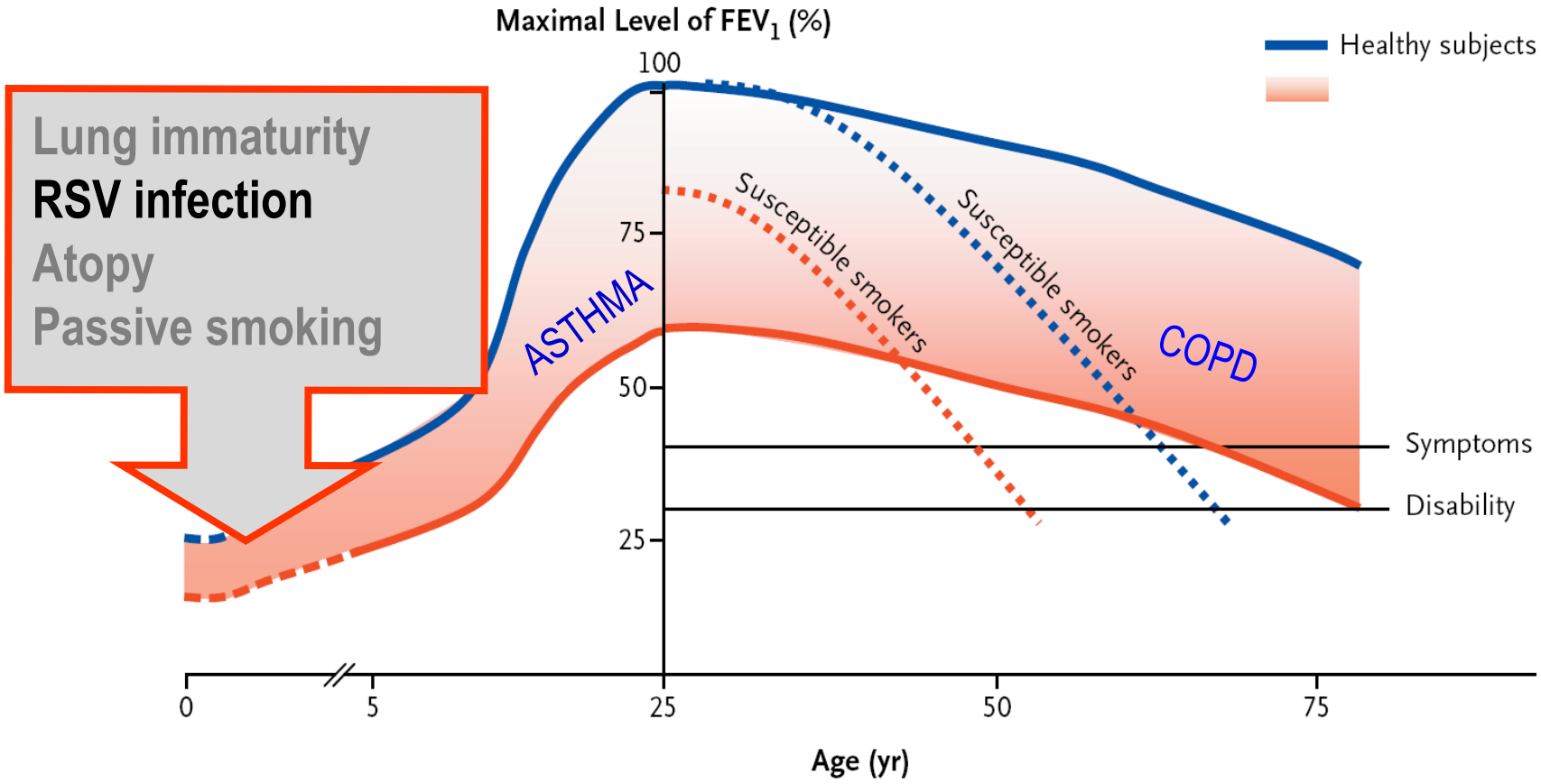
**2014**

**Preterm infants born before 29 weeks gestation** (who are younger than 12 months at the start of the RSV season)

- **BPD infants (< 1-2 yrs)**
- **Infants with CHD hemodinamically significant**
- **Infants with neuromuscolar disease or congenital pulmonary anomalies (< 1 yr)**
- **Infants with Cystic Fibrosis (< 2 yrs)**
- **Immunocompromised infants (< 2 yrs)**

PREVENTION

# EARLY INSULTS MAY CAUSE FAILURE TO ACHIEVE MAXIMAL LUNG FUNCTION AND EXPOSE INDIVIDUALS TO THE RISK OF CHRONIC RESPIRATORY DISEASES LATER IN LIFE




Baraldi & Filippone NEJM 2007

# CONCLUSIONS

aspects of bronchiolitis management are still debated

- Attention to children at risk: preterm , BPD, CHD, immunodeficiency
- Beta-agonists and steroids (systemic and inhaled) are not recommended for routine use
- Hypertonic saline may provide significant benefit but.....
- HFNC O2 therapy is a promising option for moderate-severe cases
- Prevention always and prophylaxis for infants at high-risk
- Significant association between RSV bronchiolitis and development of wheezing up to early adulthood

# THERAPY FOR BRONCHIOLITIS:: THE HISTORY GOES ON……

Grazie per l'attenzione