

LE VIE AEREE

**La bronchiolite:
ciò che è realmente
utile fare**

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CORSO
**ALLERGOLOGIA
ed IMMUNOLOGIA
PEDIATRICA**

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Centro Congressi Fra Pietro Maria de Giovanni o.h.
Ospedale Sacro Cuore di Gesù Fatebenefratelli
BENEVENTO

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

The online version of this article, along with updated information and services, is located on the World Wide Web at:

Bronchiolitis: Recent Evidence on Diagnosis and Management
Joseph J. Zorc and Caroline Breese Hall
Pediatrics 2010;125:342-349; originally published online Jan 25, 2010;
DOI: 10.1542/peds.2009-2092

The online ve



National Guideline Clearinghouse
www.guideline.gov



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. 2006 May



Scottish Intercollegiate Guidelines Network



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Bronchiolitis in children

A national clinical guideline

November 2006

- **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.”

- **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.”

-Bush A,Thomson AH.Acute Bronchiolitis BMJ 2007;335:1037

- Scottish Intercollegiate Guidelines Network.Bronchiolitis in children November 2006

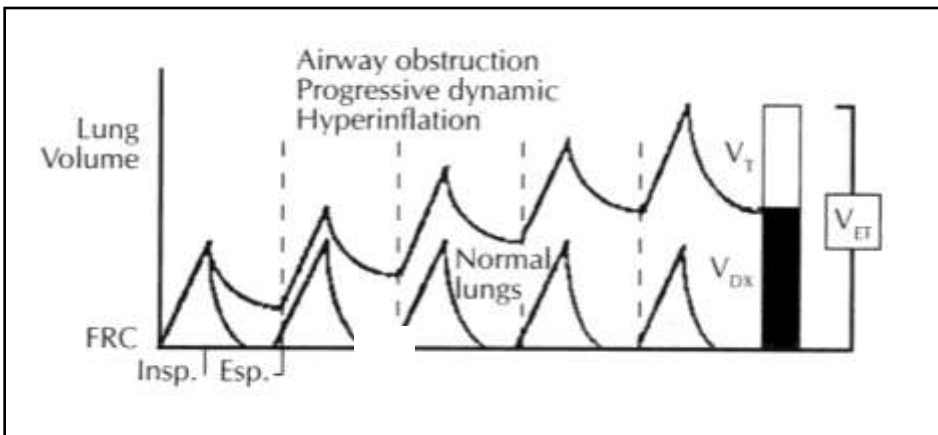
*-American Academy of Pediatrics Subcommittee on Diagnosis and Management of Bronchiolitis.
Diagnosis and management of bronchiolitis. Pediatrics 2006;118:1774*

- Cincinnati Children’s Hospital Medical Center; 2006 May

- Zorc JJ, Hall CB Bronchiolitis: Recent Evidence on Diagnosis and Management. Pediatrics 2010;125:342

Prolongation of the respiratory time-constant & Increase in respiratory frequency

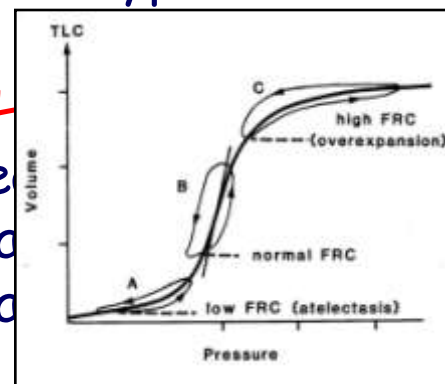
Incomplete
exhalation



airway narrowing
- alveolar hypoventilation

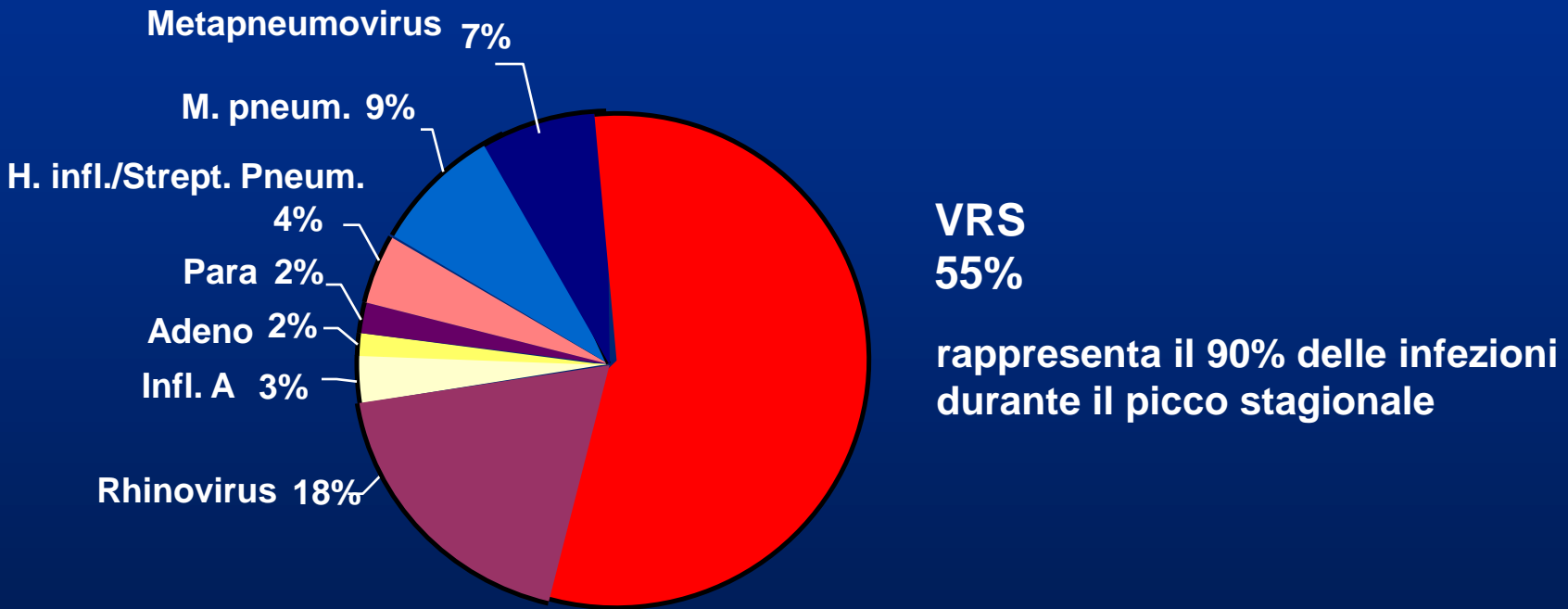
Dynamic Hyperinflation

- decreased
- increased
- increased



(\downarrow - $T_e \uparrow$)
on

Virus Respiratori responsabili di Bronchiolite



**E' necessaria la ricerca
dei virus respiratori?**

- L'utilità della ricerca dei virus respiratori nell'aspirato nasofaringeo è limitata, dal momento che il trattamento è diretto verso le manifestazioni cliniche più che verso l'agente eziologico; in genere il trattamento è lo stesso indipendente dai risultati del test.
- Il test rapido per il VRS (sensibilità tra l'80-90% e specificità > 90%) è indicato per ricerche o valutazioni epidemiologiche e nei bambini ricoverati, programmare infatti spazi dedicati in corsia riduce la trasmissione ospedaliera del VRS.

**E' necessario eseguire
la radiografia del torace?**

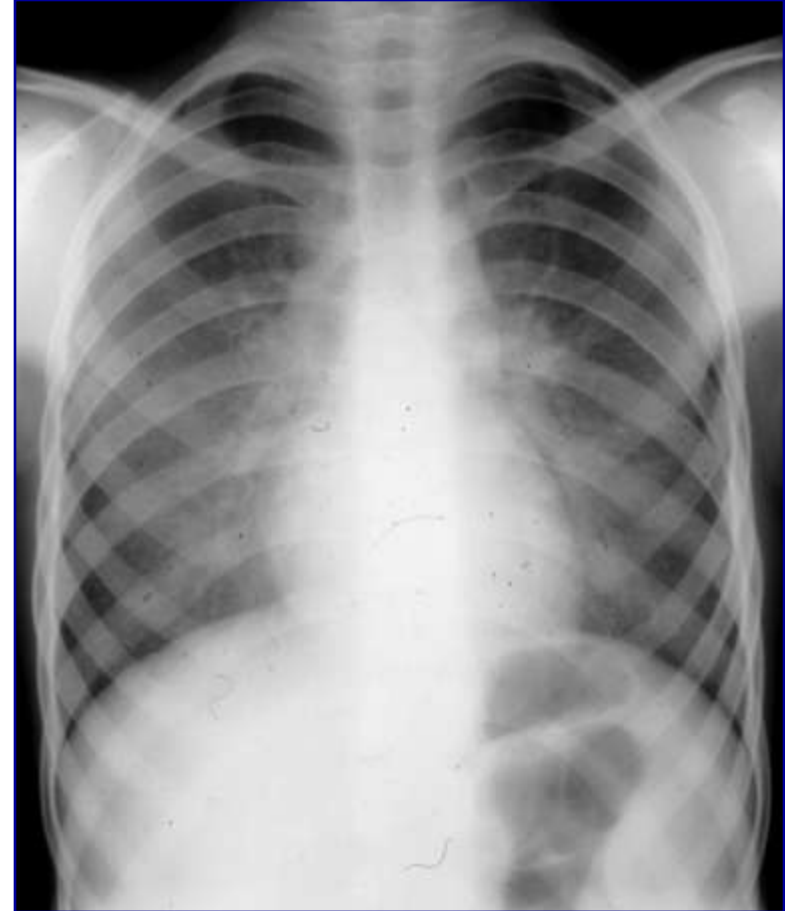
➤ La radiografia del torace non è specifica: è presente *air trapping* diffuso e, nella maggioranza dei bambini, sono visibili opacità sfumate ed infiltrati peribronchiali, suggestivi di polmonite interstiziale.

➤ È anche possibile che la radiografia del torace risulti normale in bambini ricoverati per bronchiolite grave.

Alterazioni radiografiche

Le alterazioni radiografiche più comuni sono rappresentate da infiltrati interstiziali polmonari, quasi sempre bilaterali, con iperdistensione del polmone.

In circa il 20% dei pazienti si possono osservare addensamenti segmentari o lobari che simulano una infezione batterica.



La diagnosi di bronchiolite è clinica

La diagnosi è formulata sulla base dell'anamnesi e dell'esame obiettivo, non è necessario l'impiego routinario di test di laboratorio o di esami radiologici.

Importante valutare la presenza di fattori di rischio:

- ✓ prematurità,
- ✓ malattie polmonari croniche,
- ✓ cardiopatie,
- ✓ immunodeficienza.

Selected Risk Factors for Outcomes of Bronchiolitis in 3 Prospective Studies of Outpatients

Outcome	Shaw et al ³⁸ (1991)	Mansbach et al ⁴⁰ (2008)	Voets et al ³⁹ (2006)
Risk factors	Severe disease ^a	Hospitalization	Hospitalization
Age			
<2 mo		4.5/0.78	
<3 mo	2.2/0.75		
<6 mo			2.2/0.53
Prematurity			
<34 wk	5.4/0.77		
<35 wk		1.5/0.96	
Ill appearance	3.2/0.32		
Oxygen saturation			
<94%		5.4/0.77	
<95%	16/0.69		5.2/0.37
Respiratory rate			
>45 breaths per min			3.8/0.39
At or higher than normal for age (40–45 breaths per min according to age)		1.3/0.61	
≥70 breaths per min	5.8/0.75		
Work of breathing			
Accessory muscle use	2.2/0.42		
Moderate/severe retractions		3.2/0.76	
Chest radiograph result			
Atelectasis	10.5/0.81		
Abnormal		1.2/0.73	

..... e quale terapia?

Ossigeno Liquidi

L'ossigenoterapia è indicata se la saturazione di O₂ è persistentemente <92% (<90% AAP 2006) in un bambino che prima della bronchiolite godeva di buona salute.

Somministrare l'ossigenoterapia deve essere indicata se esiste ipossiemia e ipossimetria.

Dare un adeguato supporto idratante e peridratazione

Monitorare SaO₂, FC e FR

SI

Broncodilatatori (α adrenergici)

L'efficacia dei broncodilatatori non è adeguatamente documentata, né la durata del ricovero.

Tuttavia è un agonista, come il salbutamolo, continuare il trattamento clinica favorevole ben v...

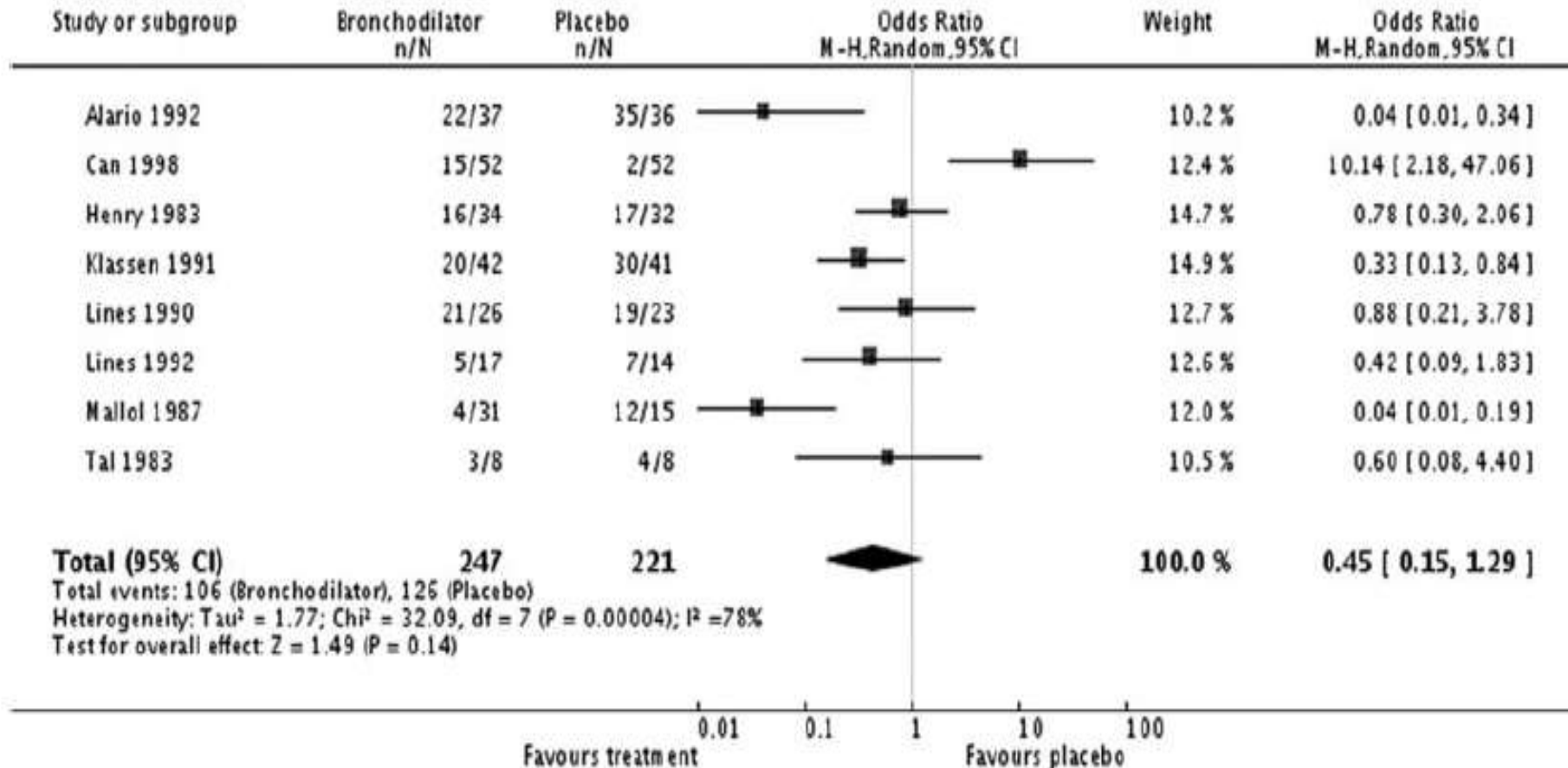
Efficacia da valutare

Gadomski AM et al Broncodilators for bronchiolitis Cochrane Database Syst Rev 2006;CD001262

Zorc JJ, Hall CB Bronchiolitis: Recent Evidence on Diagnosis and Management Pediatrics 2010;125;342-349

Rate of improvement after β 2-agonist bronchodilators or placebo among children with bronchiolitis.

Review: Bronchodilators for bronchiolitis
 Comparison: 1 Bronchodilator versus placebo
 Outcome: 1 Improvement in clinical score (dichotomous)



Adrenalina

L'adrenalina è un farmaco che viene utilizzato per il trattamento delle crisi asmatiche. I dati disponibili sono limitati e non consentono di raccomandare l'uso di adrenalina come

**Efficacia
limitata**

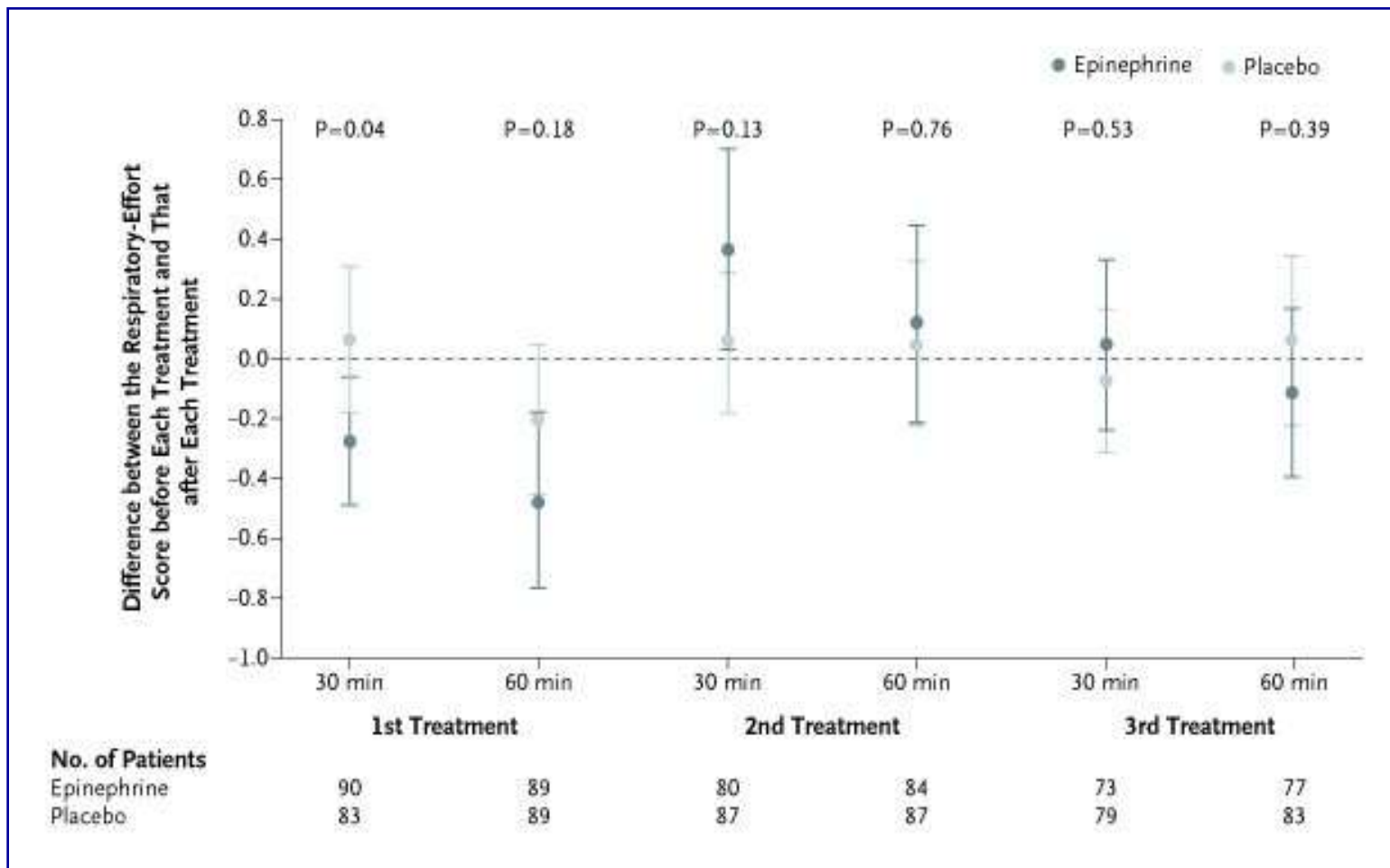
Wainwright C et al. A multicentre, randomised, double-blind, controlled trial of nebulized epinephrine in infants with acute bronchiolitis. NEJM 2003; 349:27

Hartling L et al Epinephrine for bronchiolitis. Cochrane Database Syst Rev The Cochrane Library 2011, Issue 6

Hartling L et al: Steroids and bronchodilators for acute bronchiolitis in the first two years of life: systematic review and meta-analysis BMJ 2011;342:d1714

Zorc JJ, Hall CB Bronchiolitis: Recent Evidence on Diagnosis and Management Pediatrics 2010;125;342-349

A multicenter, randomized, double-blind, controlled trial of nebulized epinephrine in infants with acute bronchiolitis.



Mean Differences between the Respiratory-Effort Score before each nebulization treatment and those 30 and 60 minutes after each treatment
Wainwright C et al. N Engl J Med 2003;349:27-35

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®**

The Cochrane Library 2011, Issue 6

Bronchodilators are commonly used for acute bronchiolitis, despite uncertain effectiveness.

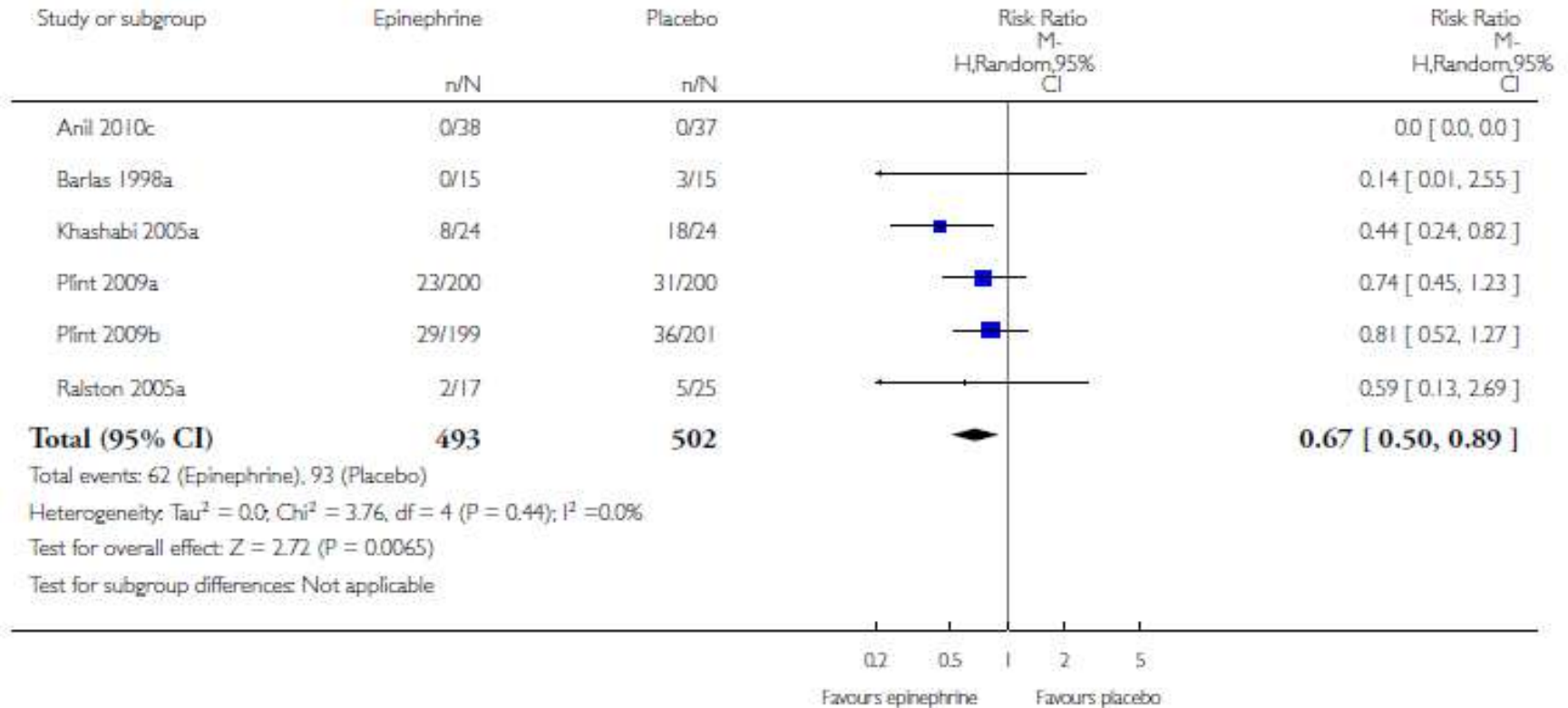
Efficacy and safety of epinephrine in children less than two with acute viral bronchiolitis.

19 studies (2256 participants).

- This review demonstrates of the **effectiveness** of epinephrine versus placebo in outpatients for outcomes of most clinical relevance, specifically **admission rates during the first 24** hours, but not at day 7 post-emergency department visit.
- **Epinephrine** versus **salbutamol** showed **no differences** among outpatients for admissions at day 1 or 7.

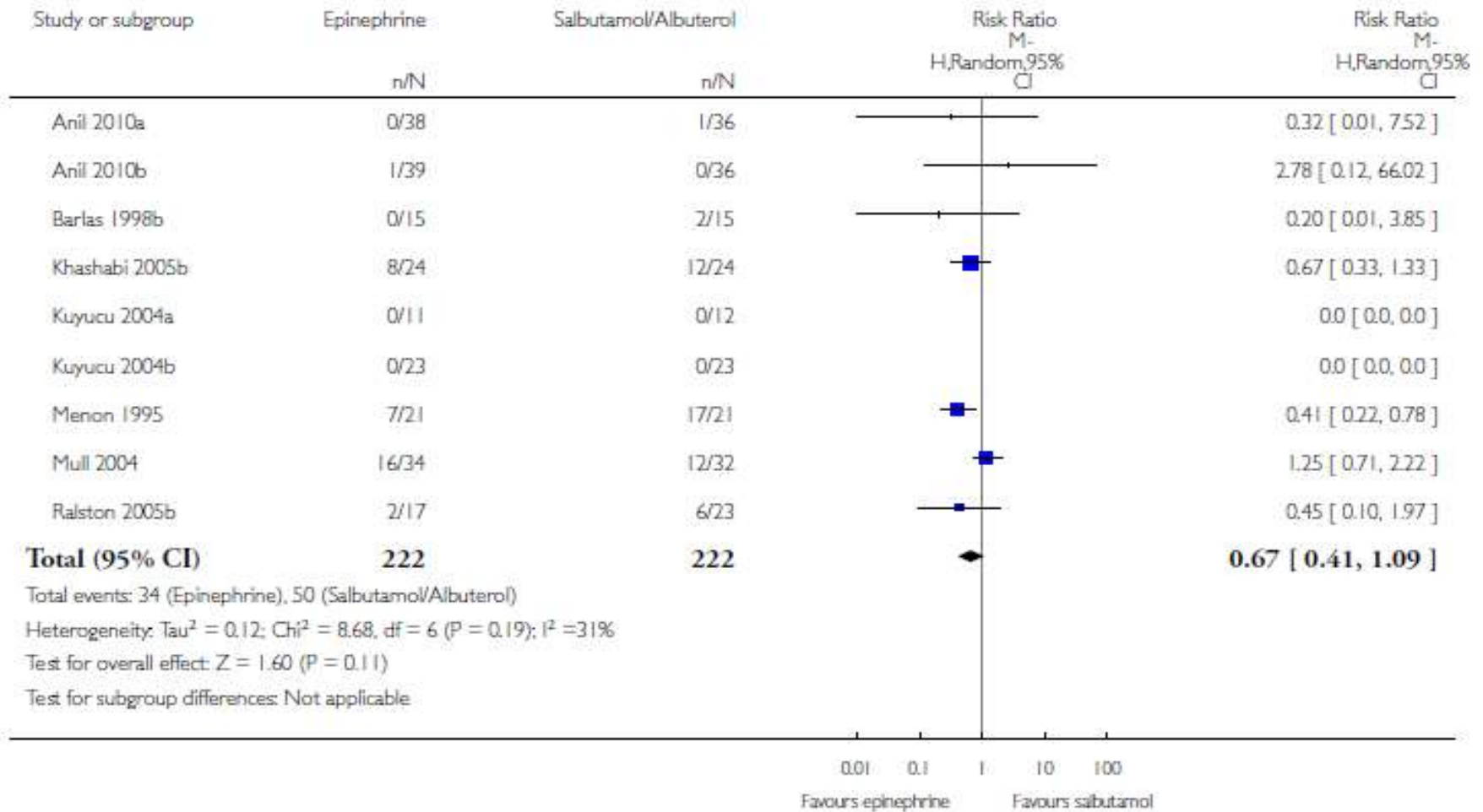
Epinephrine versus placebo

Admissions at enrollment or < 24 hours



Epinephrine versus salbutamol/albuterol

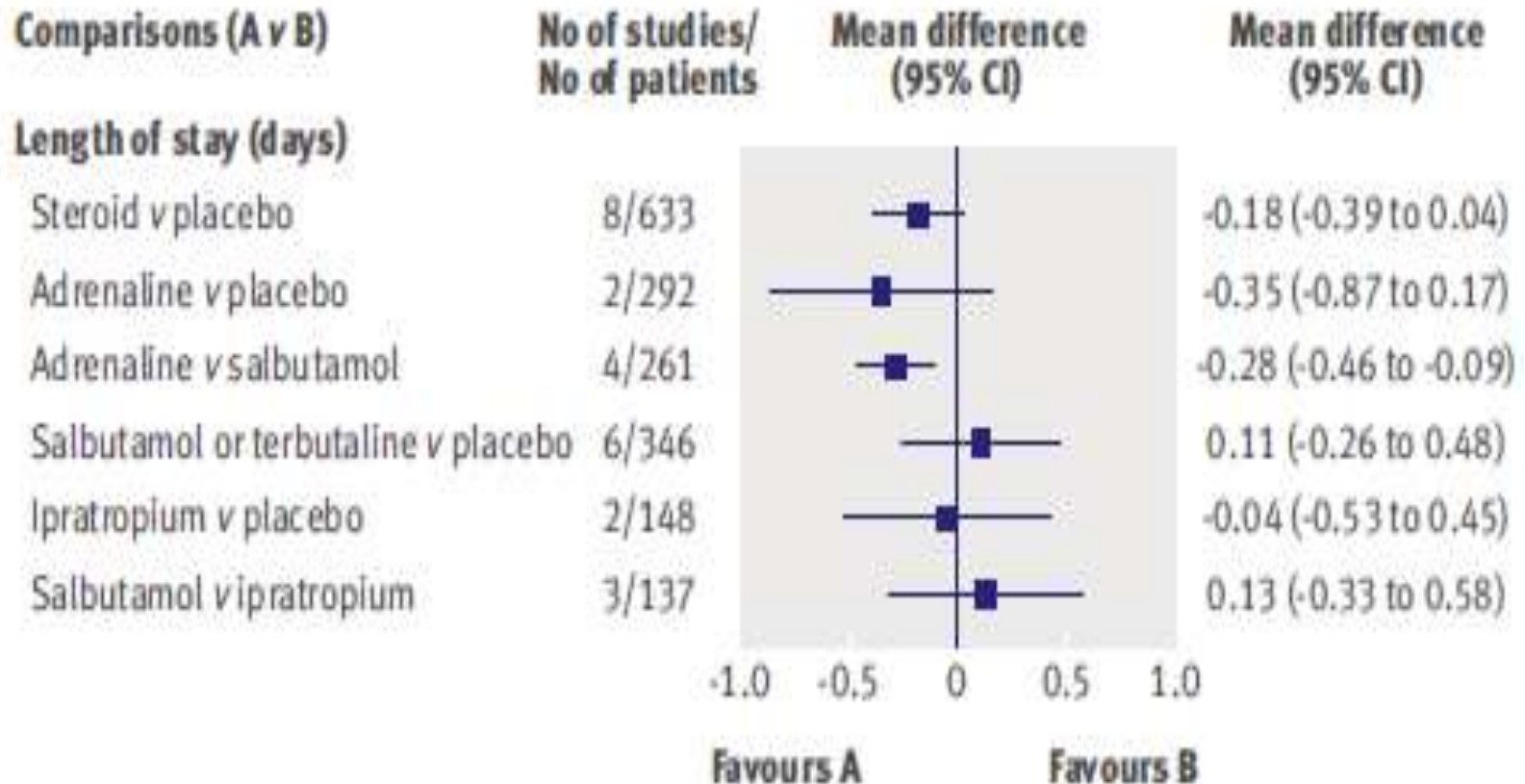
Admissions at enrollment or < 24 hours (outpatients only).



Length of stay (inpatients only)

- While epinephrine compared to salbutamol showed a significant difference for length of stay, the finding is tempered by the fact that there were no differences in length of stay for epinephrine versus placebo.
- There is **insufficient evidence** to support the prolonged use of epinephrine for the treatment of bronchiolitis among **inpatients**.

Results from meta-analysis of direct comparisons for length of stay in inpatients



Steroids and bronchodilators for acute bronchiolitis in the first two years of life: systematic review and meta-analysis

Lisa Hartling, assistant professor,¹ Ricardo M Fernandes, PhD student,² Liza Bialy, project coordinator,¹ Andrea Milne, research assistant,¹ David Johnson, professor,³ Amy Plint, associate professor,⁴ Terry P Klassen, professor,⁵ Ben Vandemeer, biostatistician¹

Objective: To evaluate and compare the efficacy and safety of **bronchodilators and steroids**, alone or combined, for the acute management of bronchiolitis in children aged **less than 2 years**.

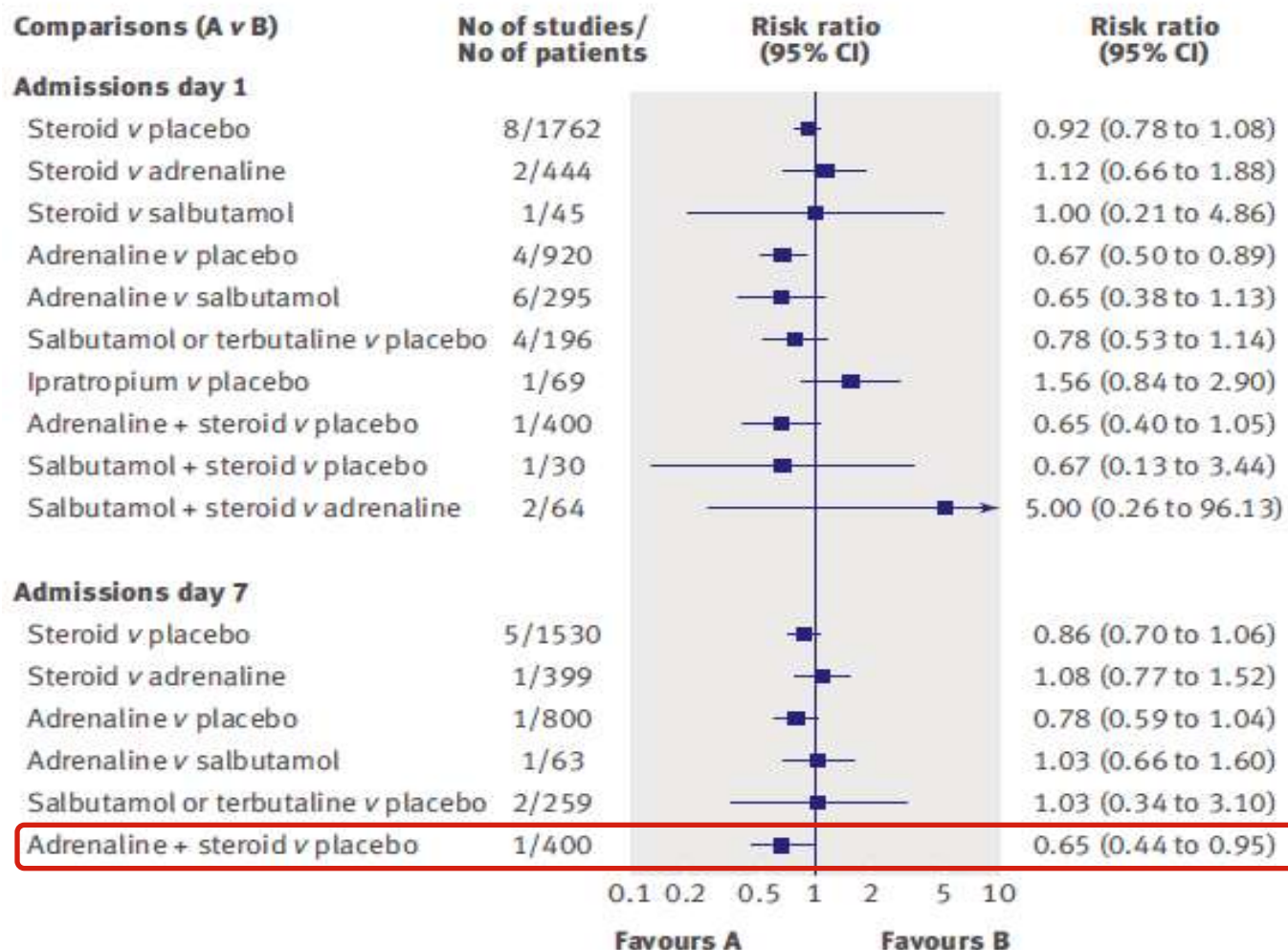
Primary outcomes: rate of **admission** for outpatients (day 1 and up to day 7) and **length of stay** for inpatients.

48 trials (4897 patients) were included.

Conclusions: Evidence suggests a benefit of **combined adrenaline and dexamethasone** for reducing admission rates seven days after the emergency department visit.

For inpatients, none of the interventions examined showed clear benefits for length of stay.

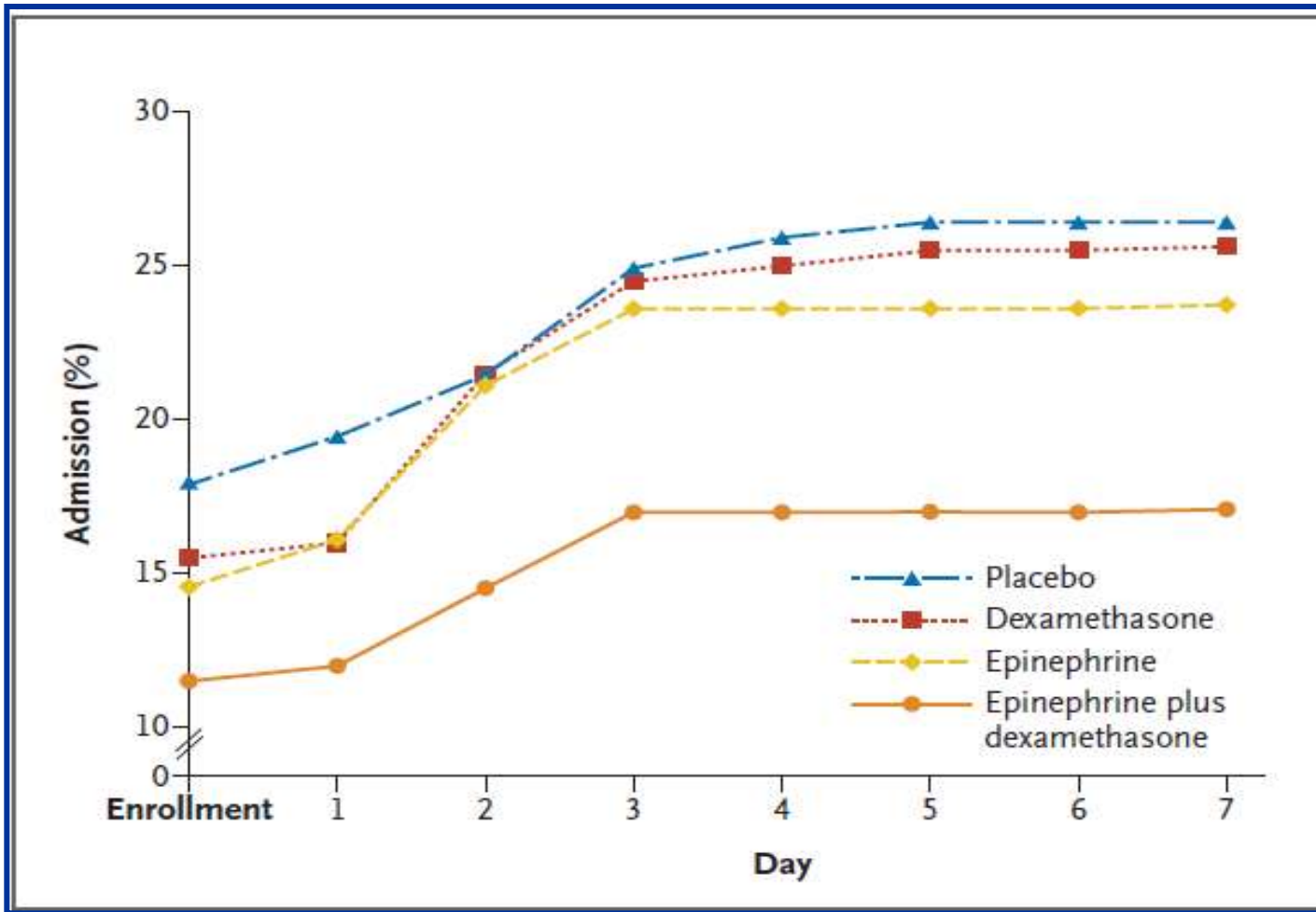
Results from meta-analysis of direct comparisons for admission rates from emergency department (day 1 and day 7) in outpatients



The results were statistically significant for only one comparison, showing a reduction of 33% for adrenaline compared with placebo (pooled risk ratio 0.67, 95% CI 0.50 to 0.89)

An similar effect was shown with combined adrenaline and dexamethasone compared with placebo (35%), (RR 0.65, 95%CI 0.44 to 0.95 P=0.07) NNT=11

Multicenter, double-blind, placebo-controlled trial with 800 infants with bronchiolitis seen in eight Canadian pediatric emergency department.



Cumulative admission rate over 7 days compared with those who were on placebo 17.1% vs 26.4% (P = 0.02) NNT= 11 (11 infants would need to be treated to prevent one hospital admission.)

Plint AC. Epinephrine and dexamethasone in children with bronchiolitis. NEJM 2009;360:2079

CORTICOSTEROIDI

non devono essere usati di routine nel trattamento della bronchiolite

**Efficacia
Controversa**

Cade A, et al. Arch Dis Child 2000;82:126-30

Wong JY et al. ERJ 2000;15:388-94

Patel H, et al. Glucocorticoids for acute viral bronchiolitis in infants and young children (Review) Cochrane Database Syst Rev 2007;CD004878

Corneli HM et al. NEJM 2007;357:331-9

Zorc JJ, Hall CB Bronchiolitis: Recent Evidence on Diagnosis and Management Pediatrics 2010;125:342-349

A multicenter, randomized, controlled trial of dexamethasone for bronchiolitis.

Table 3. Hospital Admission and Changes in Clinical Variables from Baseline to 4 Hours after Intervention.*

Variable	Dexamethasone Group	Placebo Group	Difference between Groups (95% CI)	P Value
Hospital admission (%)	39.7	41.0	-1.3 (-9.2 to 6.5)	0.74
RACS	-5.3±4.7	-4.8±4.6	-0.5 (-1.3 to 0.3)	0.21
RDAI score	-4.4±3.1	-3.9±3.2	-0.5 (-1.0 to -0.1)	0.03
Respiratory rate (breaths/min)	-8±15	-7±14	-1.0 (-3.0 to 1.0)	0.39
Oxygen saturation (%)	0.3±3.3	0.9±3.2	-0.6 (-1.0 to -0.1)	0.02
Heart rate (beats/min)	-13±24	-5±25	-8.0 (-12.0 to -5.0)	<0.001
Temperature (°C)	-0.6±0.9	-0.2±1.0	-0.4 (-0.6 to -0.3)	<0.001

* Data for all variables except hospital admission are expressed as the change from baseline to 4 hours. RACS denotes Respiratory Assessment Change Score, and RDAI Respiratory Distress Assessment Instrument.

Hospital Admission and Changes in Clinical Variables from Baseline to 4 Hours after Intervention

Corneli H et al. *N Engl J Med* 2007;357:331-339

Gli antibiotici devono essere impiegati nella bronchiolite solo in presenza di specifiche indicazioni per una forma batterica.

La fisioterapia non deve essere utilizzata nel trattamento della bronchiolite “...it is a waste of time”

Nebulized hypertonic saline solution for acute bronchiolitis in infants (Review)

2008

Zhang L, Mendoza-Sassi RA, Wainwright C, Klassen TP



Valutare l'efficacia terapeutica della soluzione salina ipertonica 3% nebulizzata in bambini affetti da bronchiolite acuta virale

4 *trials* randomizzati controllati con 254 bambini

189 ricoverati

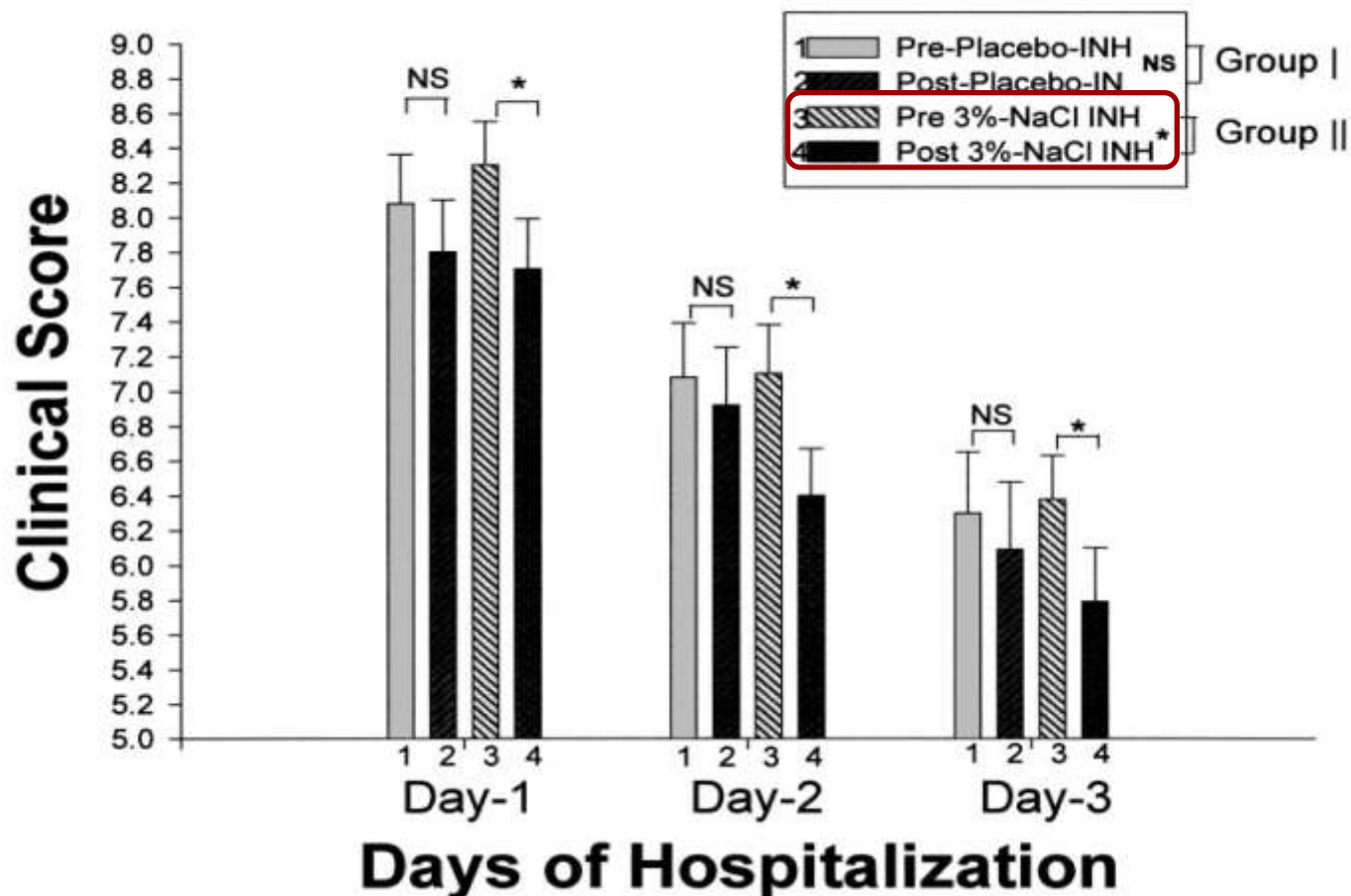
65 ambulatoriali

Salina ipertonica 3% vs salina 0.9% nebulizzate da sole o in associazione ad un broncodilatatore

Nebulized 3% Hypertonic Saline Solution Treatment in Hospitalized Infants With Viral Bronchiolitis*

Avigdor Mandelberg, Guy Tal, Michaela Witzling, Eli Someck, Sion Hourri, Ami Balin and Israel E. Priel

Chest 2003;123;481-487
DOI 10.1378/chest.123.2.481

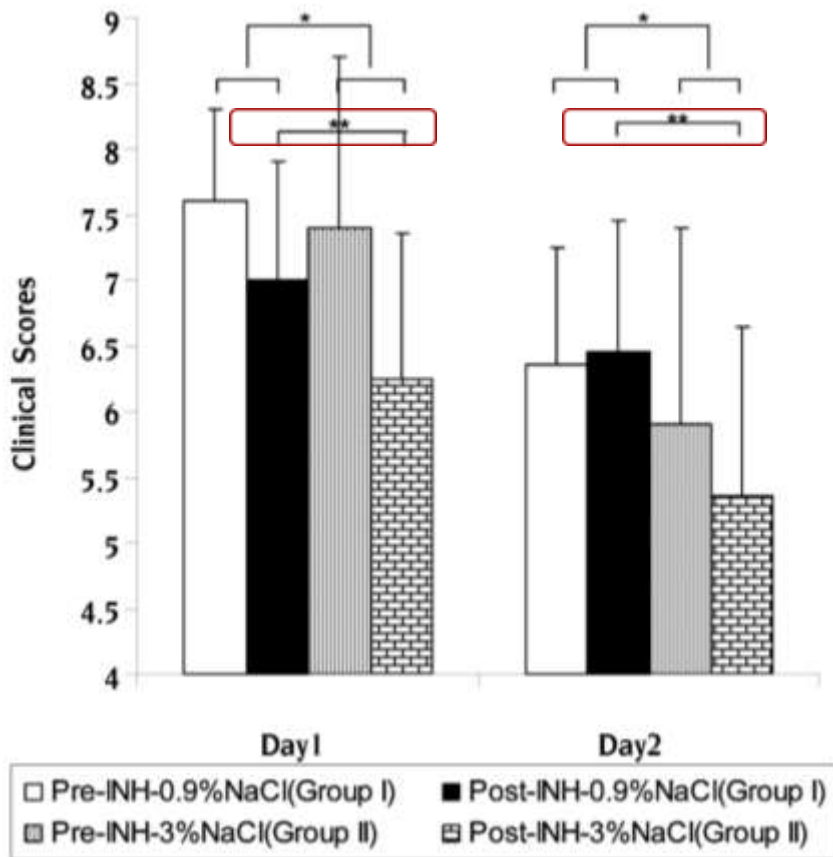


* P < 0.001

Hypertonic Saline/Epinephrine Treatment in Hospitalized Infants with Viral Bronchiolitis Reduces Hospitalization Stay: 2 Years Experience

Guy Tal MD¹, Karine Cesar MD², Anat Oron MD², Sion Houri MD³, Ami Ballin MD² and Avigdor Mandelberg MD¹

¹Pediatric Pulmonary Unit, ²Department of Pediatrics, and ³Pediatric Critical Care Unit, Wolfson Medical Center, Holon, Israel
Affiliated to Sackler Faculty of Medicine, Tel Aviv University, Ramat Aviv, Israel

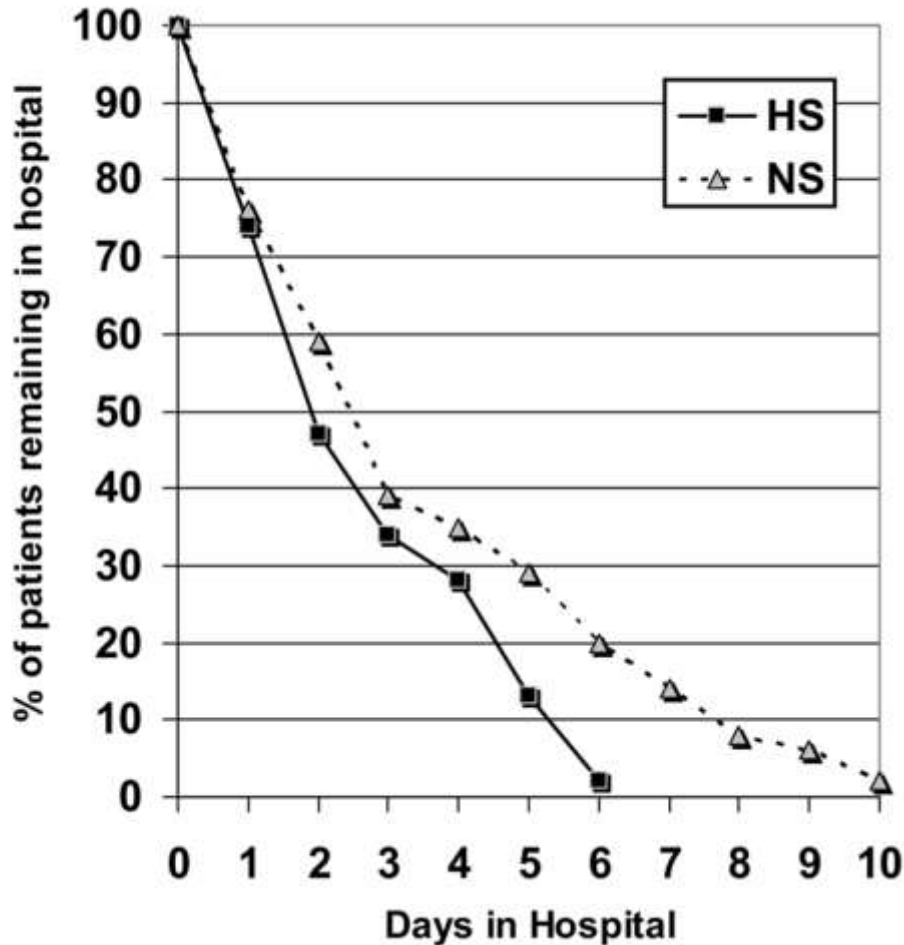


Durata della degenza

	Salina 0.9%	Salina 3%	<i>P</i>
Giorni	3.5 1.7	2.6 1.4	0.018

Nebulized Hypertonic Saline in the Treatment of Viral Bronchiolitis in Infants

Kuzik BA et al, J Pediatr 2007;151:266-70



Durata del ricovero:

salina fisiologica: 3.5 giorni

salina ipertonica 3%: 2.9 giorni

I bambini trattati con salina ipertonica 3% nebulizzata vengono dimessi con **1 giorno di anticipo** con risparmio del 26% ($p < 0.05$)



Original Article

Nebulized hypertonic saline/salbutamol solution treatment in hospitalized children with mild to moderate bronchiolitis

Zhengxiu Luo, Enmei Liu, Jian Luo, Subi Li, Fengqiong Zeng, Xiqiang Yang and Zhou Fu

*Respiratory Department, Children's Hospital, Chong Qing Medical University, Chongqing, China***Segni, sintomi e durata dell'ospedalizzazione**

Group	Sample size	Wheezing	Cough	Pulmonary moist crackles	Hospital time
Treatment group	50	2.7 ± 0.9	5.3 ± 0.8	5.4 ± 0.8	6.0 ± 1.2
Control group	43	3.8 ± 1.1	6.3 ± 0.9	6.2 ± 0.9	7.4 ± 1.5
<i>t</i> -value		5.29	5.49	4.51	4.97
<i>P</i> -value		<0.01	<0.01	<0.01	<0.01

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

Objectives: To determine whether the introduction of heated humidified high-flow nasal cannulae (HFNC) therapy was associated with decreased rates of intubation for infants <24 months old with bronchiolitis admitted to a pediatric intensive care unit (PICU).

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: 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.

Summary of Recent Evidence for Therapies Used for Bronchiolitis

Therapy	Summary	Recommendation
Bronchodilators	No improvement in duration of illness or hospitalization ^{58,59} May improve short-term clinical scores in a subset of children ⁵⁸	No routine use Use only after proven benefit in a trial of therapy, if chosen as an option
Corticosteroids	No improvement in duration of illness or hospitalization ^{7,63}	No routine use
Leukotriene receptor antagonists	No improvement in duration of illness ^{67,75}	Not recommended
Nebulized hypertonic saline	May reduce length of inpatient hospitalization ⁷⁰	None

Zorc JJ, Hall CB Bronchiolitis: Recent Evidence on Diagnosis and Management Pediatrics 2010;125;342-349

Indicazioni al ricovero

- **Condizioni generali compromesse**
- **Apporto di liquidi inadeguato**
- **FR > 70 atti/min e/o SaO₂ < 92% e/o apnee e/o cianosi**
- **Presenza di fattori di rischio: patologie croniche, età gestazionale < 32 settimane, età < 3 mesi.**

Impact of a bronchiolitis clinical care pathway on treatment and hospital stay

Claire Walker • Susan Danby • Steve Turner

Duration of stay (DOS) was compared before and after the clinical pathway was introduced (winter 2005/2006).

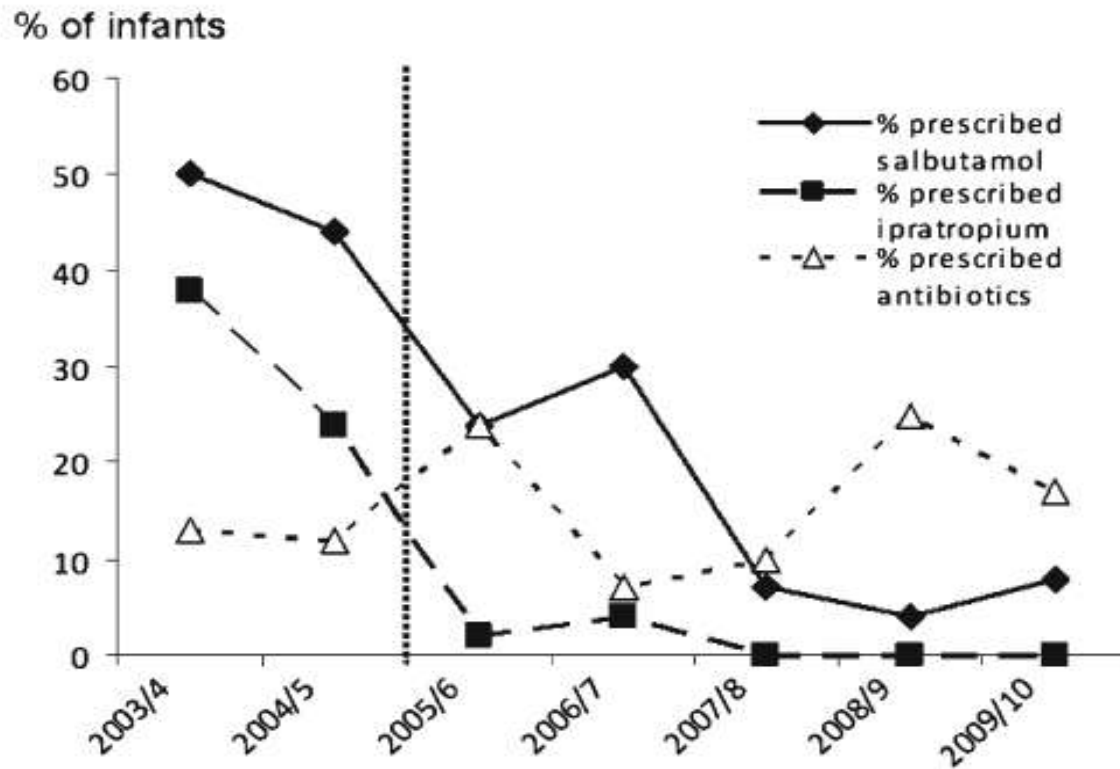
There were **328 infants** identified, mean age **75 days**,

RSV was detected in 89%,

After the clinical pathway was introduced:

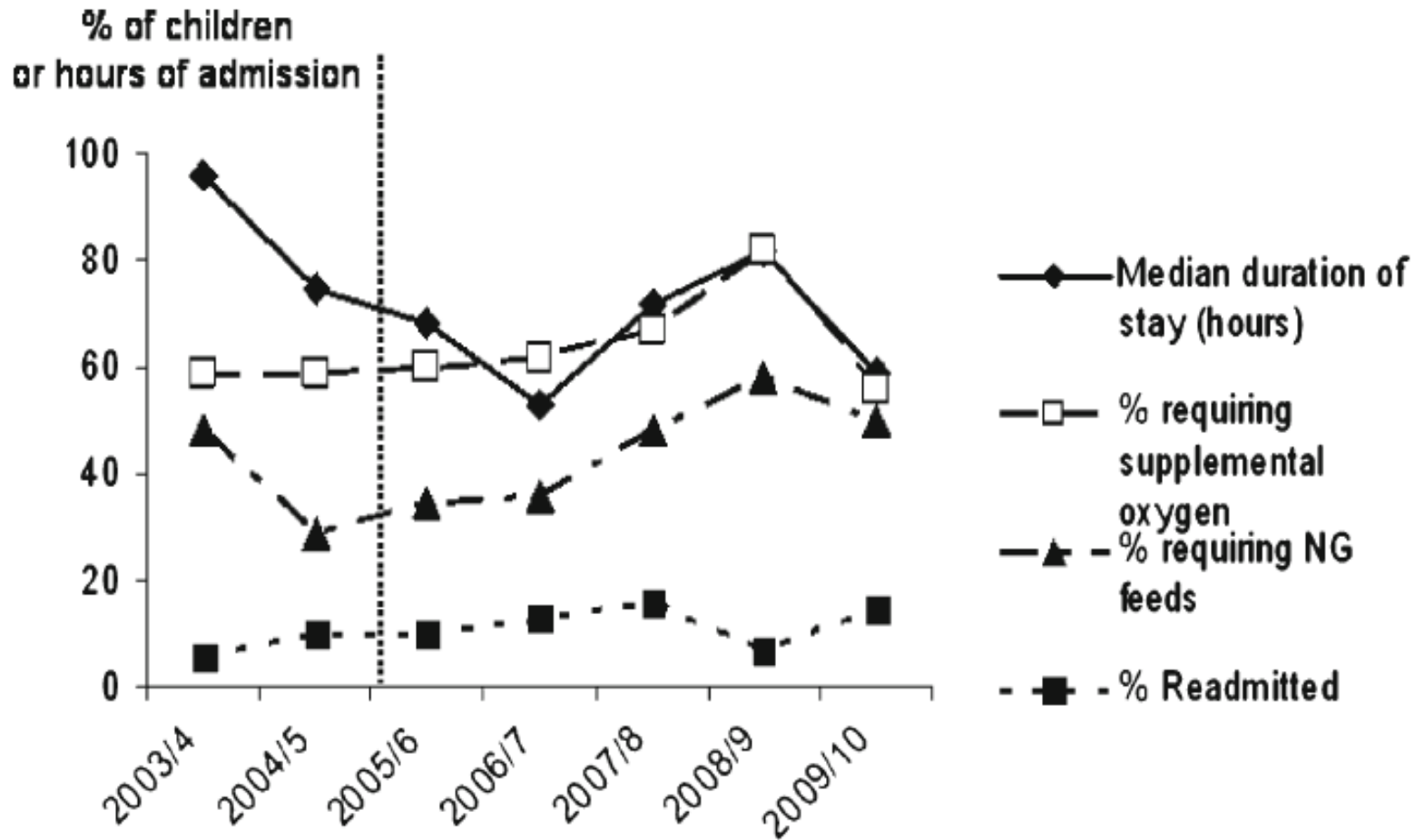
- **salbutamol fell from 50% to 8%** ($p < 0.001$),
- **ipratropium bromide from 38% to 0%** ($p < 0.001$),
- the proportion prescribed **antibiotics was unchanged**.

The median DOS was **79 h prior** to the clinical pathway and **66 h afterwards** ($p = 0.010$)



Proportions of infants with bronchiolitis prescribed bronchodilators and antibiotics over seven successive winters.

The vertical broken line corresponds with the introduction of the clinical pathway



The median duration of hospitalization and proportions of infants requiring: supplemental oxygen, nasogastric feeding and readmission over seven successive winters.