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LA GESTONE DELLA BRONCHIOLITE

DR.SSA M.CERUTTI
SCDU PEDIATRIA
AOU MAGGIORE DELLA CARITÀ NOVARA

…In ospedale…

NEL MONDO

VRS provoca circa **33 milioni** casi/aa LTRI
3,6 milioni di ospedalizzazioni
100.000 decessi

73,5% delle ospedalizzazioni per bronchiolite

RSV 60% < 1aa → 4% **RICOVERO** → 20% **TIP**

Entro il secondo anno di vita quasi tutti rsv +

40 % broncospasmo ricorrente e/o asma bronchiale.

Manti *et al. Italian Journal of Pediatrics* (2023) 49:19
https://doi.org/10.1186/s13052-022-01392-6

FATTORI DI RISCHIO

Most infants who are hospitalized with RSV bronchiolitis were born at full term with no known risk factors.[1,2] Chronologic age is the single most important predictor of the likelihood of severe bronchiolitis, given the observa-

N ENGL J MED 374;1 NEJM.ORG JANUARY 7, 2016

2/3 H < 5mesi di vita (1-3 m) riduzione Ig materne

Prognosi più grave

Vi sono fattori di rischio aggiuntivi per una prognosi più grave, quali nascita pretermine, displasia bronco-polmonare, cardiopatie congenite emodinamicamente significative, e altre malattie che implicano deficit immunitari o neuromuscolari. Tuttavia, dati italiani raccolti in 5 diverse stagioni invernali dimostrano che l'88% delle ospedalizzazioni per VRS si sono avute in bambini sani e nati a termine.

Viral Bronchiolitis in Children

H. Cody Meissner, M.D.

N ENGL J MED 374;1 NEJM.ORG JANUARY 7, 2016

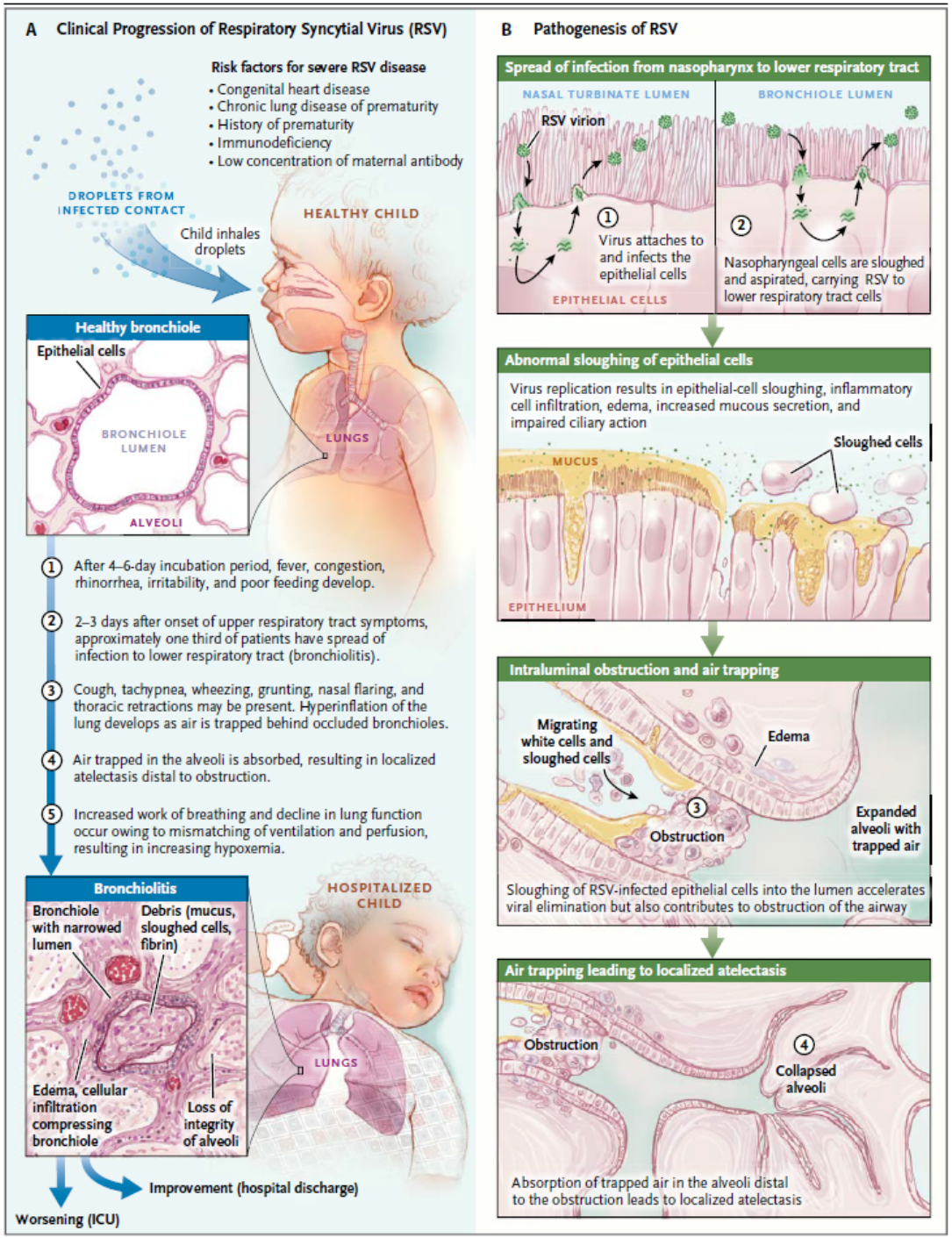


Figure 1 (facing page). Pathogenesis of Bronchiolitis Due to Respiratory Syncytial Virus (RSV).

Infection is acquired by inoculation of the nasal or conjunctival mucosa with contaminated secretions or by inhalation of large (>5 μm in diameter), virus-containing respiratory droplets within 2 m of an infectious patient. After an incubation period of 4 to 6 days, viral replication in the nasal epithelium results in congestion, rhinorrhea, irritability, and poor feeding. Fever occurs in approximately 50% of infected infants. Once in the lower respiratory tract, the virus infects the ciliated epithelial cells of the mucosa of the bronchioles and pneumocytes in the alveoli. Two RSV surface glycoproteins, F and G, mediate viral attachment to the glycocalyx of the target cell. Viral attachment initiates a conformational change in F protein to a postfusion structure that facilitates fusion of the viral envelope and the plasma membrane of the host cell, resulting in viral entry into the cell. Viral replication initiates an influx of natural killer cells, helper CD4+ and cytotoxic CD8+ T lymphocytes, and activated granulocytes. Cellular infiltration of the peribronchiolar tissue, edema, increased mucous secretion, sloughing of infected epithelial cells, and impaired ciliary beating cause varying degrees of intraluminal obstruction. During inspiration, negative intrapleural pressure is generated and air flows past the obstruction. The positive pressure of expiration further narrows the airways, producing greater obstruction, which causes wheezing. Innate and adaptive immune responses are involved in viral clearance, and most hospitalized children are discharged after 2 to 3 days. Regeneration of the bronchiolar epithelium begins within 3 to 4 days after the resolution of symptoms. ICU denotes intensive care unit.

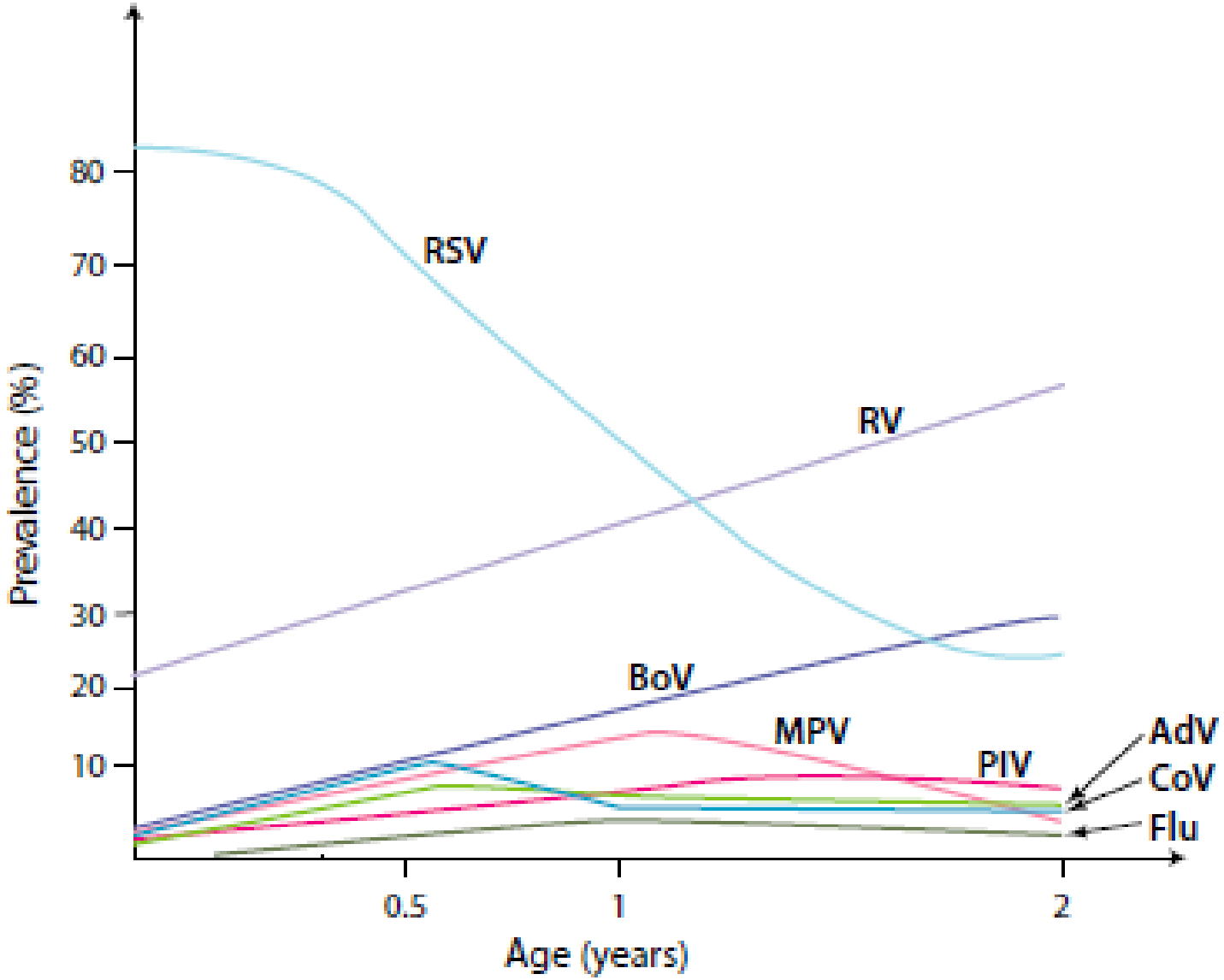
Viral Bronchiolitis in Children

H. Cody Meissner, M.D.

N ENGL J MED 374;1 NEJM.ORG JANUARY 7, 2016

Table 1. Viruses Detected in Nasopharyngeal Secretions from Hospitalized Children with Bronchiolitis.*

Virus	Type	Approximate Frequency	Seasonality in North America
		%	
Respiratory syncytial virus	A and B	50–80	November through April
Human rhinovirus	Groups A, B, and C; >100 serotypes	5–25	Peak activity in spring and autumn
Parainfluenza virus	Type 3 most common, followed by types 1, 2, and 4	5–25	Type 3 is most prominent during spring, summer, and fall in odd-numbered years
Human metapneumovirus	Subgroups A and B	5–10	Late winter and early spring; season typically peaks 1–2 mo later than RSV peak
Coronavirus	OC43, 229E NL63, and HKU1	5–10	Winter and spring
Adenovirus	>50 serotypes	5–10	Year-round, although season for certain serotypes may be more restricted
Influenza virus	A and B	1–5	November through April
Enterovirus	Echovirus and coxsackievirus	1–5	Generally June through October


Prevalence (%)
80
70
60
50
40
30
20
10
RSV
RV
BoV
MPV
PIV
AdV
CoV
Flu
0.5
1
2
Age (years)

REVIEW ARTICLE

WILEY Allergy

Bronchiolitis needs a revisit: Distinguishing between virus entities and their treatments

- «the first episode of severe bronchiolitis in under 2-years-old children is a **critical event** and an **important opportunity** for designing secondary prevention strategies for asthma»

- p **18-32%** <1° anno di vita (Jaarti et al, 2018)
- p **9-17%** 1°-2° anno (Jaarti et al, 2018)

Rischio di **WHEEZING RICORRENTE / ASMA**

70 % età prescolare

50% età scolare

→ **PREVENZIONE SECONDARIA**

EZIOLOGIA VIRALE/ medicina di precisione

Fattore di differenziazione e stratificazione all'interno di diverse coorti

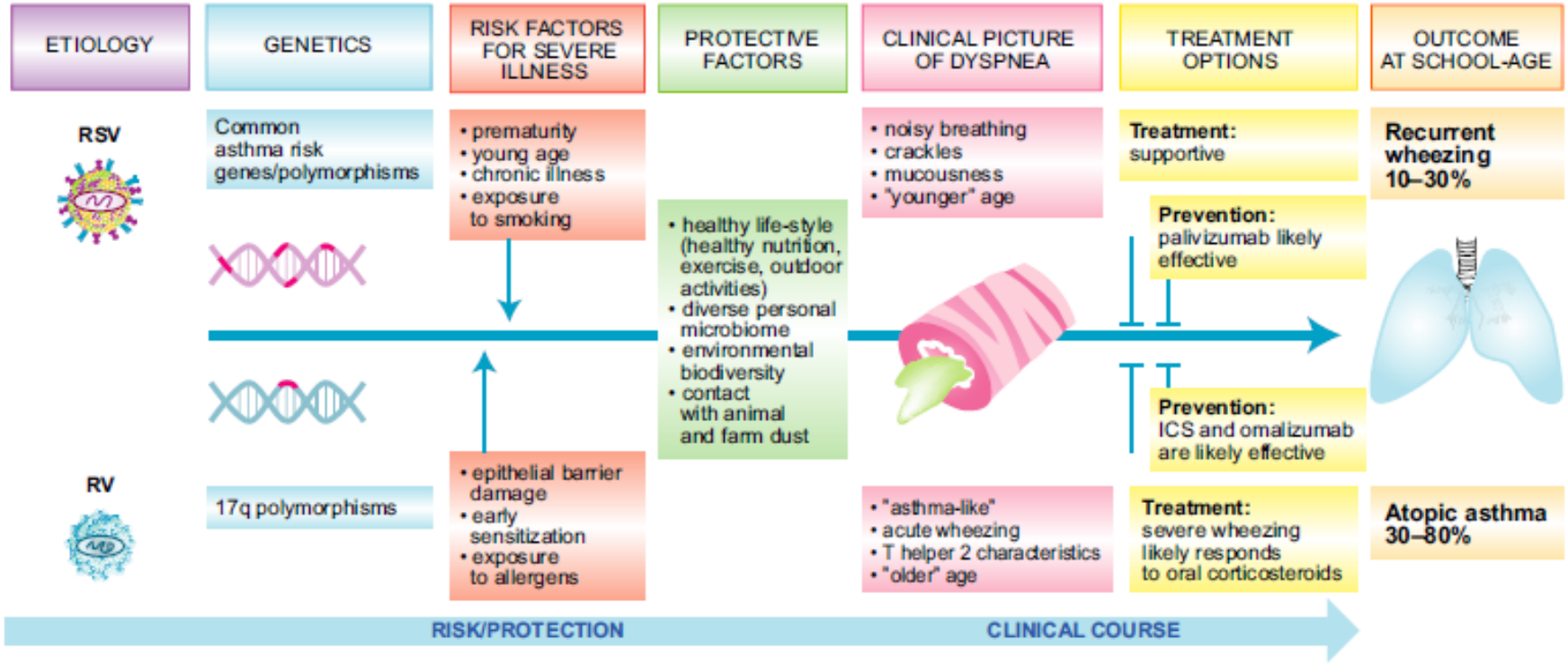
Indagine di biologia molecolare PCR 100% capacità diagnostica

CO- INFEZIONI
10-40% RSV - RV

- **RSV (50-80% H) (<1 aa)**
- **Rhinovirus (>1 aa)**
- Altri virus (BoV, MPV, PIV, AdV, CoV, Flu)

Genetica, meccanismo patogenetico, caratteristiche cliniche, risposta ai trattamenti

A breve e lungo termine



RSV / RV

REVIEW ARTICLE

WILEY Allergy

Bronchiolitis needs a revisit: Distinguishing between virus entities and their treatments

Bronchiolite / forma severa

RSV

- Genere Pneumovirus
- Famiglia Paramyxoviridae
- Enveloped ss RNA
- 2 sottotipi antigenici A e B
- Rispettivamente 11 e 23 genotipi

- **Reinfezioni sono riportate ma sono solitamente lievi**
- RF prematurità / malattia polmonare cronica / CHD, età 1-6 m, deficit risposta IFN

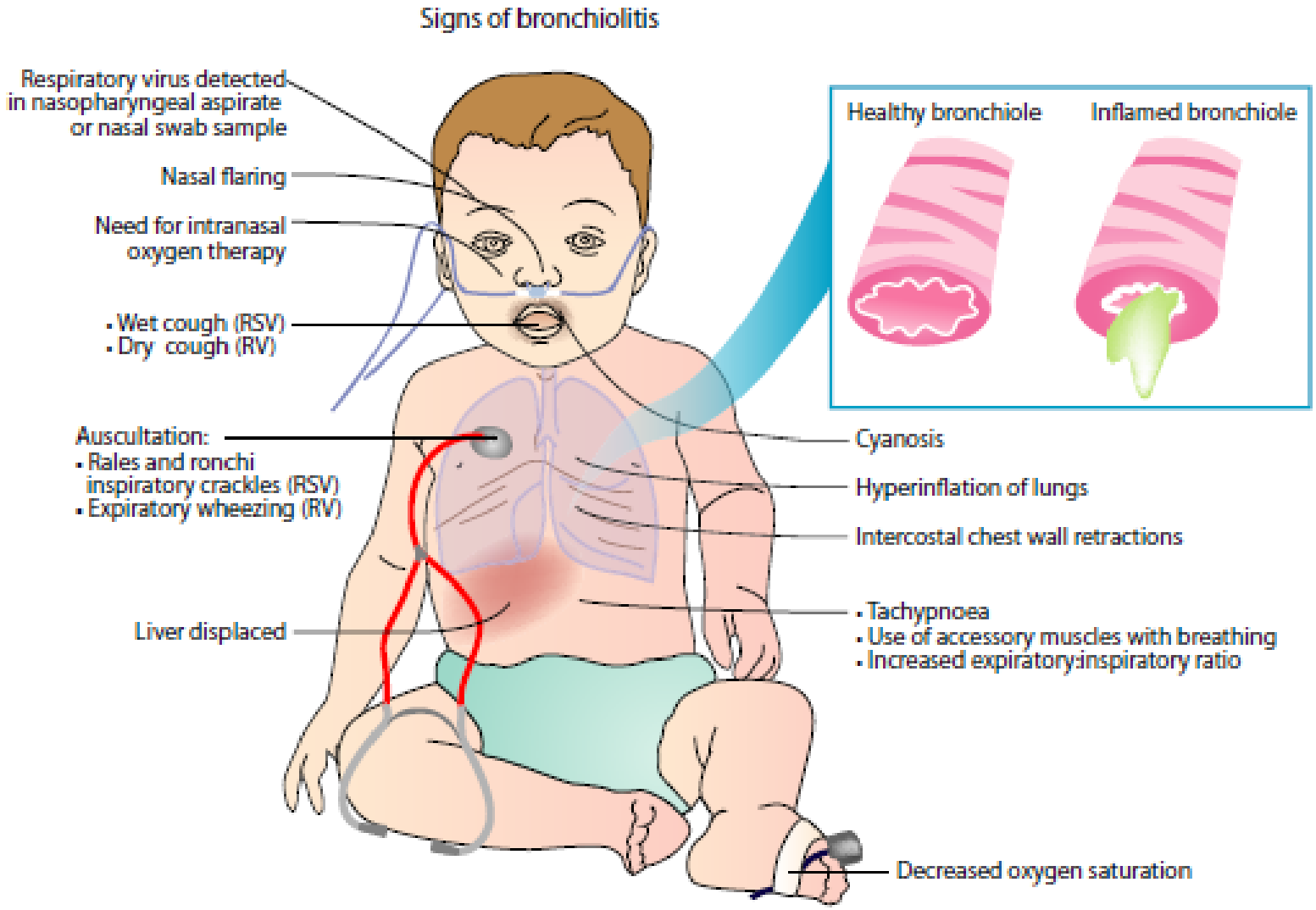
RV

- Genere Enterovirus
- Famiglia Picornaviridae
- Nonenveloped ss-RNA
- Sottogruppi A B **C** (83-32-55 genotipi)
- Risp polarizzata T2

Severity scores → 4 FENOTIPI

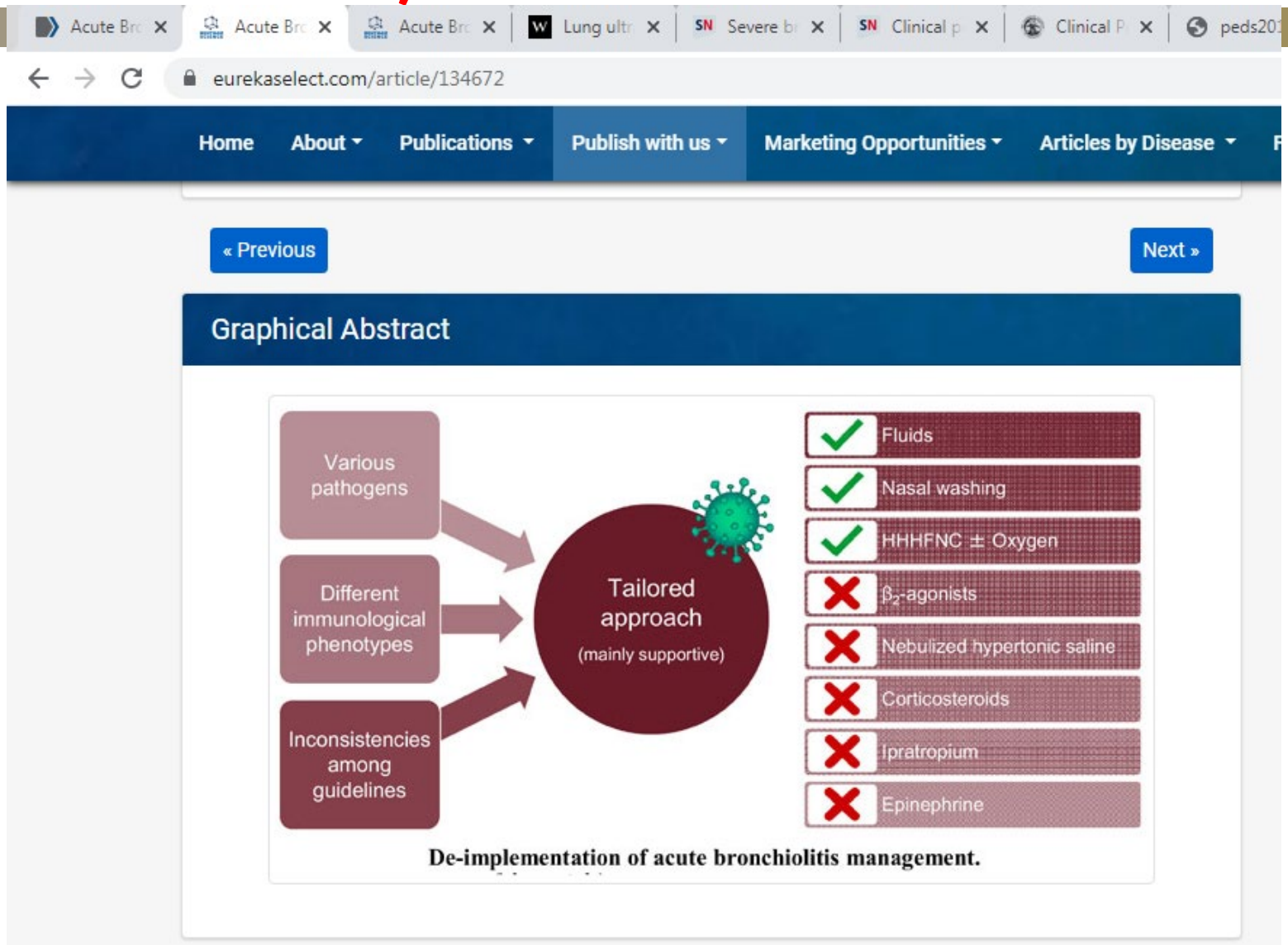
A	B	C	D
RV Storia di wheezing Wheezing alla dg Eczema Età >	Wheezing alla dg No storia di wheezing No eczema	Severità ICU Permanenza in ospedale + prolungata	Meno severi Non wheezing Durata ospedalizz breve

DIAGNOSI anamnestica + clinica



TANTE linee guida ma:

THE LESS, THE BETTER (Virgili et al, 2024)



Manti *et al. Italian Journal of Pediatrics* (2023) 49:19
https://doi.org/10.1186/s13052-022-01392-6

REVIEW Open Access

UPDATE - 2022 Italian guidelines on the management of bronchiolitis in infants

- **Interventi educazionali** → cure primarie
- **Riduzione uso tp non EBM** → cure primarie ma sptt ospedalieri

The peak severity of the disease occurs around 3-5 days from the disease onset, and improvement occurs in 7-14 days, with 90% of infants having a resolution of cough within 2-3 weeks [1, 20–32].

Table 2. American Academy of Pediatrics Guidance for Diagnosis and Management of Bronchiolitis.*

Intervention	Recommendation	Comment
Diagnostic Test		
Chest radiography	Not recommended for routine use	Poor correlation with severity of disease or risk of progression; studies show increase in inappropriate use of antimicrobial therapy owing to similar radiographic appearance of atelectasis and infiltrate
Testing for viral cause	Not recommended for routine use	May influence isolation of symptomatic patients, but infection-control procedures are similar for most respiratory viruses
Treatment		
Bronchodilator therapy	Not recommended	Randomized trials have not shown a consistent beneficial effect on disease resolution, need for hospitalization, or length of stay
Epinephrine	Not recommended	Large, multicenter, randomized trials have not shown improvement in outcome among outpatients with bronchiolitis or hospitalized children
Glucocorticoid therapy	Not recommended	Large, multicenter, randomized trials provide clear evidence of lack of benefit
Nebulized hypertonic saline	May be considered	Nebulized 3% saline may improve symptoms of mild-to-moderate bronchiolitis if length of stay is >3 days (most hospitalizations are <72 hr)
Supplemental oxygen	Routine use not recommended if oxyhemoglobin saturation is >90% in the absence of acidosis	Transient episodes of hypoxemia are not associated with complications; such episodes occur commonly in healthy children
Pulse oximetry	Not recommended for patients who do not require supplemental oxygen or if oxygen saturation is >90%	Oxygen saturation is a poor predictor of respiratory distress; routine use correlates with prolonged stays in the emergency department and hospital
Chest physiotherapy	Not recommended	Deep suctioning is associated with a prolonged hospital stay; removal of obstructive secretions by suctioning the nasopharynx may provide temporary relief
Antimicrobial therapy	Not recommended for routine use	Risk of serious bacterial infection is low; routine screening is not warranted, especially among infants 30 to 90 days of age
Nutrition and hydration	Hospitalization for observation of hydration and nutritional status may be needed for infants with respiratory distress	Intravenous or nasogastric hydration may be used

* Adapted from the clinical practice guidelines for the diagnosis and management of bronchiolitis in children 1 through 23 months of age.[9]

PRATICA

VS

EVIDENZE

Table 6 Treatment for bronchiolitis

Treatment	Indications	Evidence Quality Recommendation Strength
Supportive treatment	Recommended	Evidence Quality: A Recommendation Strength: Strong
Oxygen therapy	Recommended *(when SpO_2<92%)*	Evidence Quality: A Recommendation Strength: Strong
HFNC	Recommended when standard subnasal supplemental O2 fails in infants who are hypoxic. *(It should not be used as a primary treatment modality)*	Evidence Quality: B Recommendation Strength: Moderate
Nebulized hypertonic saline solution	Not Recommended	
Inhaled bronchodilators	Not Recommended	
Chest physiotherapy	Not Recommended	
Nebulized adrenaline	Not Recommended	
Nebulized steroids	Not Recommended	Evidence Quality: A
Systemic steroids	Not Recommended	
Antibiotics	Not Recommended *(Except in case of strong suspicion of clear evidence of a secondary bacterial infection)*	
Other *Antivirals* *Montelukast* *DNase* *Inhaled furosemide* *Inhaled ipratropium bromide* *Magnesium sulfate* *Helium* *Surfactant* *Methylxanthine*	Not Recommended	Evidence Quality: B; Recommendation Strength: Strong

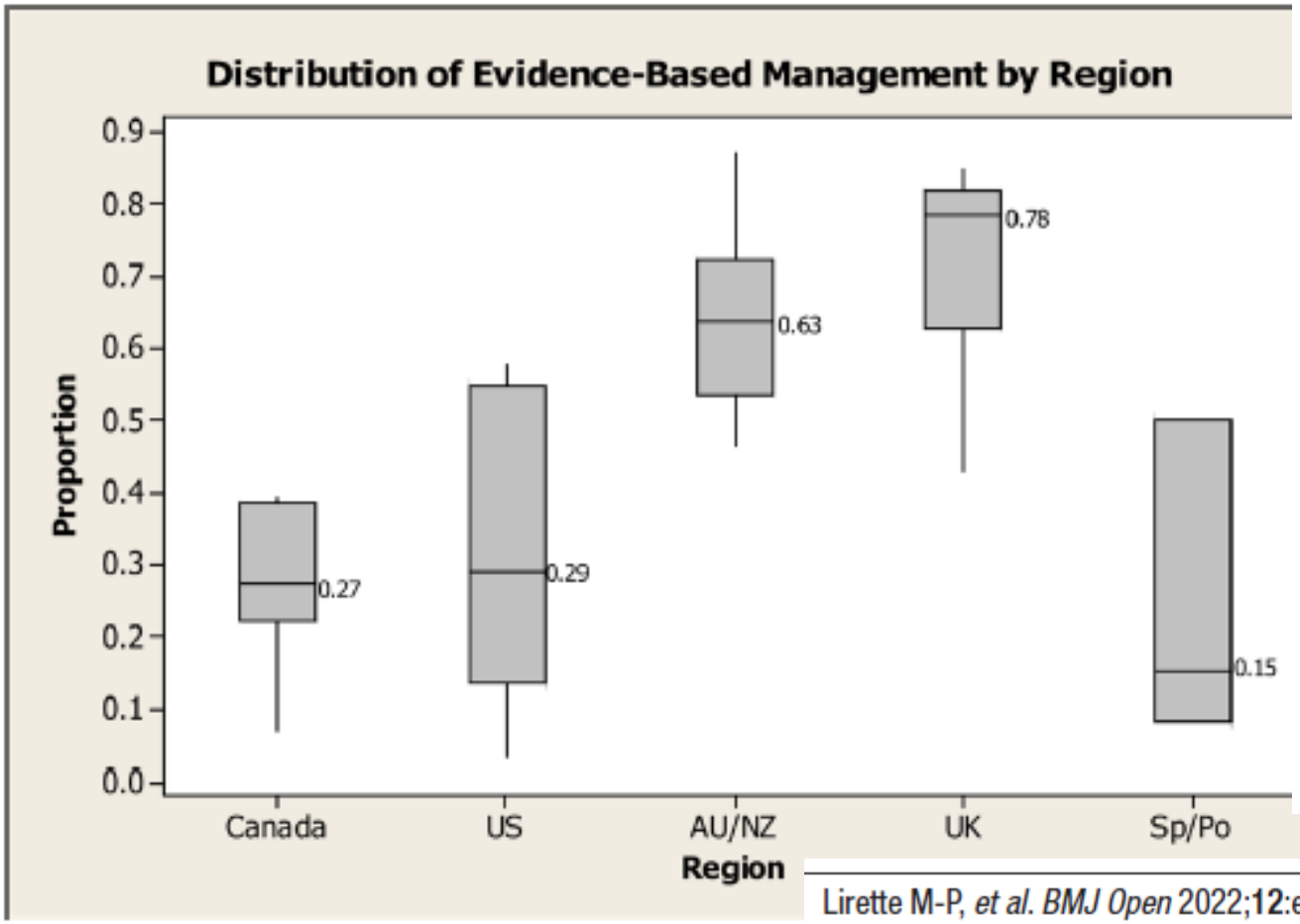
Non utilizzo routinario

More recently, a study showed that nebulized epinephrine, in addition to systemic corticosteroids, was significantly more effective in reducing ventilatory support in infants with severe bronchiolitis and admitted to ICU than standard care [98].

Nevertheless, a minority of guidelines suggest using systemic corticosteroids in exceptional circumstances, such as severe bronchiolitis admitted to ICU [48].

Recently, an RCT in ninety-one non-hospitalized infants (mean age 7.9 ± 2.6 months) with mild to moderate bronchiolitis showed that high-frequency chest wall compression (HFCWC) was effective and safe in decreasing the severity of respiratory symptoms [90]

International variation in evidence-based emergency department management of bronchiolitis: a retrospective cohort study



STRENGTHS AND LIMITATIONS OF THIS STUDY

- ⇒ While studies have examined international variation of specific aspects of bronchiolitis care, there is lack of data on the international use of practices consistent with full-evidence-based management for bronchiolitis and related association with patient outcomes.
- ⇒ Use of a large international database with patient-level data optimises generalisability of the results, enables adjustment of the associations for disease severity and provides data for emergency department-based international deimplementation strategies of low-value bronchiolitis interventions.
- ⇒ A large sample size provides high statistical precision.
- ⇒ Use of the international standards for retrospective chart reviews and the methodology to select records and to blind abstractors from the study hypotheses minimises the selection and ascertainment biases.
- ⇒ While this database was collected in 2013, the definition of the optimal bronchiolitis management used in this study remains the treatment target to this day: experts currently continue to convey the need for intensive de-implementation of low-value bronchiolitis care to enhance the adoption of best-practice management of bronchiolitis.

Lirette M-P, *et al. BMJ Open* 2022;**12**:e059784. doi:10.1136/bmjopen-2021-059784

Quando ricoveriamo/1?

Table 4 Bronchiolitis severity

	Mild	Moderate	Severe
Respiratory rate	Normal to slightly increased	Increase	Markedly increased compared to normal values per age range (< 2 months: <60/min) (2-12 months: <50/min)
Respiratory effort	Mild chest wall retraction	Tracheal tug Nasal Flare Moderate chest wall retraction	Marked chest wall retraction Nasal Flare Grunting
Oxygen saturation	No supplemental oxygen requirement, O_2 saturation > 95%	O_2 saturation 90-95%	O_2 saturation < 90%, may not be corrected by O_2
Feeding	Normal to slightly decreased	50-75% of normal feeds	< 50% of feeds, unable to feed
Apnea	Absent	May have brief episodes	May have increasing episodes

Table 5 Scoring of the acute bronchiolitis severity scale

Score	0	1	2	3	4
Wheezing	No	Wheezing at end of expiration	Wheezing throughout expiration	Wheezing during inspiration-expiration	Severe hypoventilation
Crackles	No	Crackles in 1 field	Crackles in 2 fields	Crackles in 3 fields	Crackles in 4 fields
Effort	No effort	Subcostal or lower intercostal retractions	+ Suprasternal retractions or nasal flaring	+ Nasal flaring and suprasternal retractions (universal)	
I:E ratio[a]	Normal	Symmetrical	Inverted		

[a] Inspiration-to-Expiration ratio

Manti *et al. Italian Journal of Pediatrics* (2023) 49:19

Quando ricoveriamo/2?

- **!!! Fattori di rischio**

Table 3 Risk factors for severe bronchiolitis

- Infants born prematurely (<35 weeks' gestation)
- <3 months of age at presentation
- Decreased hydration and feeding (<50% of usual fluid intake in preceding 24 h)
- Hemodynamically significant cardiac disease
- Chronic lung disease
- Neurological disorders
- Immunodeficiency
- Environmental factors: exposure to tobacco smoke and or air pollution
- Social factors: distance from the hospital or difficulty to access to the hospital; poor social circumstances; unreliable parents or parents do not able to spot red flag symptoms

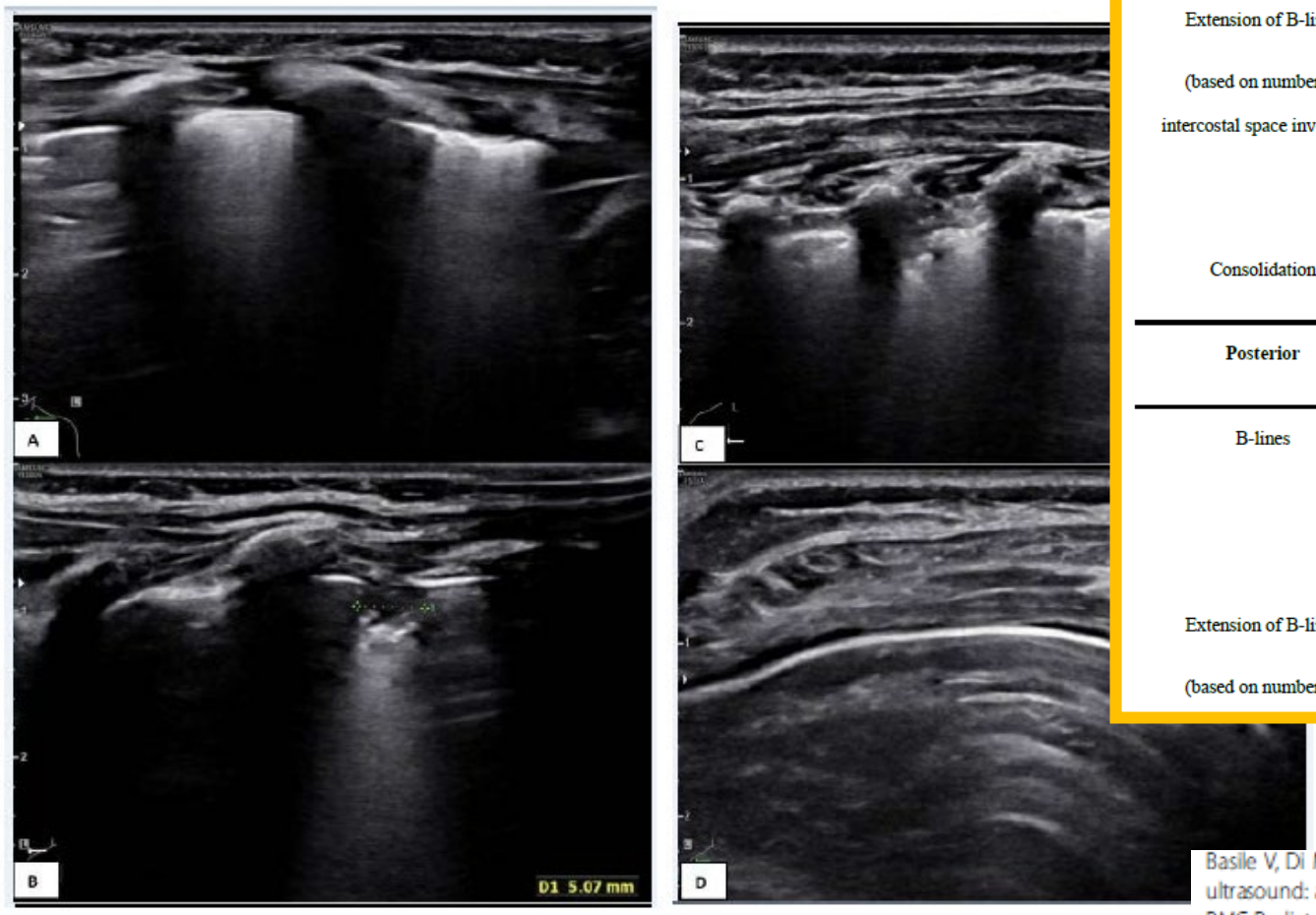
- IDRATAZIONE (**NE** continua o pasti/**ev** isotonica)
- Genitori !!!
- Dubbi su **DD**

Manti *et al. Italian Journal of Pediatrics* (2023) 49:19

Lung Ultrasound?

Title: Lung ultrasound in bronchiolitis

Authors: Domenico Paolo La Regina MD[1] *, Silvia Bloise MD[1] *, Daniela Pepino MD[2], Elio Iovine



Anterior-Lateral	0	1	2
B-lines	Limited number/Absent	Focal	Confluent
Extension of B-lines (based on number of intercostal space involved)	<1 intercostal space	1-3 intercostal spaces	>3 intercostal spaces
Consolidation	absent	< 1cm	>1 cm/multiple
Posterior	**0**	**1**	**2**
B-lines	Limited number/Absent	Focal	Confluent
Extension of B-lines (based on number of	<1 intercostal space	1-3 intercostal spaces	>3 intercostal spaces

Basile V, Di Mauro A, Scalini E, Comes P, Lofù I, Mostert M, et al. Lung ultrasound: a useful tool in diagnosis and management of bronchiolitis. BMC Pediatr. 2015;15:63.

Lung Ultrasound?

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In this regard, lung ultrasound performed in a hospital setting has been demonstrated to help stratify the risk of bronchiolitis and predict respiratory failure and the need for invasive ventilation without the risks associated with ionising radiation [40]. Accordingly, lung ultrasound ɛared to be a feasible tool that might help the physi- to confirm the clinical impression, predict hospital ission, the bronchiolitis severity, the need for res- tory support, and the length of hospital stay [41–47]. ɾever, multicenter studies are needed to determine its value in clinical routine, the most optimal setting, and the target population

posterior projections. Based on B-lines, extension of B-lines (based on number of intercostal spaces involved) and the presence of subpleural consolidation, a score from 0 to 6 was given for each projection. According to the LUS score patients were divided into 3 groups: mild (score 0-3), moderate (score 4-8) and severe (score 9-12) (Table 2)

In this study we have showed a positive correlation between a LUS score and clinical score in infants hospitalized for bronchiolitis. Furthermore, the LUS score correlated with the length of hospital stay and patient's oxygen requirement. The most frequent LUS findings were B lines, subpleural consolidation and pleural lines abnormalities. The presence of pleural lines abnormalities on LUS correlated with diffuse air trapping on chest X ray.

Biagi et al. BMC Pulmonary Medicine (2018) 18:191
https://doi.org/10.1186/s12890-018-0750-1

BMC Pulmonary Medicine

Lung Ultrasound?

RESEARCH ARTICLE Open Access

Lung ultrasound for the diagnosis of pneumonia in children with acute bronchiolitis

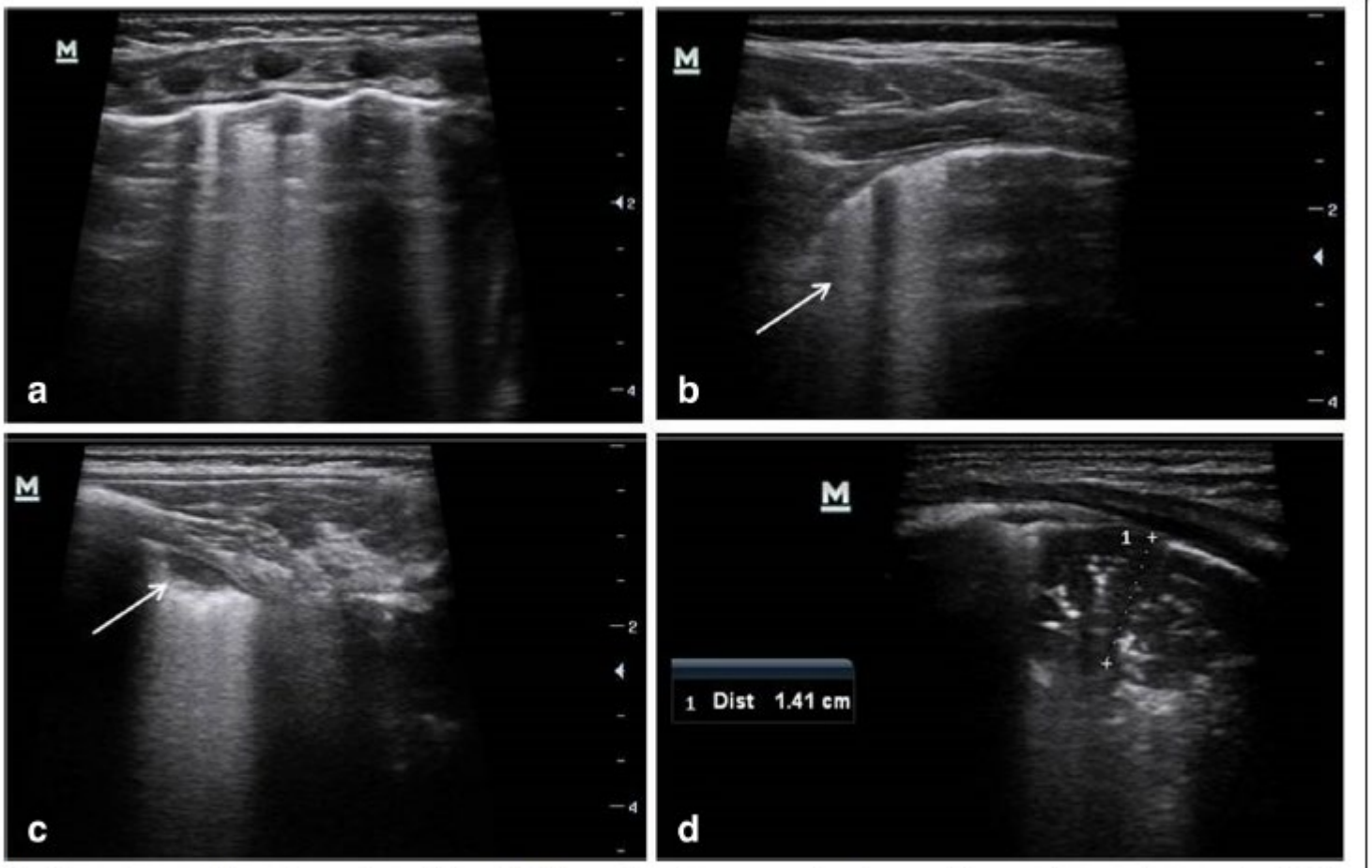

Fig. 1 Lung ultrasound images in a patient with bronchiolitis complicated by pneumonia. **a** Transversal intercostals approach showed multiple B lines, consistent with bronchiolitis. **b** Longitudinal thoracic scan, revealed irregular pleural surface and confluent B lines (arrow). **c** The left posterior lung field showed a small subpleural consolidation without sonographic air bronchograms (arrow) - a typical finding in infants with bronchiolitis – associated with focally confluent B lines arising from the margin of the consolidation. **d** The scan of the posterior region of the right lung revealed a consolidation with hyperechoic air bronchograms suggestive of pneumonia

Lung Ultrasound per ridurre CXR

Conclusions: This study shows the good accuracy of LUS in diagnosing pneumonia in children with clinical bronchiolitis. When including only consolidation size > 1 cm, specificity of LUS was higher than CXR, avoiding the need to perform CXR in these patients. Added benefit of LUS included high inter-observer agreement.

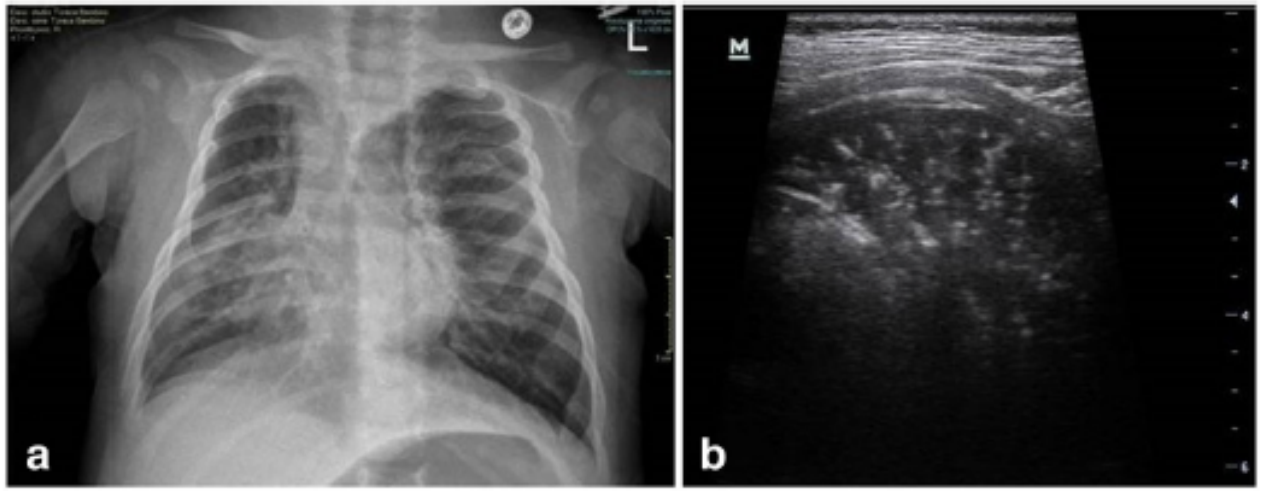

Fig. 2 Comparison of CXR and LUS in a patient with bronchiolitis complicated by pneumonia in the right lung. **a** CXR showed a right lung consolidation consistent with pneumonia, associated with hyperinflation and a mediastinal herniation of the left lung. **b** LUS revealed a large hypoechoic consolidated area with sonographic air bronchograms with branching pattern, compatible with pneumonia

Terapia? SUPPORTO

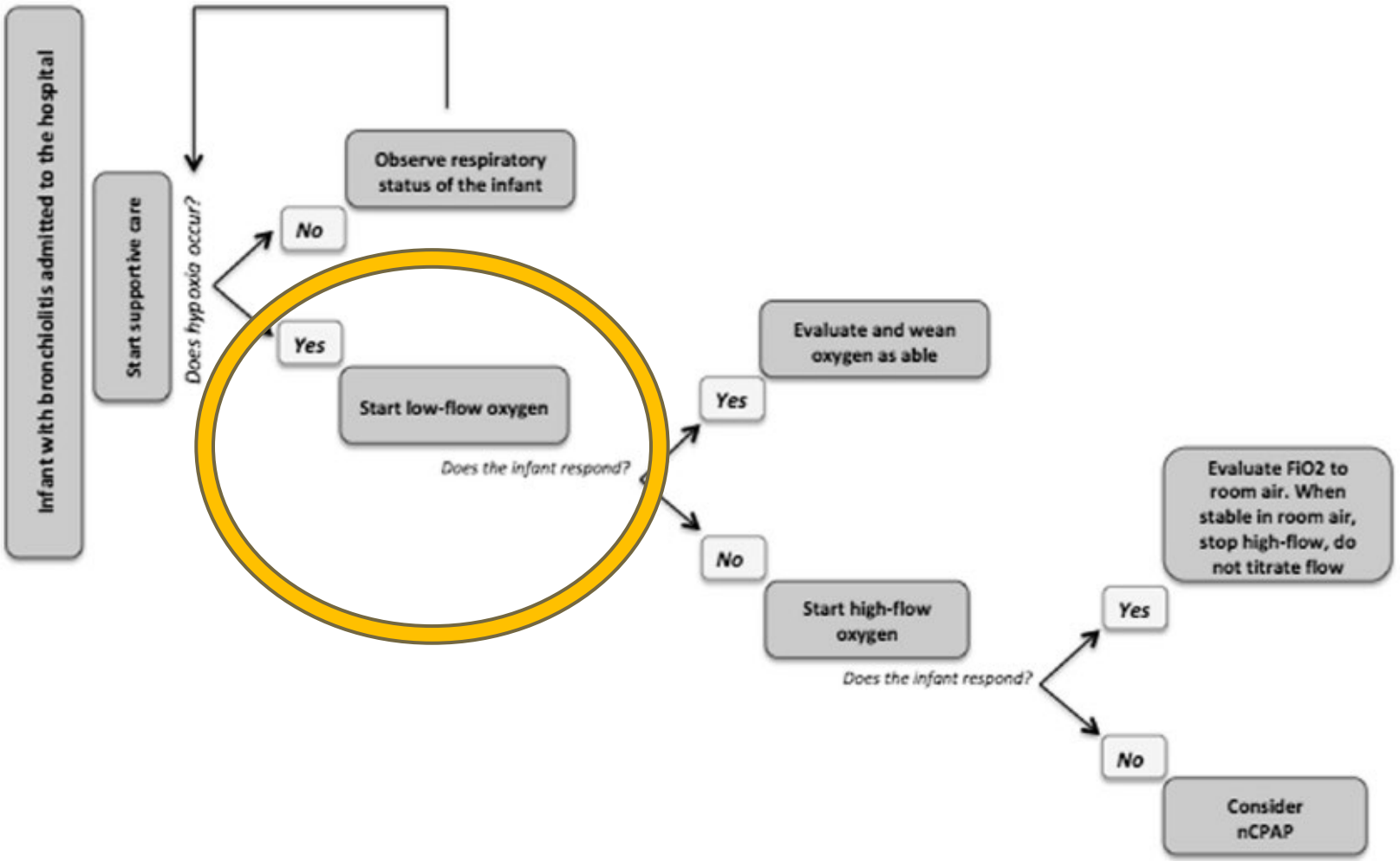

Fig. 2 Proposed approach to the use of non-invasive respiratory support in infants with bronchiolitis. FiO_2: fraction of inspired oxygen; nCPAP: nasal Continuous Positive Airway Pressure

GESTIONE IN URGENZA DEL BAMBINO CON BRONCHIOLITE IN PIEMONTE

Allegato 1: **PRESIDI PER SOMMINISTRAZIONE DI OSSIGENO A BASSO E MEDIO FLUSSO**

I presidi per la somministrazione di O2 **a performance variabile** preferibilmente utilizzabili sono:

- Cannule nasali: flusso massimo 4-6 l/min, FiO2 erogata 24%-44%
  - ogni l/min di O2 aggiunge il 3-4 % alla FiO2
- Maschera semplice: flusso massimo 8-10 l/min, FiO2 erogata 40%-60%
  - Non va mai utilizzato un flusso inferiore ai 5 l/min per evitare il rebreathing della CO2

Su spunto clinico, in casi particolari, possono essere utilizzati:

- Maschera con reservoir a parziale rebreathing: flusso di 6-10 l/min, FiO2 erogata 50%-80%
- Maschere non rebreathing con reservoir: flusso di 6-10 l/min, FiO2 erogata 60%-95%
- Cappetta: flusso di 5-7 l/min, FiO2 erogata in modo non uniforme, possibile ristagno di CO2

I presidi utilizzabili per la somministrazione di O2 **a performance fissa** sono:

- Maschere di Venturi: flusso di 8-15 l/min, FiO2 erogata 50%-70%

HFNC?

High-Flow Nasal Cannula Oxygen Therapy: Physiological Mechanisms and Clinical Applications in Children

Santi Nolasco[1], Sara Manti[2], Salvatore Leonardi[2], Carlo Vancheri[1] and Lucia Spicuzza[1]*

sembra essere uno strumento di sempre maggior utilizo la CPAP riduce atelettasie E lavoro respiratorio

- **NO** come primo approccio
- Se **ipossiemia** nonostante O2tp a basso flusso (NC 2-3 L/min- maschera facciale fino a 15 l/min)
- Sembra migliorare outcome **RDAI** (respiratory distress assesment instrument/**FR**/**SO2**)
- →2 l/kg/min
- →15 l/min

Manti *et al. Italian Journal of Pediatrics* (2023) 49:19

High-Flow Nasal Cannula Oxygen Therapy: Physiological Mechanisms and Clinical Applications in Children

Santi Nolasco[1], Sara Manti[2], Salvatore Leonardi[2], Carlo Vancheri[1] and Lucia Spicuzza[1]*

- **EASY TO USE DEVICE**
- concentrazione fissa di O2
- minima PEEP
- riduzione lavoro respiratorio
- clearence spazio morto nasofaringeo

TABLE 1 | Physiological effects of COT, HFNC and CPAP/NIV.

	Conventional oxygen therapy (COT)	High-flow nasal cannula (HFNC)	Continuous positive airway pressure (CPAP) / Non-invasive ventilation (NIV)
Deliver fixed concentrations of oxygen and other gasses	+	+++	++
Generate positive end-expiratory pressure	=	+	+++
Reduce work of breathing	=	++	+++
Anatomic dead space washout	=	+++	+
Reduce inspiratory resistance	=	+	+++
Gas conditioning	=	+++	+
Improve mucociliary clearance	=	+++	=

=, no effect; +, low effect; ++, medium effect; +++, high effect.

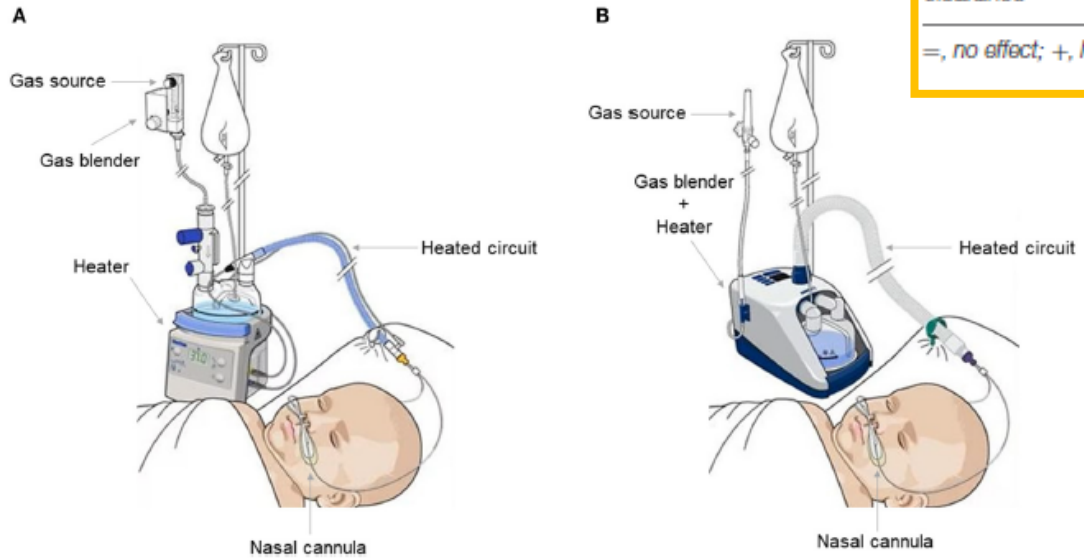

FIGURE 1 | Fisher and Paykel Optiflow system ® **(A)** and Fisher and Paykel Airvo 2 ® system **(B)**. Both allow an inhaled oxygen fraction of up to 100% and generate a flow of up to 60 L/min. The Fisher and Paykel Airvo 2 ® system combines a gas mixer and heater in one device.

Three types of HFNC devices are currently available for pediatric patients. The first type, utilized by Optiflow System® (Fisher and Paykel, Auckland, New Zealand) (**Figure 1A**), Precision Flow® (Vapotherm, Exeter, UK), and Comfort-Flo® (Teleflex Medical, Durham, NC, USA) consists of an air/oxygen blender that is connected to a system to humidify and heat the gas. The device can be equipped with a pressure relief valve that cuts off the flow when a predetermined pressure in the circuit is reached. The second type, employed by Airvo2® (Fisher and Paykel, Auckland, New Zealand) (**Figure 1B**), works through an integrated turbine generating the flow plus a heated humidifier with the advantage of not requiring an external source of gas, except from oxygen and nitric oxide. The third type is based on a CPAP or conventional ventilator with an HFNC breathing circuit connected to the humidifier.

HFNC?

Società Italiana di Pediatria

PERCORSO DIAGNOSTICO TERAPEUTICO ASSISTENZIALE

GESTIONE IN URGENZA DEL BAMBINO CON BRONCHIOLITE IN PIEMONTE

Controindicazioni all'utilizzo di HFNC

- compromissione dello stato di coscienza o condizioni critiche tali da richiedere nell'immediato un livello superiore di supporto respiratorio (es. ventilazione meccanica)
- anomalie delle vie aeree superiori (es. atresia delle coane, trauma/chirurgia del nasofaringe)
- pneumotorace

HFNC non è raccomandato inoltre nelle seguenti condizioni

- insufficienza respiratoria grave con acidosi respiratoria/ipercapnia
- crisi di apnea subentranti e/o apnee di durata superiore a 20 secondi

Miglioramento clinico atteso entro 2 ore

- FiO2 necessaria per mantenere SatO2 nell'intervallo di riferimento < 40 %
- Riduzione del 20% di frequenza cardiaca e frequenza respiratoria
- Miglioramento dei segni d'impegno respiratorio (es. rientramenti, alitamento delle pinne nasali)

- Il paziente va mantenuto sotto **monitoraggio cardiorespiratorio** continuo (pulsiossimetro)
- Effettuare **EGA** capillare arterializzato all'inizio della terapia con HFNC, indi a giudizio medico
- Rivalutazione clinica dopo 60 – 90 minuti con registrazione dei parametri di **FR, FC, SatO2**
- A seguire almeno ogni 4 ore **rivalutazione clinica** e registrazione dei parametri di **FR, FC, SatO2**.

È inoltre necessaria la rivalutazione clinica se si verifica una delle seguenti condizioni:

- il paziente non sta mostrando una stabilizzazione clinica
- la difficoltà respiratoria peggiora
- l'ipossiemia persiste nonostante un alto flusso
- il paziente richiede FiO2> 50%

Trasferimento in pICU?

Critical care of severe bronchiolitis during shortage of ICU resources

Daniele De Luca,[a,b,*] Lucilla Pezza,[a] Laura Vivalda,[a] Matteo Di Nardo,[c] Margaux Lepainteur,[d] Eugenio Baraldi,[e,f] Marco Piastra,[g,h] Walter Ricciardi,[i] Giorgio Conti,[g,h] and Maria Rosaria Gualano[i]

Chi solitamente viene trasferito?

- 60 gg
- Maschio
- Comorbidità
- Coinfezioni
- LBW/prema

1) **IPOSSIEMIA**

SpO2<90% o PaO2<60 mmHg O2 2L/min o FiO2>0.30

Utilizzo di O2 per SpO2>88% e OI<4 oppure OSI<5

- Supporto respiratorio CPAP, NIV o ventilazione invasiva
- 2) **DISTRESS RESPIRATORIO SIGNIFICATIVO**
- 3) **APNEA, RESPIRO PERIODICO o SUPERFICIALE**
- 4) **IPERCAPNIA**
- PaCO2>65 mmHg o PaCO2>60 mmHg e PH<7.25
- 5) **COMPROMISSIONE EMODINAMICA**
- 6) **COMPROMISSIONE NEUROLOGICA**
- 7) **DISIDRATAZIONE SEVERA**

Critical care of severe bronchiolitis during shortage of ICU resources

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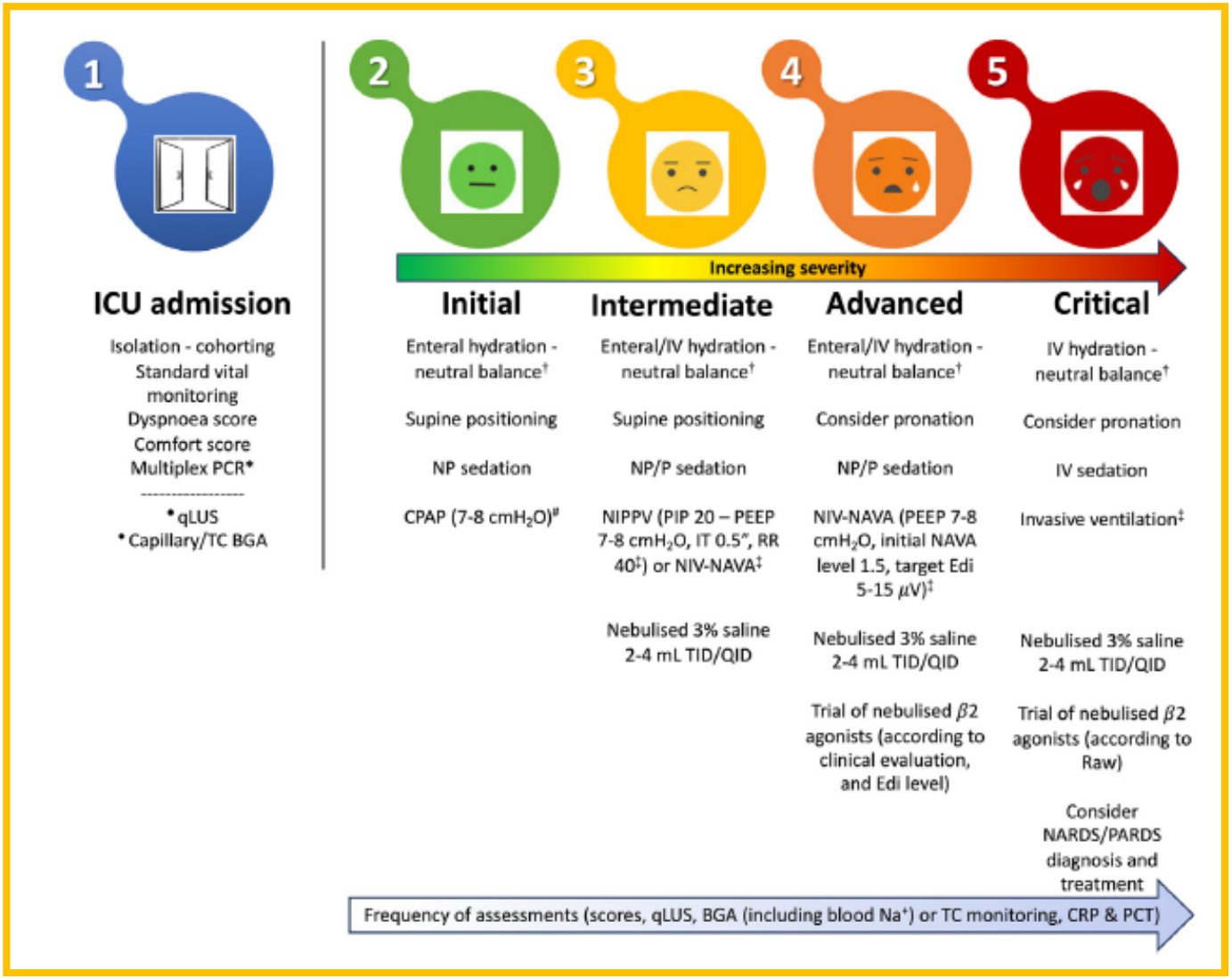


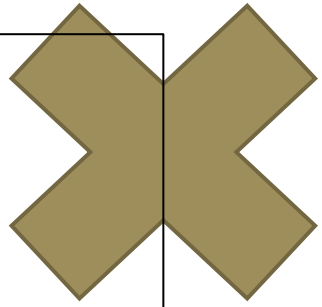
Terapia? **RIBAVIRINA**

Non vi sono terapie specifiche per la cura di infezioni gravi da RSV, il solo farmaco autorizzato (*ribavirina*) è di complessa gestione per problematiche di sicurezza di utilizzo. Pertanto, la cura delle gravi forme di malattia delle basse vie respiratorie si limita più spesso a terapie sintomatiche e misure di supporto (idratazione e ossigeno).

Anemia emolitica

Nefrotossicità

Rash



Clinical Microbiology and Infection 29 (2023) 1272–1279

Systematic review

Ribavirin treatment for respiratory syncytial virus infection in patients with haematologic malignancy and haematopoietic stem cell transplant recipients: a systematic review and meta-analysis

Profilassi? 1- PALIVIZUMAB

1. <29 sg e < 12 m nella loro prima stagione epidemica
2. 29-35 sg e < 6 mesi se fattori di rischio
3. BPD < 12 mesi o <24 mesi se in tp
4. CHD emodinamicamente significativa

- Immunodeficit
- Fibrosi cistica
- CDH
- Sindrome Down

is a key priority for the WHO [115]. The only currently licensed immunoprophylaxis for RSV is the monoclonal antibody (mAb) palivizumab produced by recombinant DNA technology and targeting the fusion (F) protein of the virus. Evidence has shown that palivizumab, approved in 1999, effectively reduces hospitalization and prevents lower respiratory tract infections in preterm infants [113–115]. It is administered via intramuscular injection once each month during the RSV season for five doses (i.e. 15 mg/kg).

Necessarie fino a 5 dosi per assicurare una protezione durante il periodo di massima circolazione del VRS.

Table 3. American Academy of Pediatrics Guidance for Palivizumab Immunoprophylaxis.*

Category	Prophylaxis Recommendation	Comment
Preterm infants without chronic lung disease of prematurity or congenital heart disease and <12 mo of age at start of RSV season		
Born at <29 wk of gestation	Maximum five monthly doses or until end of RSV season, whichever comes first	Rate of hospitalization for RSV infection is higher than among infants born at ≥29 wk of gestation[3,34,35]
Born at ≥29 wk of gestation	Not recommended	No significant difference, as compared with full-term infants, in rate of hospitalization for bronchiolitis[3,34,35]
Infants born at <32 wk of gestation with chronic lung disease of prematurity and requirement for supplemental oxygen for first 28 days of life	Maximum five monthly doses or until end of RSV season, whichever comes first	Palivizumab prophylaxis reduced rates of hospitalization for RSV by 4.9% among 762 preterm infants with chronic lung disease (12.8% in the control group vs. 7.9% in the prophylaxis group, P=0.04)[23]
Infants born with congenital heart disease		
Cyanotic disease	Not recommended routinely	No significant reduction in rates of hospitalization for RSV (7.9% in the placebo group vs. 5.6% in the palivizumab group, P=0.28)
Acyanotic disease	Five monthly doses or until end of RSV season, whichever comes first	Prophylaxis associated with a 6.8% reduction in rate of hospitalization for RSV (11.8% in the placebo group vs. 5.0% in the palivizumab group, P=0.003)[37]
Children >12 mo of age	Not recommended except for children with chronic lung disease who continue to require supplemental oxygen or diuretic or glucocorticoid therapy	Except for children with chronic lung disease, RSV hospitalization rates in second year of life are less than rates for first 6 mo of life among healthy, full-term infants for whom prophylaxis is not recommended[34]

Profilassi? 2 - NIRSEVIMAB

Posizione del Board del Calendario Vaccinale per la Vita e della Società Italiana di Neonatologia sul possibile utilizzo di anticorpi monoclonali a lunga emivita per la prevenzione universale delle malattie da Virus Respiratorio Sinciziale (VRS o RSV) nel neonato

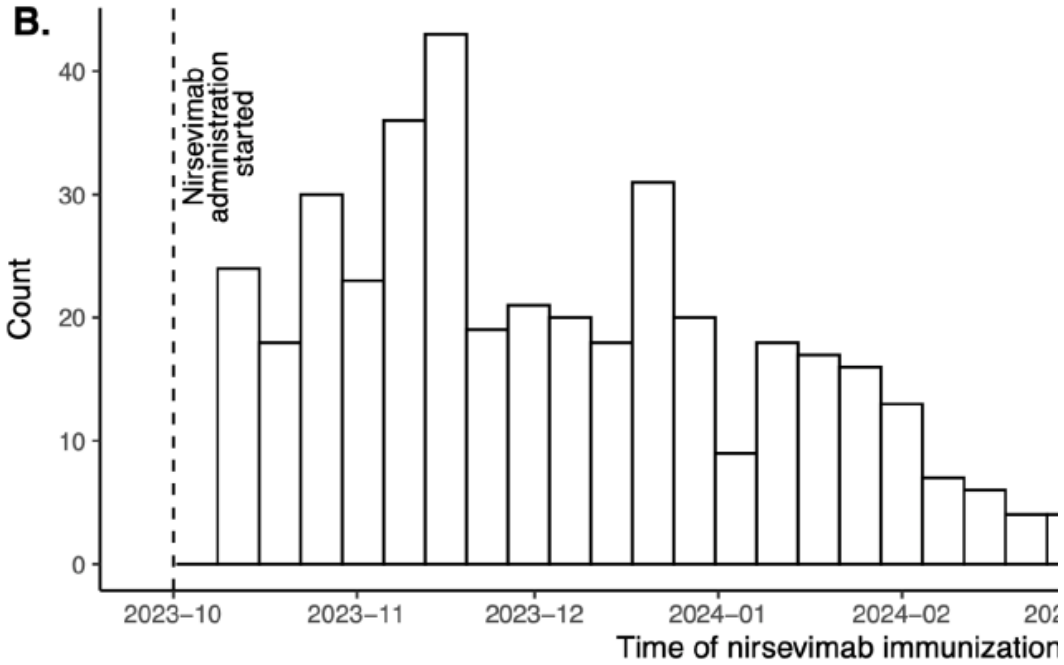
Il Nirsevimab, con Determina Aifa n. 9 del 4 gennaio 2023, è stato classificato tra i farmaci di classe C con ricetta ripetibile limitativa (RRL), e vendibile al pubblico su prescrizione di centri ospedalieri o di specialisti. Non è incluso, peraltro, nel vigente Piano Nazionale Prevenzione Vaccinale. Tale prestazione si configura pertanto come un extra Lea. Questo sta comportando delle gravi disomogeneità nel suo utilizzo sottolineate dalla stessa Società italiana di neonatologia (Sin) già ad inizio 2024.

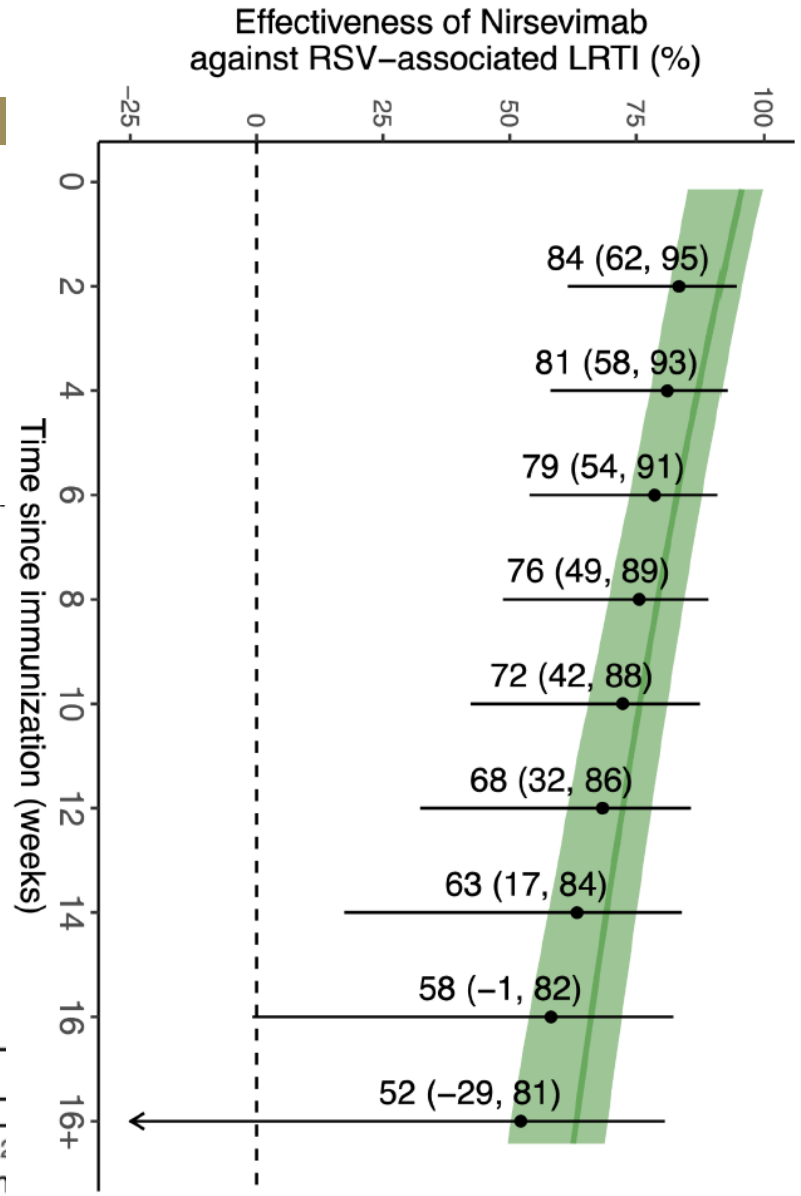
Real-World Effectiveness of Nirsevimab Against Respiratory Syncytial Virus: A Test-Negative Case-Control Study

- Efficacia USA su H e visite med
- 69% VS infezione RSV LRTI
- 81% vs OSPEDALIZZ
- **85%** vs MALATTIA SEVERA
- 79% 2 ws
- **55% 14 ws PROTEZ SIGNIFIC**
- **GAP Dosaggio / efficacia lungo termine**
- **15 su 16 studi REAL WORLD sono Europa**

- Long acting monoclonal antibody
- Studio ottobre 23 maggio 24
- Età media 6,7 mo
- 3090 pz
- FDA luglio 2023
- CDC bambini < 8 mesi
- Bambini con pato complesse 8-19 mo

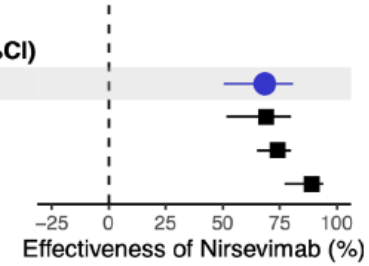
Real-World Effectiveness of Nirsevimab Against Respiratory Syncytial Virus: A Test-Negative Case-Control Study





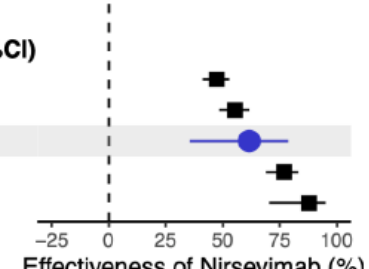
A) Medically attended RSV infection

Study	Design	Country	Time	Effectiveness (95%CI)
Current study	observational	US	Oct–May	68.4 (50.3–80.8)
Coma 2024	observational	Spain	Oct–Jan	68.9 (51.7–80)
Estrella–Porter 2024	observational	Spain	Oct–Jan	74 (65–80)
NVSN study	observational	US	Oct–Mar	89 (77–94)



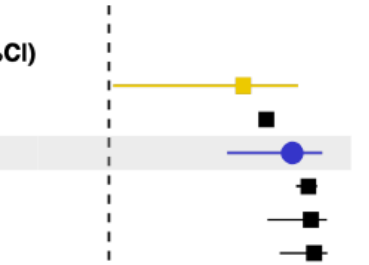
B) RSV–associated outpatient visit

Study	Design	Country	Time	Effectiveness (95%CI)
Barbas del Buey 2024	observational	Spain	Oct–Feb	47.3 (41.2–52.9)
Coma 2024	observational	Spain	Oct–Jan	55.4 (48.4–61.5)
Current study	observational	US	Oct–May	61.6 (35.6–78.6)
VISION study	observational	US	Oct–Mar	77 (69–83)
Ezpeleta 2024	observational	Spain	Oct–Jan	87.9 (70.3–95.1)



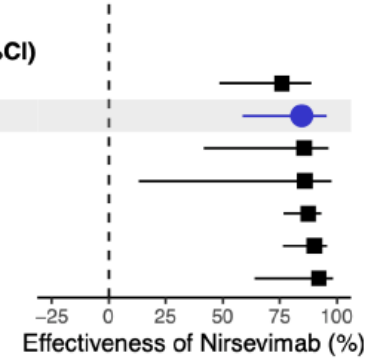
C) RSV–associated hospitalization

Study	Design	Country	Time	Effectiveness (95%CI)
Hammitt 2022	trial	Multi–country	19/20 season	59 (2.1–82.9)
Ernst 2024	observational	Luxembourg	Oct–Dec	69 (NA–NA)
Current study	observational	US	Oct–May	80.5 (52–93.5)
Coma 2024	observational	Spain	Oct–Jan	87.6 (82.1–91.4)
Ezpeleta 2024	observational	Spain	Oct–Jan	88.7 (69.6–95.8)
Moline 2024	observational	US	Oct–Feb	90 (75–96)
NVSN study	observational	US	Oct–Mar	91 (79–96)
Barbas del Buey 2024	observational	Spain	Oct–Feb	91.1 (86.9–94)
VISION study	observational	US	Oct–Mar	98 (95–99)



D) RSV–associated severe outcomes

Study	Design	Country	Time	Effectiveness (95%CI)
Paireau 2024	observational	France	Sep–Jan	75.9 (48.5–88.7)
Current study	observational	US	Oct–May	84.6 (58.7–95.6)
Aguera 2024	observational	Spain	Nov–Feb	85.6 (41.7–96.4)
Ezpeleta 2024	observational	Spain	Oct–Jan	85.9 (13.2–97.7)
Ares–Gomez 2024	observational	Spain	Sep–Dec	87.5 (76.6–93.2)
Coma 2024	observational	Spain	Oct–Jan	90.1 (76.3–95.9)
			Feb	92.1 (64–98.3)



Real-World Effectiveness of Nirsevimab Against Respiratory Syncytial Virus: A Test-Negative Case-Control Study

Article

Safety and Efficacy of Nirsevimab in a Universal Prevention Program of Respiratory Syncytial Virus Bronchiolitis in Newborns and Infants in the First Year of Life in the Valle d'Aosta Region, Italy, in the 2023–2024 Epidemic Season

Alessandra Consolati [1], Mariapaola Farinelli [1], Paolo Serravalle [2], Christine Rollandin [3,4], Laura Apprato [1], Susanna Esposito [5,*] and Salvatore Bongiorno [1]

Valle d'Aosta

apripista **stagione 2023-2024**

prevenzione univers

1 aa (71%).

→**NO** casi di ospedalizzazione per infezioni respiratorie gravi causate dall'RSV

→vs neonati non immunizzati **9,7%.**

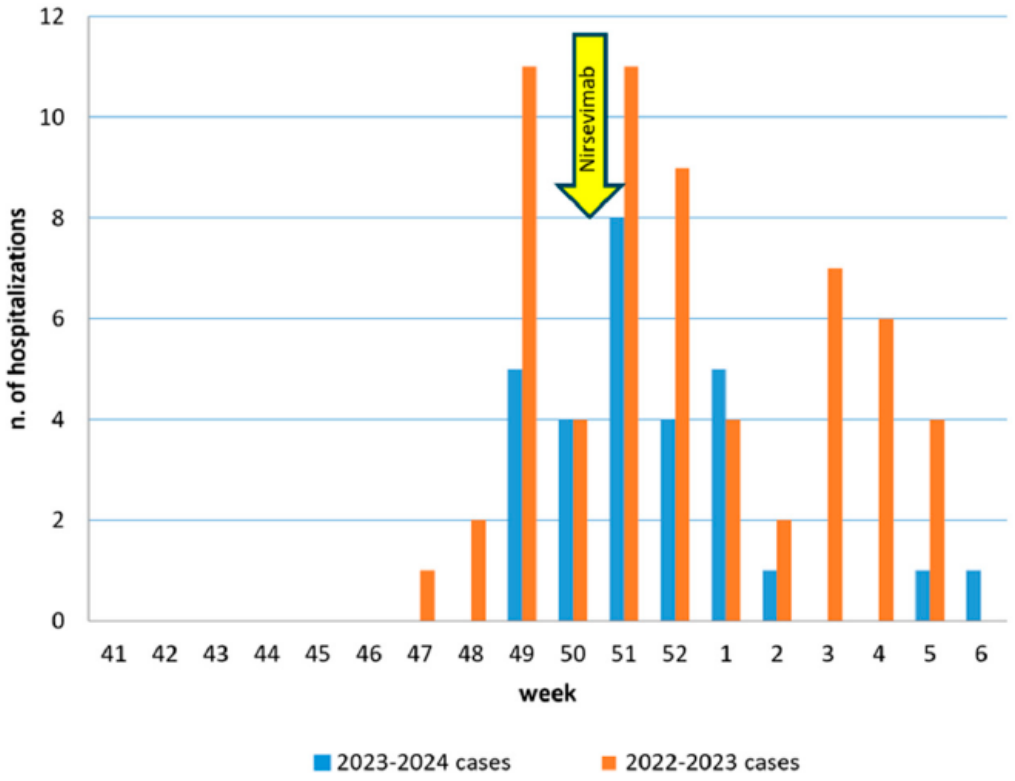


Figure 1. Hospitalizations for RSV bronchiolitis in Valle d'Aosta in the last two epidemic seasons.

Effetti collaterali?

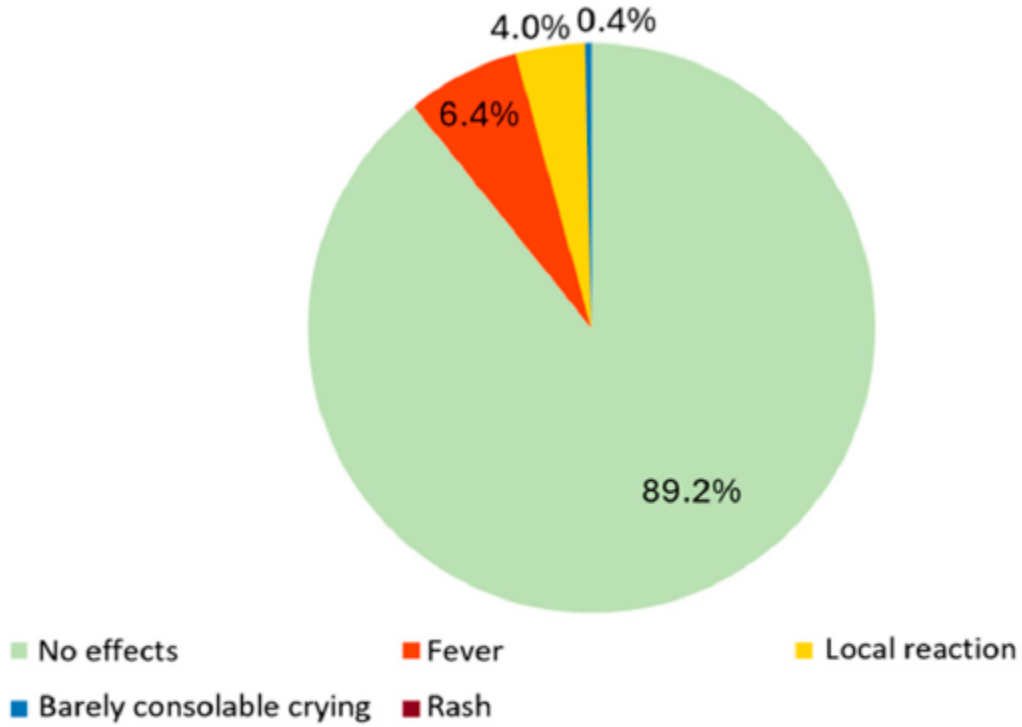


Figure 2. Side effects reported in the two weeks following nirsevimab administration. The percentage of rash was 0%.