CONVEGNO ECM: COVID
E MALATTIE INFETTIVE STAGIONALI:
DIAGNOSI DIFFERENZIALE E STRATEGIE
DI PREVENZIONE E CONTROLLO.

26 febbraio 2022

Responsabile Scientifico e Moderatore
Dr. Ernesto Cappellano

Virus Respiratorio Sinciziale: nuova emergenza pediatrica nel 2021

Melania Evangelisti
UOC Pediatria, AOU Sant'Andrea, Roma
Università La Sapienza, facoltà Medicina e Psicologia

SISTEMA SANITARIO REGIONALE
AZIENDA OSPEDALIERO-UNIVERSITARIA SANT'ANDREA

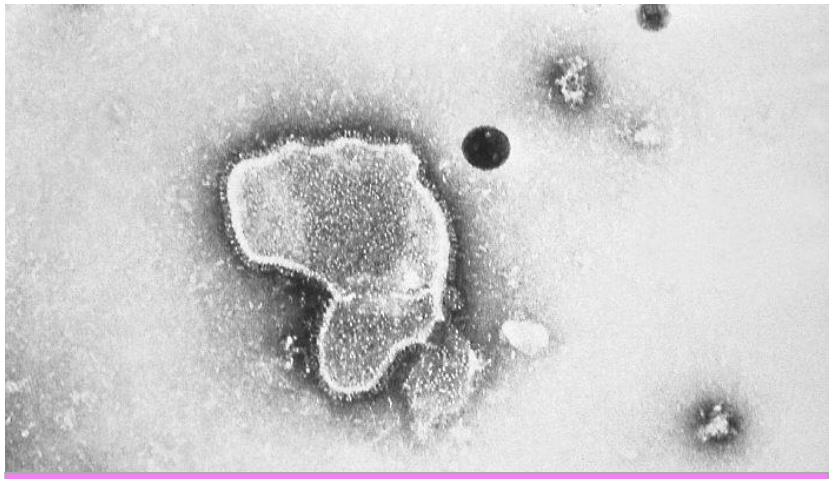
SAPIENZA UNIVERSITÀ DI ROMA

h-VIRUS RESPIRATORIO SINCIZIALE

- Il virus respiratorio sinciziale (RSV) è stato isolato per la prima volta nel 1955 in una scimmia, mentre quello umano (hRSV) è stato descritto nel 1957 in due lattanti con infezione respiratoria.

- ha un genoma costituito da RNA a a singolo filamento.

- La particella infettiva ha forma eterogenea riconducibile essenzialmente a due morfologie principali; una forma rotonda o reniforme del diametro di 150-250 nm, e una forma filamentosa di lunghezza fino a 10 µm.



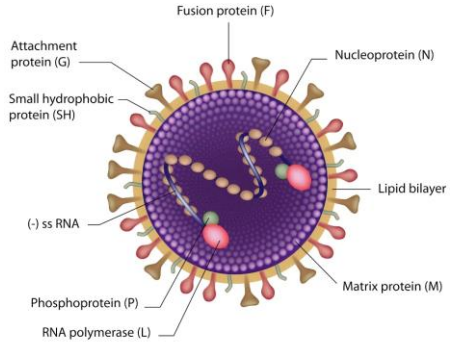
Classificazione dei virus	
Dominio	Acytota
Gruppo	Gruppo V
Ordine	*Mononegavirales*
Famiglia	*Paramyxoviridae*
Sottofamiglia	Pneumovirinae
Specie	
respiratory syncitial virus	

h-VIRUS RESPIRATORIO SINCIZIALE

- In colture di cellule umane il hRSV provoca la comparsa di sincizi (cellule pseudo-giganti). Anche altri *Paramyxoviridae* (ad es. morbillivirus, virus della parotite) formano sincizi nelle colture di cellule umane; ma, a differenza di questi, il virus respiratorio sinciziale è l'unico a non possedere emoagglutinine.

- Per mezzo di anticorpi monoclonali sono stati descritti due gruppi antigenici di virus respiratorio sinciziale, il gruppo A e B, in base alle differenze nella glicoproteina G presente sul capside virale; la glicoproteina G media l'adesione del virus alle cellule ospite.

- Le infezioni dovute a ceppi del sottogruppo A appaiono più severe. le differenze antigeniche sono dovute a differenze del virione.



Nasal Microbiota in RSV Bronchiolitis

Abstract: Respiratory Syncytial Virus (RSV) is the leading cause of bronchiolitis, and the severity may be influenced by the bacterial ecosystem. Our aim was to analyze the nasal microbiota from 48 infants affected by bronchiolitis from RSV virus and 28 infants with bronchiolitis but negative for the virus. Results showed a significantly lower biodiversity in the RSV-positive group with respect to the RSV-negative group, a specific microbial profile associated with the RSV-positive group different from that observed in the negative group, and significant modifications in the relative abundance of taxa in the RSV-positive group, as well as in the RSV-A group, with respect to the negative group. Furthermore, microbial network analyses evidenced, in all studied groups, the presence of two predominant sub-networks characterized by peculiar inter- and intra-group correlation patterns as well as a general loss of connectivity among microbes in the RSV-positive group, particularly in the RSV-A group. Our results indicated that infants with more severe bronchiolitis disease, caused by RSV-A infection, present significant perturbations of both the nasal microbiota structure and the microbial relationships. Patients with a milder bronchiolitis course (RSV-B-infected and patients who have cleared the virus) presented less severe alterations.

SCHIPPA S et al. Microorganisms **2020**, *8*, 7

Nasal Microbiota in RSV Bronchiolitis

Table 1. Clinical characteristics of the studied population. Qualitative clinical variables are reported as number of occurrences and percentage, while continuous variables are expressed as mean ± SD. The reported *p* values are relative to chi square tests or Mann–Whitney U tests performed between the V_{neg} group and the RSV_{pos} group. $p < 0.05$ was considered statistically significant.

Characteristics	V_{neg} ($N = 28$)	RSV_{pos} ($N = 48$)	*p* Value
Male	13 (46.4%)	25 (52.1%)	0.634
Caesarean section	12 (42.9%)	27 (43.8%)	0.940
Age (days)	65.7 ± 3 4.8	76.3 ± 34.5	0.139
Weight	5.0 ± 1.2	5.3 ± 1.0	0.291
Hospitalization (days)	3.7 ± 1.6	4.8 ± 2.4	0.071
Severity score	3.0 ± 1.6	3.9 ± 1.5	0.016
O_2 therapy	3 (10.7%)	18 (37.5%)	0.012
Admission to PICU	0 (0.0%)	3 (6.3%)	0.018
White blood cells	11083.2 ± 3615.9	9784.4 ± 2965.8	0.189
Lymphocytes absolute	5683.2 ± 1689.1	4797.4 ± 2039.4	0.030
Neutrophils absolute	3323.7 ± 2464.9	3166.5 ± 1967.3	0.834
Eosinophil absolute	212.7 ± 192.9	136.7 ± 190.5	0.062
Eosinophil > 400	4 (14.3%)	2 (4.2%)	0.115
Breastfeeding	15 (55.61%)	31 (64.6%)	0.441

SCHIPPA S et al. Microorganisms **2020**, *8*, 7

Nasal Microbiota in RSV Bronchiolitis

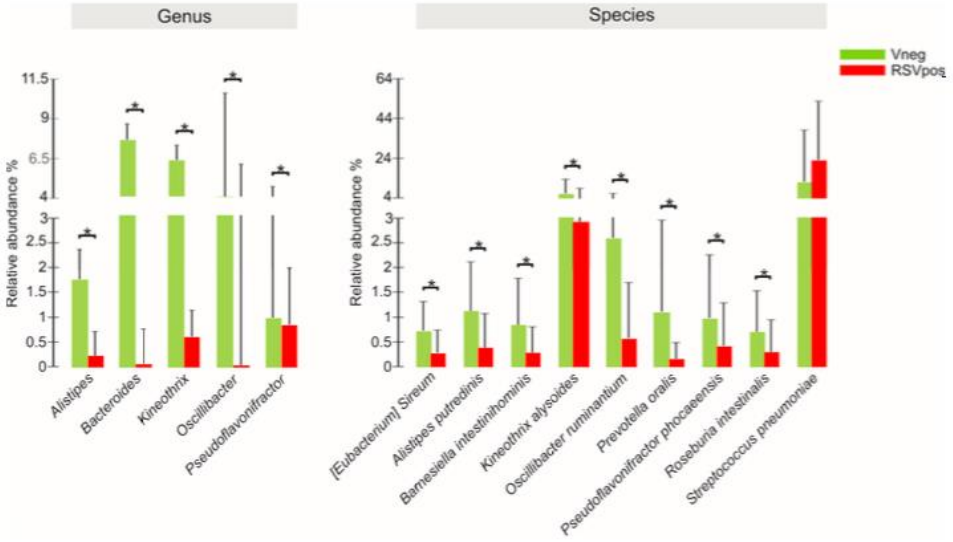


Figure 3. Color-coded bar plot showing differential abundance analysis at genus and species levels performed by Mann–Whitney U tests. * p value ≤ 0.05.

We highlighted significant differences among the groups; in particular, we showed the following:
(i) a significantly higher biodiversity in the virus-negative group with respect to the RSV-positive and to the RSV-A groups;
(ii) a specific nasal microbiota composition in the virus-negative group, different from that of the RSV-positive and RSV-A groups; and
(iii) a significant modification in taxa relative abundance, among RSV-positive, in particular the RSV-A, with respect to the virus-negative group.

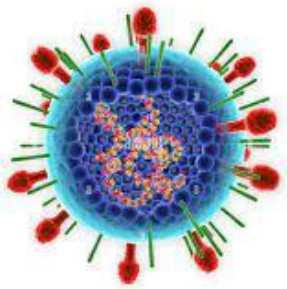
SCHIPPA S et al. Microorganisms **2020**, *8*, 7

h-VIRUS RESPIRATORIO SINCIZIALE

- L'immunità acquisita dopo una infezione da hRSV è incompleta e di breve durata.

- L'infezione con RSV di adulti volontari ha dimostrato che la reinfezione si verifica facilmente anche nei volontari che, della inoculazione del virus, avevano livelli di anticorpi neutralizzanti da moderati ad alti.

- Pertanto, bronchioliti e polmoniti hRSV sono frequenti nei lattanti fino all'età di 3-4 mesi, nonostante la possibile presenza in circolo di livelli elevati di anticorpi anti-hRSV di origine materna trasmessi col latte.



Serological Study of Respiratory Syncytial Virus Infections in Infancy and Childhood

P. S. GARDNER,* M.D., DIP.BACT. ; F. M. ELDERKIN,† M.B., B.S., M.R.C.P.ED., D.C.H. ;
A. H. WALL,* M.B., B.S., B.SC.

Brit. med. J., 1964, **2**, 1570–1573

A serological investigation has been carried out on paired sera from 148 children over the last three years in Newcastle upon Tyne. The great majority of these children had serious infection of the lower respiratory tract, mainly bronchiolitis and pneumonia. Serological evidence is presented that about 60% of severe respiratory infections in the children are due to respiratory syncytial virus. The immunological responsiveness of infants to R.S.V. infection increases with age ; this is directly related to the decrease in maternal antibody, which disappears by 3 months and is replaced by acquired antibody. Few of the older children showed antibody responses, and this coincided with high acquired antibody titres to R.S.V. Evidence is presented which suggests that an antigenic relationship between measles and R.S.V. is unlikely.

Over the three years of the investigation suitably paired sera were received from 148 children with acute respiratory illness ; 125 of these were under 1 year of age, 89 of whom were less than 16 weeks and 68 less than 12 weeks old. Table I shows the types of illness studied during these three winters. It

TABLE I.—*Clinical Categories in 148 Children Admitted to Hospital From Whom Paired Sera Were Obtained*

Winter	Infection of Upper Respiratory Tract	Croup	Bronchitis	Bronchiolitis	Pneumonia
1961–2	0	0	1	17	8
1962–3	0	1	0	19	9
1963–4	4	3	5	67	14
Totals ..	4	4	6	103	31
Seropositives	1 (25%)	0 (—)	3 (50%)	63 (61%)	17 (55%)

TABLE III.—*Serological Responses in Four Clinical Categories of Acute Respiratory Illness*

	Infection of Upper Respiratory Tract	Bronchitis	Bronchiolitis	Pneumonia
Total No. of children ..	4	6	103	31
Antigen :				
R.S.V.	0	3	61	15
Measles	0	0	0	3§
Adenovirus	1†	0	2	1‡
Influenza A	1	0	0	0
Mycoplasma pneumoniae	0	0	2*	0

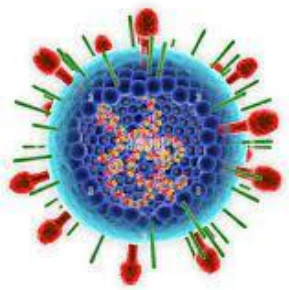
* Associated with a rising titre of antibodies to adenovirus in one case and with R.S.V. in another.
† Associated with a rising titre of antibodies to influenza A.
‡ Associated with a rising titre of antibodies to R.S.V.
§ Two of these rising titres were associated with rising titres of antibodies to R.S.V.

h-VIRUS RESPIRATORIO SINCIZIALE

- Si trasmette per via aerea - attraverso l'inalazione di goccioline generate da uno starnuto o dalla tosse - o per contatto diretto delle secrezioni nasali infette con le membrane mucose degli occhi, della bocca o del naso.

- **Il periodo di maggiore contagiosità è compreso tra novembre e aprile, con un picco nei mesi di gennaio, febbraio e marzo in Italia**.

- Il periodo di incubazione (tempo che intercorre tra l'esposizione e i sintomi) è di circa quattro-sei giorni.



h-VIRUS RESPIRATORIO SINCIZIALE

- Il Virus Respiratorio Sinciziale (VRS) è la causa più comune di **bronchiolite** (infiammazione delle piccole vie aeree dei polmoni) e di **polmonite** nei bambini sotto i due anni, ma può infettare bambini di qualsiasi età, anche se è più comune in quelli tra i 2 e gli 8 mesi.

- La maggior parte dei bambini viene infettata almeno una volta nei primi due anni di vita ma non sempre sviluppano manifestazioni gravi.

- I bambini **possono anche essere reinfettati dal virus** perché una prima infezione da Virus Respiratorio Sinciziale non li rende completamente immuni; in genere, però, le infezioni successive sono più lievi della prima.

- I bambini più piccoli - neonati o nei primi mesi di vita - sono a maggior rischio di sviluppare una forma più grave di malattia.

h-VIRUS RESPIRATORIO SINCIZIALE

RSV is the most common cause of acute lower respiratory tract infections in the pediatric population, with almost 33.8 million cases worldwide in children under 5 years of age, 3.4 million (10%) of hospitalizations, and 66,000–199,000 deaths.

Forty-four percent of hospitalized infants have less than 2 months of age and 99% of deaths occur in developing countries.[9]

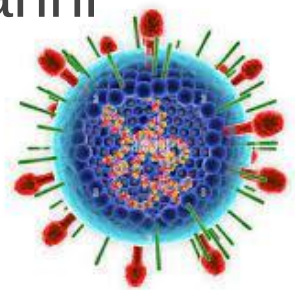
RSV is not only a pediatric virus, but represents a significant cause of morbidity and mortality also in the elderly (>65 years old) and in immunocompromised patients.[10]

Di Mattia G et al. Pediatric Pulmonology. 2021;1–4.

h-VIRUS RESPIRATORIO SINCIZIALE

- Nei **nati prematuramente** o con una **malattia polmonare cronica**, o che hanno alcune **malattie cardiache** e neuromuscolari, l'infezione da VRS può portare a gravi complicazioni respiratorie (insufficienza respiratoria con mancanza di ossigenazione) e polmonite, che può diventare pericolosa per la vita.

- Inoltre sembra accertato che l'infezione da VRS nel lattante sia collegata allo sviluppo di **asma** negli anni successivi.



Association between early bronchiolitis and the development of childhood asthma: a meta-analysis

The combined results demonstrated the association between early bronchiolitis and the development of wheezing/asthma.

In the first year of life, both the respiratory tract and the immune system mature rapidly, and it seems that postnatal development is affected by viral infection. A variety of potential biological mechanisms might underlie the association of bronchiolitis with wheezing/asthma.

(1) Induction of inflammation typical of allergic asthma by T lymphocyte differentiation into Th2,
(2) activation of Th17 cells and induction of IL-17 production. Activated Th17 cells regulate the production of other proinflammatory cytokines (IL-6, tumor necrosis factor (TNF)-α, metalloproteinases etc), which may play important roles in the pathogenesis of asthma,
(3) upregulation of IL-4 and downregulation of interferon (IFN)-γ levels,
(4) induction of bronchial hyperactivity by inflammatory cells and sensory C-fibre neuropeptide,
(5) imbalance of respiratory microbial communities.

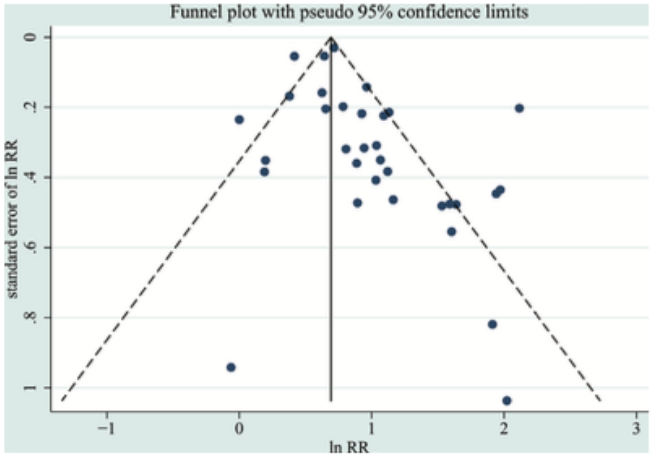
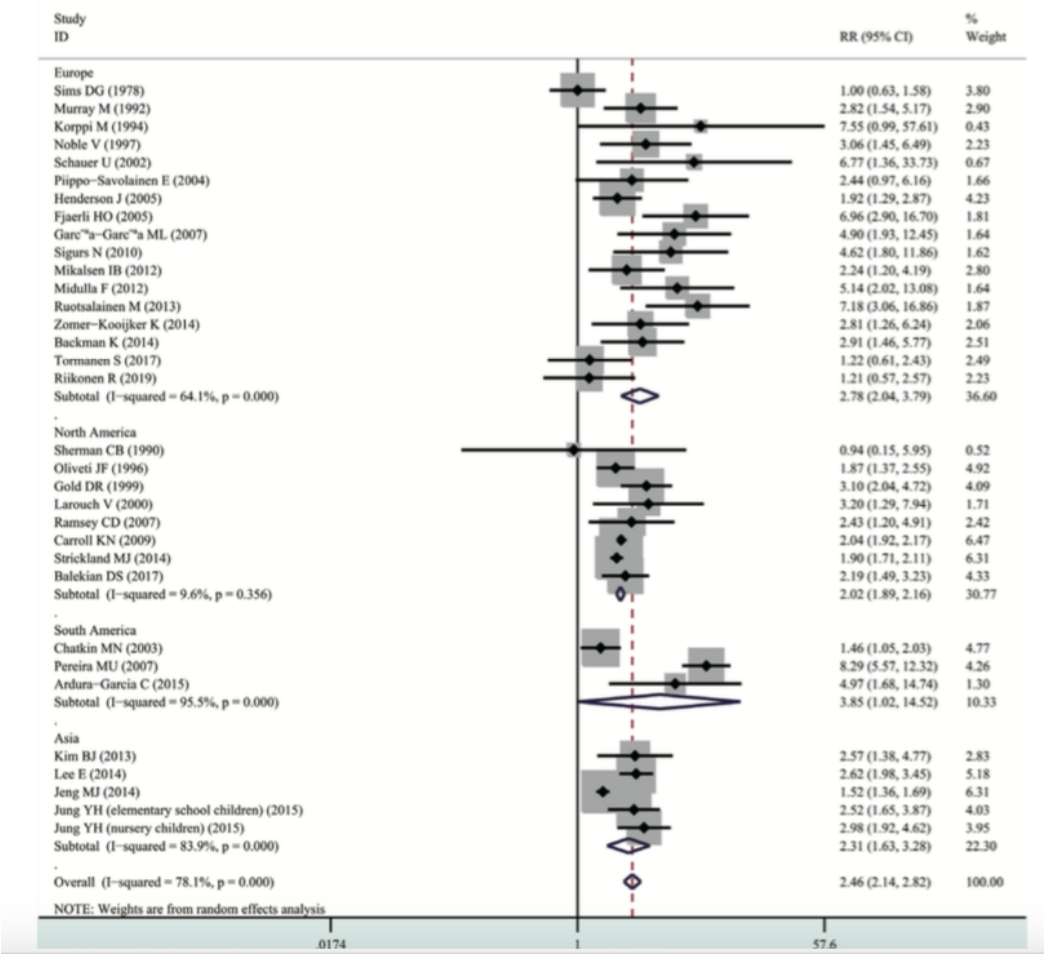


Figure 6 Funnel plot of publication bias for the association between bronchiolitis before 2 years of age and the subsequent development of wheezing/asthma. The horizontal axis represents lnRR and the vertical axis means the SE of lnRR. Vertical line and sloping lines in funnel plot represent summary RR and expected 95% CI for a given SE, respectively. RR, relative risk.

Wang G, et al. BMJ Open 2021;**11**:e043956.

Association between early bronchiolitis and the development of childhood asthma: a meta-analysis

Conclusions The meta-analysis indicates an association between bronchiolitis before 2 years of age and the wheezing/asthma in later life. Well-designed and highly standardised prospective studies that better address bias due to potential confounding factors are needed to validate the risk identi ed in our meta-analysis.



Wang G, et al. BMJ Open 2021;**11**:e043956.

Combined Plasma and Urinary Metabolomics Uncover Metabolic Perturbations Associated with Severe Respiratory Syncytial Viral Infection and Future Development of Asthma in Infant Patients

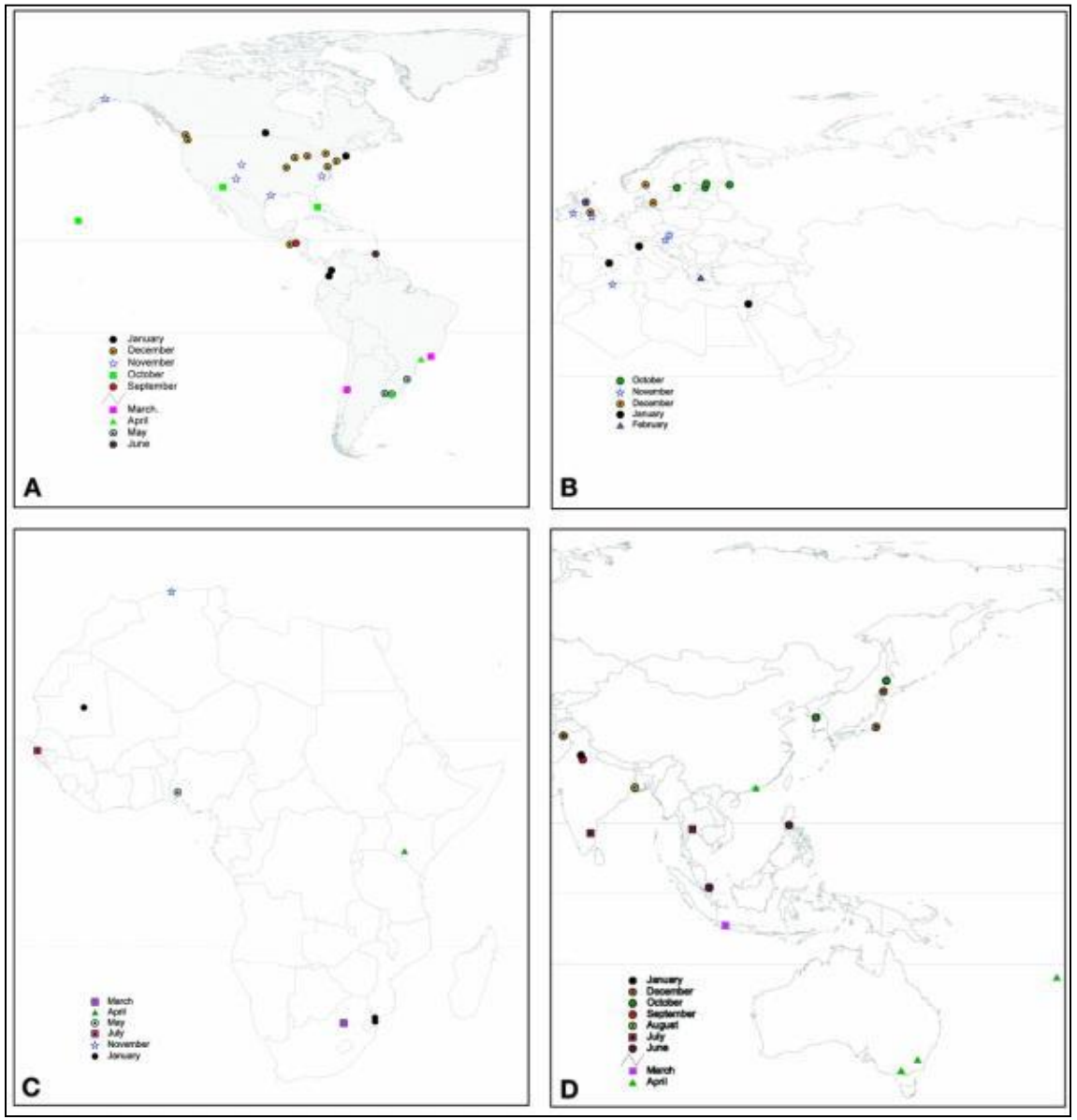
Abstract

A large percentage of infants develop viral bronchiolitis needing medical intervention and often develop further airway disease such as asthma. To characterize metabolic perturbations in acute respiratory syncytial viral (RSV) bronchiolitis, we compared metabolomic profiles of moderate and severe RSV patients versus sedation controls. RSV patients were classified as moderate or severe based on the need for invasive mechanical ventilation. Whole blood and urine samples were collected at two time points (baseline and 72 h). Plasma and urinary metabolites were extracted in cold methanol and analyzed by liquid chromatography coupled with tandem mass spectrometry (LC-MS/MS), and data from the two biofluids were combined for multivariate data analysis. Metabolite profiles were clustered according to severity, characterized by unique metabolic changes in both plasma and urine. ***Plasma metabolites that correlated with severity included intermediates in the sialic acid biosynthesis, while urinary metabolites included citrate as well as multiple nucleotides***.

Furthermore, metabolomic profiles were predictive of future development of asthma, with urinary metabolites exhibiting higher predictive power than plasma. These metabolites may offer unique insights into the pathology of RSV bronchiolitis and may be useful in identifying patients at risk for developing asthma.

Teoh ST Metabolites. 2022 Feb 14;12(2):178.

Respiratory syncytial virus epidemics: the ups and downs of a seasonal virus.
STENSBALLE, LONE et al.



Maps of North, Central and South America (A), Europe and Mediterranean countries (B), Africa (C) and Southeast Asia and Eastern Pacific Rim countries (D), illustrating temporal trends in the appearance of RSV epidemics. Different colors (consistent throughout the four panels) refer to the month of the onset of the RSV season in cities in the five continents.

- **Nord Nov-marzo**
- **Sud giugno-settembre**

Pediatric Infectious Disease Journal. 22(2) Supplement:S21-S32, February 2003.

Bronchiolitis: Analysis of 10 Consecutive Epidemic Seasons

Summary. Bronchiolitis is the leading cause of hospitalization in infants under 12 months. Our aims were to analyze epidemiological characteristics of infants with bronchiolitis over 10 consecutive seasons and to evaluate whether there are any clinical differences between infants hospitalized for bronchiolitis during epidemic peak months and infants in non-peak months. We enrolled consecutive enrolled 723 previously healthy term infants hospitalized at the Paediatric Emergency Department, "Sapienza" University of Rome over the period 2004–2014. Fourteen respiratory viruses were detected from nasopharyngeal aspirates by molecular methods. Clinical and demographic data were extracted from clinical charts. Viruses were detected in 351 infants (48.5%): RSV in 234 (32.4%), RV in 44 (6.1%), hBoV in 11 (1.5%), hMPV in 12 (1.6%), co-infections in 39 (5.4%), and other viruses in 11 (1.5%). Analyzing the 10 epidemic seasons, we found higher incidence for bronchiolitis every 4 years with a peak during the months December–January. Infants hospitalized during peak months had lower family history for asthma ($P=0.003$), more smoking mothers during pregnancy ($P=0.036$), were slightly higher breastfed (0.056), had lower number of blood eosinophils ($P=0.015$) and had a higher clinical severity score ($P=0.017$). RSV was detected mostly during peak months, while RV was equally distributed during the seasons. We found some variations in bronchiolitis incidence during epidemics, and discriminative characteristics in infants hospitalized for bronchiolitis during peak months and in non-peak months, that might reflect two different populations of children. **Pediatr Pulmonol. 2016; 9999:XX–XX.**

Cangiano et al. Pediatr Pulmonol. 2016; 999

Bronchiolitis: Analysis of 10 Consecutive Epidemic Seasons

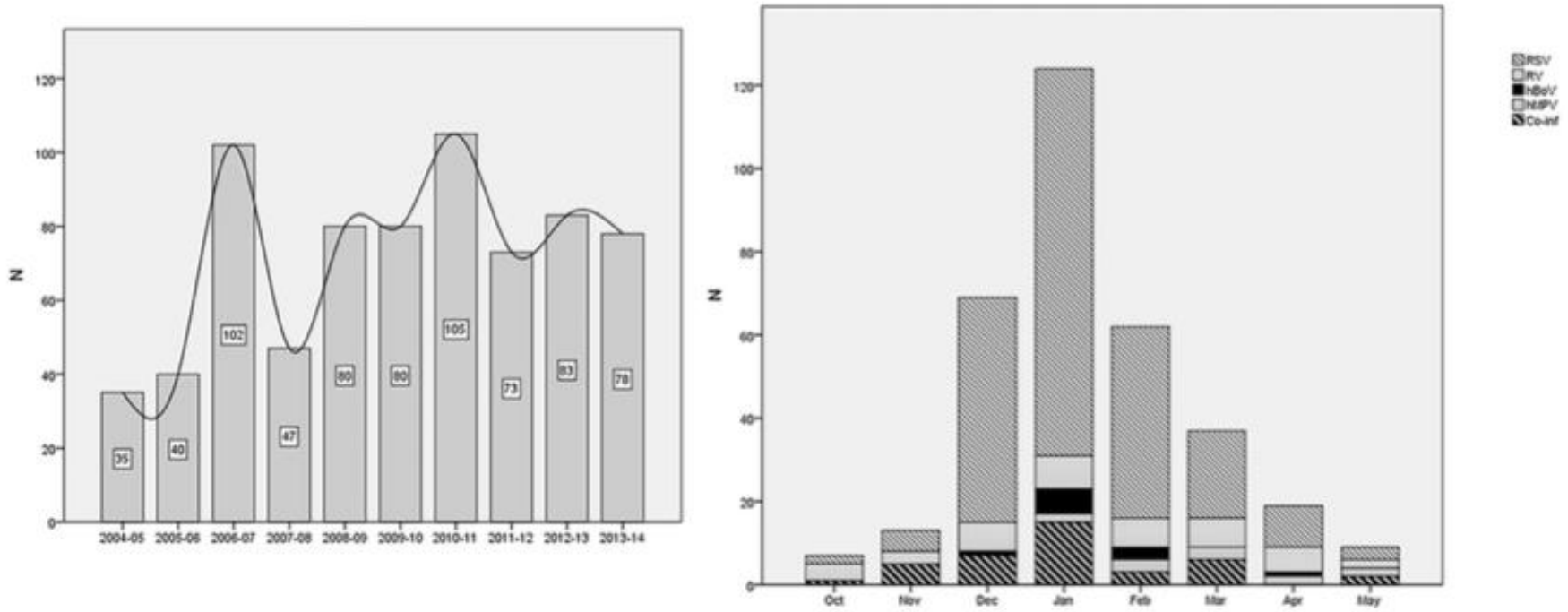
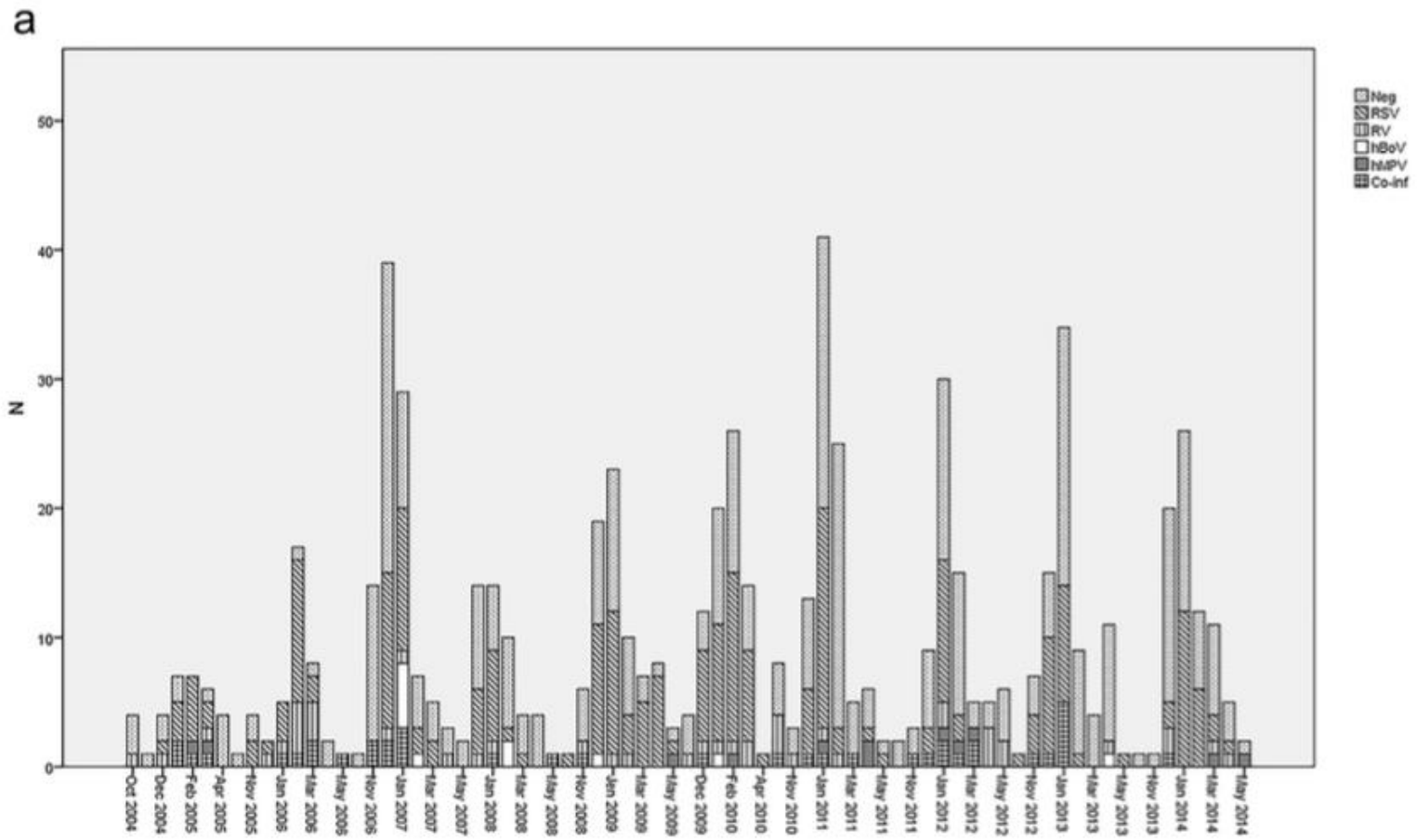


Fig. 1. (a) Number of infants hospitalized for bronchiolitis over 10 epidemics. (b) Number of infants hospitalized for bronchiolitis by infection type (RSV, RV, hBoV, hMPV, and coinfections) during the 10 epidemics divided by month.

Cangiano et al. Pediatr Pulmonol. 2016; 999

Bronchiolitis: Analysis of 10 Consecutive Epidemic Seasons



Cangiano et al. Pediatr Pulmonol. 2016; 999

Bronchiolite

La ***bronchiolite*** è una malattia respiratoria che si riscontra in età pediatrica, comunemente causata da un' infezione virale che coinvolge le basse vie aeree.

Non esiste una concordanza però nella ***definizione*** :

Gli autori nordamericani, infatti, identificano con il termine di bronchiolite, più genericamente, il primo episodio di wheezing associato ad un'infezione respiratoria in bambini al di sotto dei 24 mesi d'età.

Gli autori Europeo-Canadesi definiscono come bronchiolite il primo episodio acuto di infezione delle basse vie respiratorie caratterizzato da tachipnea e rantoli crepitanti (raramente sibili espiratori) all'auscultazione del torace in bambini di età inferiore a 12 mesi.

Pneumologia Pediatrica 2002

Age Limit in Bronchiolitis Diagnosis: 6 or 12 Months?

WHAT IS KNOWN

- Bronchiolitis is a common cause of lower respiratory tract infection in infants and the major responsible factor of hospitalization under the age of one year.
- Respiratory syncytial virus is major involved virus in bronchiolitis

WHAT THIS PAPER ADDS

- Infants younger than 6 months had more frequently respiratory syncytial virus infection and a more severe disease.
- Infants older than 6 months had slightly more tobacco smoking exposure and slightly higher recurrent wheezing after the hospitalization.
- The human bocavirus has been identified almost entirely in infants older than 6 months.

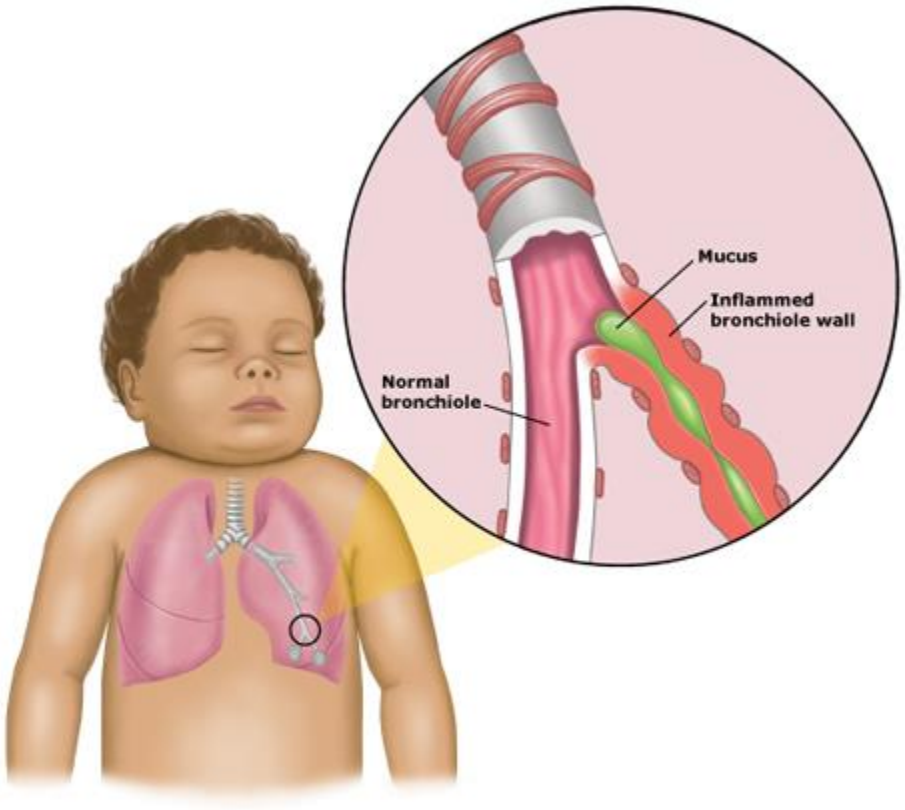
TABLE 1 | Clinical characteristics of 824 infants hospitalized for bronchiolitis divided in ≤6 months /> 6 months old infants.

Items	≤ 6 months old infants (*N* = 773)	> 6 months old infants (*N* = 51)	*p*
Male sex	54.1%	47.1%	ns
Passive smoking exposure	45.4%	58.0%	0.107
Virus negative	50.1%	45.1%	ns
Virus positive			
RSV	68.1%	42.9%	0.007
hRV	11.7%	14.3%	ns
hBoV	1.3%	21.4%	<0.0001
hMpV	3.6%	0	ns
Others	3.9%	3.6%	ns
Coinfections	11.4%	17.8%	ns
Clinical severity score median (IQR)	3 (2–5)	3 (2–4)	0.011
IV fluids	55.1%	29.4%	0.001
Days of hospitalization (IQR)	5 (4–6)	4 (4–6)	0.216

Data were expressed as percentage or median and interquartile range (IQR).
IV, intravenous.

NENNA R ET AL. Front. Pediatr. 8:144. 2020

Bronchiolite



E' caratterizzata da un'infiammazione acuta, edema e necrosi delle cellule epiteliali che rivestono i bronchioli terminali e respiratori, e da maggiore produzione di muco.

Bronchiolite

- E' la più frequente malattia delle basse vie aeree nella popolazione pediatrica al di sotto del secondo anno di età ed è responsabile della **maggior parte dei ricoveri nei primi 12 mesi di vita.**

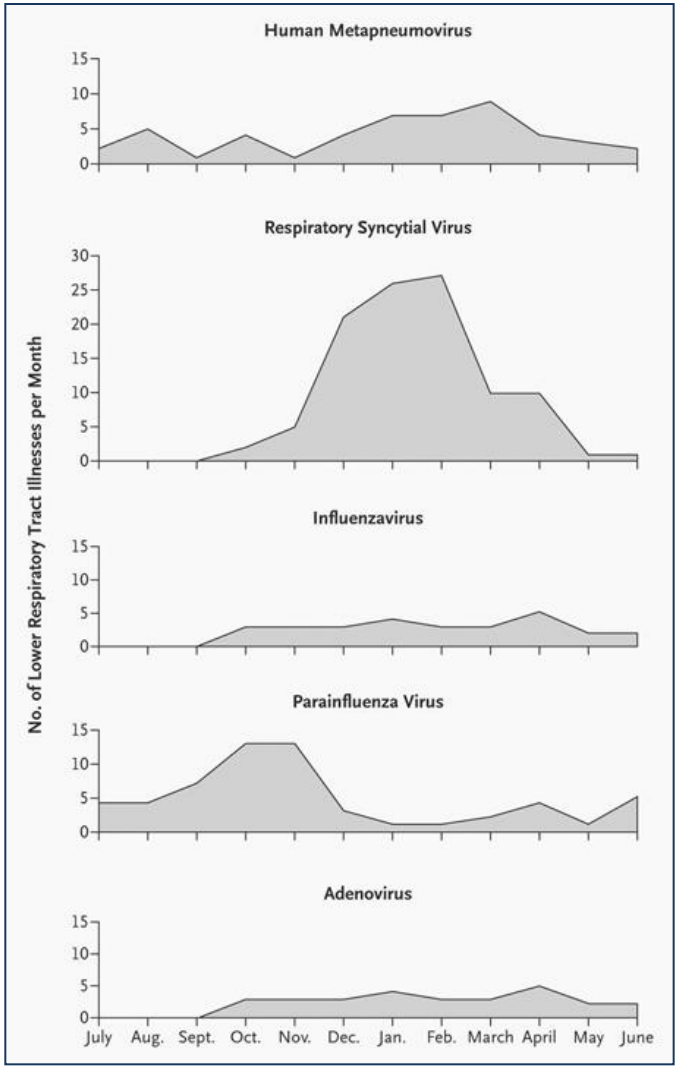
- L'uso di tecniche diagnostiche classiche e molecolari ha dimostrato che il **97% dei casi di bronchiolite è di eziologia virale.**

- Il principale agente eziologico è il **virus respiratorio sinciziale (VRS) responsabile del 45-75%** dei casi di bronchiolite, soprattutto di quelle che si verificano in forma epidemica, seguito dal rhinovirus, dal bocavirus, dal metapneumovirus, dai virus parainfluenzali di tipo 1, 2 e 3, dagli adenovirus e dagli enterovirus. Più raramente sono responsabili i virus influenzali, gli echovirus, o batteri come il Mycoplasma Pneumoniae.

Bronchiolite

EPIDEMIOLOGIA :

- **Età <2 aa** (prevalentemente lattanti di 2-8 mesi).
- Predilige il **sesso maschile**
- L'infezione è altamente contagiosa e viene trasmessa per contatto diretto dalle **secrezioni nasali di soggetti infetti**.
- **Autoinoculazione** (mani infette) mediante sfregamento degli occhi e del naso che costituiscono le più importanti vie di penetrazione del virus.
- Si contrae più frequentemente in **comunità** (asilo nido) o attraverso il contatto con un **membro della famiglia** che presenta un'infezione delle vie aeree superiori..
- Predilige i **mesi invernali** e l'inizio della primavera, talora manifestandosi con piccole epidemie in collettività.



Bronchiolite

FATTORI DI RISCHIO:

- Nascita nel periodo epidemico o immediatamente precedente;
- Basso livello di anticorpi specifici alla nascita;
- Mancato allattamento al seno;
- Sovraffollamento ambientale (numero di fratelli, fumo in casa) ;
- Ospedalizzazione.

150 milioni di nuovi casi di bronchiolite/anno, di cui il 7-13% rappresentato da una delle categorie a rischio di sviluppare forme gravi, tali da richiedere il ricovero in ambiente Ospedaliero.

Tabella 1. Fattori favorenti il decorso grave della bronchiolite

NATO A TERMINE SANO	PATOLOGIE CRONICHE	NATO PRETERMINE
Età < 6 settimane	Fibrosi cistica	EG <32 settimane
Basso livello socio-economico	Cardiopatia congenita	Displasia broncopolmonare
Esposizione a fumo passivo e inquinamento atmosferico	Deficit immunitario	Ventilazione meccanica in epoca neonatale
Anamnesi familiare positiva per asma e atopia		Dimissione in corso di stagione epidemica
Infezioni da enterovirus		

Chi è a rischio di andare incontro a una infezione grave da VRS?

- Bambini prematuri nati prima delle 29 settimane di gravidanza; i bambini prematuri nascono prima di aver ricevuto la quota sufficiente di anticorpi anti VRS dalla propriamadre
- Lattanti e bambini di meno di 24 mesi con displasia broncopolmonare (BPD, una malattia polmonare legata alla prematurità)
- Sono a rischio anche alcuni bambini con cardiopatia congenita o altre malattie respiratorie croniche
- Bambini e adulti che hanno un sistema immunitario depresso o indebolito a causa di una malattia o di un trattamento medico
- Adulti sopra i 65 anni

Lancet 2014; 383: 1581–92

Outdoor air pollution and asthma

Michael Guarnieri, John R Balmes

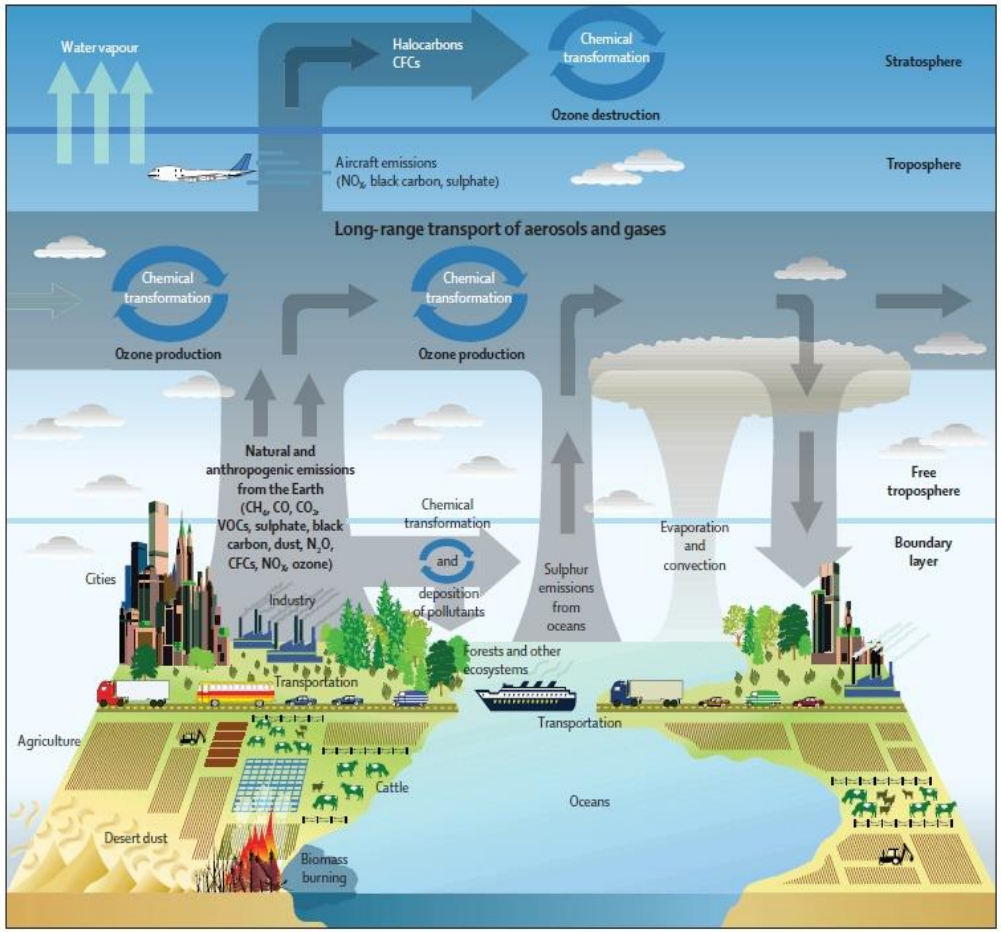


Figure 1: Sources, transport, transformation, and fate of atmospheric pollutants
Reproduced from the US Climate Change Science Program. CFC=chlorofluorocarbon. CH_4=methane. CO=carbon monoxide. CO_2=carbon dioxide. N_2O=nitrous oxide. NO_x=nitrogen oxides.

Agli inquinanti naturali (attività vulcaniche, incendi boschi, semplice metabolismo e decomposizione vegetale e animale) si aggiungono poi altre sostanze provenienti dalle attività umane che, se uniformemente distribuite, non porterebbero particolari modifiche della composizione dell'aria.

Ma il problema dell'inquinamento di origine antropica deriva proprio dal fatto di essere altamente concentrato in piccole aree (sopratutto urbane ed industriali) e di non essere in grado di diffondersi nell'intera atmosfera per la presenza o di barriere geomorfologiche naturali o create dall'uomo che ne limitano la diffusione laterale.

Si assiste, quindi, ad un vero e proprio accumulo, accentuato in alcuni giorni anche da particolari condizioni meteorologiche.

Inquinamento ambientale ed infezioni respiratorie

Exposure to Traffic and Early Life Respiratory Infection: A Cohort Study

Mary B. Rice, MD,[1,2]*

(95% CI 0.98, 1.13) higher risk of respiratory infection. Our findings suggest that living close to a major roadway during pregnancy may predispose the developing lung to infection in early life.

Pediatr Pulmonol.

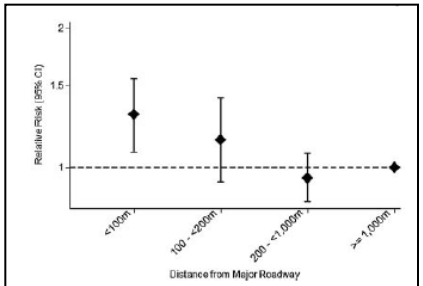


Fig. 1. Distance to major roadway and relative risk of respiratory infection by early childhood. Data from 1,263 mother-infant pairs participating in Project Viva. Adjusted for maternal race/ethnicity, maternal education, smoking during pregnancy, breastfeeding, smokers in household after birth, other children <12 years in household, census tract income (quartile), census tract education, infant sex, gestational age, birth weight for gestational age Z-score, season of birth, childcare attendance, and time.

Air Pollution and Acute Respiratory Infections Among Children 0–4 Years of Age: An 18-Year Time-Series Study

Lyndsey A. Darrow et al.

Upper and lower respiratory infections are common in early childhood and may be exacerbated by air pollution. We investigated short-term changes in ambient air pollutant concentrations, including speciated particulate matter less than 2.5 μm in diameter ($PM_{2.5}$), in relation to emergency department (ED) visits for respiratory infections in young children. Daily counts of ED visits for bronchitis and bronchiolitis ($n = 80,399$), pneumonia ($n = 63,359$), and upper respiratory infection (URI) ($n = 359,246$) among children 0–4 years of age were collected from hospitals in the Atlanta, Georgia, area for the period 1993–2010. Daily pollutant measurements were combined across monitoring stations using population weighting. In Poisson generalized linear models, 3-day moving average concentrations of ozone, nitrogen dioxide, and the organic carbon fraction of particulate matter less than 2.5 μm in diameter ($PM_{2.5}$) were associated with ED visits for pneumonia and URI. Ozone associations were strongest and were observed at low (cold-season) concentrations; a 1–interquartile range increase predicted a 4% increase (95% confidence interval: 2%, 6%) in visits for URI and an 8% increase (95% confidence interval: 4%, 13%) in visits for pneumonia. Rate ratios tended to be higher in the 1- to 4-year age group compared with infants. Results suggest that primary traffic pollutants, ozone, and the organic carbon fraction of $PM_{2.5}$ exacerbate upper and lower respiratory infections in early life, and that the carbon fraction of $PM_{2.5}$ is a particularly harmful component of the ambient particulate matter mixture.

Am J Epidemiol. 2014;180(10):968–977

Respiratory syncytial virus bronchiolitis, weather conditions and air pollution in an Italian urban area: An observational study

Background: In this study we sought to evaluate the association between viral bronchiolitis, weather conditions, and air pollution in an urban area in Italy.

Methods: We included infants hospitalized for acute bronchiolitis from 2004 to 2014. All infants underwent a nasal washing for virus detection. A regional agency network collected meteorological data (mean temperature, relative humidity and wind velocity) and the following air pollutants: sulfur dioxide, nitrogen oxide, carbon monoxide, ozone, benzene and suspended particulate matter measuring less than 10 μm (PM_{10}) and less than 2.5 μm ($PM_{2.5}$) in aerodynamic diameter. We obtained mean weekly concentration data for the day of admission, from the urban background monitoring sites nearest to each child's home address. Overdispersed Poisson regression model was fitted and adjusted for seasonality of the respiratory syncytial virus (RSV) infection, to evaluate the impact of individual characteristics and environmental factors on the probability of a being positive RSV.

Results: Of the 723 nasal washings from the infants enrolled, 266 (68%) contained RSV, 63 (16.1%) rhinovirus, 26 (6.6%) human bocavirus, 20 (5.1%) human metapneumovirus, and 16 (2.2%) other viruses. The number of RSV-positive infants correlated negatively with temperature ($p < 0.001$), and positively with relative humidity ($p < 0.001$). Air pollutant concentrations differed significantly during the peak RSV months and the other months. Benzene concentration was independently associated with RSV incidence ($p = 0.0124$).

Conclusions: Seasonal weather conditions and concentration of air pollutants seem to influence RSV-related bronchiolitis epidemics in an Italian urban area.

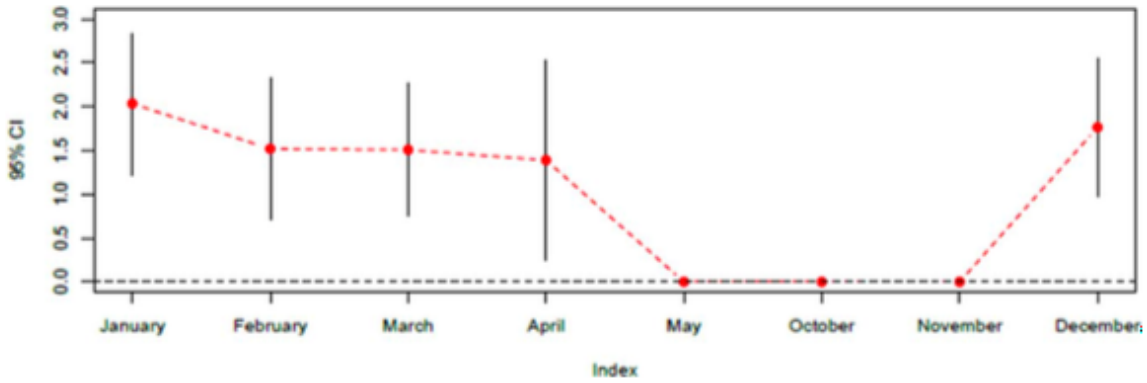


Fig. 1. 95% confidence intervals of the month effect in the Poisson regression model.

Respiratory syncytial virus bronchiolitis, weather conditions and air pollution in an Italian urban area: An observational study

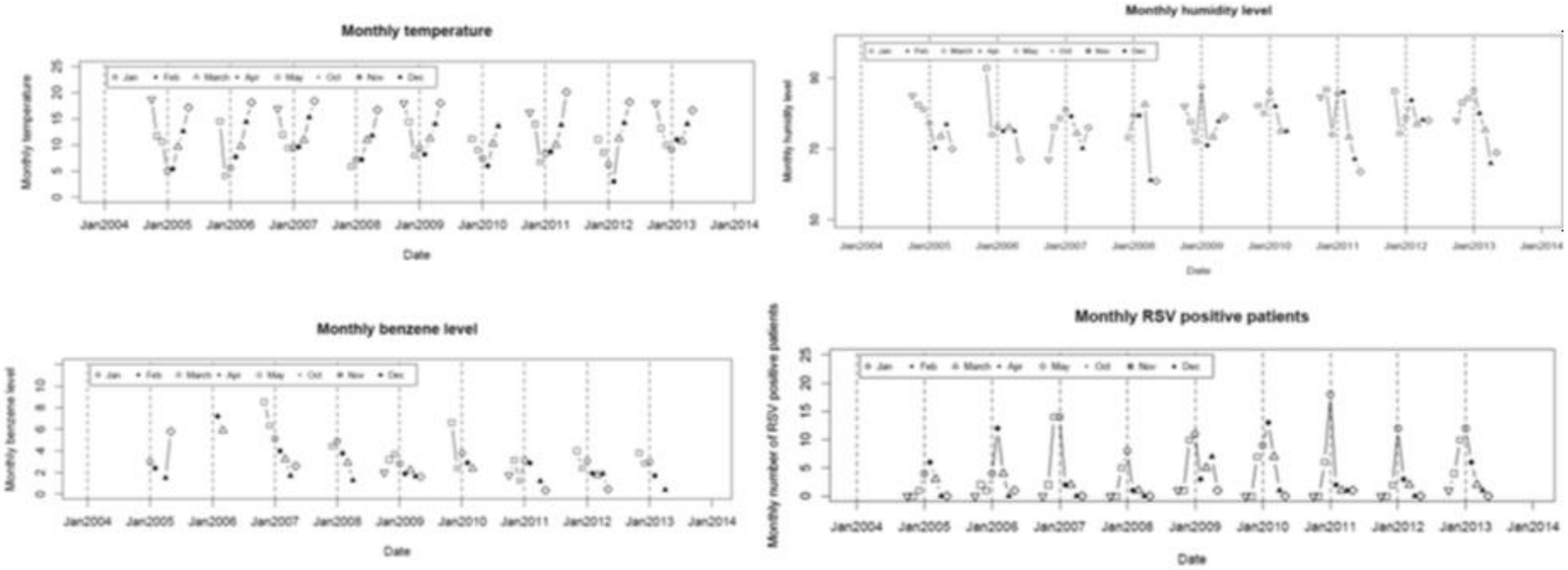


Fig. 2. Trend of temperature, humidity, benzene and respiratory syncytial virus (RSV) positive cases over the study period.

The number of RSV-positive infants correlated negatively with temperature ($r = -0.46$, $p < 0.001$), and positively with relative humidity ($r = 0.36$, $p < 0.001$). No correlation was found with wind velocity.

Nenna R et al. Environmental Research 158 (2017) 188–193

Respiratory syncytial virus bronchiolitis, weather conditions and air pollution in an Italian urban area: An observational study

Table 1
Differences in air pollutant concentrations during the months when respiratory syncytial virus (RSV) activity peaks and during other months.

Air pollutants	Months when RSV peaks	Other months	p values[a]
SO_2 µg/m^3	1.0 (0.7–1.3)	0.9 (0.6–1.3)	ns
BZ µg/m^3	3.2 (2.5–4.2)	2.2 (1.5–3.7)	0.001
CO mg/m^3	1.0 (0.7–1.2)	1.1 (0.6–1.5)	ns
NO_2 µg/m^3	59.0 (50.0–70.0)	55.5 (42.0–66.7)	0.002
NO_x µg/m^3	133.0 (102.5–185.0)	101.0 (64.0–159.0)	0.001
O_3 µg/m^3	17.0 (12.0–26.0)	35.0 (21.2–47.2)	0.001
PM10 µg/m^3	42.0 (34.0–52.0)	39.0 (29.0–47.5)	0.001
PM2.5 µg/m^3	29.0 (22.5–34.0)	11.2 (8.7–14.4)	0.001

Data are expressed as median and interquartile range (IQR). sulfur dioxide (SO_2), nitrogen oxide and dioxide (NO_x, NO_2); carbon monoxide (CO); ozone (O_3); benzene (BZ); levels of suspended particles less than 10 µm (PM10) and less than 5 µm (PM2.5) in aerodynamic diameter.

[a] Mann–Whitney *U* test.

Factors responsible for increasing the risk of virus-related bronchiolitis in Italy probably include meteorological factors and chronic traffic-derived air pollution combined.

Vegna R et al. Environmental Research 158 (2017) 188–193

Traffic density and stationary sources of air pollution associated with wheeze, asthma, and immunoglobulin E from birth to age 5 years among New York City children

.

Abstract

We examined associations of residential proximity and density of traffic and stationary sources of air pollution with wheeze, asthma, and immunoglobulin (Ig) E among New York City children between birth and age 5 years.

……Longitudinal investigation suggests that among Dominican and African American children living in Northern Manhattan and South Bronx during ages 0-5 years, residence in neighborhoods with high density of traffic and industrial facilities may contribute to chronic respiratory morbidity, and concurrent, prenatal, and earlier childhood exposures may be important. These findings may have broad implications for other urban populations that commonly have high asthma prevalence and exposure to a high density of traffic and stationary air pollution sources.

M.M. Patel et al. / Environmental Research 111 (2011) 1222–1229

Air pollution interacts with past episodes of bronchiolitis in the development of asthma

Kim BJ[1] et al.

Background: Exposure to ambient air pollution and bronchiolitis are risk factors for asthma. The aim of this study was to investigate the effect of air pollution on the development of asthma in children with past episodes of bronchiolitis.

Methods: A prospective 2-year follow-up survey consisting of parental responses to the International Study of Asthma and Allergies in Childhood (ISAAC) questionnaire, and allergy evaluations were conducted in 1743 children with a mean age of 6.8 years. Recent 5-year exposure to air pollution was estimated using a geographic information system.

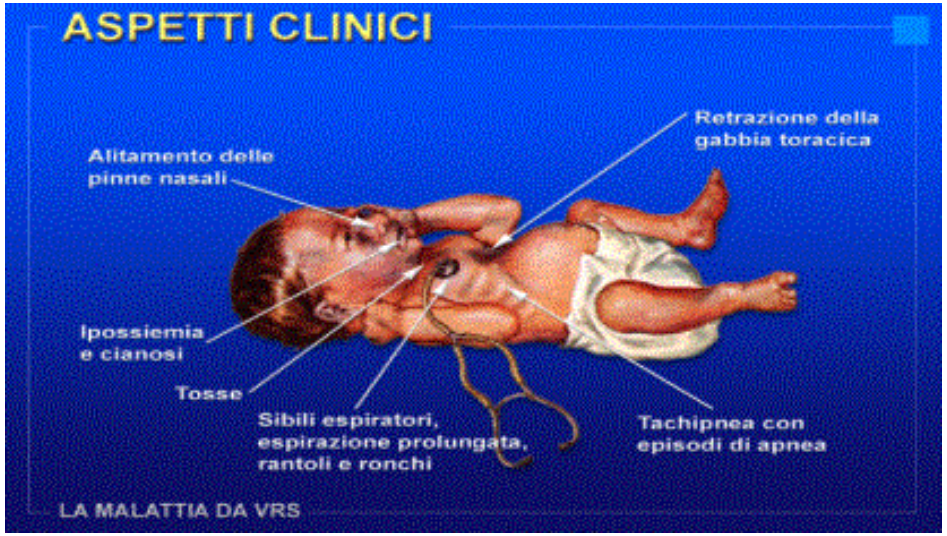
Conclusion: In children, the interaction between air pollution and past episodes of bronchiolitis resulted in a greater prevalence of asthma and pointed to an association with bronchial hyper-reactivity and decreased lung function. These results suggest mechanisms underlying the development of asthma.

Allergy. 2013 Apr;68(4):517-23.

Bronchiolite

Manifestazioni cliniche

La maggior parte dei bambini affetti presenta in anamnesi un ***contatto recente*** (meno di una settimana) con bambini e/o adulti affetti da malattie respiratorie lievi.



- ***Incubazione di 3-6 giorni***, l'esordio è abitualmente rappresentato da una ***sindrome infiammatoria febbrile delle vie aeree superiori*** con abbondante secrezione sierosa che nei giorni successivi spesso si attenua sino a scomparire.
- L'estensione del processo infiammatorio ai bronchioli può quindi manifestarsi anche dopo alcuni giorni e si rende evidente per la ***comparsa di tosse, difficoltà respiratoria, tachipnea e irritabilità.***
- L'***alimentazione*** al seno o con il biberon può risultare particolarmente difficile a causa dell'elevata frequenza respiratoria che non consente al bambino di bere o deglutire normalmente.

Bronchiolite

La diagnosi di bronchiolite è clinica, supportata dalla fascia di età del bambino, rinforzata dal dato epidemiologico (in particolare da VRS) in famiglia e in comunità.

Radiografia Torace

Nei bambini con bronchiolite da VRS ospedalizzati:

- normale (10% circa dei casi)
- air trapping o iperspansione polmonare (50% circa)
- inspessimento peribronchiale o pneumopatia interstiziale (50-80%)
- addensamento segmentale (10-25%).
- Effusione pleurica (molto rara, possibilità di una polmonite batterica).

Laboratorio

- Conta leucocitaria: solitamente normale, a volte elevata.
- Formula leucocitaria: può essere normale;
- Proteina C reattiva (PCR) aumentata nelle sovrainfezioni batteriche.

Diagnosi eziologica (su aspirato nasofaringeo).

- Immunofluorescenza
- ELISA o Immunocromatografia (test rapido)
- Polymerase Chain Reaction (PCR)
- Coltura virale

Bronchiolite

Il ***trattamento*** della bronchiolite è a tutt'oggi oggetto di numerose controversie.

- Nei pazienti ospedalizzati, la ***SaO2 deve essere mantenuta al di sopra di 92-94%,*** attraverso la somministrazione, quando necessario, di O2 riscaldato e umidificato.
- È importante ***mantenere lo stato di idratazione***, anche attraverso la somministrazione parenterale, ed evitare nello stesso tempo di sovraccaricare il bambino di liquidi e nel contempo controllare che non si instauri un'inappropriata secrezione di ADH.
- La ***rimozione delle secrezioni dalle cavità nasali e l'aspirazione delle vie respiratorie*** è un momento fondamentale delle cure di supporto.

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

TREATMENT

Clinicians should not administer albuterol (or salbutamol) to infants and children with a diagnosis of bronchiolitis (Evidence Quality: B;

Clinicians should not administer systemic corticosteroids to infants with a diagnosis of bronchiolitis in any setting (Evidence Quality: A; Recommendation Strength: Strong Recommendation).

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

Clinicians should not administer antibacterial medications to infants and children with a diagnosis of bronchiolitis unless there is a concomitant bacterial infection, or a strong suspicion of one. (Evidence

Clinicians may administer nebulized hypertonic saline to infants and children hospitalized for bronchiolitis (Evidence Quality: B; Recommendation Strength: Weak

Clinicians may choose not to administer supplemental oxygen if the oxyhemoglobin saturation exceeds 90% in infants and children with a diagnosis of bronchiolitis (Evidence Quality: D; Recommendation Strength:

h-VIRUS RESPIRATORIO SINCIZIALE

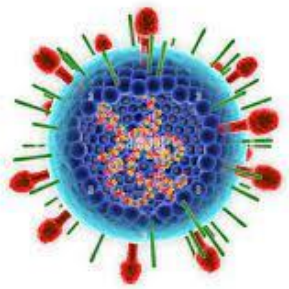
Non ci sono farmaci specifici per trattare le malattie causate da questo virus.

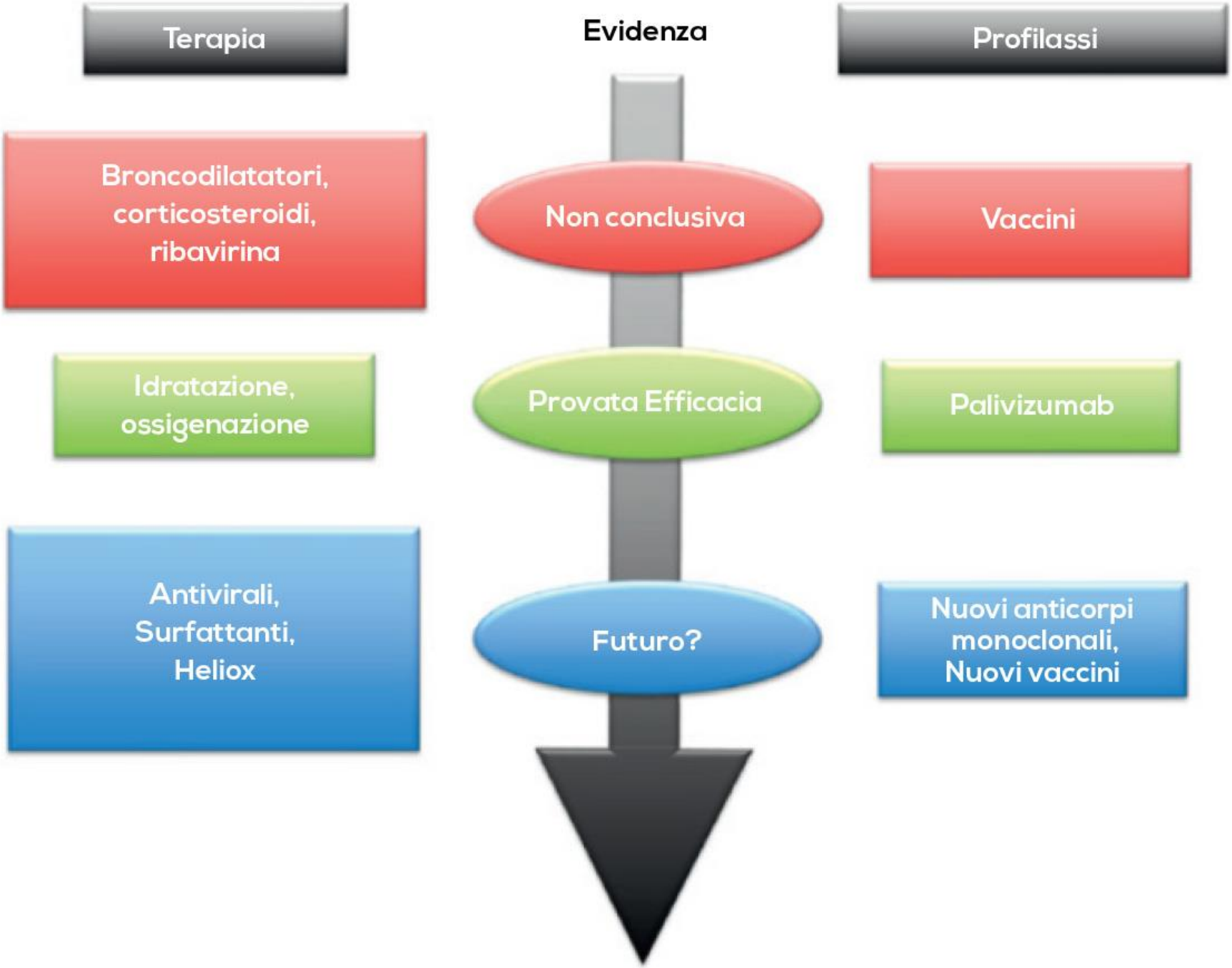
La cura si basa sul **trattamento degli effetti del virus sul sistema respiratorio**.

Inoltre essendo la malattia di tipo virale gli antibiotici sono totalmente inutili.

Il trattamento dei sintomi nei casi più gravi può includere:
-Fornire ossigeno supplementare se vi è insufficienza respiratoria (saturazione ossigeno inferiore a 92%);
-Infondere liquidi per via endovenosa (per prevenire la disidratazione);
-Alimentare tramite sondino se necessario;

Controverso: Usare farmaci broncodilatatori per aerosol , CS per via sistemica, Impiegare farmaci antivirali (raramente, solo per bambini molto gravi o ad alto rischio).




Terapia
Evidenza
Profilassi
Broncodilatatori, corticosteroidi, ribavirina
Non conclusiva
Vaccini
Idratazione, ossigenazione
Provata Efficacia
Palivizumab
Antivirali, Surfattanti, Heliox
Futuro?
Nuovi anticorpi monoclonali, Nuovi vaccini

Virus sinciziale (RSV), da Vittoria (figlia di Fedez e Ferragni) l'allarme ai bimbi. Burioni: «Il vaccino non c'è»

Un post del rapper ha messo in guardia i genitori sulla malattia che ha colpita la loro bimba. Il virologo: un pericolo non indifferente

Anche la figlia della Ferragni ne soffre

Anche la figlia di Chiara Ferragni e Fedez, la piccola Vittoria Lucia di soli 7 mesi

"Non sottovalutatelo". Il virus sinciziale spaventa l'Italia

27 Ottobre 2021 - 18:44

-L’allarme era stato inizialmente lanciato da Stati Uniti e Nuova Zelanda, ma anche nel nostro Paese è arrivata una pesante epidemia di VRS, appunto il virus respiratorio sinciziale che sta colpendo i più piccoli.

-Molti i ricoveri che hanno portato i reparti pediatrici e le terapie intensive a essere pieni.

La situazione negli ospedali

I piccoli pazienti mostrano bronchioliti e polmoniti causate proprio dal virus.

A Padova ci sono al momento 16 bimbi ricoverati, dei quali quattro sono stati intubati e si trovano in rianimazione.

Come riportato dal Corriere, al Policlinico Umberto I di Roma sono 10 i ricoverati, di cui 2, che hanno solo un mese di vita, si trovano in terapia intensiva. La situazione non è molto diversa nelle altre regioni.

A Milano Gianvincenzo Zuccotti, responsabile del reparto di Pediatria all'Ospedale Buzzi di Milano ha confermato che *"il virus Vrs sta circolando, i reparti e i pronto soccorso sono sotto pressione".* Al Buzzi ci sono in questo momento 7 bimbi ospedalizzati con bronchiolite da virus respiratorio sinciziale e 5 con bronchioliti Vrs negativa. Una sola bambina si trova nel reparto di terapia intensiva con bronchiolite da Vrs.

La situazione negli ospedali

-Antonino Reale, responsabile Pediatria emergenza dell'ospedale Bambino Gesù di Roma ha spiegato che *"negli ultimi 15 giorni stiamo assistendo ad un **aumento esponenziale** dei ricoveri per bronchioliti, anche gravi, che sono la conseguenza del virus respiratori sinciziale.*
Spesso dagli esami risulta la presenza di più virus, anche 3-4, quindi c'è un'associazione di più patogeni". Reale ha poi aggiunto che al Bambino Gesù vi sono attualmente *"una quindicina di pazienti, neonati nei primi mesi di vita, con bronchiolite e il 40% ha forme leggere. Sono 2 in terapia con ossigeno".*

"Dal 15 ottobre al 15 novembre abbiamo ricoverato circa 120 pazienti nelle terapie intensive neonatali - afferma il prof. Giovanni Chello, presidente SIN Campania e primario UOC neonatologia e terapia intensiva neonatale Ospedale Monaldi di Napoli - Si tratta di bambini sotto il primo mese di vita, che vivono quindi situazioni delicate. La degenza media è intorno ai 10giorni. Con l'abbassamento delle temperature è lecito aspettarsi un incremento dei ricoveri.

Secondo i dati epidemiologici provenienti anche dall'estero, rispetto agli scorsi anni l'aumento dell'incidenza della malattia è di 5-10 volte"

American Academy of Pediatrics
DEDICATED TO THE HEALTH OF ALL CHILDREN®

From: **Delayed Seasonal RSV Surge Observed During the COVID-19 Pandemic**

Pediatrics. 2021;148(3). doi:10.1542/peds.2021-052089

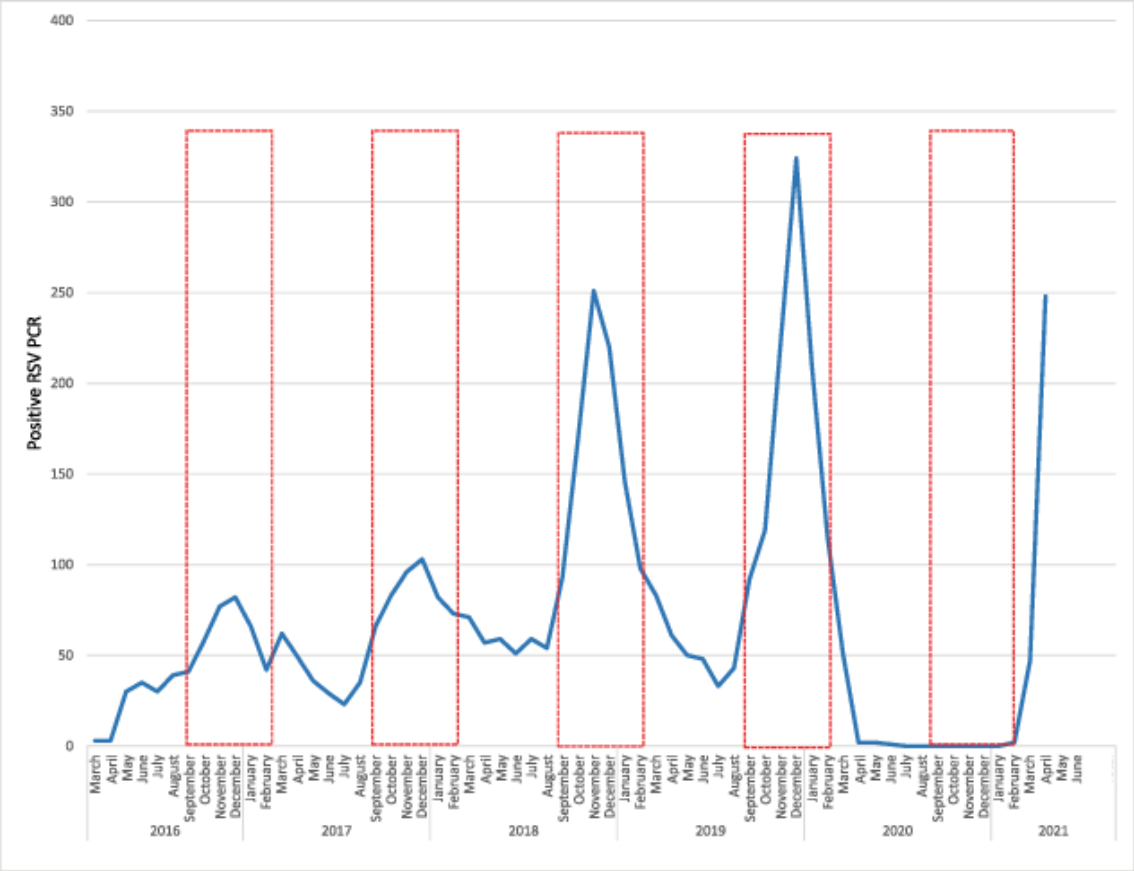


Figure Legend:

Annual RSV trends at our hospital from 2016 to April 30, 2021. The dashed red boxes represent the typical RSV season. No RSV cases were recorded for the 2020 Fall or Winter season. PCR, polymerase chain reaction.

American Academy of Pediatrics
DEDICATED TO THE HEALTH OF ALL CHILDREN®

From: **Delayed Seasonal RSV Surge Observed During the COVID-19 Pandemic**

Pediatrics. 2021;148(3). doi:10.1542/peds.2021-052089

Our data indicate more severe disease in younger infants, possibly because of diminished immunity from a lack of exposure to RSV in the previous season. Continuing closures of day care centers and virtual schooling may have resulted in less spread of the disease to older children.

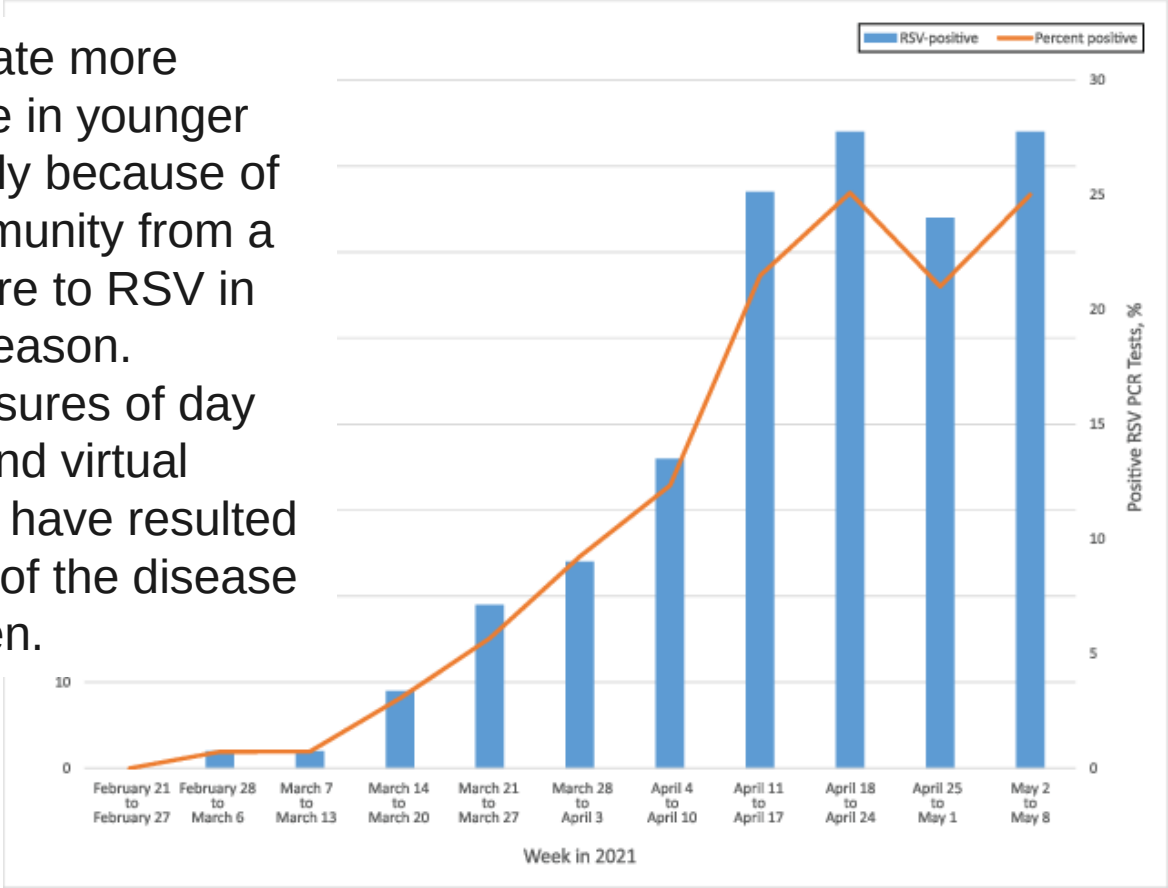
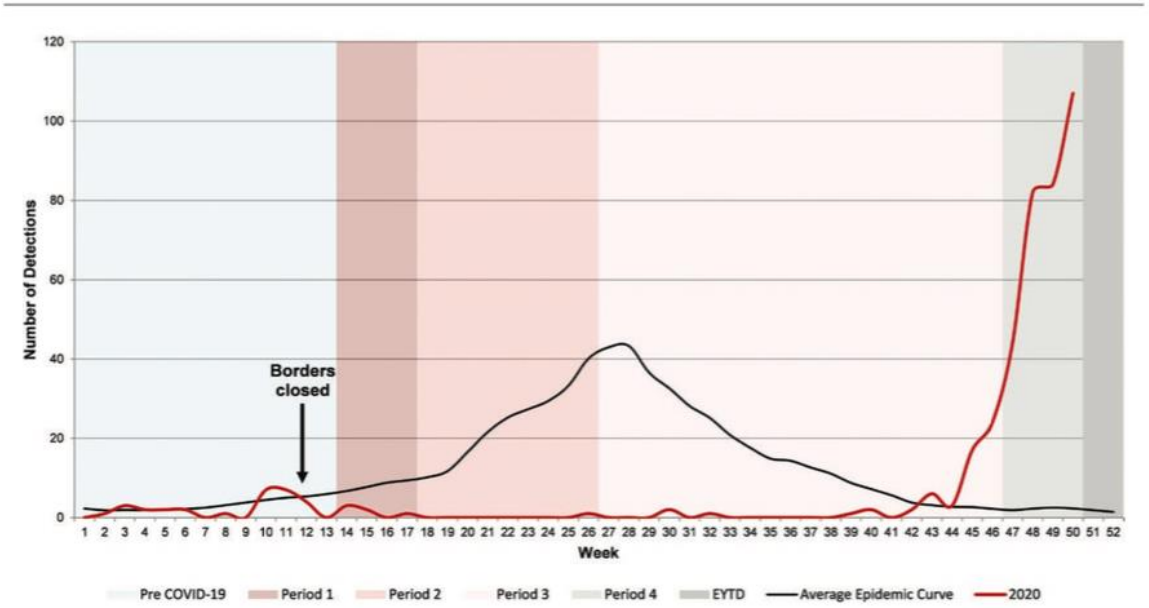


Figure Legend:

Weekly RSV positive cases in numbers from March 1 to May 8, 2021. The red line represents the percent positivity of RSV of all tested. PCR, polymerase chain reaction.

The Interseasonal Resurgence of Respiratory Syncytial Virus in Australian Children Following the Reduction of Coronavirus Disease 2019–Related Public Health Measures



RSV activity increased from late September, in the setting of relaxed physical distancing recommendations, ahead of the opening of interstate borders.

median patient age this year was 18.4 months, signi cantly higher than the upper range between 2012 and 2019 (7.3–12.5 months) ($P < .001$).

Clinical Infectious Diseases® 2021

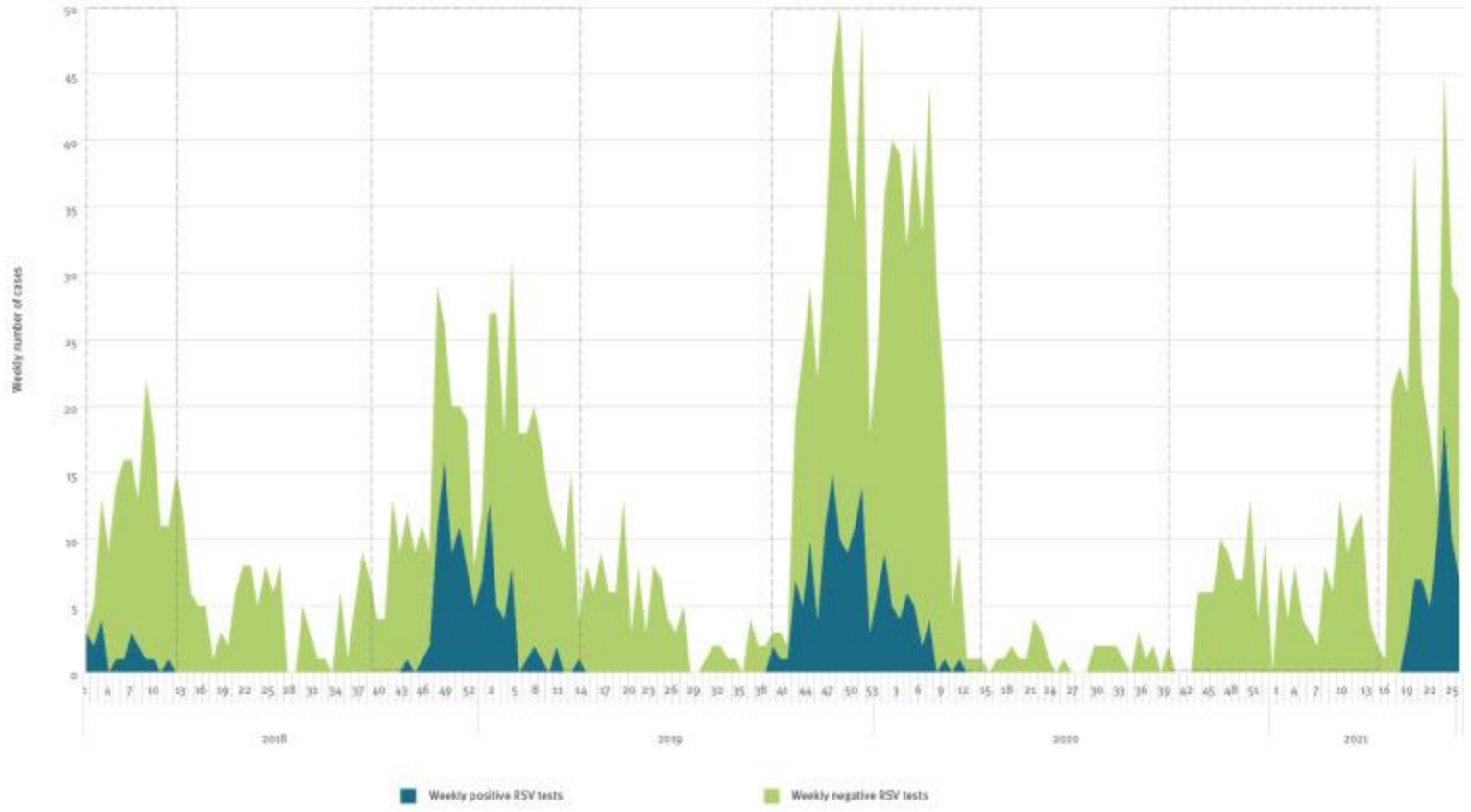
The Interseasonal Resurgence of Respiratory Syncytial Virus in Australian Children Following the Reduction of Coronavirus Disease 2019–Related Public Health Measures

- These data demonstrate the fragility of RSV control and the critical impact of physical distancing and respiratory hygiene practices. e rise in numbers and change in median age suggest that the expanded cohort of RSV-naïve patients, including an increased number of older children coupled with waning population immunity

- Our findings raise concerns for RSV control in the Northern Hemisphere, where a shortened season was experi- enced last winter [8]. e eventual reduc- tion of COVID-19–related public health measures may herald a signi cant rise in RSV [9].

Clinical Infectious Diseases® 2021

Delayed respiratory syncytial virus epidemic in children after relaxation of COVID-19 physical distancing measures, Ashdod, Israel, 2021



Weekly number of positive and negative respiratory syncytial virus tests, 1 January 2018−24 June 2021. Weekly positive RSV tests (blue area), with negative tests stacked on top (green area). The dashed rectangles mark the autumn/winter RSV seasons (calendar weeks 40–14). During 2021, no positive RSV cases were noted in autumn/winter but have appeared since week 19.

Weinberger Opek M et al. Euro Surveill. 2021 Jul;26(29):2100706.

Delayed respiratory syncytial virus epidemic in children after relaxation of COVID-19 physical distancing measures, Ashdod, Israel, 2021

Our study showed a temporal shift of the RSV epidemic during 2021 among hospitalised children in Ashod, with complete absence of cases during the autumn/winter of 2020/21, and a resurgence of cases in May to June 2021.

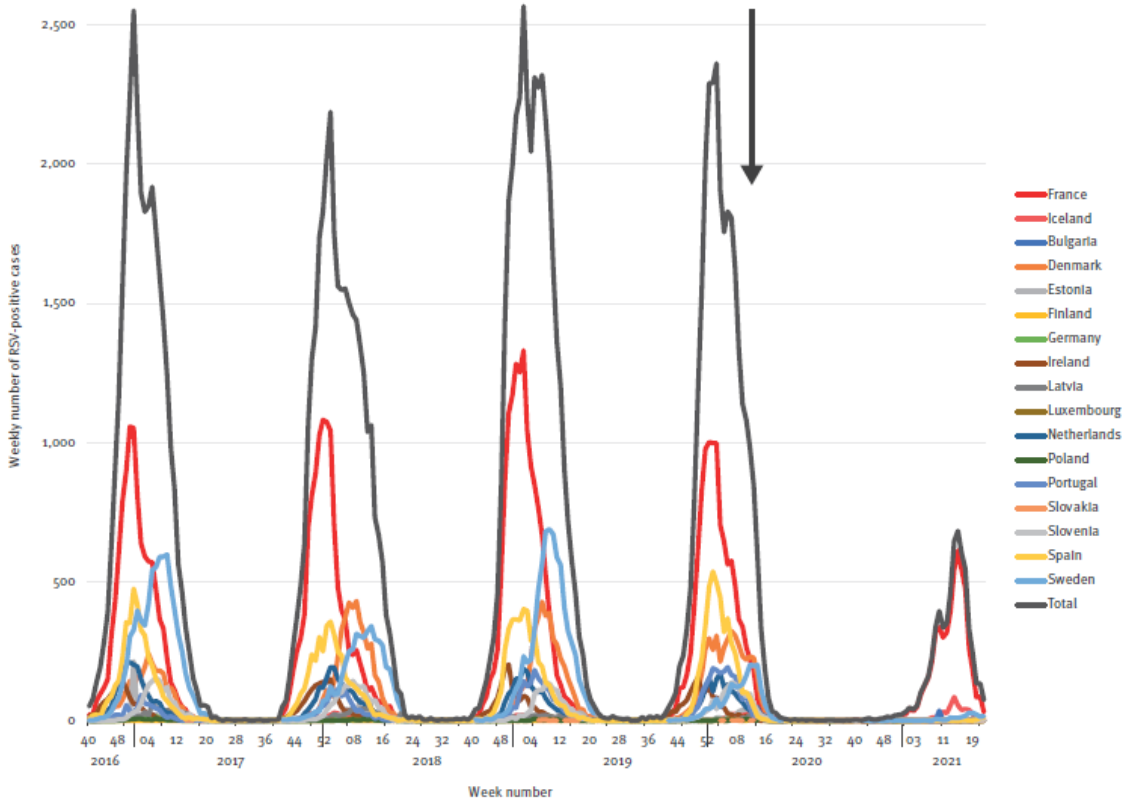
The 2021 spring/summer epidemic exceeded previous autumn/winter seasons in terms of weekly case counts and incidence in our paediatric population. Compared with previous seasons, the 2021 spring/summer epidemic included more children from the city of Ashdod as opposed to suburbs, and mainly from neighbourhoods with lower SES.

This pattern suggests higher incidence in more densely populated areas but might also represent earlier relaxation of COVID-19-related physical distancing measures in these populations.

Weinberger Opek M et al. Euro Surveill. 2021 Jul;26(29):2100706.

Low levels of respiratory syncytial virus activity in Europe during the 2020/21 season: what can we expect in the coming summer and autumn/winter?

Respiratory syncytial virus activity in Europe, week 40 2016 to week 20 2021 (n = 17 European Union countries)



Since the introduction of non-pharmacological interventions to control COVID-19, respiratory syncytial virus (RSV) activity in Europe has been limited.

Surveillance data for 17 countries showed delayed RSV epidemics in France (≥ 12 w) and Iceland (≥ 4 w) during the 2020/21 season.

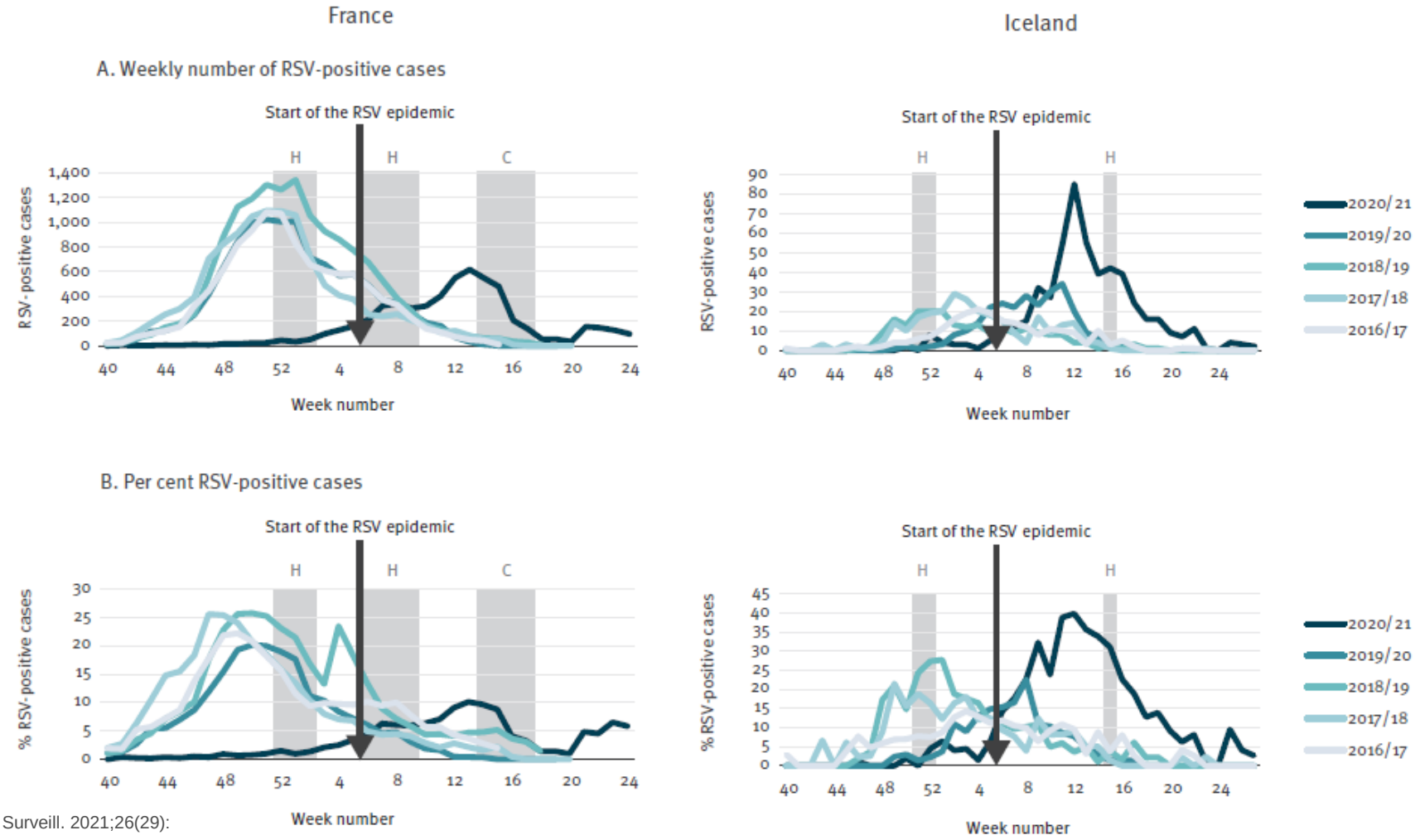
RSV cases (predominantly small children) in France and Iceland were older compared with previous seasons.

We hypothesise that future RSV epidemic(s) could start outside the usual autumn/ winter season and be larger than expected. Year-round surveillance of RSV is of critical importance.

Euro Surveill. 2021;26(29):

Low levels of respiratory syncytial virus activity in Europe during the 2020/21 season: what can we expect in the coming summer and autumn/winter?

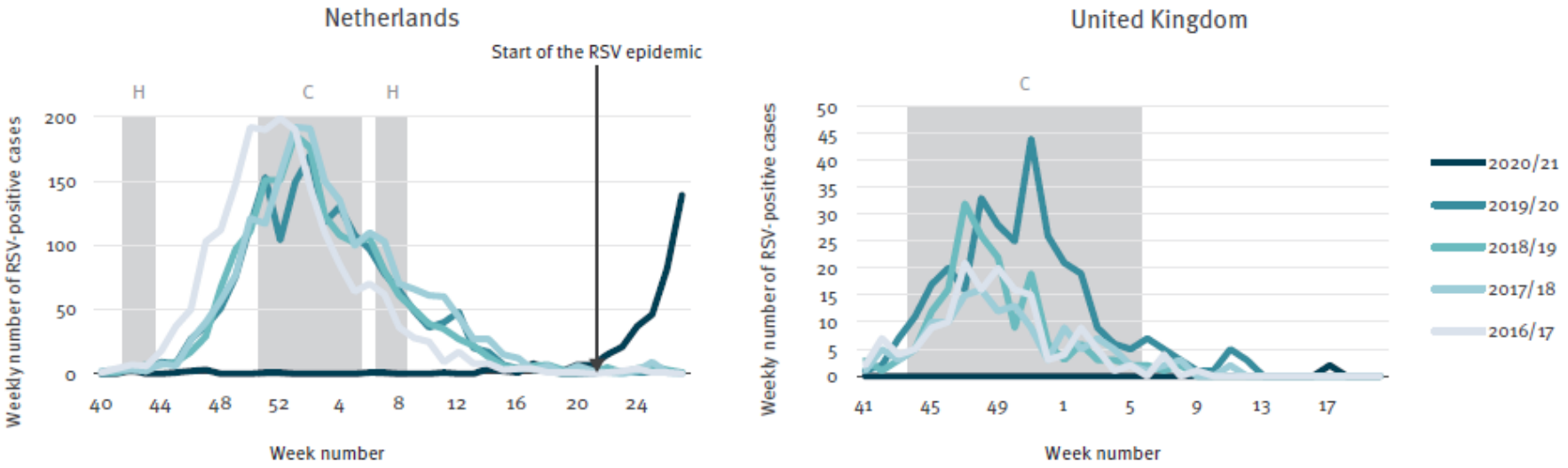
Respiratory syncytial virus activity in France, week 40 2016–week 24 2021 and Iceland, week 40 2016–week 27 2021



Euro Surveill. 2021;26(29):

Low levels of respiratory syncytial virus activity in Europe during the 2020/21 season: what can we expect in the coming summer and autumn/winter?

Respiratory syncytial virus activity in the Netherlands, week 40 2016-week 27 2021 and the United Kingdom, week 41 2016-week 20 2021



It might be hypothesised that primary school and day care facilities closures have an important impact on RSV transmission, as RSV is predominantly detected in young children [17]. In countries without an RSV epidemic, primary schools and day care centres were closed due to COVID-19 restrictions between November and March for at least 8 weeks (the Netherlands) and 9 weeks (UK) (Figure 3). On the contrary, in France and Iceland, primary schools and day care facilities were not closed, but some additional restrictions in schools were applied (Figure 2). Australia and South Africa also did not have primary school closures due to COVID- 19 restrictions in the weeks before their RSV epidemics started [7,10,16].

Euro Surveill. 2021;26(29):

Impact of COVID-19 social distancing on viral infection in France: A delayed outbreak of RSV

Abstract

Introduction: COVID-19 pandemic and associated lockdown measures have deeply modified the natural course of seasonal viral infections, such as respiratory syncytial virus (RSV).

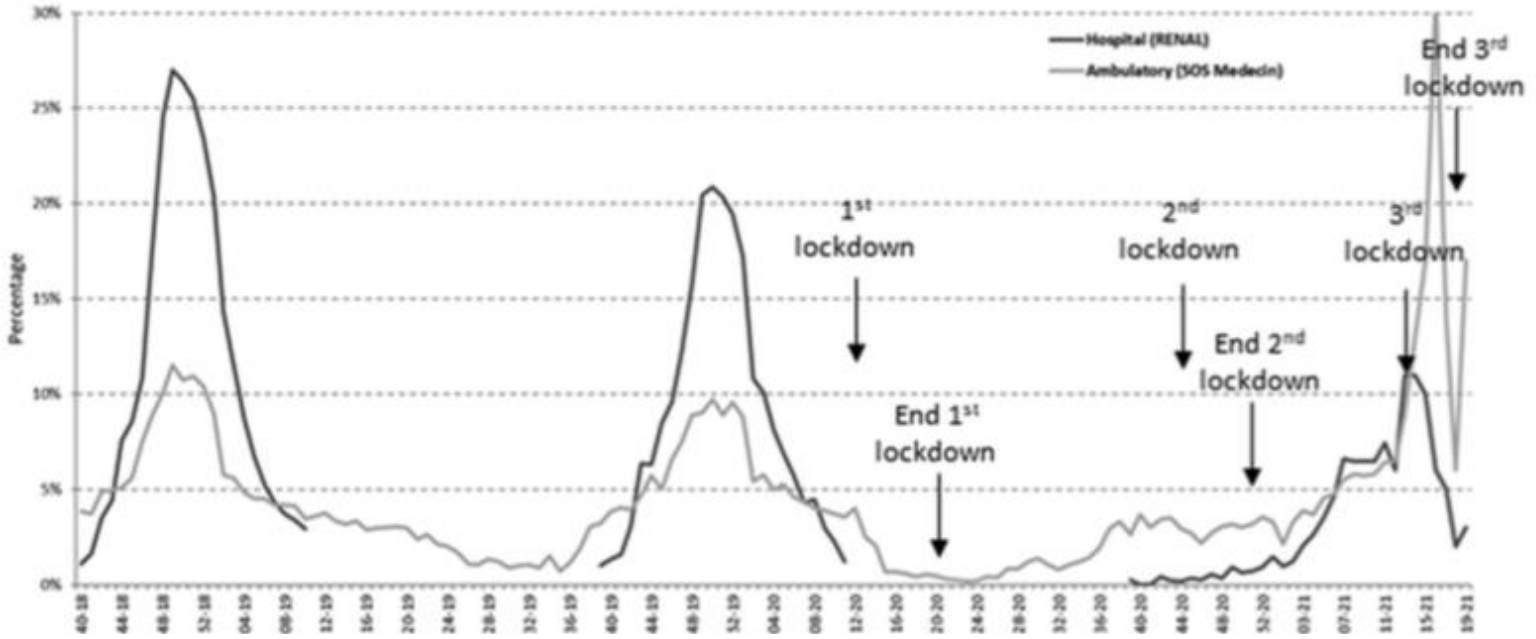
Methods: We analyzed French national data from three networks: emergency departments (ED) of French hospitals, general practitioners (GP), and hospital laboratories. We compared the number of ED or GP visits for bronchiolitis in children <2 years of age, and the percentage of RSV positive tests in the 2020 to 2021 season with those of the two previous seasons (2018–2019 and 2019–2020). We used time series of the previous 5 years to calculate epidemic thresholds.

Results: During the 2020–2021 season, the epidemic begun in February (Week 05) in the Ile de France (Paris and suburbs) region, 12 weeks later compared with the previous seasons and progressively spread across all the French metropolitan regions. The highest number of bronchiolitis cases in 2021 (Week 12) occurred 10–12 weeks after the previous seasonal peaks of previous seasons, but the number of cases remained lower than in the previous seasonal peaks.

Conclusion: We identified a delayed RSV epidemic in the period that usually corresponds at the end of the epidemic season, raising concerns for the burden of RSV in the already strained healthcare systems during the COVID-19 pandemic.

Céline Delestrain et al Pediatric Pulmonology. 2021;56:3669–3673

Impact of COVID-19 social distancing on viral infection in France: A delayed outbreak of RSV



In conclusion, we observed in France a delayed outbreak in the period that usually corresponds at the end of the epidemic season. At the end of the third lockdown, our findings together with the Australian reports raise concerns for RSV control in the Northern Hemisphere, where a rise in RSV may occur after a shortened winter season increasing the burden in the pediatric structures and the al- ready strained healthcare systems.

Céline Delestrain et al Pediatric Pulmonology. 2021;56:3669–3673

Bronchiolitis, epidemiological changes during the SARS-CoV-2 pandemic

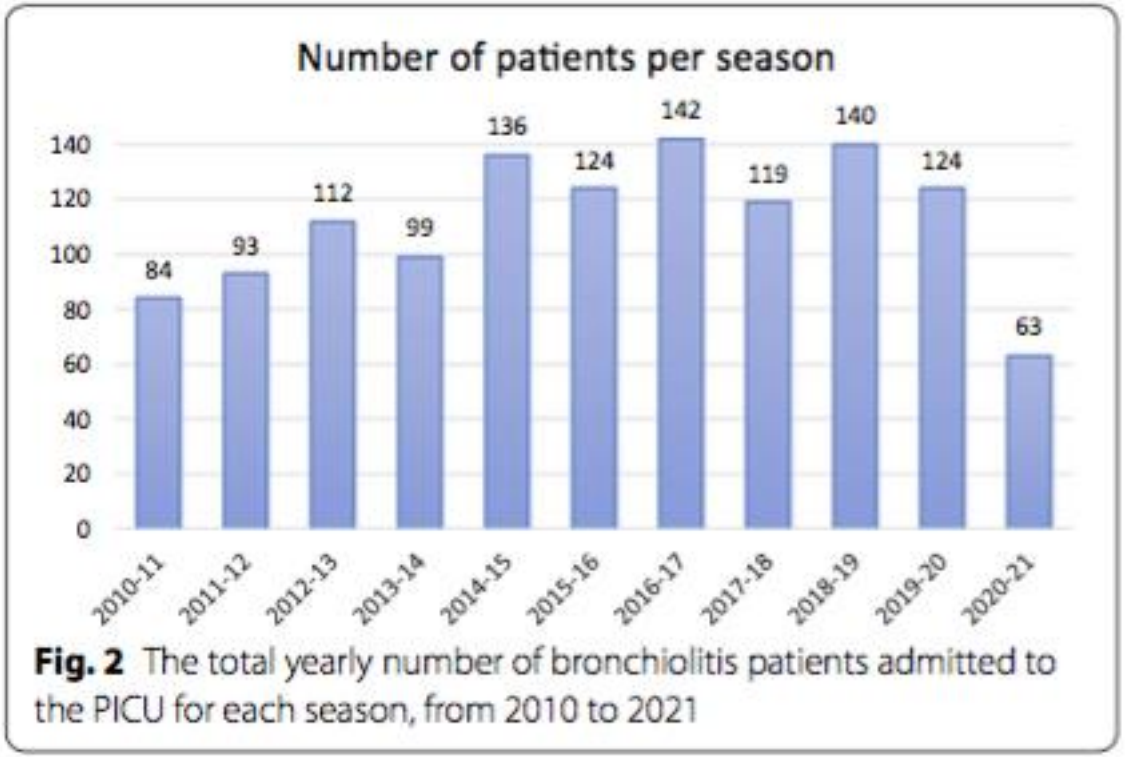


Fig. 2 The total yearly number of bronchiolitis patients admitted to the PICU for each season, from 2010 to 2021

Guitart *et al. BMC Infectious Diseases (2022) 22:84*

Bronchiolitis, epidemiological changes

Influence of the environmental temperature does not seem to have induced the viral distribution seen this last year, related to severe bronchiolitis, and thus other factors beyond temperature should be investigated.

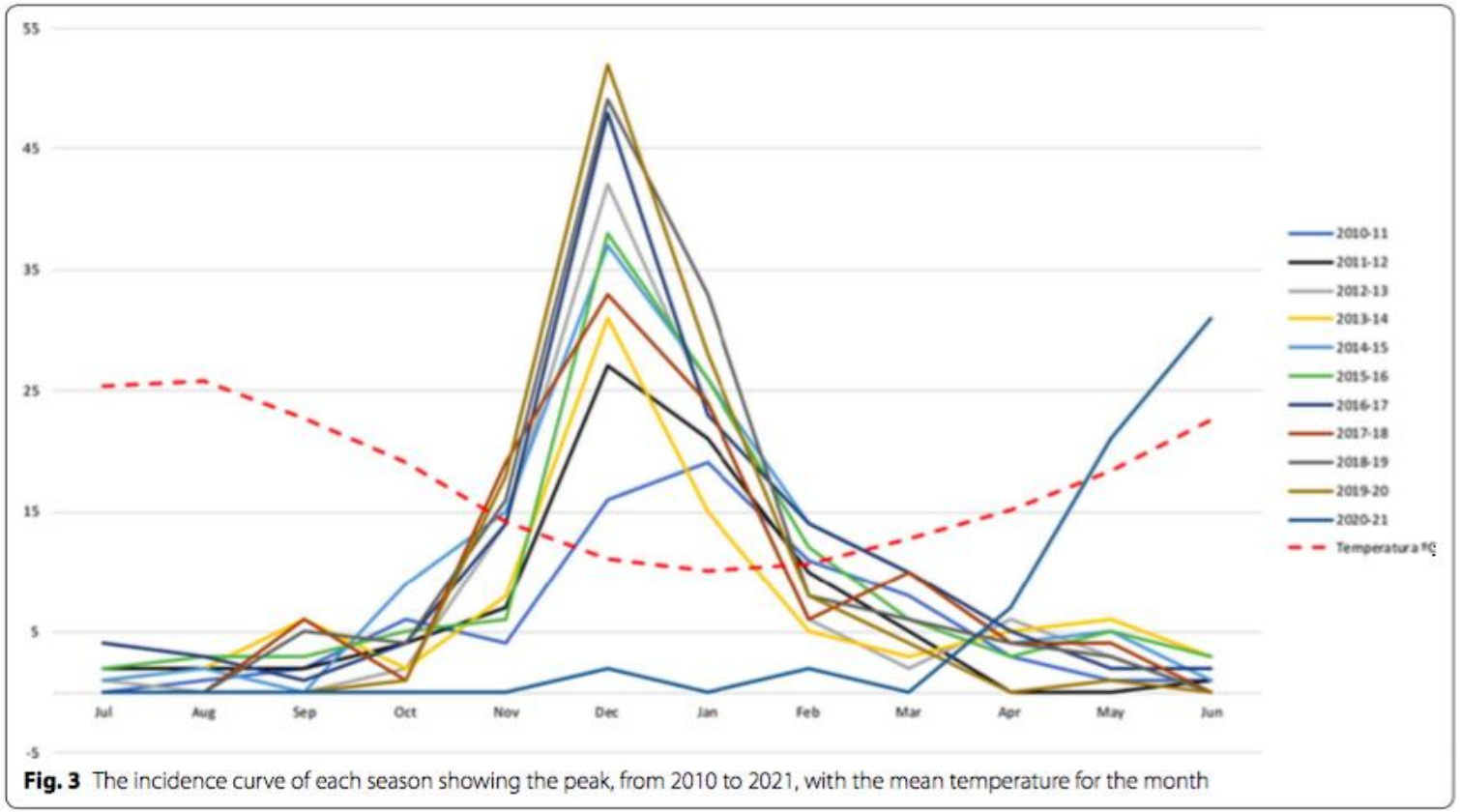


Fig. 3 The incidence curve of each season showing the peak, from 2010 to 2021, with the mean temperature for the month

Guitart *et al. BMC Infectious Diseases (2022) 22:84*

During the COVID-19 pandemic where has respiratory syncytial virus gone?

Abstract

The diffusion of the SARS-CoV-2 virus and the implementation of restrictive measures led to a drastic reduction of respiratory syncytial virus (RSV) diffusion. Few RSV cases have been detected worldwide, even after the removal of the restrictions. We review the current literature and present possible explanations on why there has been a significant reduction of RSV detection during the COVID-19 pandemic. We also hypothesize what may happen when RSV begins to circulate again. The increase of an immunologically naïve population, with infants born from mothers who have not reinforced their immunity to RSV, could lead to greater RSV epidemics in the coming seasons. It is crucial to prepare the scientific community and to keep RSV surveillance active to avoid dramatic consequences.

Di Mattia G et al. Pediatric Pulmonology. 2021;1–4.

During the COVID-19 pandemic where has respiratory syncytial virus gone?

- The coronavirus disease 2019 (COVID-19) was declared a pandemic on March 11, 2020, and restrictive measures have been implemented worldwide, with the aim of reducing social contacts.
- These measures had a positive effect not only on SARS-CoV-2 diffusion, but also significantly reduced the spread of respiratory infections caused by other respiratory viruses.
- The most evident impact is the significant reduction of respiratory syncytial virus (RSV) cases from March 2020, both in the Southern and in the Northern Hemisphere.

Di Mattia G et al. Pediatric Pulmonology. 2021;1–4.

During the COVID-19 pandemic where has respiratory syncytial virus gone?

Thus, the risk is that when RSV will circulate again, like in Western Australia, it will find a larger cohort of immunologically naïve individuals and will cause major and more severe epidemics. A mathematical model predicted that the longer the control measures will reduce the RSV diffusion, the larger the future epidemics will be.[34]

Considering the high mortality rate of RSV infection not only in infants but also in the elderly, efforts are needed to prevent a future RSV severe epidemic.[35]

RSV surveillance must be implemented, reservoirs and circulating variants need to be isolated, and research for potential vaccines needs to be accelerated.

Even in the presence of the SARS-CoV-2 pandemic, the other respiratory pathogens should not be forgotten, as the consequences could be dramatic.

Di Mattia G et al. Pediatric Pulmonology. 2021;1–4.

The Disappearance of Respiratory Viruses in Children during the COVID-19 Pandemic

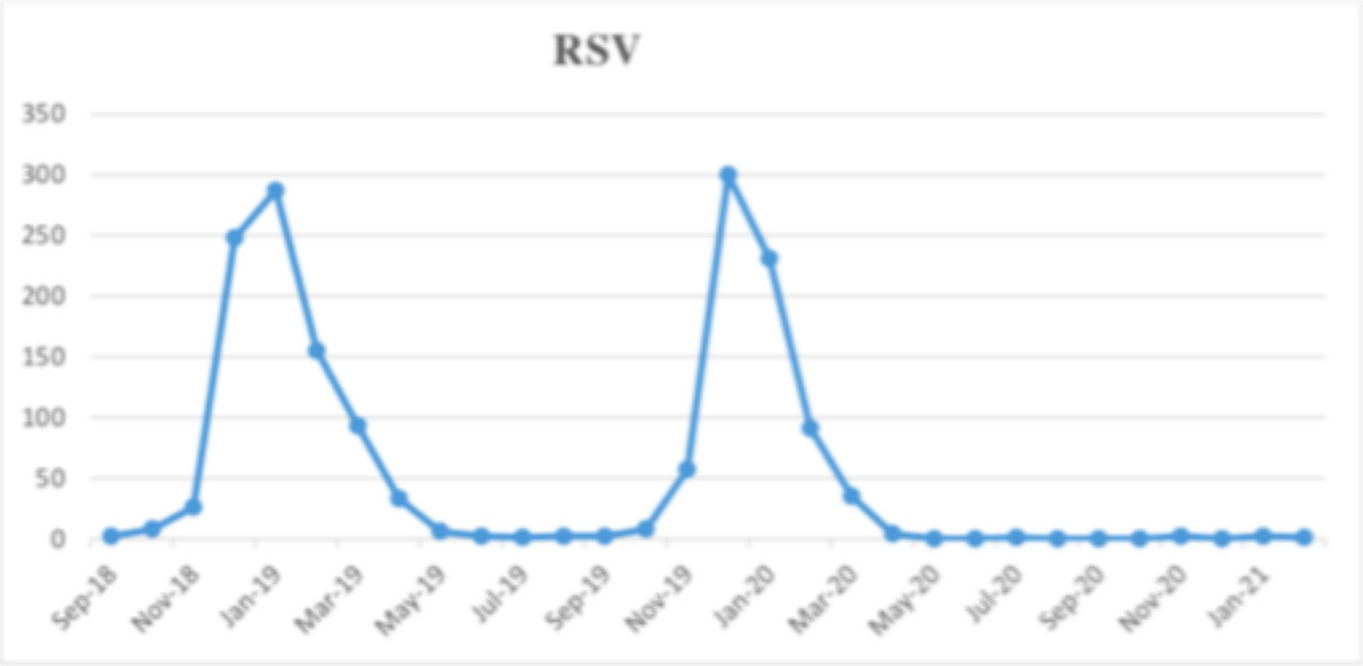
Background: Social distancing measures are used to reduce the spreading of COVID-19. The aim of this study was to assess the impact of local restrictions on the transmission of respiratory virus infections. Methods: we retrospectively analyzed the nasopharyngeal samples of all patients (0–18 years old) admitted with respiratory symptoms in a large Italian tertiary hospital during the last three seasons from 2018 to 2021. Results: A strong reduction in all viral respiratory infections was observed in the last season (2020–2021) compared to the two previous seasons (−79.69% and −80.66%, respectively). In particular, we found that during the epidemic period 2018–2019 and 2019–2020, the total number of Respiratory Syncytial Virus (RSV) cases was, respectively 726 and 689, while in the last season a total of five cases was detected. In the first months of 2018–2019 and 2019–2020, the total flu infections were 240 and 354, respectively, while in the last season we did not detect any influenza virus. As other viruses, the presence of Rhinovirus declined, but to a lesser extent: a total of 488 cases were assessed compared to the 1030 and 1165 cases of the two previous respective epidemic seasons. Conclusions: Public health interventions and distancing (including continuous use of face masks) settled to counter the pandemic spread of COVID-19 had a macroscopic impact on all respiratory virus transmission and related diseases, with a partial exception of Rhinovirus. ***The absence of viruses' circulation could result in a lack of immunity and increased susceptibility to serious infections in the next seasons.***

Vittucci AG et al. Int. J. Environ. Res. Public Health **2021**,*18*,9

The Disappearance of Respiratory Viruses in Children during the COVID-19 Pandemic

A strong reduction was observed in the third season: −79.69% compared to 2018–2019 and −80.66% compared to 2019–2020.

Figure 1 shows the epidemiological curves of RSV, flu, and HRV, the three most involved respiratory viruses, during the last 3 years.



(a)

Figure 1. *Cont.*

The Disappearance of Respiratory Viruses in Children during the COVID-19 Pandemic

Table 1. Infections detected at Bambino Gesù Children's Hospital.

	ADV	BoV	CoV	EV	Flu	MPV	PIV	RV	RSV
Season 2018–2019: total 3029									
Sep-18	12	8	7	54	0		31	128	2
Oct-18	23	15	11	43	3		43	188	8
Nov-18	42	14	23	28	0	1	55	148	26
Dec-18	64	39	59	31	10	5	52	214	248
Jan-19	39	39	56	23	105	12	28	210	287
Feb-19	32	44	53	10	122	17	20	142	155
	212	159	209	189	240	35	229	1030	726
Season 2019–2020: total 3180									
Sep-19	13	6	4	11	1	0	13	123	2
Oct-19	26	8	1	21	0	0	34	191	8
Nov-19	36	18	6	38	2	2	69	167	57
Dec-19	49	42	20	68	22	9	36	283	300
								239	231
								162	91
								165	689
								63	0
								135	0
								82	2
								66	0
								66	2
								76	1
								488	5
								eumovirus (MPV)	

- Public health measures imposed to prevent COVID-19 pandemic spread (social distancing, face masks, and non-pharmaceutical interventions) were effective at mitigating the diffusion of all respiratory infections, with a partial exception of Rhinovirus.
- The reduction in respiratory viruses' circulation could result in a lack of immunity in a cohort of children and increased susceptibility to serious infections in the next seasons.
  - Proper preparation of the health system and good education of caregivers will provide fundamental help.

www.mdpi.com/journal/ijerph *Int. J. Environ. Res. Public Health* **2021**, *18*, 9

A single centre study of viral community-acquired pneumonia in children: No evidence of SARS-CoV-2 from October 2019 to March 2020

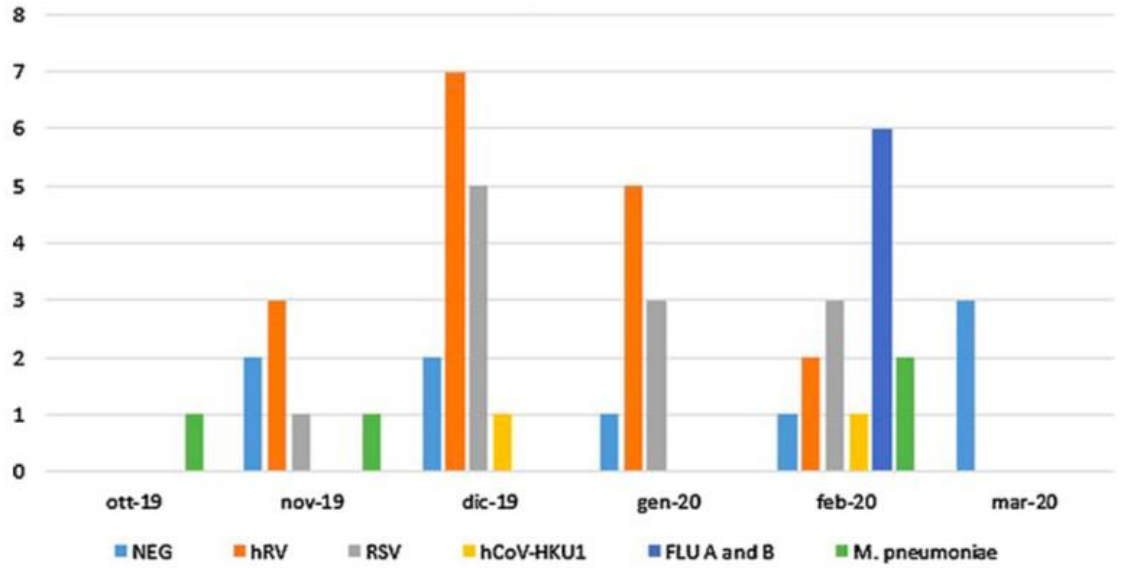


Fig. 1. Pathogens distribution (hRV, RSV, hCoV-HKU1, FLU A and B, M. pneumoniae) in children hospitalized for CAP, between October 2019 and March 2020.

Environmental risk factors such as household crowding and air pollution, as well as viru- lence factors, play a fundamental role in developing lower respiratory infection [13] and particularly pneumonia [14].

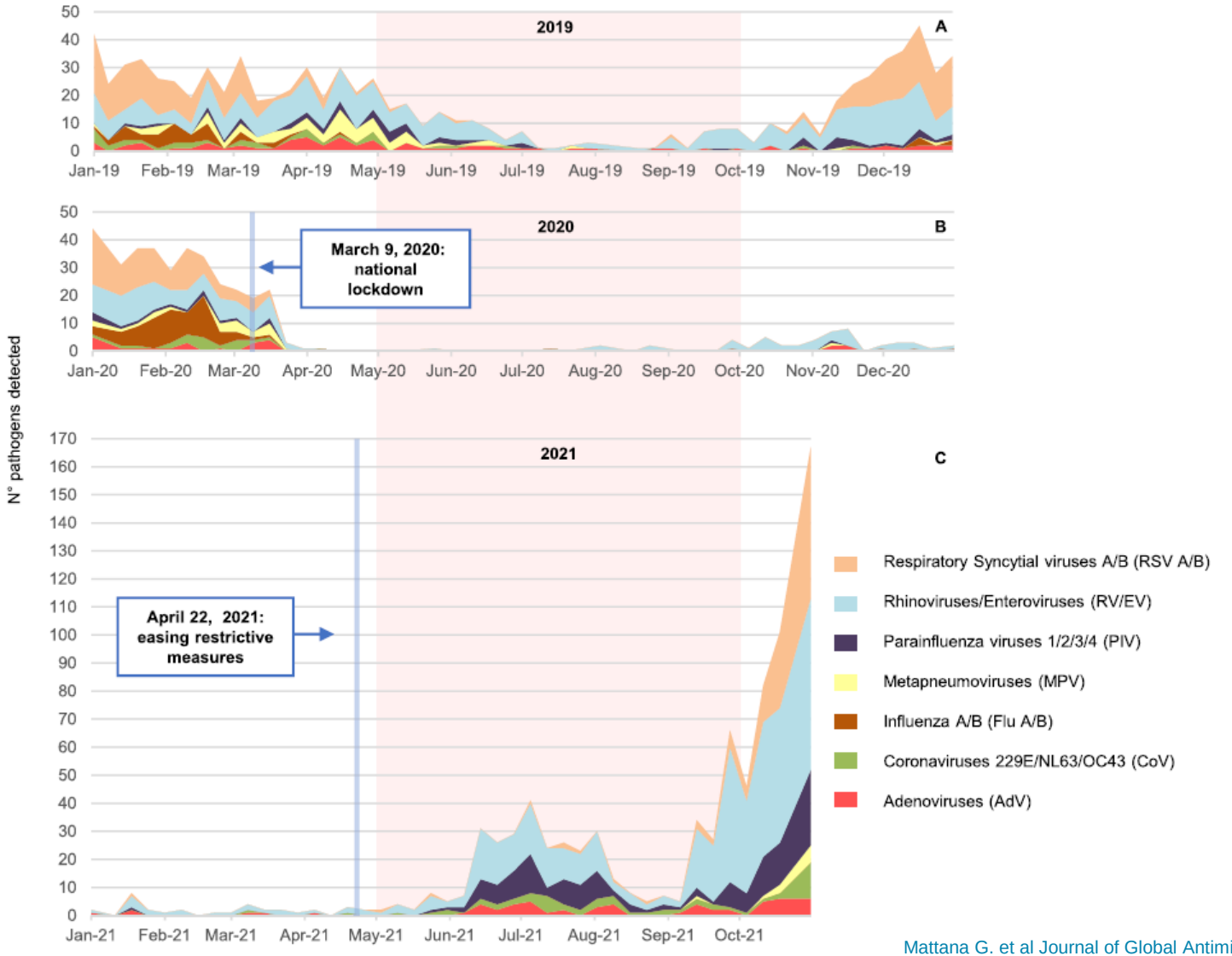
Accordingly, the lockdown that Italian authorities established to confine COVID-19 and the resulting decrease in social interactions (schools and day nurseries closure) were likely determinant in reducing CAP which required hos- pitalization.

Il virus arrivato in anticipo di 2 mesi

Anche Fabio Midulla, presidente della Società italiana per le malattie respiratorie infantili (Simri), professore ordinario all'Università La Sapienza e responsabile del Pronto Soccorso pediatrico del Policlinico Umberto I di Roma, ha confermato che l'epidemia è arrivata con due mesi di **anticipo**.
Si tratta di uno dei virus respiratori che circola maggiormente nel mondo, in particolare durante la stagione invernale. Colpisce a tutte le età, ma in maniera più grave i neonati, i lattanti nei primi mesi di vita e gli anziani con più patologie. Nei più piccoli sotto l'anno di età può portare a bronchiolite e apnee. Esistono poi anche dei soggetti ritenuti particolarmente a rischio, come i bambini cardiopatici o con una grave prematurità o che hanno problemi del neurosviluppo. Nelle persone anziane con comorbidità è un virus pericoloso al pari del Covid.

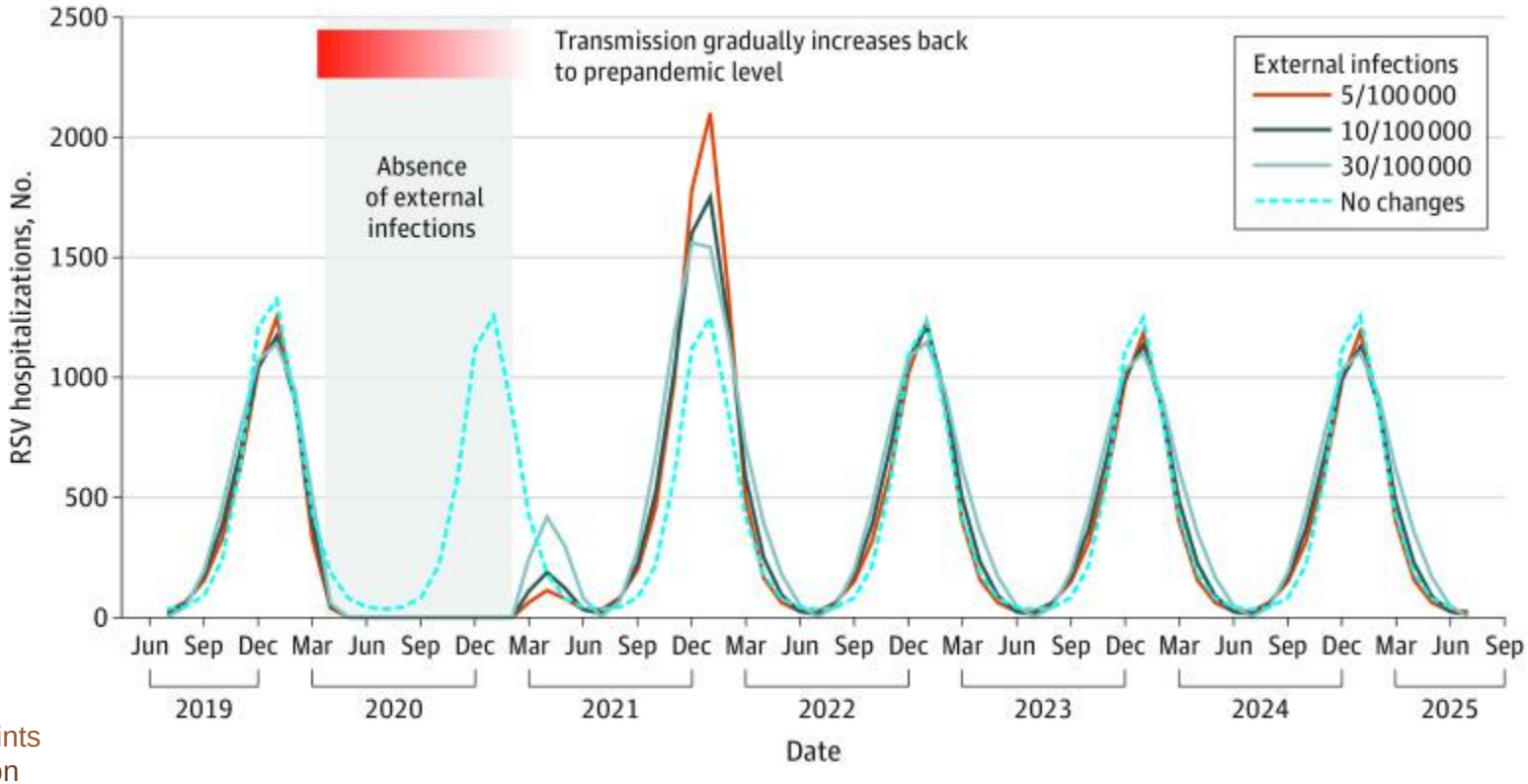
In tutto il mondo si contano 33milioni di infezioni respiratorie all'anno che colpiscono bambini sotto i 5 anni di età e il 20% è legata al virus respiratorio sinciziale, con 3milioni di ricoveri e circa 100mila morti ogni anno, soprattutto nei Paesi in via di sviluppo.

Back to the future (of common respiratory viruses)



Mattana G. et al Journal of Global Antimicrobial Resistance 28 (2022) 223–22

Estimation of the Timing and Intensity of Reemergence of Respiratory Syncytial Virus Following the COVID-19 Pandemic in the US



Key Points

Question

What are the factors associated with the timing and intensity of reemergent respiratory syncytial virus (RSV) epidemics following the COVID-19 pandemic?

Findings

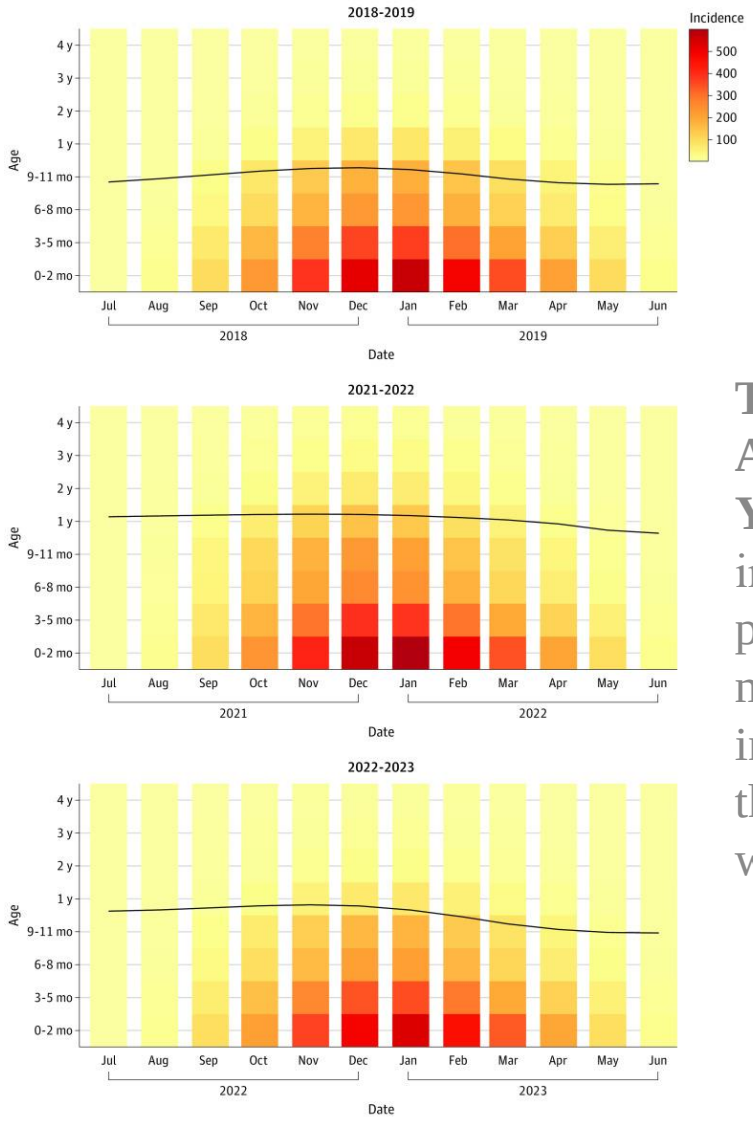
In this simulation modeling study of a simulated population of 19.45 million people, virus introduction from external sources was associated with the spring and summer epidemics in 2021. Reemergent RSV epidemics in 2021 and 2022 were projected to be more intense and to affect patients in a broader age range than in typical RSV seasons.

Meaning

These findings suggest that the timing and intensity of reemergent RSV epidemics might be different from the usual RSV season, depending on the duration of mitigation measures and the extent of virus introduction from other regions.

Zhe Zheng ET AL. JAMA Netw Open. 2021 Dec; 4(12): e2141779.

Estimation of the Timing and Intensity of Reemergence of Respiratory Syncytial Virus Following the COVID-19 Pandemic in the US



The Mean Age of RSV Hospitalizations Among Children Aged Younger Than 5 Years The background color represents the incidence of RSV hospitalization per 100 000 people per month in each age group in each month. Darker red colors indicate a higher incidence. The black line and values indicate the mean age of hospitalization (in years) varies with time.

Zhe Zheng ET AL. JAMA Netw Open. 2021 Dec; 4(12): e2141779.

Estimation of the Timing and Intensity of Reemergence of Respiratory Syncytial Virus Following the COVID-19 Pandemic in the US

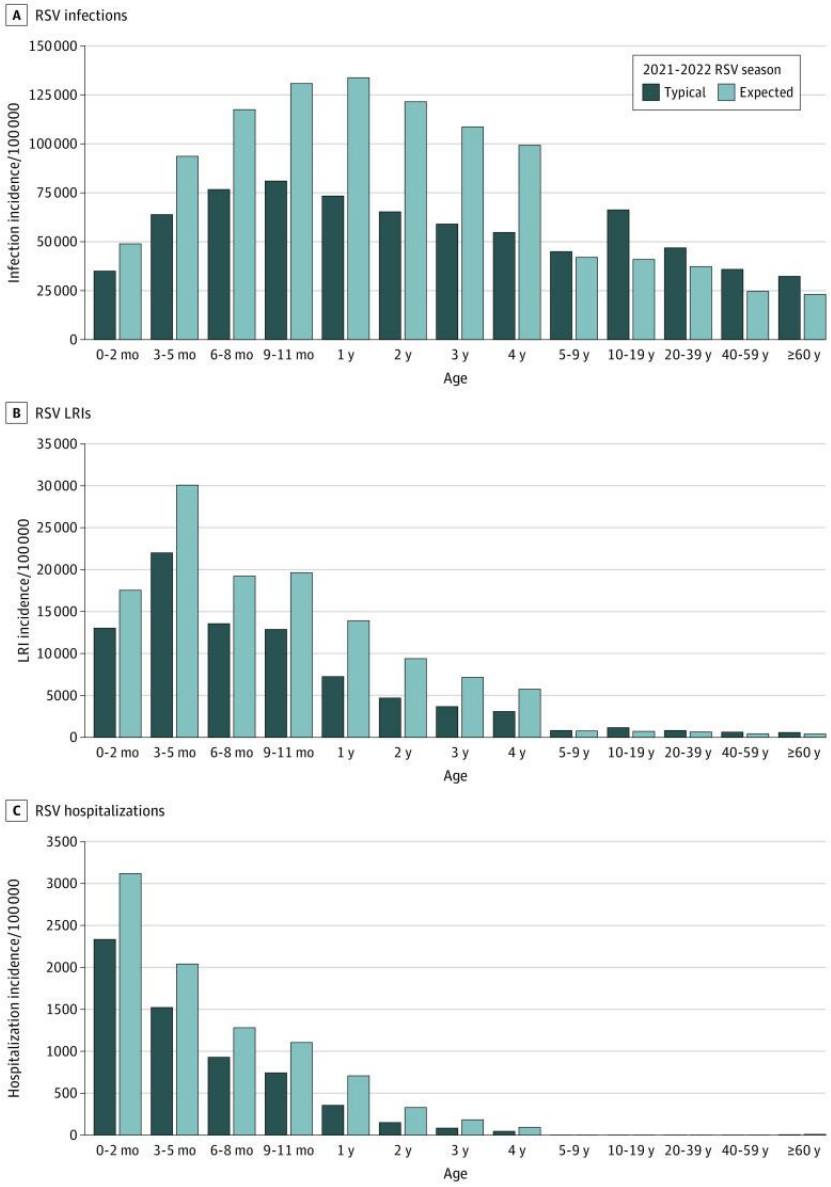


Figure 3.. Age Distribution of Respiratory Syncytial Virus (RSV) Infections, Lower Respiratory Infections (LRIs), and Hospitalizations, 2021-2022 RSV Season The figures show a comparison of RSV infections (A), RSV LRIs (B), and RSV hospitalizations (C) during a typical season (counterfactual incidence of RSV cases during the 2021-2022 RSV season if there was no COVID-19 pandemic and no mitigation measures in place) and the expected season (expected incidence of RSV cases during the 2021-2022 RSV season under the assumption that substantial virus importation was disrupted by mitigation measures between April 2020 and February 2021).

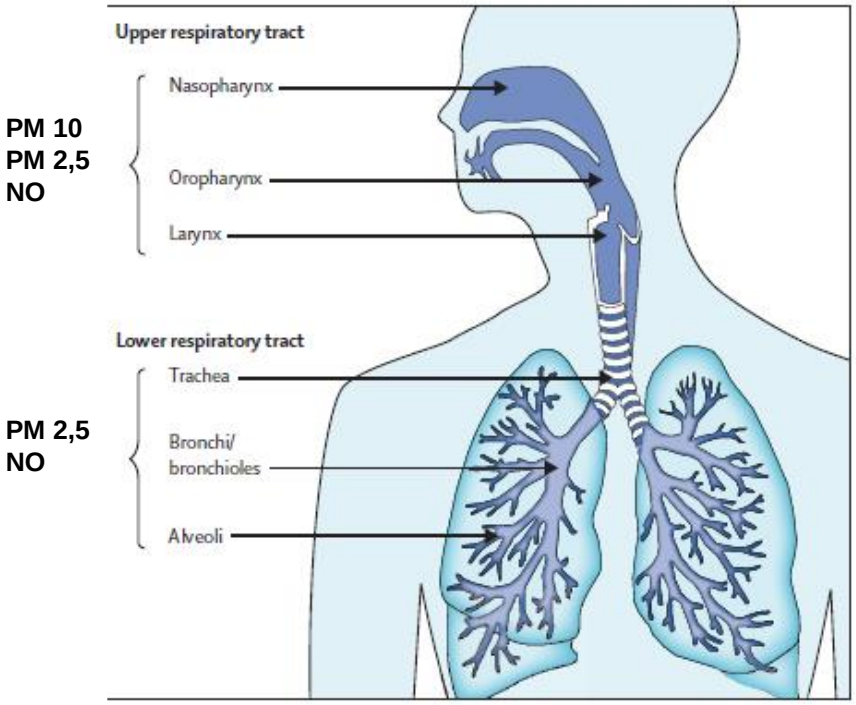
Zhe Zheng ET AL. JAMA Netw Open. 2021 Dec; 4(12): e2141779.

Discussione

- ***L'inquinamento ambientale porta all'aumento dei sintomi respiratori*** (irritazione di naso e gola, seguiti da tosse e difficoltà respiratoria), ad una ***ridotta funzione polmonare*** ed ***un'aumentata reattività bronchiale***. Vari studi si sono concentrati sugli effetti sulla salute di detti inquinanti, sia nel periodo prenatale che post-natale .

- ***I bambini risultano essere più suscettibili agli inquinanti ambientali.*** La loro peculiarità e vulnerabilità risiede nel fatto che ***l'epitelio delle vie aeree è più permeabile agli inquinanti*** ed i loro ***meccanismi di difesa sono incompleti ed immaturi.***

- Altro dato fondamentale è che i bambini hanno una ***frequenza respiratoria più alta*** che l'adulto e per questo inalano un volume di aria maggiore per superficie corporea.



Discussione

Cosa potete fa

Le cose che p
vostro e del v
evitarne l'ulte

- Accurato la
  altri prima
- Evitate di t
- Pulite le su
  con il virus,
  piani dei ta
- Se possibile
  da persone
- Evitate l'es
  rischio di in

Piano d'azione

- ✔ Evitate l'esposizione ai virus quali il VRS lavando spesso e accuratamente le mani
- ✔ Evitate i contatti con persone malate e superfici che possano essere contaminate
- ✔ Se pensate che il vostro bambino possa essere ad alto rischio, parlate con il vostro medico per capire se deve essere sottoposto a terapia con palivizumab durante la stagione epidemica VRS
- ✔ Se il vostro bambino è ad alto rischio, evitate di frequentare asili e posti affollati che possono aumentare i contatti con soggetti infetti.

Le persone che hanno sintomi da raffreddore dovrebber

- Riparare i propri colpi di tosse e gli starnuti
- Lavare frequentemente e correttamente le mani
- Astenersi dal baciare gli altri e stare il più lontano possibile da soggetti ad alto rischio

Autori: Marianna Sockrider MD DrPH, **Testo originale:** www.thoracic.org

DISCUSSIONE

- Per proteggere i bambini più piccoli esiste una profilassi con anticorpi monoclonali, rivolta a tutti i bambini nati entro 34 settimane e 6 giorni, che al momento dell'inizio dell'epidemia abbiano meno di 6 mesi

- Per i nati sotto le 29 settimane la somministrazione viene effettuata, invece, fino ai 12 mesi.

-Per i piccoli che presentano fattori di rischio a causa di altre patologie, si prosegue fino ai 2 anni.

- Consiste in 5 iniezioni intramuscolari da effettuare una volta ogni 30 giorni, durante la stagione epidemica.

DISCUSSIONE

Le attuali politiche di immunizzazione passiva per i bambini ad alto rischio potrebbero dover essere riconsiderate in relazione a:

(i) estendere le indicazioni dell'immunizzazione passiva a bambini leggermente più grandi,

(ii) somministrare l'immunizzazione passiva al di fuori della consueta stagione invernale

(iii) somministrare l'immunizzazione passiva per un periodo di tempo più lungo.

DISCUSSIONE

- Gli sforzi di ricerca e sviluppo del vaccino RSV sono progrediti significativamente negli ultimi anni, con circa diciannove vaccini e due anticorpi monoclonali di nuova generazione.

- È possibile che un vaccino materno RSV per prevenire l'infezione da RSV nei neonati sia autorizzato nei prossimi anni.[16]

- Le linee guida prevedono la gestione della bronchiolite basata sull'evidenza. La profilassi passiva è un modo sicuro ed efficace per proteggere i bambini a rischio di malattia da virus respiratorio sinciziale grave ma non è costo-efficace.

DISCUSSIONE

- La nuova emergenza di epidemia di RSV che stiamo vivendo è dovuta principalmente a:

- Riduzione delle norme di distanziamento sociale, ripresa delle attività all'aperto e scolastiche

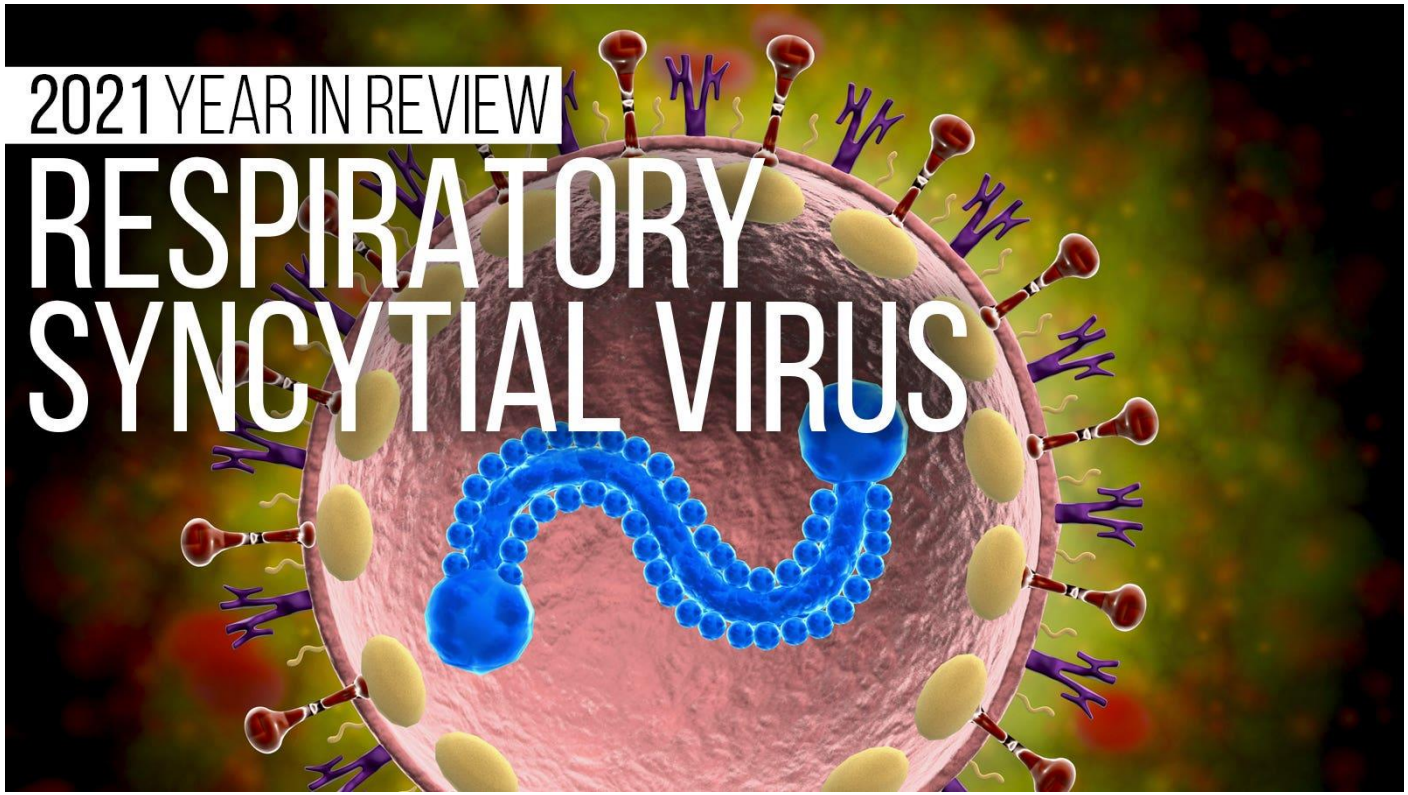
- Scarsa immunità sviluppata durante il lockdown sia nelle madri che nei bambini

CONCLUSIONI

-L’RSV è una delle principali sfide rimaste nelle malattie infettive e una delle principali cause di ricovero in ospedale tra i bambini piccoli, in particolare nei neonati pretermine.

-Le principali sfide per il futuro consistono soprattutto nella messa a punto di nuovi vaccini e di anticorpi monoclonali per potenziare la fase preventiva evitando, così, ospedalizzazioni e complicanze.

-La conoscenza dell’epidemiologia, attuabile tramite programmi di sorveglianza ad hoc, è utile per pianificare strategie preventive, sia nel caso di immunizzazione passiva con anticorpi monoclonali ricombinanti sia nel caso di immunizzazione attiva materna o infantile.



Progress continued on a vaccine against respiratory syncytial virus (RSV) for older adults, while the country experienced a resurgence in infections among young children this year that caused the CDC to issue a Health Advisory on the illness.

GRAZIE