Infezione da RSV: impatto su famiglie e pediatri

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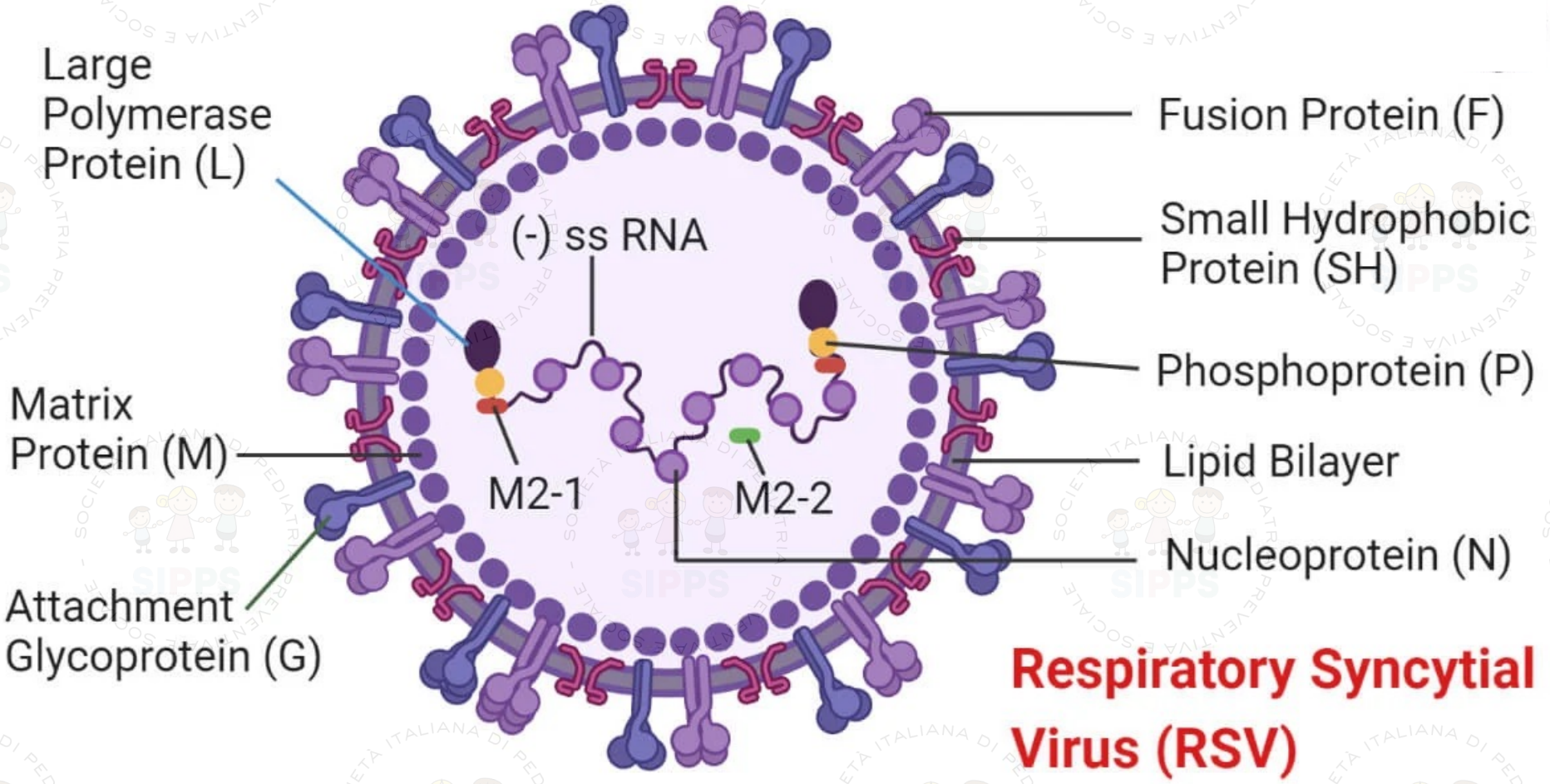
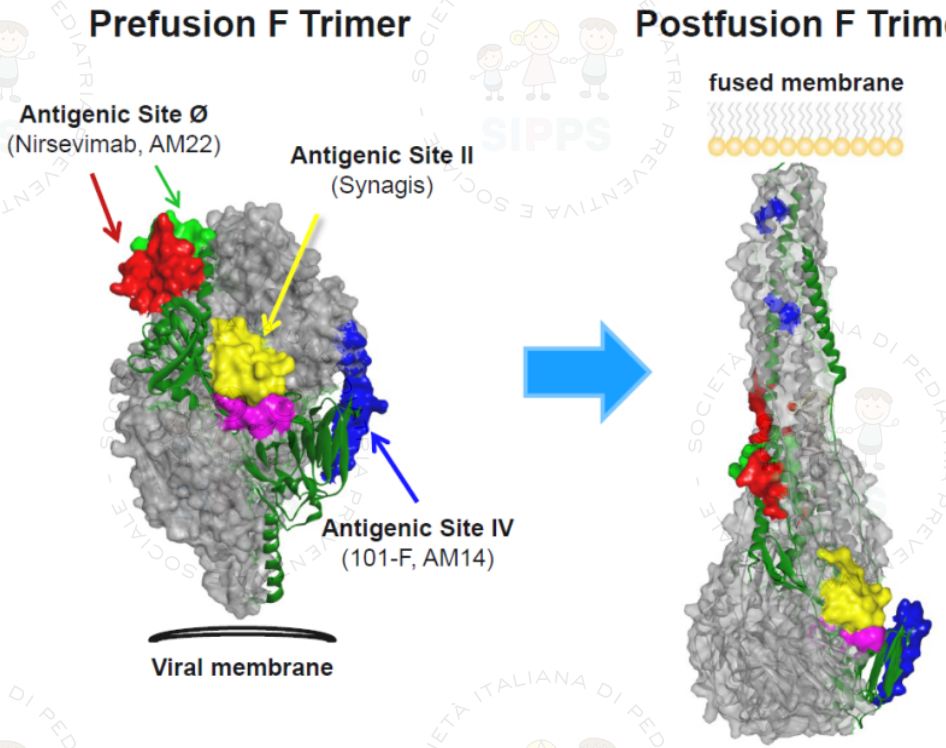

Large Polymerase Protein (L)
Matrix Protein (M)
Attachment Glycoprotein (G)
(-) ss RNA
M2-1
M2-2
Fusion Protein (F)
Small Hydrophobic Protein (SH)
Phosphoprotein (P)
Lipid Bilayer
Nucleoprotein (N)
Respiratory Syncytial Virus (RSV)

Groundbreaking Structural Work by NIH Elucidated that RSV F on the Virus Exists as an Unstable Prefusion Form



Only prefusion F can bind host cells for RSV to infect

Antibodies specific to the prefusion form are most effective at blocking virus infection

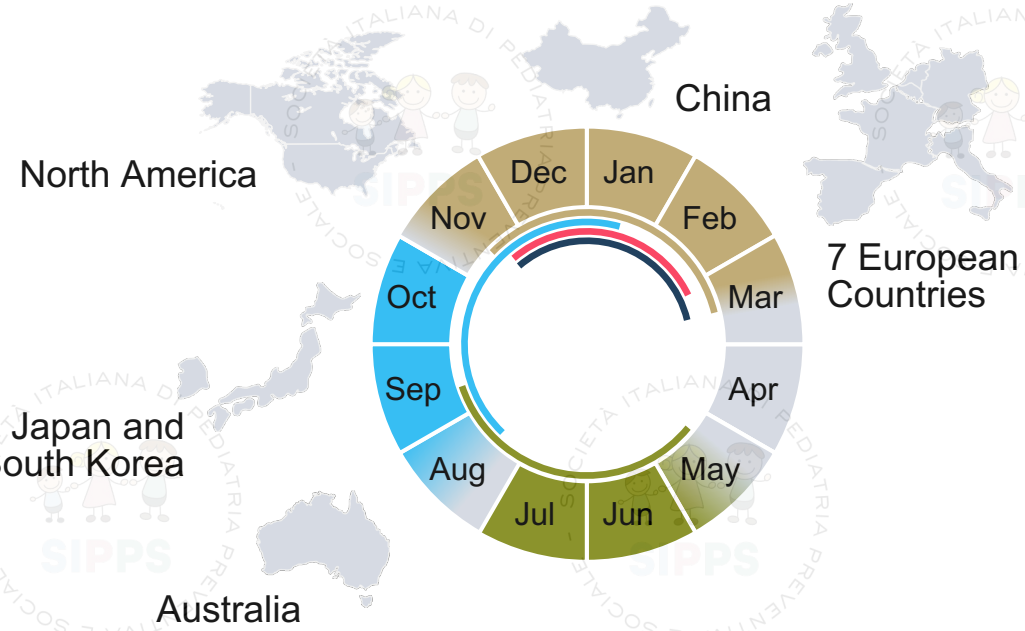
McLellan et al. *Science*, Nov 2013

Comparison of individual RSV infections by demographic, clinical and laboratory variables

(from Esposito S, et al. PLoS ONE 2015)

Characteristic	RSV-A n = 131	RSV-B n = 34	P value A vs B	RSV- A/NA1 n = 62	RSV- A/ON1 n = 69	P value A/NA1 vs A/ON1
	n/N (%)	n/N (%)		n/N (%)	n/N (%)	
Demographic and clinical presentation						
Males (%)	79 (60.3)	22 (64.7)	0.78	35 (56.5)	44 (63.8)	0.49
Mean age ± SD, yrs	0.87 ± 0.81	0.97 ± 1.06	0.82	0.88 ± 0.65	0.86 ± 0.93	0.21
Presence of fever" (%)	126 (96.2)	30 (88.20)	0.08	59 (95.2)	67 (97.1)	0.66
High-grade fever° (%)	83 (63.3)	15 (44.1)	0.06	45 (72.6)	38 (55.1)	0.05
Respiratory rate, bpm	50.0 ± 13.4	42.2 ± 9.9	0.43	52.3 ± 9.3	47.9 ± 16.5	0.52
Mean SpO_2 in room air ± SD, %	95.9 ± 2.8	97.3 ± 2.7	0.88	96.4 ± 2.5	95.0 ± 3.0	0.79
Diagnosis						
Upper respiratory tract infection	59 (45.0)	15 (44.1)	0.92	10 (16.1)	49 (71.0)	**<0.0001**
Lower respiratory tract infection	72 (55.0)	19 (55.9)		52 (83.9)	20 (29.0)	
Clinical outcome						
Hospitalisation, No.(%)	45 (34.3)	16 (47.0)	0.24	29 (46.8)	16 (23.2)	**0.007**
Mean duration of hospitalisation, days ± SD	5.7 ± 2.5	6.8 ± 1.8	0.06	5.6 ± 2.7	6.0 ± 2.1	0.32
Drug use, No. (%)						
Antibiotics	126 (96.1)	34 (100.0)	0.58	59 (95.2)	67 (97.1)	0.66
Antipyretics	126 (89.0)	30 (88.2)	0.08	61 (98.4)	65 (94.2)	0.36
Aerosol therapy	120 (91.6)	27 (82.3)	0.06	57 (91.9)	63 (91.3)	0.85
Mean absence from community, days ± SD	10.1 ± 4.2	16.5 ± 12.0	0.08	10.9 ± 4.7	8.2 ± 2.0	0.44
Similar illness within the family	62 (47.3)	19 (55.9)	0.48	27/62 (43.5)	13/23 (56.5)	0.29
Laboratory data						
White blood cell count, cells/μL	11453 ± 4361	9208 ± 2511	0.05	11248 ± 4840	11997 ± 2770	0.29
Neutrophils, %	42.9 ± 17.2	46.5 ± 13.0	0.40	39.4 ± 16.0	51.8 ± 17.4	**0.02**
Lymphocytes, %	43.3 ± 14.5	40.9 ± 12.2	0.71	44.4 ± 14.0	21.7 ± 5.2	**0.03**
Monocytes, %	13.6 ± 4.8	12.6 ± 3.9	0.65	13.9 ± 4.8	8.7 ± 2.3	**0.04**
Basophils, %	0.4 ± 0.3	0.5 ± 0.7	0.90	0.4 ± 0.4	0.5 ± 0.2	0.71
Eosinophils, %	0.4 ± 0.5	0.5 ± 0.4	0.64	0.4 ± 0.5	0.1 ± 0.1	0.76
CRP, μg/dL	16.9 ± 80.8	2.6 ± 3.8	0.56	3.4 ± 4.7	47.6 ± 144.1	0.48

RSV Is Seasonal, With Peak Incidence Varying by Region[1,2]



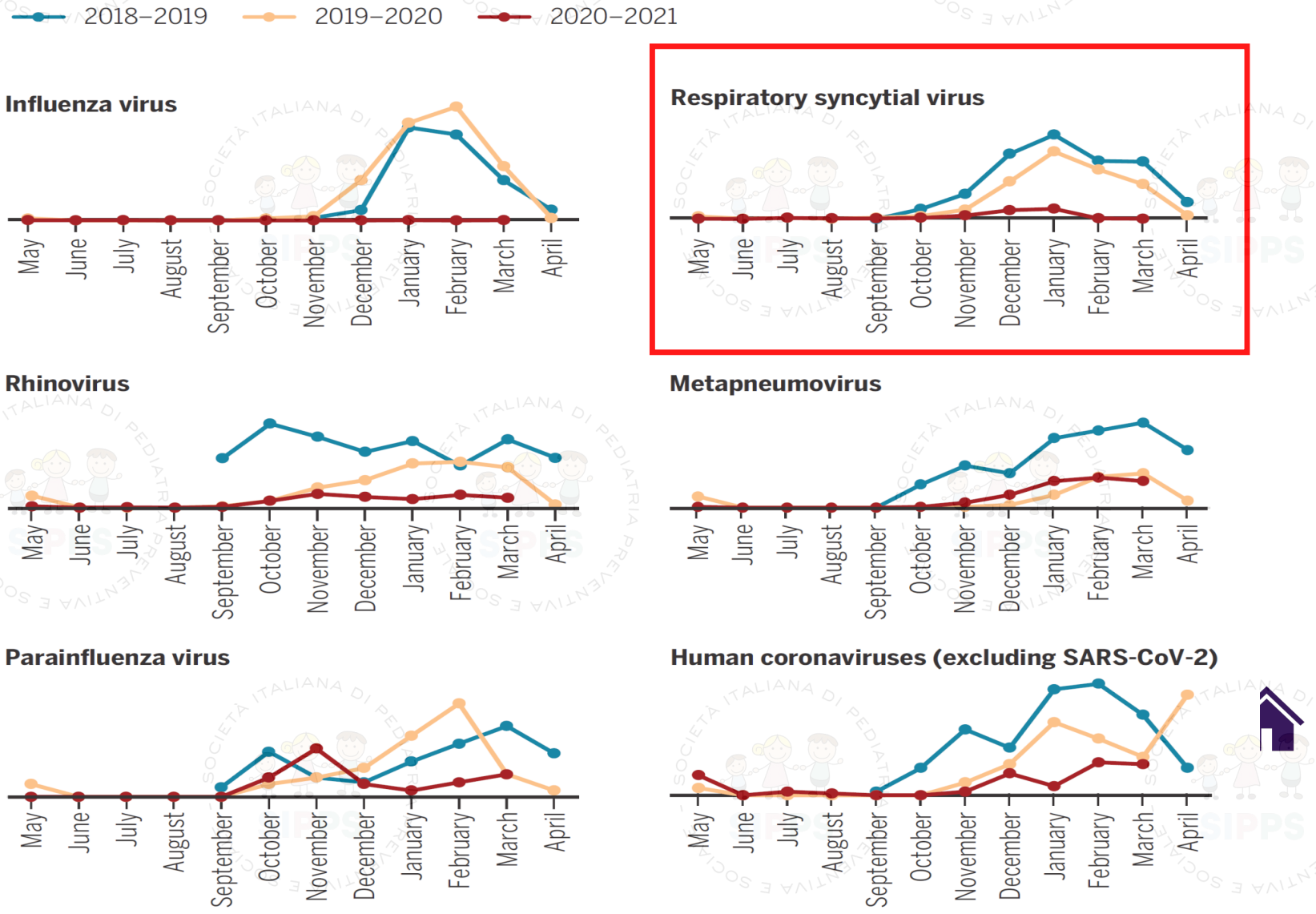
Northern Hemisphere: generally, between September and January.

Southern Hemisphere: generally, between March and June (aligned with cold season temperatures)

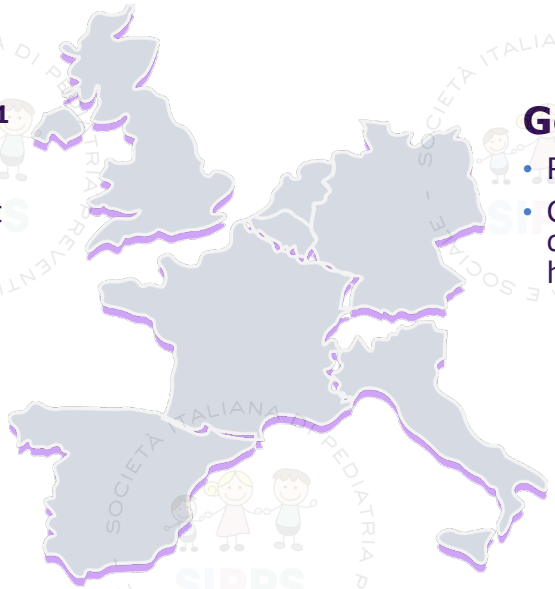
Tropical and Subtropical Climates: less consistent—peak closely aligned with rainy season and/or higher temperatures

1. Staadegaard L, et al. *Influenza Other Respir Viruses.* 2021;10.1111/irv.12885.
2. Obando-Pacheco P, et al. *J Infect Dis.* 2018;217:1356-1364.

Modified Circulation Patterns of Respiratory Viruses
(from Gomez GB, et al. Science 2021)



RSV Epidemiology Around Europe in 2021



England, United Kingdom[1]

- Increased RSV observed in May
- RSV peak identified around August

Germany[2]

- RSV season began at the end of August
- Cases of severe acute respiratory infections doubled within 1 week, reaching twice as high as in previous years

France[3]

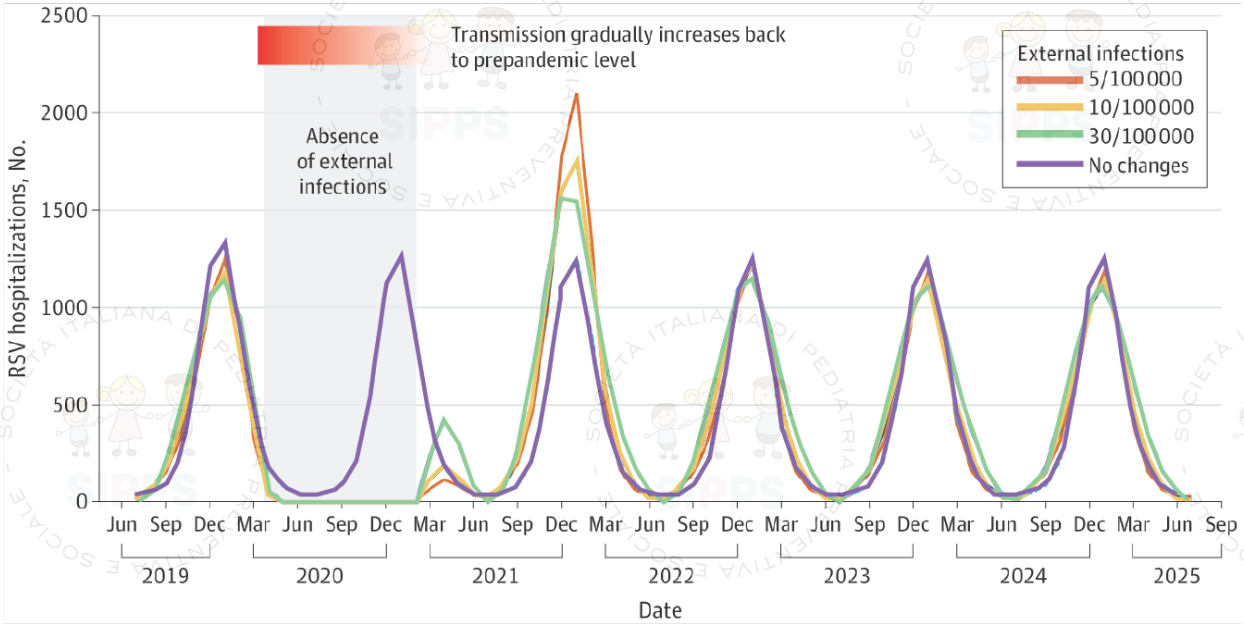
- Late and prolonged RSV epidemic
- Amplitude much lower than that in previous years

Switzerland[4]

- Unusual RSV activity with regional differences
- Case numbers peaked in August and subsequently declined

1. UK Health Security Agency. Weekly national Influenza and COVID-19 surveillance report: Week 41 report (up to week 40 data). 14 October 2021. Accessed November 3, \2021. https://assets.publishing.service.gov.uk/government/uploads/system/uploads/attachment_data/file/1025510/Weekly_Flu_and_COVID-19_report_w41.pdf/ 2. Robert Koch Institut. Epidemiologisches Bulletin 38/2021. 23 September 2021. Accessed November 3, 2021. https://www.rki.de/DE/Content/Infekt/EpidBull/Archiv/2021/Ausgaben/38_21.pdf?__blob=publicationFile/ 3. Santé publique France. Bulletin épidémiologique bronchiolite. Bilan de la surveillance 2020-2021. 12 April 2021. Accessed November 3, 2021. https://www.santepubliquefrance.fr/maladies-et-traumatismes/maladies-et-infections-respiratoires/bronchiolite/documents/bulletin-national/bulletin-epidemiologique-bronchiolite.-bilan-de-la-surveillance-2020-2021/ 4. Pédiatrie suisse. Épidémiologie des infections VRS. Accessed November 3, 2021. https://www.paediatrieschweiz.ch/news/epidemiologie-von-rsv-infektionen-2/

Modelling Study Suggests That Future RSV Epidemics May Reflect Pre-Pandemic Trend



Association of External Infections and RSV Hospitalizations

Modelling study suggests:

"Pediatric departments should be alert to large RSV outbreaks in the coming seasons, the intensity of which could depend on the size of the spring and summer epidemic in that location"[1]

– Zheng Z, et al.

1. Zheng Z, et al. *JAMA Netw Open.* 2014;4(12):e2141779.

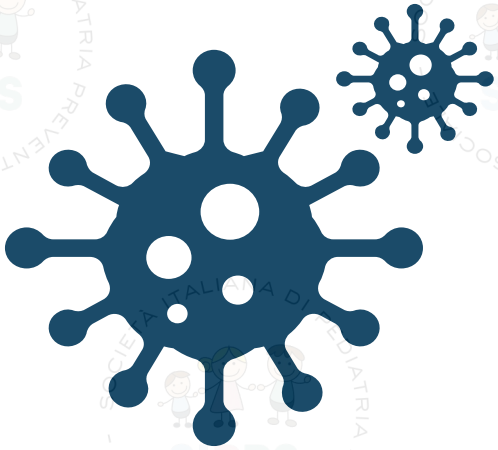
RSV: perché è importante in Pediatria

a) Altissima frequenza di infezione
b) Rischio elevato di quadri clinici molto significativi, anche nel soggetto senza fattori di rischio, specie nel primo anno di vita
c) Scarsissima possibilità di prevenzione
d) Nessuna disponibilità di antivirali efficaci e sicuri.

RSV Is Transmitted by Respiratory Droplets

RSV

is transmitted by respiratory droplets and considered “highly contagious”[1-3]

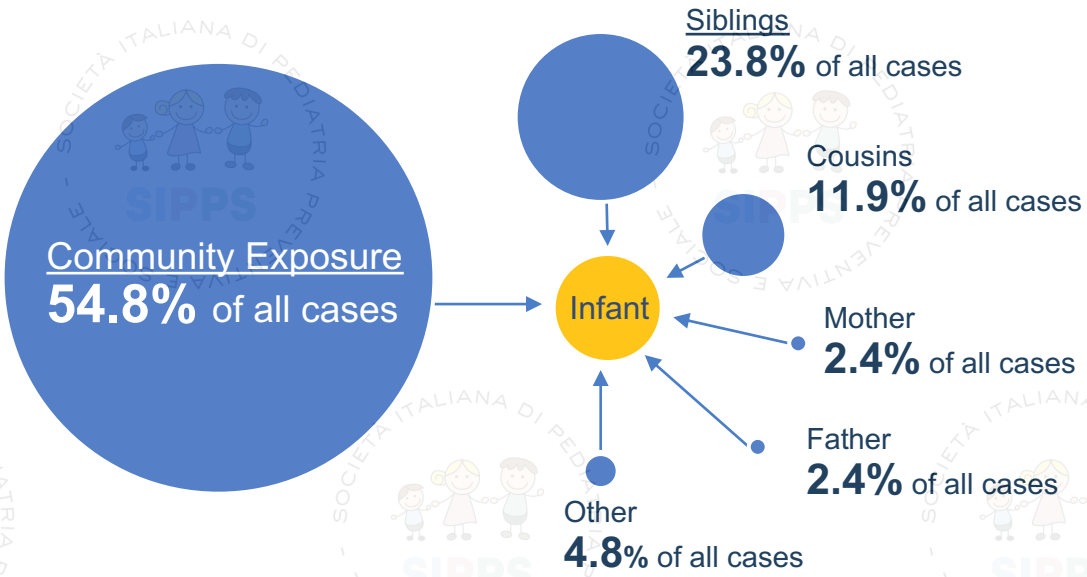


R_0 of 4.5

mean R_0 ranging from 1.7 to 8.2[4]

1. Heylen E, et al. *Biochem Pharmacol*. 2017;127:1-12. **2**. Carvajal JJ, et al. *Front Immunol*. 2019;10:2152. **3**. Drajac C, et al. *J Immunol Res*. 2017;2017:8734504. **4.** Reis J et al. *Infect Dis Mod*. 2018;3:23-34.

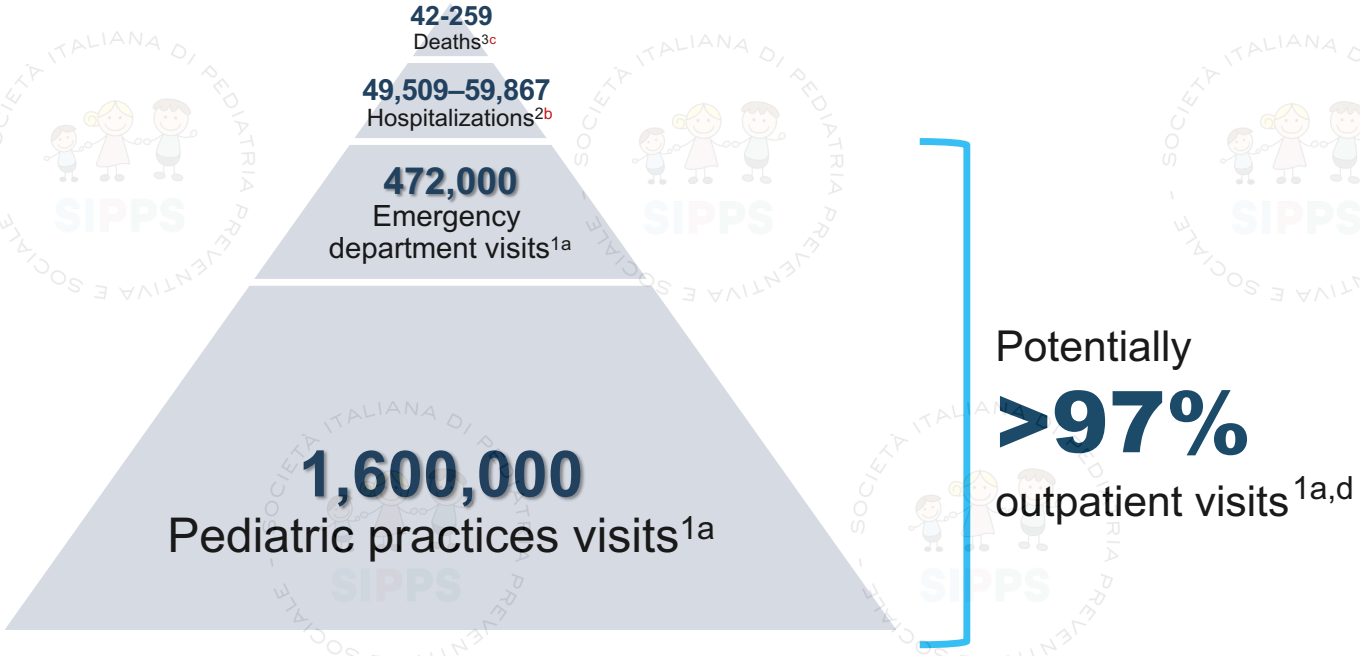
Most Infants Are Exposed to RSV Infection in the Community And Through Other Children[1-3]



Network showing the sources of infection to the infant as identified by social relationships in Kenya.[1] The size of the circles is proportional to the number of cases.

1. Adapted from Kombe IK. et al. *Sci Rep*. 2021;11:1463. **2**. Thomas E et al, Burden of Respiratory Syncytial Virus Infection During the First Year of Life. J Infect Dis. 2021;223(5): 811–817
3. Hall CB, et al Respiratory syncytial virus infections within families. N Engl J Med. 1976 Feb 19;294(8):414-9.

Most of the Healthcare Utilization Related to RSV in Children <2 Years Occurs in Outpatient Settings in the US



a. Estimates based on extrapolation of rates from 2004–2009 in the US. **b**. Estimates based on extrapolation of rates from October 2014 through April 2015 in the US. **c.** Deaths were identified from the Project Kids' Inpatient Database (KID) for 2000, 2003, 2006, and 2009 and the Pediatric Health Information System (PHIS) administrative data from 2000 to 2011 in the US. **d.** Estimate based on multiple sources and over different years.

1. Lively JY, et al. J Pediatric Infect Dis Soc. 2019;8(3):284-286. **2.** Arriola CS, et al. J Pediatric Infect Dis Soc. 2020;9(5):587-595. **3.** Byington CL, et al. Pediatrics. 2015;135(1):e24-e31.

RSV Hospitalization Rates: EU

- A systematic review of global studies (all passive, hospital-based, inpatient) showed annual incidence rates of RSV-associated ALRI ranging from 10–28 per 1,000 in children <1 year of age in the EU
- Incidence rates from passive studies may be underestimated as compared with active studies

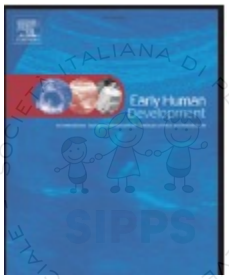
Incidence estimates of RSV-associated ALRI at hospital in children <5 years

Country (region)	Incidence of RSV-associated ALRI (per 1,000 children per year)		
	Age <1 year	Age <2 year	Age <5 year
Spain (Gipuzoka)	26	15	6
Germany (Kiel)	16	9	5
Germany (multicentric)	28	16	8
UK (Shropshire)	28	16	8
Sweden (N. Stockholm)	14	8	4
Austria (S. Austria)	12	7	4
UK	28	16	8
the Netherlands	10	6	3

ALRI, acute lower respiratory infection

Nair HN, *et al. The Lancet.* 2010;375(9725):1545–1555.

High risk for RSV bronchiolitis in late preterms and selected infants affected by rare disorders: a dilemma of specific prevention



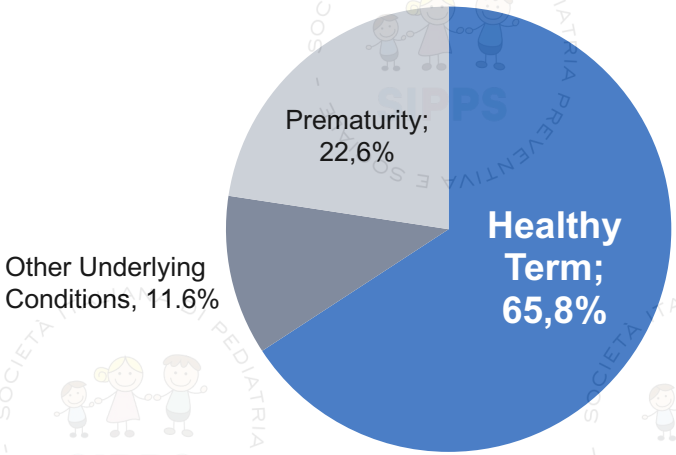
- Prematurity and BPD
- Age less than 12 weeks
- Congenital cardiac illness
- Immunodeficiency
- Congenital pulmonary anomalies
- Chronic pulmonary disease (CF, PCD….)
- Neuromuscolar diseases
- Down syndrome

Manzoni - Early Human Dev 2012

RSV Infant ICU Admissions and Mechanical Ventilation in the US[1]

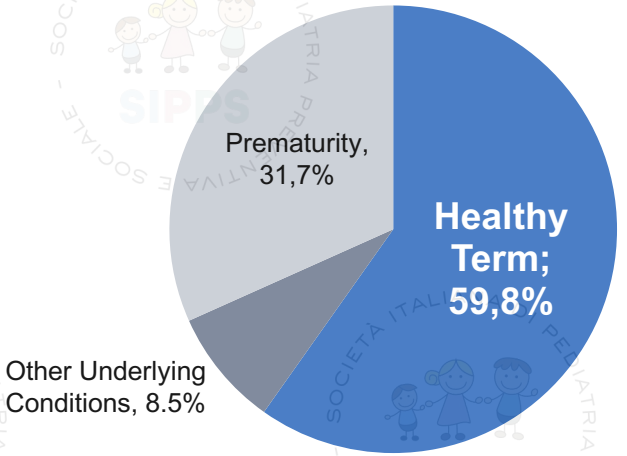
Surveillance through the Influenza Hospitalization Surveillance Network from October 2014-April 2015

Infant RSV ICU Admissions (n=336)



26% (221/851) of hospitalized **healthy term infants** were admitted to **ICU**[1]

Infant RSV Requiring Mechanical Ventilation (n=82)

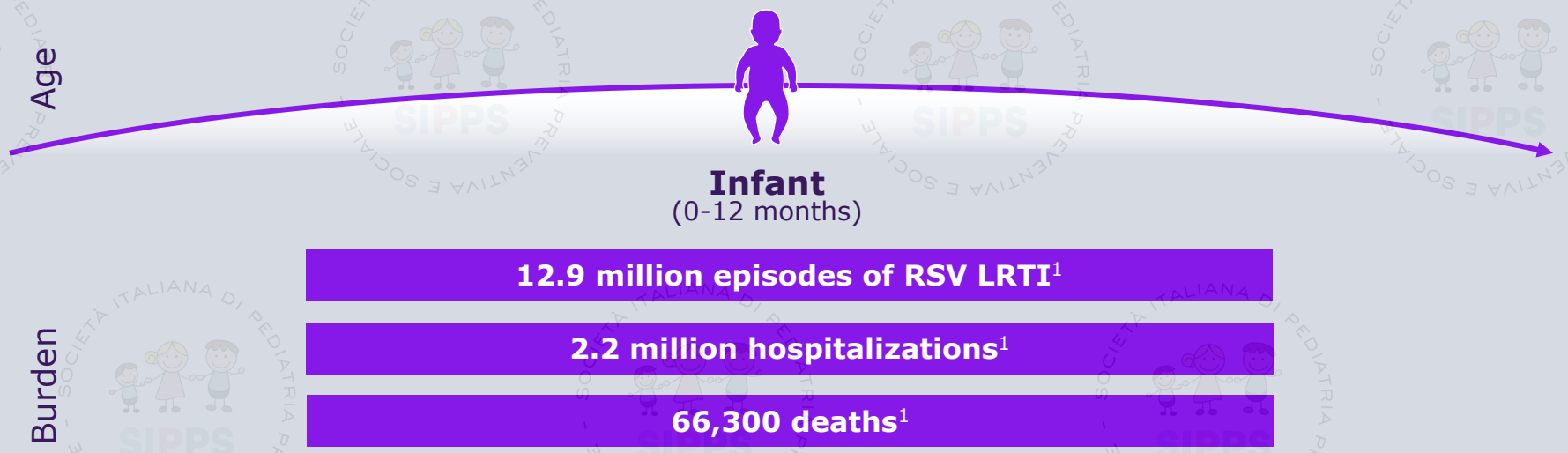


22% (49/221) of ICU admitted **healthy term infants** required **mechanical ventilation**[1]

CMC: chronic medical condition (includes chronic lung disease, cardiovascular disease, upper airway abnormality, asthma, neurologic/neuromuscular conditions, blood disease, renal disorder, immunocompromised, chronic metabolic disease, liver disease, and other); ICU: Intensive Care Unit; Preterm: born at <37 weeks gestational age; Term: born at 37+ weeks gestational age. Data from the US, % of Infant RSV ICU admissions may vary in other countries.

1. Arriola CS, et al. *J Ped Inf Dis Soc*. 2019; 9(5): 587-595. Supplemental Tables 4-6.

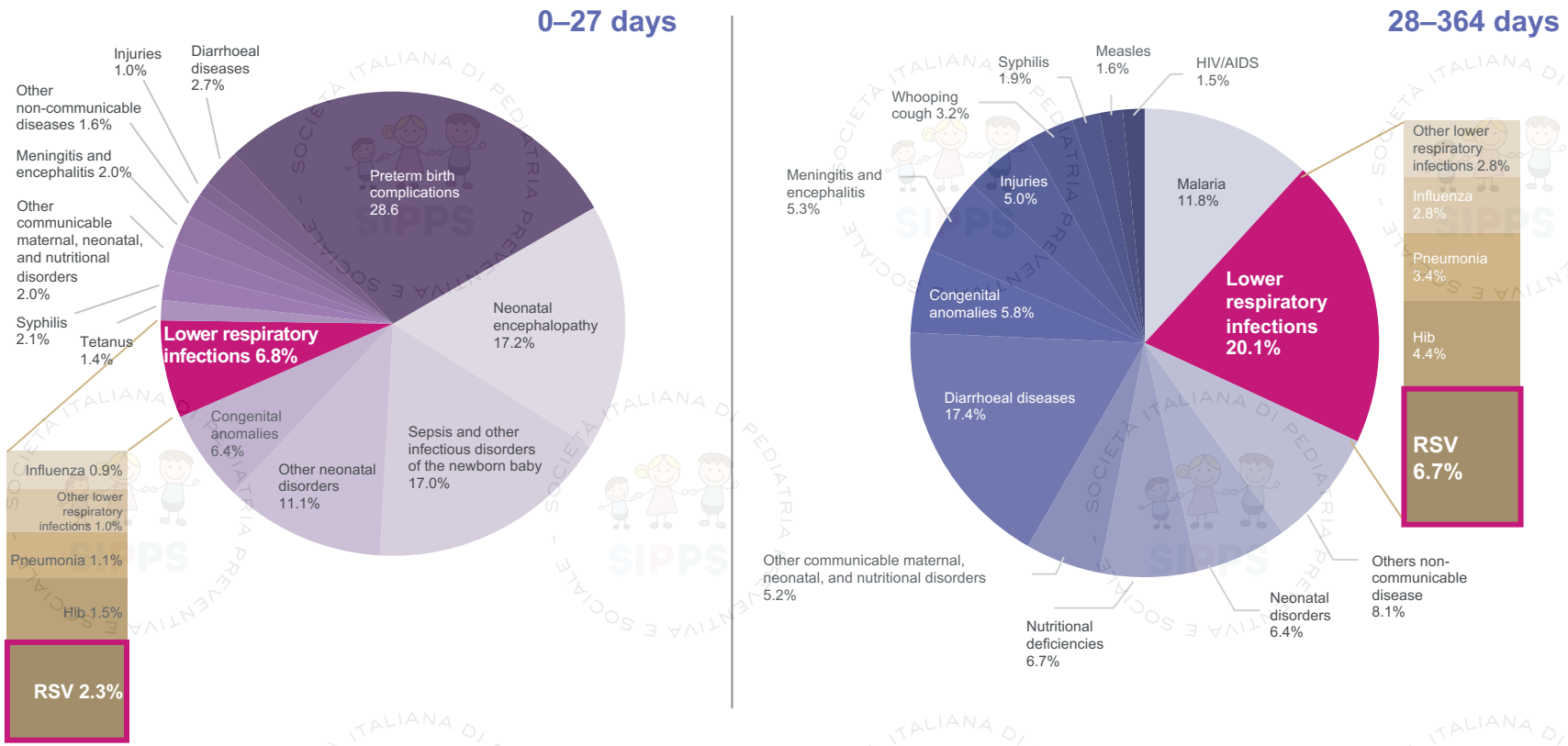
RSV Causes Substantial Disease Burden for Newborns and Infants Globally



Based on 2019 global data.

1. Li Y, et al. Lancet. 2022:S0140-673600478-0.

RSV is the Most Significant Cause of LRTI-related Death in First Year of Life

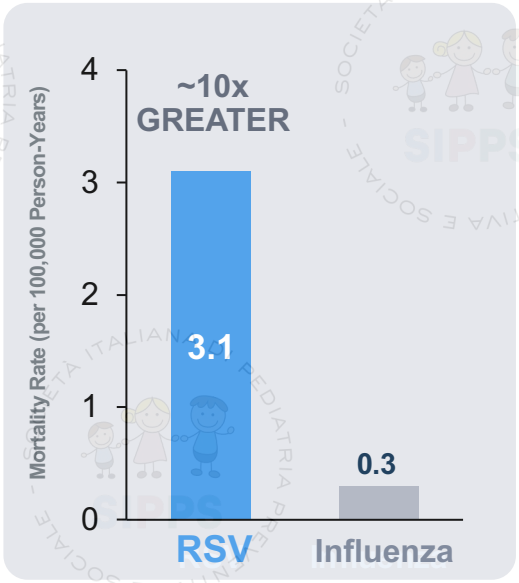


AIDS, acquired immune deficiency syndrome; ALRI, acute lower respiratory infection; EPEC, enteropathogenic Escherichia coli; ETEC, enterotoxigenic Escherichia coli; Hib, Haemophilus influenzae type b; HIV, human immunodeficiency virus.

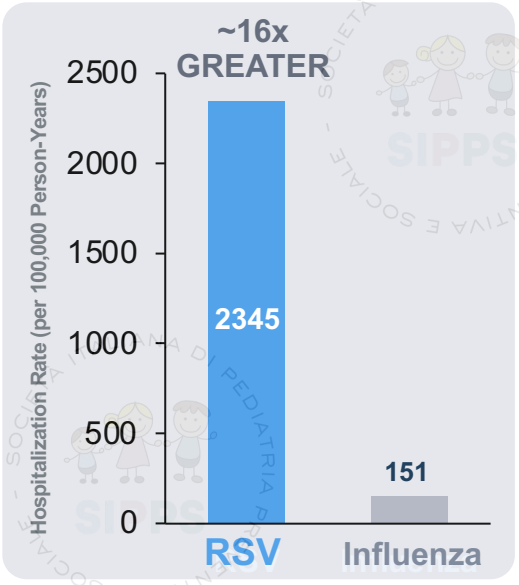
Lozano R, *et al. The Lancet.* 2012;380(9859):2095–2128.

RSV Burden Remains High Compared to Influenza in US Infants[d]

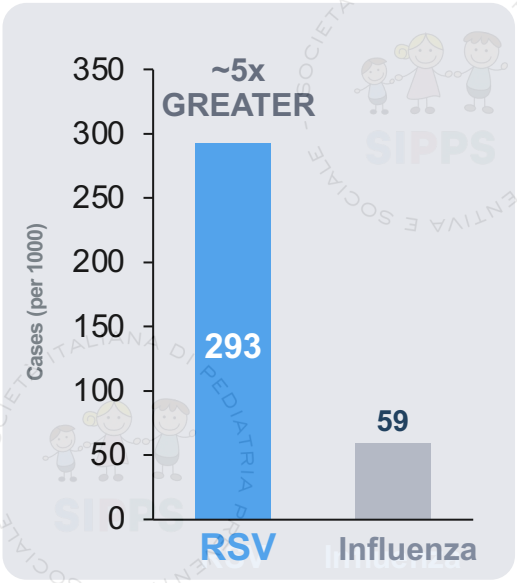
Mortality
(0-11 months)[1a]



Hospitalization
(0-11 months)[2b]



Medically Attended
(6-11 months)[3c]



Note: Influenza vaccination of all children 6-23 months of age was recommended by ACIP beginning in 2004-2005 season[4].

a. Estimated infant RSV-associated mortality for pneumonia and influenza deaths; CDC Data, 1990-1999. **b.** Infant hospitalization rates for RSV and influenza; CDC Data, 1993-2008. **c.** Estimated seasonal incidence of medically-attended RSV and influenza; Marshfield, 2006-2007 through 2009-2010. **d.** Data derives from different studies and over different years.

1. Thompson WW, et al. *JAMA*. 2003; 289(2):179-186. **2.** Zhou H, et al. *Clin Infect Dis*. 2012; 54(10):1427-1436. **3.** Simpson MD, et al. *Open Forum Infect Dis*. 2016; 3(2):ofw081. **4.** CDC. *MMWR Recomm Rep*. 2004 May 28;53(RR-6):1-40.

Burden of RSV Extends Beyond the Initial Medical Care

Short Term

RSV infection is associated with

increased incidence of otitis media and pneumonia, and excessive antibiotic use[1a]

Long Term

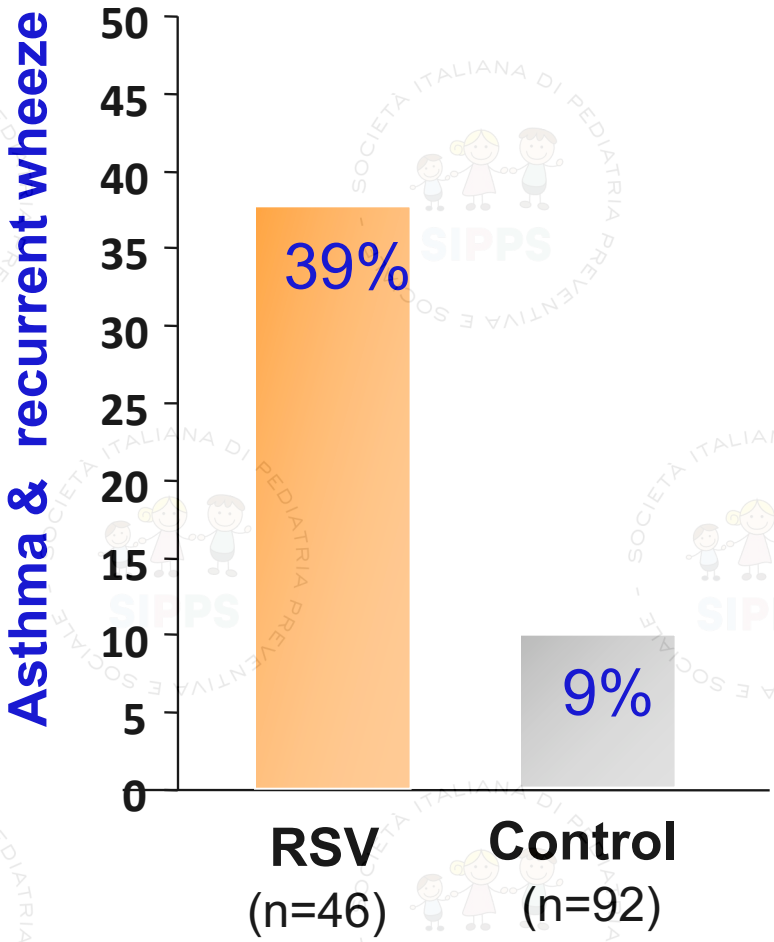
RSV infection may be possibly associated with

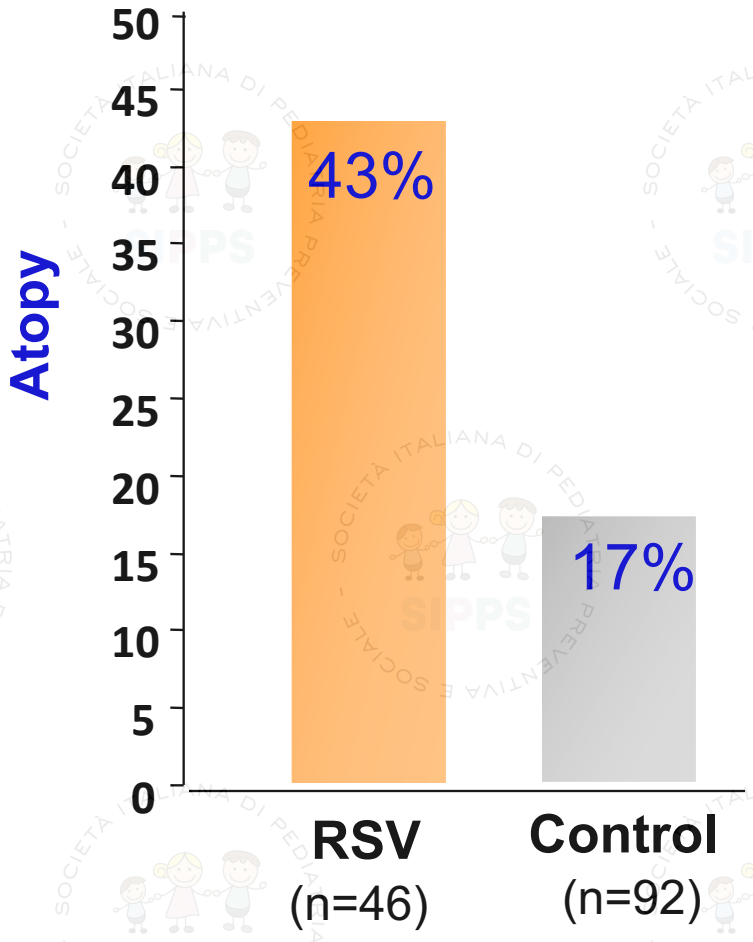
recurrent wheezing, reduced pulmonary function, and increased healthcare utilization[2-4]

a. Data representative for the second 6 months of life after considering an RSV infection in the first 6 months of life.

1. Abreo A, et al. *Clin Infect Dis.* 2020;71(1):211-214. **2**. Piedimonte G, Perez MK. *Pediatr Rev.* 2014;35(12):519-30. Erratum in: *Pediatr Rev.* 2015;36(2):85. **3**. Driscoll AJ, et al. *Vaccine.* 2020;38(11):2435-2448. **4.** Simoes EAF, et al. *J Infect Dis.* 2020;221(8):1256-1270.

Infants hospitalized for RSV bronchiolitis: 18 years follow-up





Sigurs, Thorax 2010

Only Supportive Care Is Available for Infants With Severe RSV

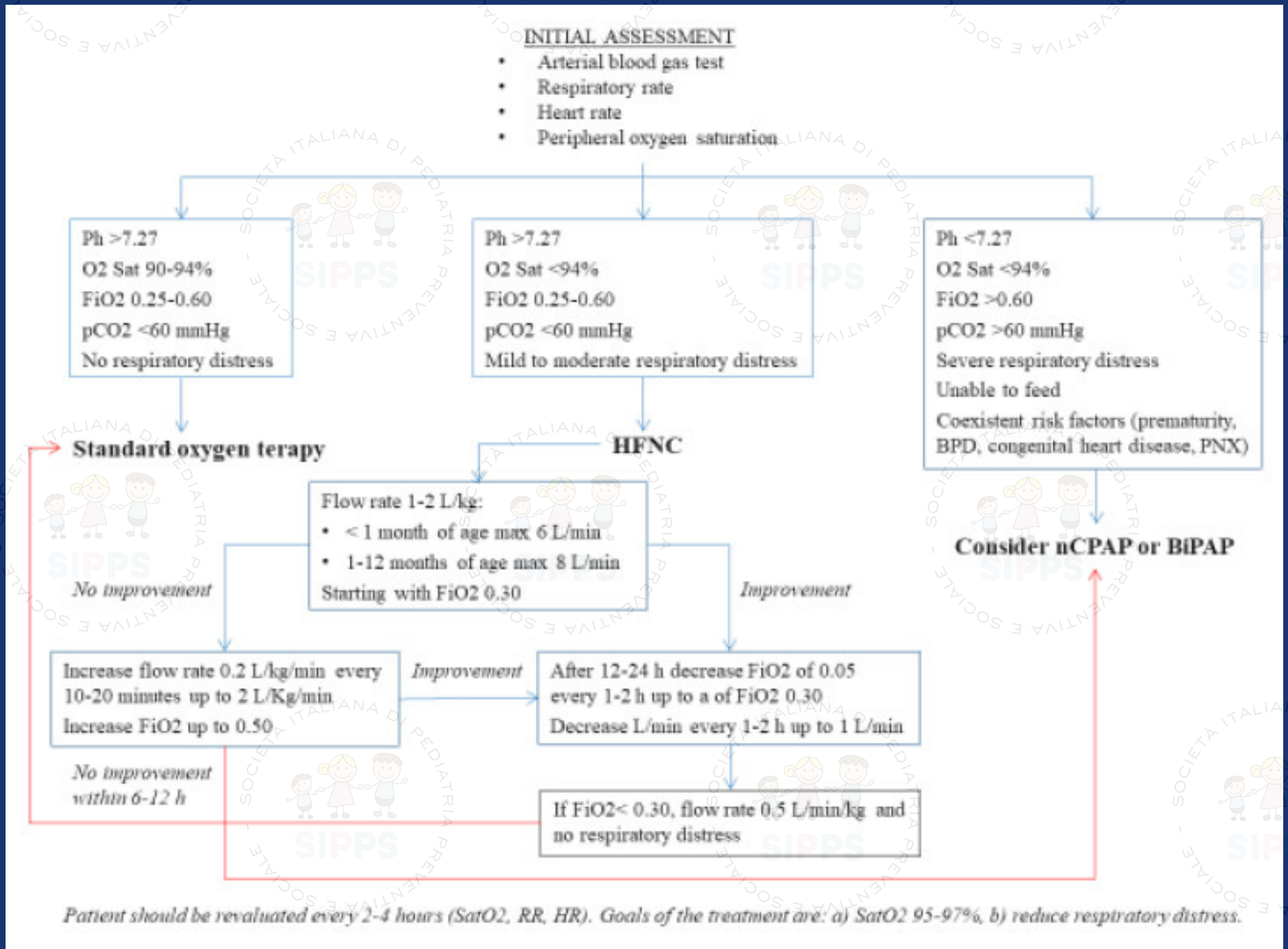
Once hospitalized, infants may require supportive care such as supplemental oxygen, IV fluids, and mechanical ventilation.[1-4]

- **1**. American Academy of Pediatrics. Respiratory syncytial virus. In: Kimberlin DW, Brady MT, Jackson MA, editors. Red Book: 2018–2021 Report of the Committee on Infectious Diseases. Elk Grove Village: American Academy of Pediatrics; 2018;682–92 **2.** Piedimonte G, Perez MK. Respiratory syncytial virus infection and bronchiolitis [published correction appears in Pediatr Rev. 2015 Feb;36(2):85]. Pediatr Rev. 2014;35(12):519-530. **3.** Ralston SL, Lieberthal AS, Meissner HC, et al; American Academy of Pediatrics. Clinical practice guideline: the diagnosis, management, and prevention of bronchiolitis. Pediatrics. 2014;134(5):e1474-e1502. **4.** Centers for Disease Control and Prevention. Respiratory Syncytial Virus (RSV): Symptoms and Care. https://www.cdc.gov/rsv/about/symptoms.html Accessed July 21, 2021.

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	Evidence Quality: B Recommendation Strenght: Moderate
Inhaled bronchodilators	Not Recommended	Evidence Quality: B Recommendation Strength: Strong
Chest physiotherapy	Not Recommended	Evidence Quality: A Recommendation Strength: Moderate
Nebulized adrenaline	Not Recommended	Evidence Quality: B; Recommendation Strength: Strong
Nebulized steroids	Not Recommended	Evidence Quality: A Recommendation Strength: Strong
Systemic steroids	Not Recommended	Evidence Quality: A Recommendation Strength: Strong
Antibiotics	Not Recommended *(Except in case of strong suspicion or clear evidence of a secondary bacterial infection)*	Evidence Quality: B; Recommendation Strength: Strong
Other *Antivirals* *Montelukast* *DNase* *Inhaled furosemide* *Inhaled ipratropium bromide* *Magnesium sulfate* *Helium* *Surfactant*	Not Recommended	Evidence Quality: B; Recommendation Strength: Strong

Practical flowchart about when to start standard oxygen therapy (SOT), high-flow nasal cannula (HFNC), or other methods of non-invasive ventilation in infants with bronchiolitis

(from Fainardi V et al. Children 2021)



Unmet Medical Need: no approved prophylaxis options for all infants[1]

Infants and children			
	Preterm and high-risk[a] newborns	Term infants <1 year of age	Children 1–5 years of age
Prophylaxis	Palivizumab	None	None
Treatment	Inhaled ribavirin[b]	Inhaled ribavirin[b2,3]	None

Approved

Approved in some cases but not routinely used*

Unmet medical need

[a]High-risk defined as: premature infants born at ≤35 weeks' gestational age, children with chronic lung disease, and children with hemodynamically significant congenital heart disease; [b]Approved by the FDA and by EMA for some EU member states for treatment of RSV infection but not routinely used and not recommended for use in most instances.; FDA, Food and Drug Administration. 1. Villafana T, *et al. Expert Rev Vaccines*. 2017;16(7):1–13. 2. https://www.ema.europa.eu/en/documents/scientific-guideline/guideline-clinical-evaluation-medicinal-products-indicated-prophylaxis-treatment-respiratory_en.pdf 3. AAP : https://pediatrics.aappublications.org/content/118/4/1774

Palivizumab: limiti attuali

(from Esposito S, et al. Front Immunol. 2023)

Bassa efficacia

La comparsa di mutazioni nel sito antigenico verso il quale è rivolto l'anticorpo, ha ridotto le stime di efficacia nella riduzione del rischio di ospedalizzazione, di morte e di sviluppo a distana di asma)

Difficoltà di utilizzo

L'anticorpo ha semivita di 17-26 giorni e deve, quindi essere somministrato 5 volte per coprire i 5 mesi di circolazione dell'RSV

Alto costo.

L'itero ciclo di profilassi costa più di 2.500 euro e il calcolo costo/efficacia ha dimostrato possibile vantaggio solo per i lattanti con displasia broncopolmonare e cardiopatia congenita oltre che per i prematuri

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

American Academy of Pediatrics

DEDICATED TO THE HEALTH OF ALL CHILDREN™

- Preterm infants born before 29 weeks gestation (who are younger than 12 months at the start of the RSV season)
- BPD infants (< 1-2 yrs)
- Infants with CHD hemodinamically significant
- Infants with neuromuscolar disease or congenital pulmonary anomalies (< 1 yr)
- Infants with Cystic Fibrosis (< 2 yrs)
- Immunocompromised infants (< 2 yrs)

2014

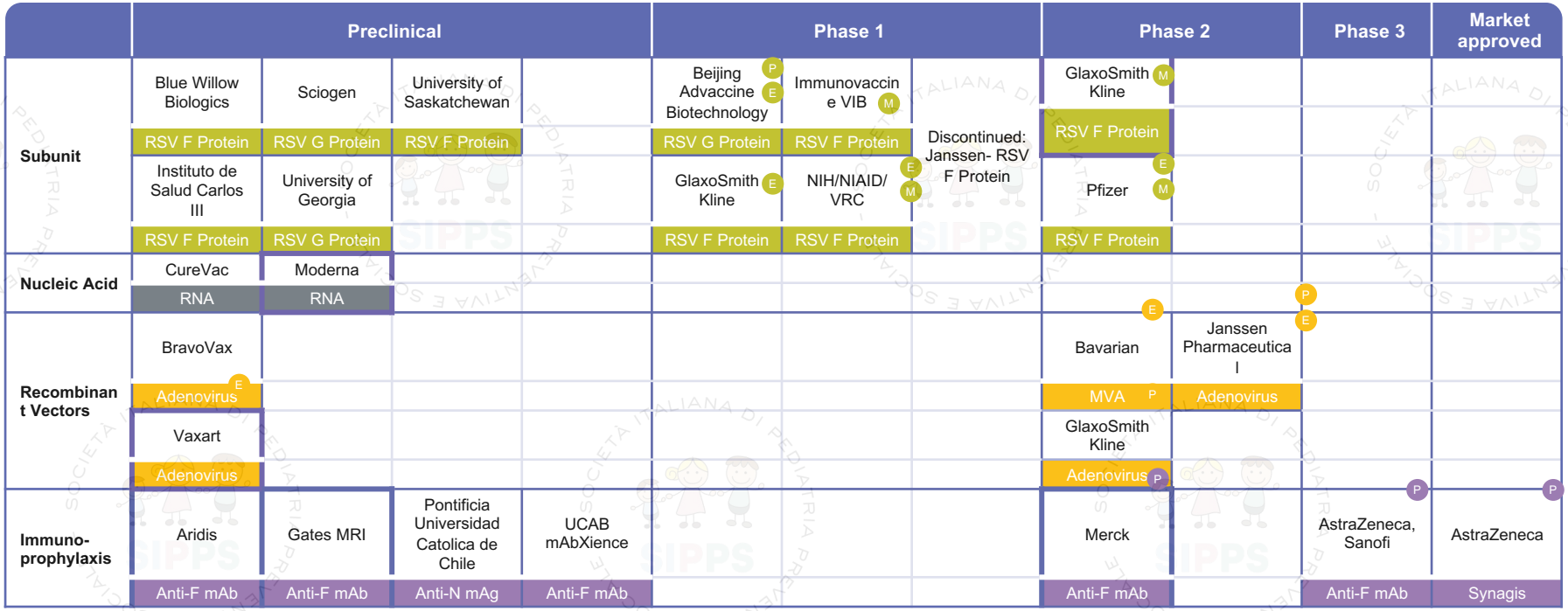
RSV Vaccines and mAb in Development Worldwide (1)

	Preclinical				Phase 1			Phase 2	Phase 3	Market approved
Live – attenuated/ chimeric	Codagenix, LID/NIAID/NIH	LID/NIAID/NIH			Intravacc (P)	Pontificia Universidad Catolica de Chile (P)	Sanofi, LID/NIAID/NIH (P)			
	RSV	RSV			RSV-AG	BCG/RSV	RSV 276			
	LID/NIAID/NIH				Meissa Vaccines (P)	SIIPL, St. Jude Hospital (P)	RSV ANS2/A1313/i 1314L			
	RSV				RSV	Sev/RSV	RSV 6120/ANS/103 0s			
Whole-inactivated	Blue Willow Biologics									
	RSV									
Particle-based	Fraunhofer	Icosavax	University of Massachusetts	Discontinued: Artificial Cel Technologies	Novavax (P)			Novavax (E)	[a]Novavax (M)	
	VLP	VLP	VLP		RSV F Nanoparticle			RSV F Nanoparticle	RSV F Nanoparticle	
	Georgia State University	Sanofi (E)	Virometix						[a]Ph3 primary endpoint not met	
	VLP	RSV F Nanoparticle	VLP							

Indicates change

E, elderly; LID, Laboratory of Infectious Diseases; M, maternal; mAb, monoclonal antibody; NIAID, National Institute of Allergy and Infectious Diseases; NIH, National Institutes of Health; P, pediatric; Ph3, Phase 3; VLP, virus-like particle. Path – Vaccine Resource Library. RSV Vaccine and mAb Snapshot. Updated March 26, 2020. https://path.azureedge.net/media/documents/RSV-snapshot-2020_03_26_High_Resolution_PDF_1.pdf. [Last accessed November 2020].

RSV Vaccines and mAb in Development Worldwide (2)



Indicates change

E, elderly; M, maternal; mAb, monoclonal antibody; NIAID, National Institute of Allergy and Infectious Diseases; NIH, National Institutes of Health; P, pediatric; VRC, Vaccine Research Center. Path – Vaccine Resource Library. RSV Vaccine and mAb Snapshot. https://path.azureedge.net/media/documents/RSV-snapshot-2020_03_26_High_Resolution_PDF_1.pdf. [Last accessed November 2020].

PRINCIPALI CARATTERITICHE DI NIRSEVIMAB IN CONFRONTO A PALIVIZUMAB

- **Più efficace** sia nel prematuro che nel nato a termine
- **Più comodo da utilizzare** perchè ad emivita più lunga, sufficiente a consentire una sola somministrazione per coprire i 5 mesi della durata del periodo epidemico di RSV
- **Meno costoso** perchè di fatto la prevenzione viene a costare 1/5 di quello che costa la prevenzione con Palivizumab. La singola dose costa grossolanamente come la singola dose di Palivizumb.

RESEARCH SUMMARY

Nirsevimab for Prevention of RSV in Healthy Late-Preterm and Term Infants

Hammitt LL et al. DOI: 10.1056/NEJMoa2110275

CLINICAL PROBLEM

Nirsevimab — a monoclonal antibody against the respiratory syncytial virus (RSV) fusion protein that has an extended half-life — has been shown to protect healthy preterm infants from RSV-associated lower respiratory tract infection, but its efficacy and safety in late-preterm and term infants are unknown.

CLINICAL TRIAL

Design: A multinational, phase 3, randomized, placebo-controlled trial assessed the efficacy and safety of nirsevimab for preventing RSV-associated lower respiratory tract infection in healthy infants born at a gestational age of at least 35 weeks.

Intervention: 1490 infants were randomly assigned, in a 2:1 ratio, to receive a single intramuscular injection of nirsevimab or placebo before entering their first RSV season. The primary efficacy end point was medically attended RSV-associated lower respiratory tract infection through day 150 after the injection.

RESULTS

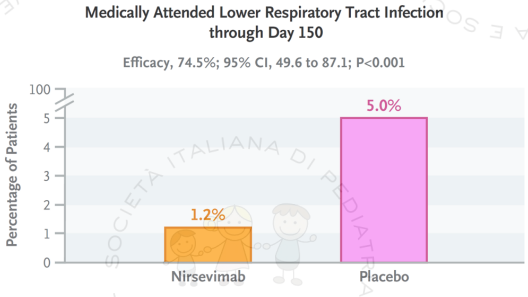
Efficacy: The incidence of medically attended RSV-associated lower respiratory tract infection was significantly lower in the nirsevimab group than in the placebo group.

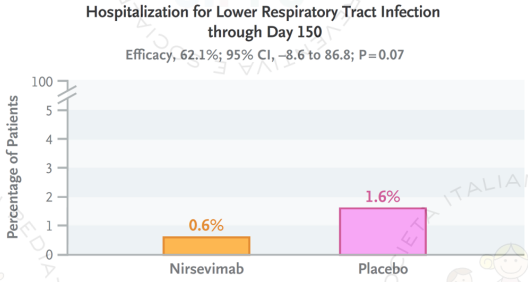
Safety: Similar types of adverse events occurred in the two groups, at similar frequencies. Most adverse events were grade 1 or 2 in severity.

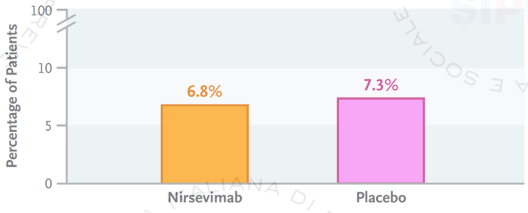
LIMITATIONS AND REMAINING QUESTIONS

- The efficacy of nirsevimab was relatively lower among younger infants (≤3 months vs. >3 months of age) and among those who weighed less (<5 kg vs. ≥5 kg), although small numbers preclude firm conclusions.
- The trial enrolled infants in the northern hemisphere and in South Africa (southern hemisphere). Although the overall incidence of RSV during the trial was as expected in the northern hemisphere, measures to control the Covid-19 pandemic in South Africa limited RSV circulation, resulting in low enrollment there.

Links: Full Article | NEJM Quick Take







CONCLUSIONS

A single dose of nirsevimab given before the RSV season lowered the risk of medically attended RSV-associated lower respiratory tract infection in healthy late-preterm and term infants, with no safety concerns.

Efficacy of nirsevimab weight-band dose on different case definitions of medically attended LRTI to 150 days post-dose

	Placebo group (n=786)	Nirsevimab group (n=1564)	Relative risk reduction (95% CI)	p value
Medically attended RSV LRTI*	51 (6%)	19 (1%)	79·5% (65·9–87·7)	<0·0001
Hospital admission for medically attended RSV LRTI†	21 (3%)	9 (1%)	77·3% (50·3–89·7)	0·0002
Very severe RSV LRTI‡	18 (2%)	5 (<1%)	86·0% (62·5–94·8)	<0·0001
Medically attended LRTI of any cause‡§	149 (19%)	191 (12%)	35·4% (21·5–46·9)	<0·0001
Hospital admission for respiratory illness of any cause‡§	51 (6%)	57 (4%)	43·8% (18·8–61·1)	0·0022

Relative risk reduction (95% CI) and p values were estimated on the basis of Poisson regression with robust variance across all case definitions. LRTI=lower respiratory tract infection. RSV=respiratory syncytial virus. *The model included study code, treatment group, and stratification factors (age at randomisation and hemisphere) as covariates obtained from PROC MIANALYZE after missing data imputation. †The model included study and treatment group as covariates for pooled studies obtained from PROC MIANALYZE after missing data imputation. ‡The model included treatment as a factor. §Included are all medically attended LRTIs according to the investigator's judgement, regardless of whether they met the clinical criteria for the definition of medically attended LRTI (appendix p 4).

Nirsevimab Administration Visual Guide

American Academy of Pediatrics
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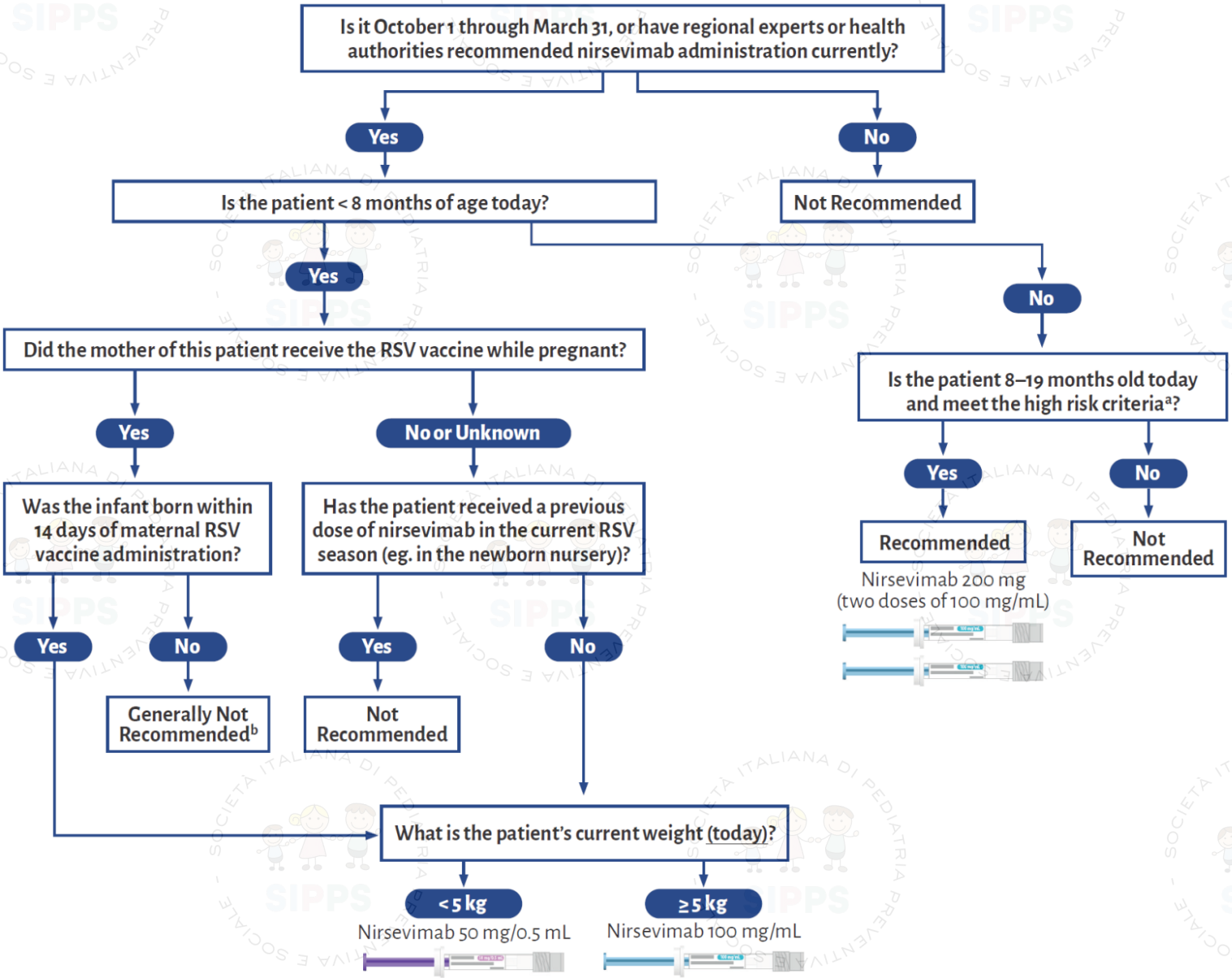
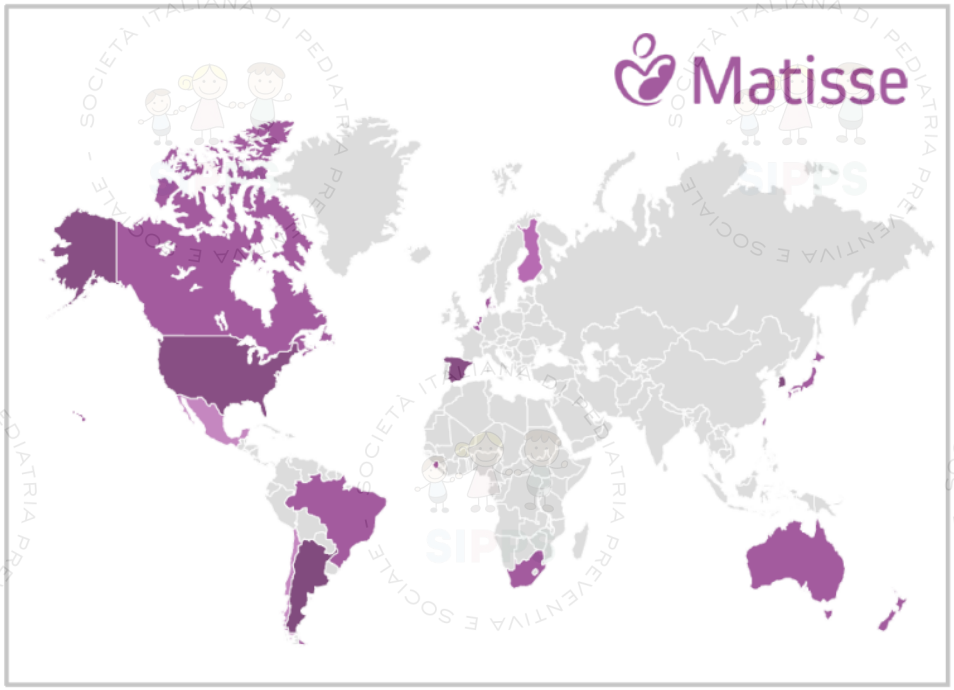


MATISSE: A Phase 3 Trial to Evaluate the Efficacy and Safety of RSVpreF in Infants Born to Women Vaccinated During Pregnancy

7,392 Maternal Participants in 18 Countries
Randomized 1:1 RSVpreF 120µg or Placebo

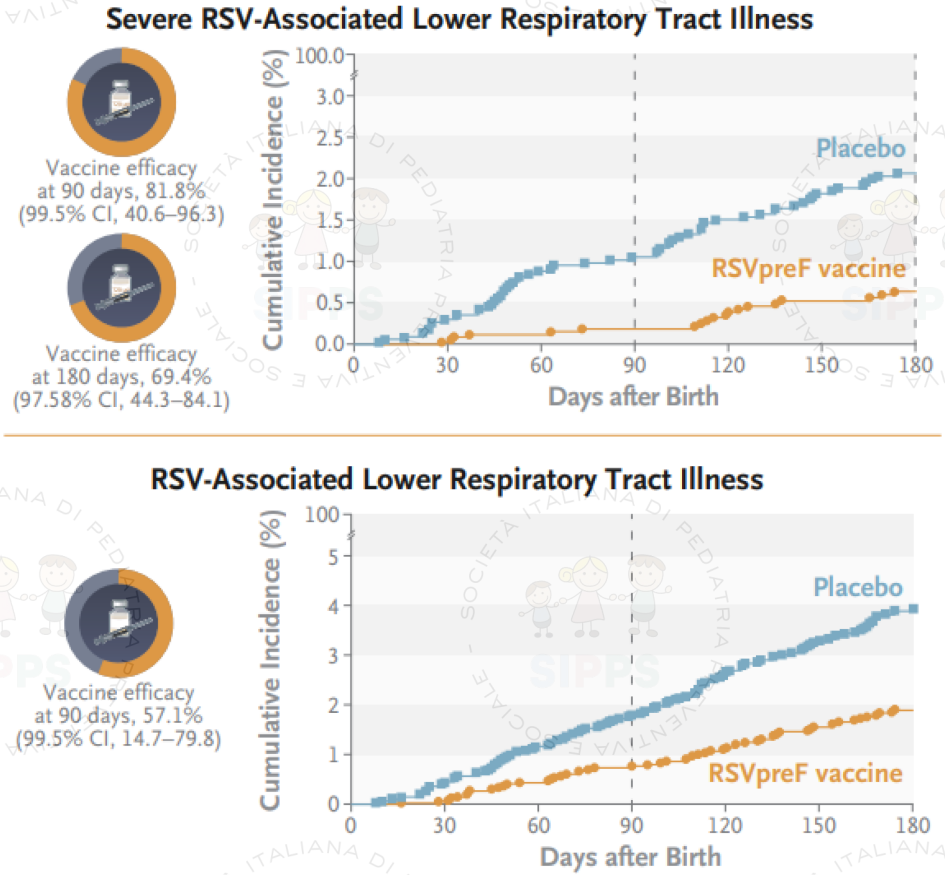
Pregnant persons ≤49 years between ≥24 and ≤36 weeks gestation

7,128 Infants enrolled

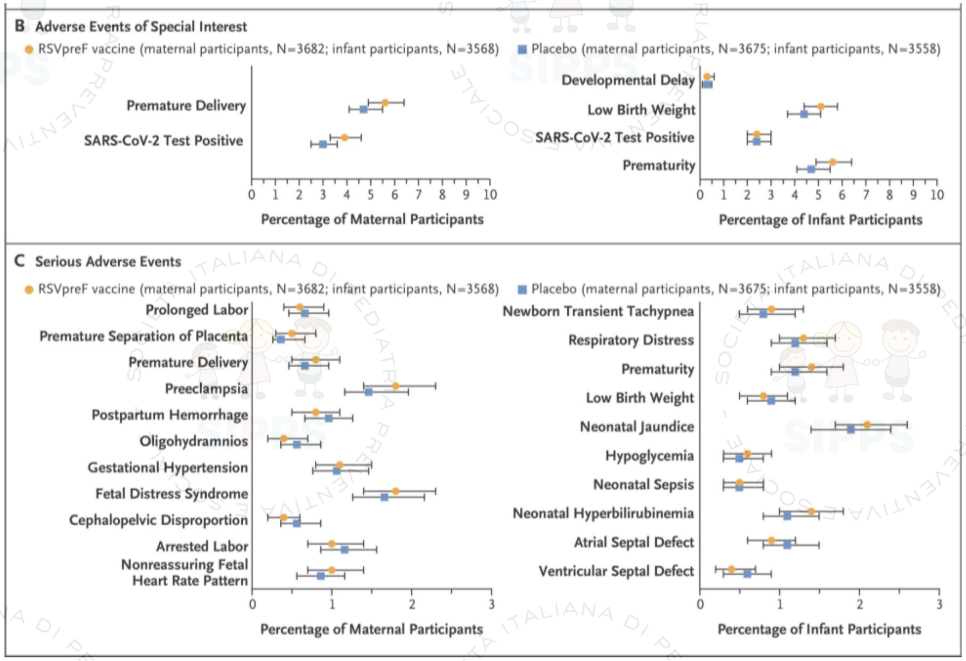


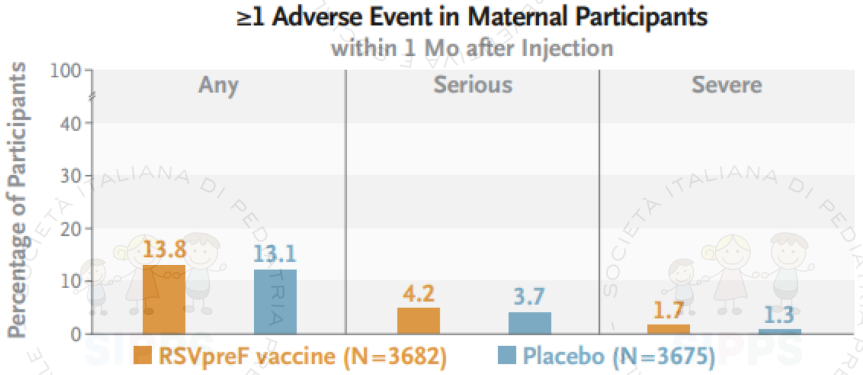
A Trial to Evaluate the Efficacy and Safety of RSVpreF in Infants Born to Women Vaccinated During Pregnancy. NCT04424316.

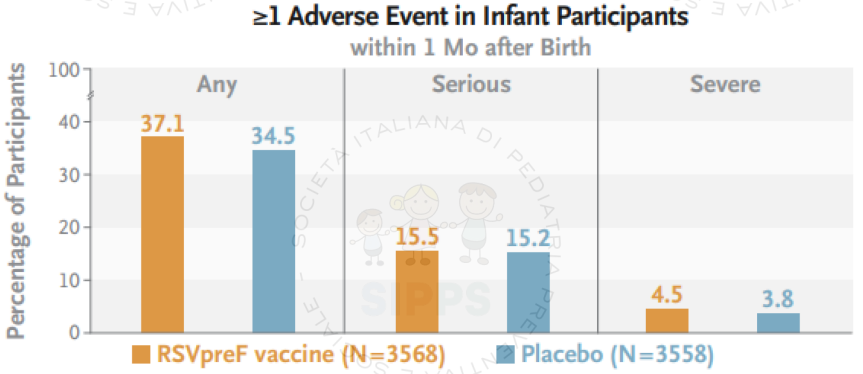
Vaccine Efficacy



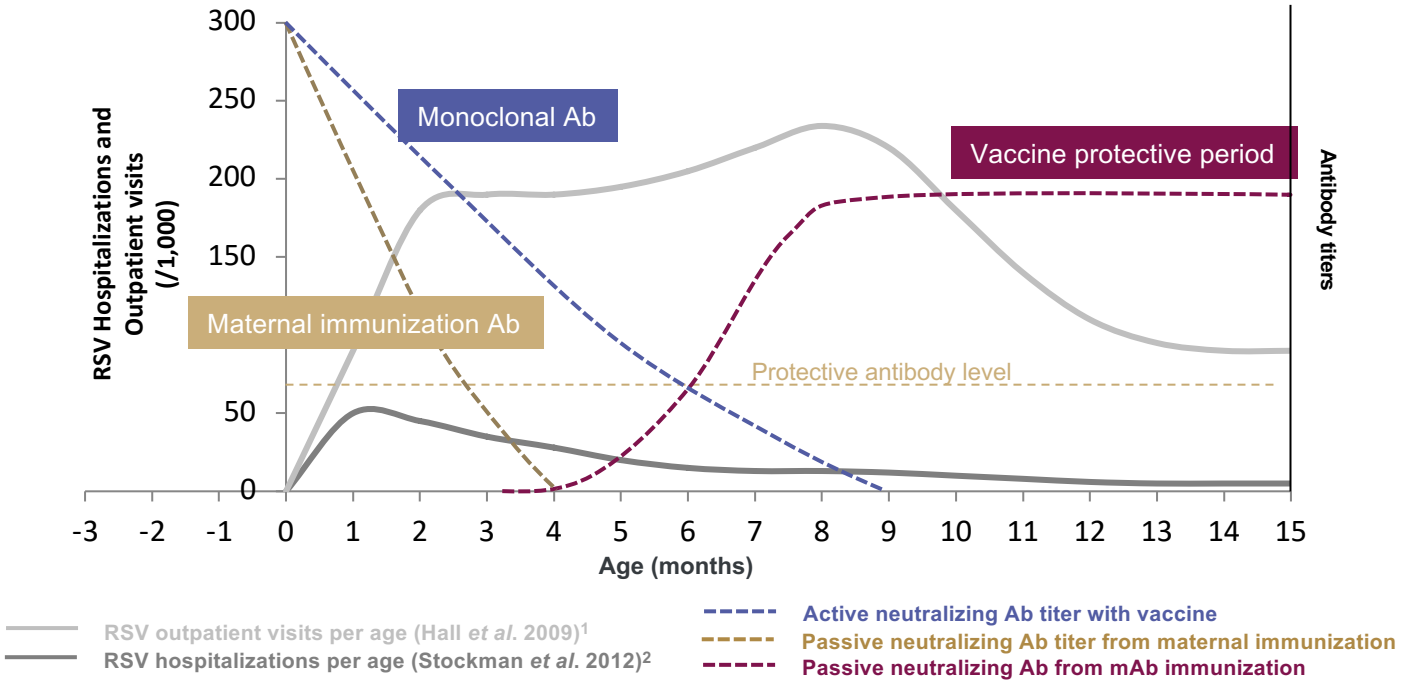
Vaccine Safety and Side Effects







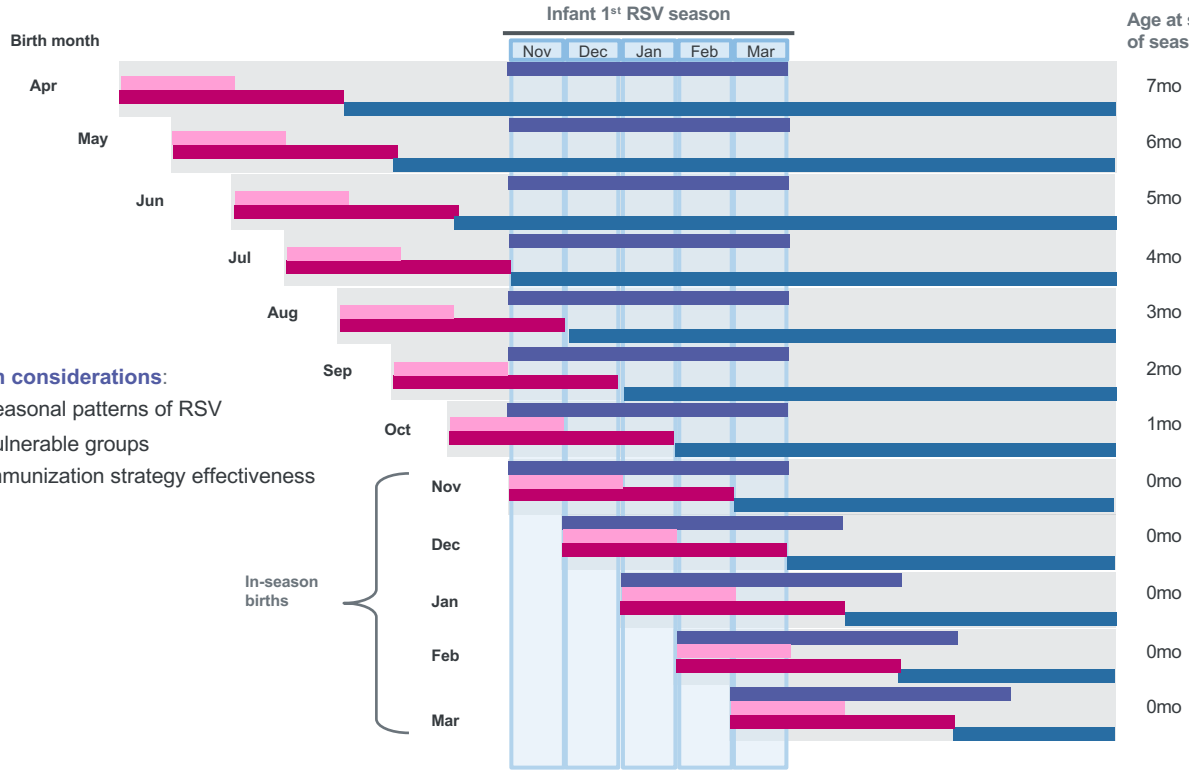
Prevention of Disease: Vaccine and Passive modelling Approaches[1–3]



Disclaimer: Graph from model based on Hall *et al.* 2009 and Stockman *et al.* 2012. Ab, antibody; mAb, monoclonal antibody.

1. Hall CB, *et al. N Engl J Med.* 2009;360(6):588–598; 2. Stockman LJ, *et al. Pediatr Infect Dis J.* 2012;31(1):5–9; 3. World Vaccine Congress, April 14–17, 2019, Washington, D.C.

RSV Immunization Programmatic Considerations



Main considerations:

- Seasonal patterns of RSV
- Vulnerable groups
- Immunization strategy effectiveness

Infant 1st RSV season (Nov–Mar)

STRATEGIES

Protection through passive immunization by monoclonal antibody

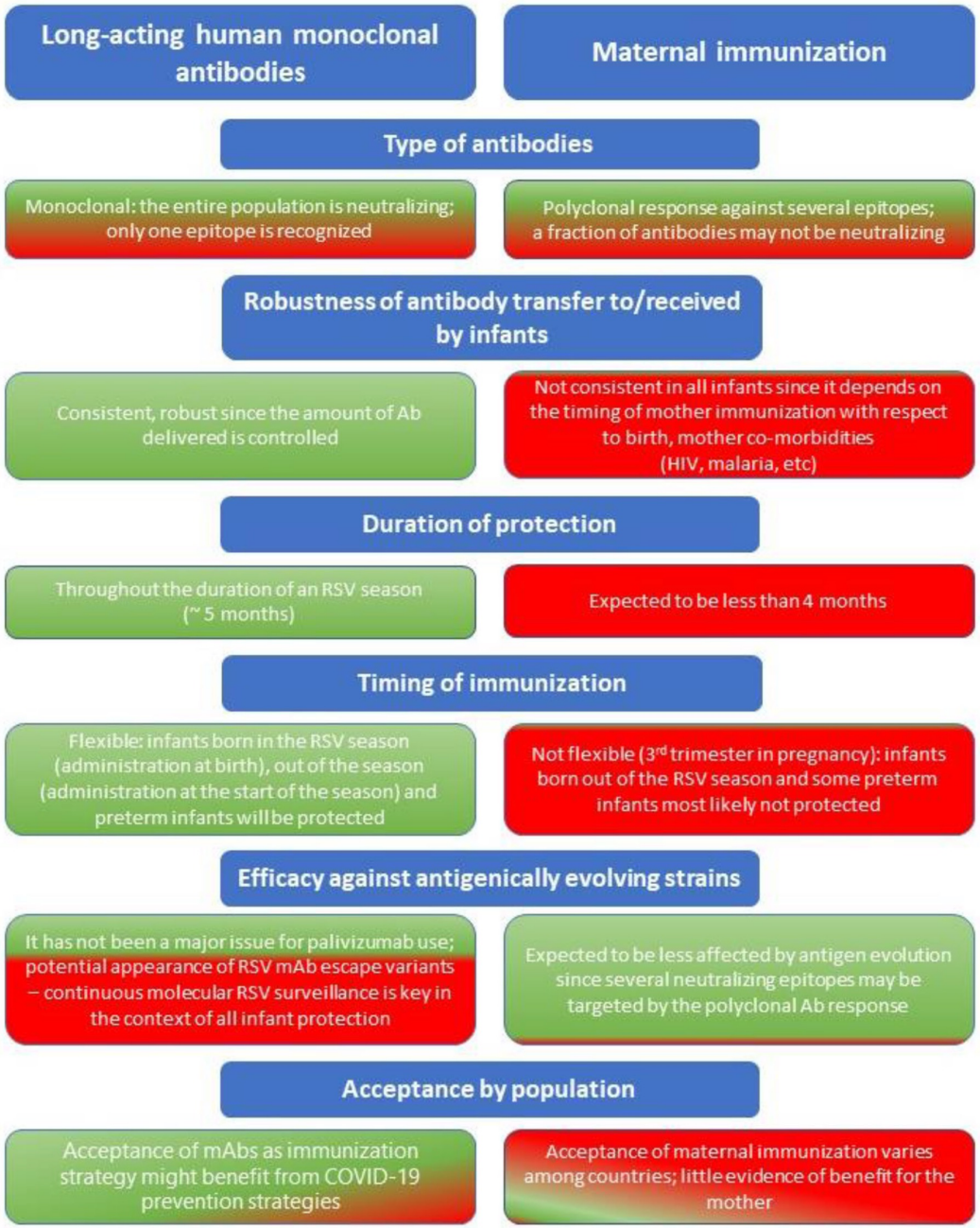
Protection through maternal immunization assumes 2 mo protection

Protection through maternal immunization assumes 4 mo protection

Protection through active immunization assumes 1+ dose and protection from 4 mo of age

mo, month

Adapted from Janet S, *et al. Hum Vacc Immunother.* 2018;14(1):234–244.



Considerations regarding long-acting human monoclonal antibodies and maternal immunization as prevention strategies against RSV for all infants entering their first RSV season.
Green = advantage;
Red = disadvantage.

(from Esposito S, et al. Front Immunol 2022)