

Position paper

Respiratory syncytial virus (RSV) in preterm and ill infants



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1. General background

1.1. What is RSV

The Respiratory Syncytial Virus (RSV) is a virus that causes infections of the lungs and airways. It commonly appears during the coldest and wettest months of the year, similarly to the influenza virus. In adults and older children the symptoms of infection might be very mild, with cold-like symptoms such as rhinitis or coughing; some adults who are infected with the virus do not have any symptoms at all. However, if more vulnerable patients (e.g. preterm infants, ill infants or elderly people) are infected with the virus, they may develop a severe lower respiratory tract infection (LRTI), such as bronchiolitis or pneumonia. These complications often result in admission to a hospital or to the neonatal intensive care unit (NICU) and sometimes in the need for mechanical ventilation, all of which are a burden not only for the infant but for the whole family. Furthermore, an infection with RSV does not mean that the person has gained protective immunity, therefore reinfections are common.¹



Four important facts about how RSV is transmitted



The virus is transmitted mainly by passing on droplets from one person to another through sneezing or coughing, or by touching an infected person, or surfaces that have previously been touched by an infected person.



The incubation period, the time between infection and the first occurrence of symptoms, is usually between 2 and 8 days, on average 5 days.



Normally, a person infected with RSV is contagious for 3 to 8 days. Particularly preterm and immune-compromised persons can shed the virus for a considerable length of time (up to 4 weeks after the infection).



The virus can survive outside the host on objects and surfaces: for about 20 minutes on hands, about 45 minutes on tissues and cotton lab coats, and for several hours on objects and surfaces (e.g. tables, mobile phones, crib rails).²



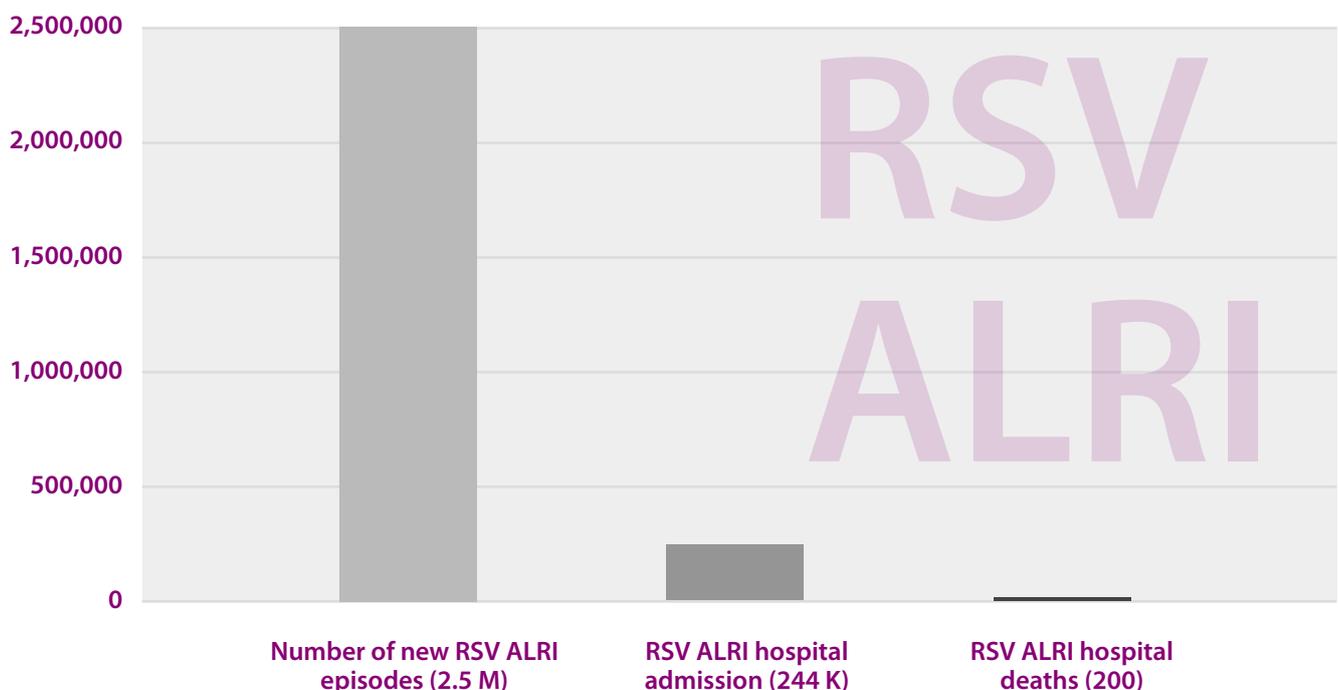
1.2. Infants who are at risk of a more severe infection

For some infants an RSV infection can lead to serious complications and can even become life threatening if the infection reaches the lower respiratory tract. It is particularly dangerous for preterm infants and infants with bronchopulmonary dysplasia (BPD) or congenital heart disease. There are other non-medical risk factors that make severe infections more likely. According to the guidelines published in 2018 by the German Society of Paediatric Infectious Diseases (DGPI), the most important risk factors are age under 6 months during RSV season, multiple birth (twins, triplets, etc.), male gender, siblings in kindergarten and school, passive smoking, close domestic conditions, malnutrition, lack of breastfeeding, and a family history of allergic diseases or asthma.³

1.3. Burden of disease

RSV infections are found worldwide. RSV is the most frequent cause of respiratory infections in children and, as a result, a major cause of hospital admissions globally. In developing countries it is also a major cause of death in children.⁴ In Europe, RSV is the most widespread pathogen causing infections of the lower respiratory tract of infants in their first 2 years of life, and the majority of children who are hospitalised with bronchiolitis have an RSV infection.³

Burden of RSV ALRI* in children 0 to 5 years of age in 2015 in industrialised countries⁵



*Acute lower respiratory infections



1.4. Short-term consequences of severe RSV infections

The most immediate consequence is that infants with a severe infection often need to be hospitalised. As a matter of fact, RSV infections result in 16 times more hospitalisations and emergency department visits in children under five years of age compared to infections caused by influenza virus.⁶

In hospital, doctors and nurses need to relieve the symptoms of the respiratory infection. The most frequent infection is bronchiolitis, an acute inflammatory injury of the bronchioles, the smallest airways in the lungs, which is caused mainly by RSV but also by other viruses, e.g. rhinoviruses. If the bronchiolitis is more severe, it can lead to sounds in the lungs (wheezing, rales etc.), respiratory distress and signs of dehydration. Some infants may also develop pneumonia; its symptoms are very similar to those of bronchiolitis but might also include chest and/or abdominal pain or vomiting. If the infant's condition worsens, it may need to receive supportive care measures, such as supplemental oxygen, fluid replacement or feeding support.



Please see infographic on bronchiolitis on page 8

1.5. Long-term consequences of severe RSV infections

RSV infections do not only lead to an increased number of hospitalisations, but may also have negative long-term effects on the health of children. Some studies have shown that RSV infections might be a significant risk factor for pulmonary problems later in life, such as asthma, recurrent wheezing or impaired lung function. These long-term consequences can have negative effects on the overall quality of life of the children and the family.⁷

A recent study showed, however, that wheezing is more frequent in bronchiolitis caused by rhinoviruses than by RSV.⁸

1.6. Need for evidence-based guidelines and more information for parents

Currently, there are no European-wide standards, guidelines or recommendations on RSV prevention, prophylaxis and treatment. There are several guidelines on a national level, however, with wide variations between individual countries. Differences between national guidelines pertain to recommendations for preventive measures, immunoprophylaxis, as well as follow-up. But not only the guidelines vary within Europe, also the reimbursement models sometimes do not follow national guidelines. To end these inconsistencies and the inequity throughout Europe and to give all preterm and newborn infants equal and evidence-based care, a European-wide consensus needs to be established. This position paper could be a starting point for this endeavour.

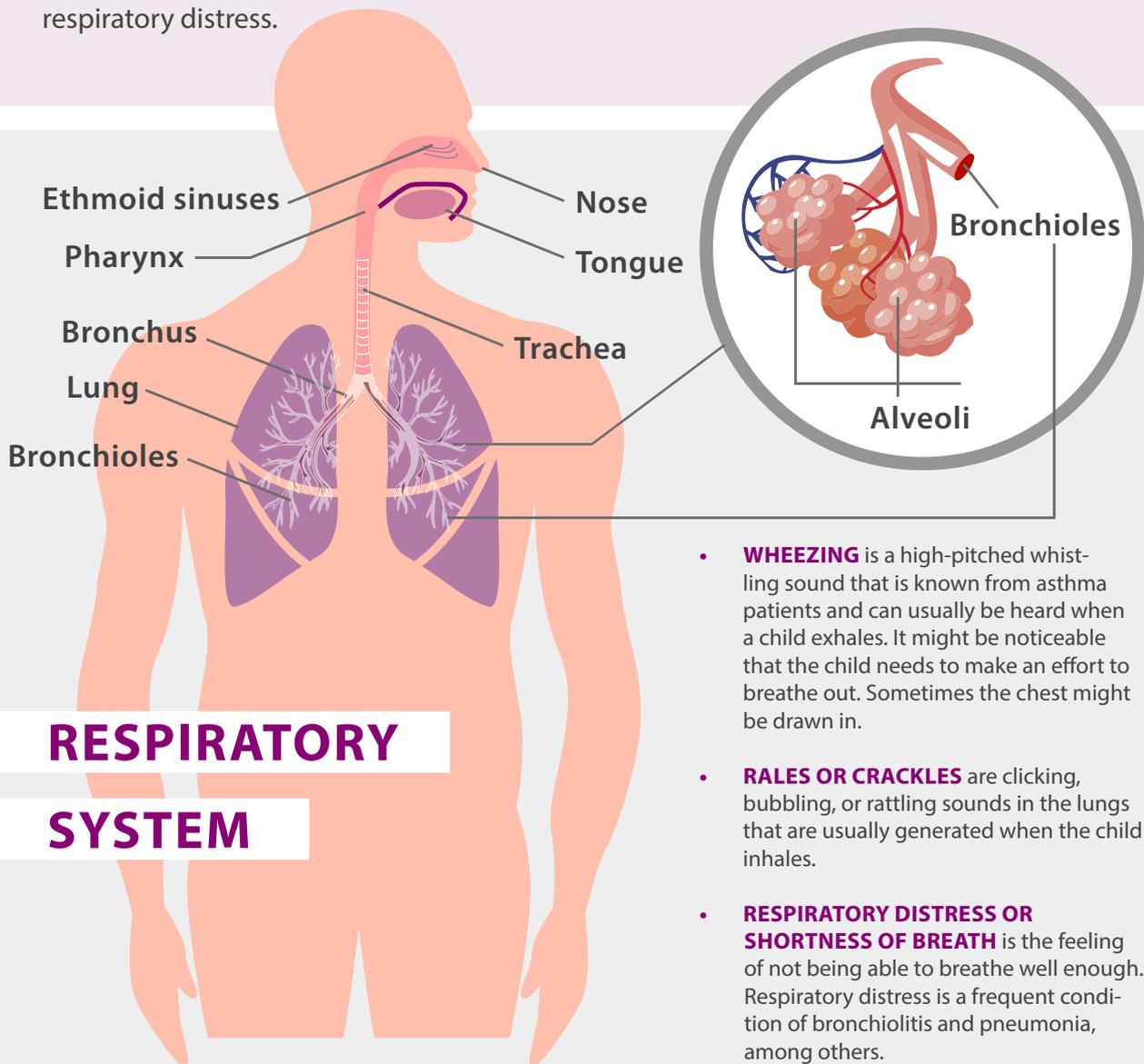


1.7. RSV vaccines in development

There is no vaccine available against RSV, but researchers and pharmaceutical companies worldwide are working on developing a vaccine that can prevent an RSV infection. RSV has alternating strains (a slight variation of the same virus) which makes the development of a vaccine difficult. At present, a few vaccine candidates are being tested, but it may still take years until they are on the market.¹

WHAT IS BRONCHIOLITIS

Bronchiolitis is a common infection of the lower respiratory airways which is mainly seen in infants and young children. It is mostly caused by RSV but also by other viruses, for example rhinoviruses. Bronchiolitis is an inflammation and congestion of the terminal and respiratory bronchioles (smaller airways) and starts out with symptoms similar to those of a common cold but sometimes progresses to coughing, wheezing and even respiratory distress.



- **WHEEZING** is a high-pitched whistling sound that is known from asthma patients and can usually be heard when a child exhales. It might be noticeable that the child needs to make an effort to breathe out. Sometimes the chest might be drawn in.
- **RALES OR CRACKLES** are clicking, bubbling, or rattling sounds in the lungs that are usually generated when the child inhales.
- **RESPIRATORY DISTRESS OR SHORTNESS OF BREATH** is the feeling of not being able to breathe well enough. Respiratory distress is a frequent condition of bronchiolitis and pneumonia, among others.



2. RSV prevention at home

2.1. Hygiene and behavioural measures

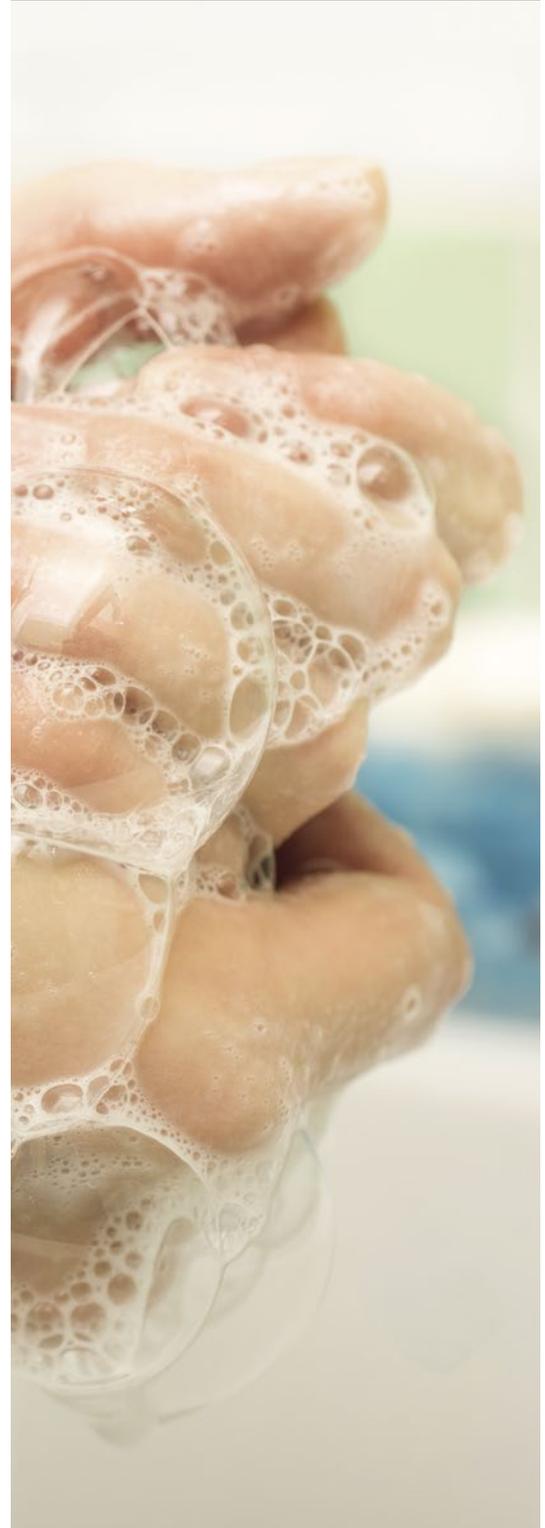
RSV is transmitted by droplet infection and by touching an infected person, infected surfaces and objects, so the single most effective preventive measure for a family with a preterm or ill infant is to follow basic hygiene rules, such as washing hands frequently and thoroughly, keeping surfaces clean, and covering mouth and nose with a tissue when coughing or sneezing. These rules do not only help to protect against RSV and other viruses, but also against other disease-causing microorganisms, like bacteria. Not smoking near a child, breastfeeding and avoiding public places during RSV season are among the many behavioural measures that reduce the risk of infection.



Practical advice on hygiene and behavioural measures can be found in the appendix on pages 32-35

2.2. Pertussis vaccinations during pregnancy

Currently there is no RSV vaccination on the market. However, as pertussis (whooping cough) and influenza can lead to serious and life-threatening conditions in newborn infants, in many countries it is recommended that pregnant women get vaccinated against both. Vaccinating the pregnant woman shall give the infant protection against these microorganisms until they are old enough to be vaccinated themselves. Besides the mothers, other household contacts, e.g. fathers, siblings and grandparents, should have their vaccination status checked/completed as well. Preventing avoidable diseases protects the infant's immune system making it less vulnerable to other infections, like e.g. RSV infections.^{9,10}



3. RSV prevention in hospital

To avoid potentially severe infections, neonatal wards need to follow very strict guidelines to guarantee a clean environment as newborn, preterm and ill infants are extremely vulnerable and thus at high risk of being harmed. Hospital-acquired RSV infections are often due to pathogen contamination of surfaces and hand carriage of pathogens. Therefore, continuous improvement of patient safety and hygiene standards in hospital is an important component of high-quality care and requires an appropriate system of specific procedures, including identification and reporting of gaps to facilitate learning from safety, hygiene, and quality issues.¹¹



Please see detailed recommendations for preventive measures in hospital in the appendix on pages 32-33

4. RSV prophylaxis with palivizumab

4.1. What is palivizumab

Currently, there is neither a vaccine nor a curative treatment available against RSV infections. Once an infection of the lungs has occurred, supportive care strategies are applied to ameliorate infective symptoms, such as administration of oxygen and symptomatic treatment with anti-inflammatory medication. However, immunoprophylaxis can be given with a monoclonal antibody against RSV. The medication currently on the market is called palivizumab; it contains specific antibodies that can help the body fight an RSV infection before it reaches the lungs. As any prophylactic medication, it is not used to treat an active RSV infection.

Palivizumab is given once monthly during the peak of RSV activity, which in Europe is in the autumn and winter season (similarly to flu season), but RSV seasons vary from country to country and also from year to year. To find out the local RSV season ask relevant health authorities or check disease surveillance websites, such as www.eurosurveillance.org.

Besides the seasonal aspects, there are other factors that are important when deciding if a prophylaxis should be given, mainly the chronological and gestational age of an infant and additional serious health conditions.

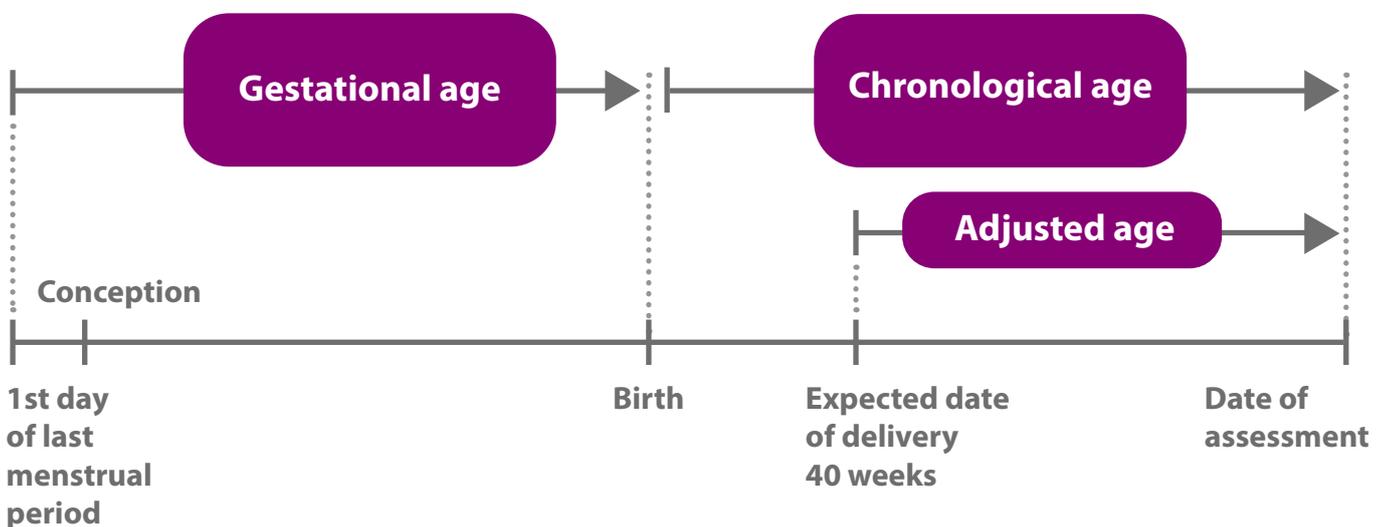


Important terminology in preterm birth

Gestational age is the amount of time an infant was in the womb before birth. The term is used to determine the degree of preterm birth. Regular term birth is a birth between 37 to 40 weeks of gestation or about 280 days from the first day of the mother's last menstrual period.

Chronological age is the age of an infant counting from the day it was born.

Adjusted age begins at the expected date of delivery (not the actual date of delivery) and continues until the date of assessment.



Preterm birth is defined by the WHO as birth before 37 weeks of pregnancy are completed. There are subcategories of preterm birth, based on gestational age:

- extremely preterm (<28 weeks gestational age)
- very preterm (28 to <32 weeks gestational age)
- moderate to late preterm (32 to <37 weeks gestational age)



4.2. European marketing authorisation of palivizumab

In 1999, the European Medicines Agency (EMA) gave the marketing authorisation for palivizumab as a prophylaxis (passive immunisation) against RSV. The EMA approval is mainly based on two studies and authorises prophylaxis with palivizumab in the following cases:

- During the first year of chronological age in infants born in week 35 or earlier (gestational age)
- During the first two years of chronological age in infants born in week 35 or earlier who suffer from bronchopulmonary dysplasia (BPD)
- During the first two years of chronological age in infants of any gestational age who suffer from haemodynamically significant congenital heart defects (CHD)^{12,13}



4.3. Administration of palivizumab

If an infant meets the criteria and RSV season is about to start or is already in progress, palivizumab is usually given in five monthly injections into the thigh muscles. The dosage is determined by the weight of the infant.¹³

Five palivizumab injections should be given during RSV season in an interval of 4 weeks, up to 5 times. Especially between the first and second injection, the interval of 4 weeks should be strictly adhered to in order to avoid breakthrough infections (an infection occurring despite prophylaxis between the first and the second injection).³



4.4. Safety and efficacy

Palivizumab has been on the market since 1999. Its efficacy and safety have been evaluated in randomised controlled trials (RCTs), and reported adverse effects were similar to placebo. The most frequent adverse events were fever, nervousness, and a temporary redness at the injection site. These events were generally mild and of short duration.¹²

4.5. Differing national guidelines on palivizumab in Europe

So far, no common European guideline on the use of palivizumab exists, and some European countries do not have any published guidelines at all. Since the majority of RSV infections has a mild course and palivizumab prophylaxis is costly, current national guidelines weigh cost-effectiveness considerations differently. This is why guidelines vary between different European countries. The most-followed guidelines on a global level are the US-American guidelines published by the American Academy of Pediatrics AAP.¹⁴ They recommend a more restrictive use of palivizumab due to cost-effectiveness considerations.



For a detailed comparison of national guidelines in Europe please see pages 14 – 23

4.6. Which infants should receive palivizumab remains a disputed issue

Besides cost effectiveness, the dispute is ongoing if palivizumab should be offered to a larger group of preterm infants, contrary to the existing guidelines. Supporters of this perspective argue that giving palivizumab even to moderate to late preterm infants ≤ 35 weeks without additional complications but with at least two risk factors* would decrease the RSV-related hospitalisation rate in this group by 62-75%.¹⁵

In addition to bronchopulmonary dysplasia and congenital heart disease, palivizumab can be considered in other high-risk populations such as in infants with Down syndrome, cystic fibrosis, anatomic pulmonary abnormalities, neuromuscular disorders and profoundly immunocompromised infants.¹⁵

* The study lists three major risk factors: birth three months before and two months after the RSV season start date, smokers in household and/or smoking during pregnancy, and siblings (excluding multiples) and/or (planned) day care.



Different European guidelines on the use of palivizumab in preterm infants without BPD

Country*	Preterms < 28 wGA (extremely preterm)	Preterms 28 to < 32 wGA (very preterm)	32 to < 37 wGA (moderate to late preterm)
Austria	≤ 12 mCH/< 29 wGA	≤ 6 mCH plus risk factors/ 29 – 32 wGA	≤ 3 mCH plus risk factors/ 33 – 35 wGA
Belgium	Recommended; < 12 mCH	Recommended; < 6 mCH; + > 48 hrs ventilatory support in NICU	Not recommended
Bosnia	<28+6d < 12 mCH	With 2 or more risk factors at the start of the first RSV season (< 6 mCH)	Not recommended
Bulgaria	≤ 30 wGA + < 12mCH	30-32 wGA + < 6 mCH	Not recommended
Croatia	<28+6d wGA and ≤ 9 mCH	29+0d – 31+6d wGA and ≤ 6 mCH	32+0d – 35+6d wGA and risk factors (birth 3 months before to 2 months after start of RSV season, smokers in household and/or smoking while pregnant, siblings and/or daycare)
Cyprus	< 29+0 wGA in the 1st year of life		Not recommended
Czech Republic	28+6d wGA (or with a birth weight ≤ 1000g) and ≤ 6 mCH	29+0d – 31+6d wGA with weight ≤ 1500g and ≤ 6 mCH	Not recommended
Denmark	Not recommended		
Estonia	< 28+6d wGA and < 12 mCH	29+0d – 32 wGA: only moderate/ severe BPD or CHD < 12 mCH	Only with severe BPD, or CHD < 12 mCH
Finland	< 29+0d wGA and < 12 mCH		Not recommended
France	< 28+6d wGA and < 12 mCH at beginning of RSV season	Between 29+0d and 31+6d wGA and < 6 mCH at the beginning of RSV season	Not recommended
Germany	≤ 28+6d wGA and ≤ 6 mCH at the beginning of RSV season may receive prophylaxis	29+0d – 34+6d wGA and ≤ 6 mCH at the beginning of RSV season with at least 2 of the following risk factors can be considered for prophylaxis: discharge from neonatal ward before or during RSV season, being in day care or having siblings in day care, or severe underlying neurologic disease	
Greece	≤ 28+0d wGA and ≤ 12 mCH at the beginning of RSV season	29+1d wGA – 31+6d wGA and ≤ 6 mCH at the beginning of RSV season	32+0d wGA – 34+6d wGA and ≤ 6 mCH at the beginning of RSV season with ≥ 2 risk factors
Hungary	≤ 6 mCH		Not recommended
Ireland	< 30+0d wGA in the 1st year of life		Not recommended
Italy	< 29 wGA/≤ 12 mCH	29 to < 36 wGA can be considered	
Latvia	≤ 28+6d wGA and ≤ 12 mCH	≥ 29 wGA Not recommended	
Lithuania	≤ 28 wGA until ≤ 12 mCH	28-30 wGA and ≤ 6 mCH	>30 wGA If they have additional risk factors for RSV infection, Palivi- zumab is prescribed ex consilio.
Macedonia	No specific guideline (Palivizumab not available)		



Different European guidelines on the use of palivizumab in preterm infants without BPD

Country*	Preterms < 28 wGA (extremely preterm)	Preterms 28 to < 32 wGA (very preterm)	32 to < 37 wGA (moderate to late preterm)
Malta	No specific guideline (except if BPD)		
Montenegro	<28+6d wGA: any child without conditions until ≤12 mCH	29-32 + 6d wGA: O2 > 21% longer than 28 days, with 2 or more risk factors at the beginning of the first RSV season (< 6 mCH) (risk factors: discharge in the RSV season, child care attendance or siblings in day care, neurological disease: 2 out of 3 needed)	Doctor's decision on the seriousness of the child's disease: respiratory anomalies, cystic fibrosis, neuromuscular diseases
Netherlands	< 32 wGA and < 6 mCH at start of RSV season		Not recommended
Norway	Not recommended		
Poland	≤ 28+6d wGA and ≤ 12 mCH	29 – 32+6d wGA and ≤ 6 mCH	> 33 wGA not recommended Except all triplets or more ≤35+6d wGA and ≤6 mCH
Portugal	< 28+6d wGA and < 9 mCH	29 – 31+6d wGA and < 3 mCH with mild BPD or 3 – 6 mCH with mild BPD and contagion risk factors	32 – 33+6d wGA if < 46 days mCH with mild BDP or if 46 days – 3 mCH with mild BPD and contagion risk factors
Russia	≤ 28 wGA until ≤ 12 mCH	29 wGA – 32+6d wG and ≤ 6 mCH	33 to 35 wGA who are < 6 mCH
Serbia	< 28+6d wGA and < 12 mCH at beginning of RSV season	Between 29+0d and 31+6d wGA and < 6 mCH at the beginning of RSV season	Not recommended
Slovakia	< 6 mCH	< 6 mCH Preterm infants < 32 wGA during their hospital stay at ICU who were in contact with another patient with RSV infection	33 to 35 wGA who are < 3 mCH and have at least 1 of the risk factors (listed below) 33 to 35 wGA who are < 6 mCH and have at least 2 of the risk factors (listed below) Risk factors: <ul style="list-style-type: none"> • Breastfeeding < 2 months • Birth weight <10-th percentile for gestational age or < 1500 g • Neuromuscular disease • History of severe respiratory distress at neonatal period • Discharge during RSV season • Positive family history of wheezing • Cystic fibrosis • Day care of a child at a nursery school • More than 7 persons living together in the household • Multiple pregnancy



Different European guidelines on the use of palivizumab in preterm infants without BPD

Country*	Preterms < 28 wGA (extremely preterm)	Preterms 28 to < 32 wGA (very preterm)	32 to < 37 wGA (moderate to late preterm)
Slovenia	< 29 wGA and < 12 mCH	29 – 31+6d wGA age/< 6 mCH if sibling < 6 years (preschool)	Not recommended
Spain	≤ 28+6d wGA and ≤ 9 mCH	29+0d – 31+6d wGA and ≤ 6 mCH	32+0d wGA – 34+6d wGA AND age < 10 weeks at beginning of RSV season AND with at least 1 sibling attending school or child-care centre
Sweden	< 26 wGA/≤ 6 mCH	Not recommended	
Switzerland	Not recommended		
Turkey	< 29 wGA/ ≤ 12 mCH	29+0d – 31+6d wGA and ≤ 3 mCH	Not recommended
Ukraine	No specific guideline (Palivizumab not available)		
United Kingdom	Not recommended		

* See list of national guidelines on page 23



Different European guidelines on the use of palivizumab in preterm infants with BPD

Country*	1st year	2nd year
Austria	Treated for BPD in the last 6 months before start of RSV season	
Belgium	Recommended if need for chronic oxygen therapy or ventilatory support	Recommended if need for chronic oxygen therapy or ventilatory support
Bosnia	Preterm infants with BPD in the first RSV season	If they received therapy in the last 6 months (corticosteroids, oxygen, bronchodilators)
Bulgaria	<ul style="list-style-type: none"> • preterm infants ≤ 28 wGA + < 12 mCH • preterm infants 29-35 wGA + < 6 mCH • preterm infants ≤ 35 wGA + < 24 mCH if oxygen or bronchodilators or diuretics or corticosteroids are prescribed 	if oxygen or bronchodilators or diuretics or corticosteroids are prescribed
Croatia	≤ 12 mCH	Children with high risk (oxygen-dependent and/or medical therapy- e.g. use of bronchodilators) (*)
Cyprus	$< 32+0$ wGA with BPD (defined as requirement of $> 21\%$ oxygen for minimum 28d after birth)	BPD and continue to require medical intervention (supplemental oxygen, chronic corticosteroids or diuretic therapy) during second RSV season (*)
Czech Republic	≤ 28 wGA; Infants > 28 wGA if need for any treatment for BPD/CLD within 6 months before start of RSV season (i.e. oxygen therapy, bronchodilators, corticosteroids, diuretics)	If any treatment for BPD/CLD is prescribed within 6 months before start of RSV season (i.e. oxygen therapy, bronchodilators, corticosteroids, diuretics)
Denmark	$< 32+0$ d wGA with severe BPD and need for oxygen supplementation, CPAP or ventilation at term (40 weeks)	Might be considered after expert assessment (*)
Estonia	< 32 wGA with BPD > 32 wGA- if severe BPD	Only to those who receive medical support (inhaled or systemic corticosteroids, bronchodilators, oxygen) within 6 months before beginning of RSV season
Finland	$< 32+0$ d wGA and requirement of $> 21\%$ oxygen for minimum 28d after birth	Only if continued medical support required (chronic corticosteroid therapy, diuretic therapy, or supplemental oxygen) during the 6-month period before the start of the second RSV season
France	< 24 mCH at the beginning of RSV season and with BPD treated within 6 months with mechanical ventilation and/or prolonged oxygen therapy and/or continuous drug therapy (corticosteroids, bronchodilators, diuretics)	
Germany	≤ 24 mCH at the beginning of RSV season and moderate or severe BPD and treated with oxygen in the last 3 months before RSV season should receive prophylaxis	
Greece	$\leq 32+0$ d wGA and ≤ 12 mCH at the beginning of RSV season	$\leq 32+0$ d wGA requiring medical therapy (oxygen, bronchodilators, diuretics or chronic steroids) in the six months preceding the beginning of RSV season
Hungary	< 32 wGA and need for any medication to treat BPD	
Ireland	< 32 wGA with BPD (< 32 wGA and requiring $> 21\%$ oxygen for at least 28 days after birth)	Children with BPD who required at least 28 days of supplemental oxygen after birth and require medical intervention for 6 months preceding the RSV season (*)
Italy	All infants with BPD	Children with BPD with persistent need of medical treatment or in whom it is considered appropriate due to the high risk of the patient based on clinical condition.
Latvia	< 32 wGA with BPD / chronic lung disease (≤ 12 mCH)	Not recommended



Different European guidelines on the use of palivizumab in preterm infants with BPD

Country*	1st year	2nd year
Lithuania	All	
Macedonia	No specific guideline (Palivizumab not available)	
Malta	<36 wGA with moderate or severe BPD who receive supplemental oxygen or respiratory support Children < 2 years requiring treatment for bronchopulmonary dysplasia within the last 6 months (*)	
Montenegro	CLD/BPD	Children < 2 years of age with BPD / chronic lung disease who have been treated (continuous corticosteroids, O ₂ , bronchodilators and/or diuretics) in the last 6 months
Netherlands	Prematures with BPD (28 days > 21% FiO ₂) who are treated for BPD in the 6 months before start of RSV season or infants with other severe pulmonary problems (e.g. CF or autoimmune disease) should be considered for prophylaxis	Ex-prematures with BPD who are treated for BPD in the 6 months before start of RSV season may be considered for prophylaxis
Norway	< 32 wGA and BPD (defined as oxygen need at 36 w), if discharge from hospital in winter season, or 3 months before winter season	Only if oxygen at home, or severe recurrent airway infection
Poland	Recommended for children of all gestational ages < 12 mCH	Not recommended
Portugal	All Infants with severe / moderate BPD (for mild BPD depending on wGA and mCH, see table above)	Moderate or severe BPD and treated with oxygen in the last 6 months before RSV season
Russia	< 24 mCH with BPD who received therapy (corticosteroids, oxygen, bronchodilators) in the last 6 months before beginning of RSV season	
Serbia	All infants with BPD	Infants who required medical therapy (oxygen, bronchodilators, diuretics or chronic steroids) in the six months preceding the beginning of RSV season
Slovakia	Infants with BPD requiring treatment (inhaled or systemic corticosteroids, oxygen, bronchodilators) in the last 6 months before beginning of RSV season	
Slovenia	If treated in the last 6 months before beginning of RSV season	Not recommended (except for children with severe BPD on home ventilator support)
Spain	All infants with BPD	Children with BPD with persistent need of medical treatment or in whom it is considered appropriate due to the high risk of the patient based on clinical condition.
Sweden	Continued oxygen therapy, or oxygen therapy that was discontinued < 6 months before RSV season	Prophylaxis can be considered in severe BPD
Switzerland	Severe BPD: recommended Moderate BPD: individual indication Mild BPD: not recommended	Not recommended
Turkey	All preterm infants with BPD (< 32 0/7 wGA who required supplemental oxygen therapy at least 28 days > 21% FiO ₂)	Ex-premature infants with BPD who require medical therapy including oxygen, bronchodilators or diuretics in the last 6 months before the start of RSV season.
Ukraine	No specific guideline (Palivizumab not available)	
United Kingdom	Infants with moderate and severe BPD and: ≤ 24+0d wGA and ≤ 9 mCH ≤ 28+0d wGA and ≤ 6 mCH ≤ 32+0d wGA and ≤ 3 mCH ≤ 34+0d wGA and ≤ 1.5 mCH	

* See list of national guidelines on page 23



(*) Several countries include into their guideline other high risk infants such as Down syndrome, cystic fibrosis, anatomic pulmonary abnormalities, neuromuscular diseases, immunocompromised infants¹⁵. These were however not systematically collected for this table and therefore incomplete.

Abbreviations used (in order of appearance):

wGA	Complete weeks of gestational age
mCH	Months of chronological age at the beginning of RSV season
BPD	Bronchopulmonary dysplasia
CHD	Congenital heart disease/defect
d	days
CF	Cystic fibrosis
HS-CHD	Haemodynamically significant heart disease/defect



Different European guidelines on the use of palivizumab in infants with CHD

Country*	1st year	2nd year
Austria	HS-CHD (if awaiting corrective surgery or transplantation possible for more than 24 months), pulmonary hypertension, cardiomyopathy (not haemodynamically significant CHD excluded)	
Belgium	Indication has to be confirmed by a pediatric cardiologist. Recommended if: <ul style="list-style-type: none"> • < 2 years CH + HS-CHD <ul style="list-style-type: none"> o During the period waiting for surgical intervention o During the month of surgical intervention • During RSV season + at least one of the following criteria: <ul style="list-style-type: none"> o CHD o SaO₂ < 90 % o Pulmonary arterial hypertension 	
Bosnia	HS-CHD	< 24 mCH in patients with cyanotic or acyanotic CHD with haemodynamic instability, (with uncorrected or palliated cyanotic and non-cyanotic CHD with pulmonary hypertension; need for medicines for congestive heart failure, children listed for heart transplantation)
Bulgaria	Specific diagnoses with CHD with left to right shunt, Complex CHD, Obstructive CHD: If the children with these diagnoses have at least one of the following: <ul style="list-style-type: none"> • circulatory insufficiency grade III IV • waiting for operation or operated but with complications • need for medical treatment • Pulmonary hypertension > 25mm Hg 	<ul style="list-style-type: none"> • previous course of palivizumab • treatment with medications in the previous 6 months
Croatia	≤ 12 mCH with HS-CHD	< 24 mCH in patients with cyanotic or acyanotic CHD with haemodynamic instability (with uncorrected or palliated cyanotic and non-cyanotic CHD with pulmonary hypertension; need for medicines for congestive heart failure, children listed for heart transplantation)
Cyprus	For certain infants with HS-CHD (consultation of cardiologist)	Not recommended
Czech Republic	HS-CHD (with single-ventricular circulation or with severe hypoxemia or with heart failure - significant left to right shunt indicated for surgery or dilated cardiomyopathy or with severe pulmonary hypertension or after heart transplant)	
Denmark	Recommended for cyanotic CHD or HS-CHD	May be indicated in rare cases
Estonia	HS-CHD	Only if severe HS-CHD
Finland	HS-CHD (especially infants with acyanotic heart disease who are receiving medication to control congestive heart failure and will require cardiac surgical procedures or infants with moderate to severe pulmonary hypertension)	Not recommended
France	< 24 mCH at the beginning of RSV season and with HS-CHD	



Different European guidelines on the use of palivizumab in infants with CHD

Country*	1st year	2nd year
Germany	<p>≤ 6 mCH at the beginning of RSV season: Infants with HS-CHD (mostly defects requiring surgery in combination with pulmonary hypertension, pulmonary venous congestion or cyanosis) or severe CHD requiring medical treatment should be given prophylaxis</p> <p>6 – 12 mCH at the beginning of RSV season: Infants with HS-CHD (mostly defects requiring surgery in combination with pulmonary hypertension, pulmonary venous congestion or cyanosis) or severe CHD requiring medical treatment may be given prophylaxis</p>	Not recommended
Greece	<p>Infants ≤ 12 mCH with HS-CHD at the beginning of RSV season (infants with non-cyanotic CHD on therapy for congestive heart failure and scheduled for surgery); infants ≤ 12 mCH with moderate to severe pulmonary hypertension at the beginning of the epidemic season; infants ≤ 12 mCH suffering from congestive cardiomyopathy on treatment at the beginning of the epidemic season</p> <p>Infants with surgically repaired CHD who continue to need therapy for congestive heart failure; infants with cyanotic CHD prior to the surgical procedure or after a palliative procedure, on indication of the paediatric cardiologist based on the haemodynamic status of the patient</p>	
Hungary	HS-CHD	HS-CHD
Ireland	Certain infants with HS-CHD, specifically those with acyanotic CHD requiring medication for congestive cardiac failure and/or moderate to severe pulmonary hypertension, infants with cyanotic CHD	Not recommended
Italy	HS-CHD awaiting corrective surgery or transplantation, pulmonary hypertension, cardiomyopathy; cyanotic infants after corrective surgery (Exclusion: not hemodynamically significant defects at the heart and central blood vessels)	Infants with heart transplant during RSV season can receive prophylaxis (Exclusion: not hemodynamically significant defects at the heart and central blood vessels)
Latvia	Recommended for premature child with acyanotic HS-CHD OR a child with acyanotic or cyanotic CHD with serious comorbidities, usually with multiple organ involvement (≤ 12 mCH)	Not recommended
Lithuania	All CHD if cardiologists prescribe	
Macedonia	No specific guideline (Palivizumab not available)	
Malta	Children < 2 years with HS-CHD; Children with cyanotic or acyanotic CHD plus significant co-morbidities Acyanotic HS-CHD with one of the following age criteria: ≤ 24+0d wGA and <9 mCH; 24+1d – 28+0d wGA and < 6 mCH; 28+1d – 32+0d wGA and <3 mCH; 32+1d – 34+0d wGA and <1,5 mCH.	
Montenegro	HS-CDH ≤12 mCH	Not recommended
Netherlands	Infants with HS-CHD	Infants with severe HS-CHD may be considered for prophylaxis
Norway	HS-CHD, palliative heart shunt and moderate or serious Persistent Pulmonary Hypertension (PPHN)	
Poland	HS-CHD	Not recommended
Portugal	All Infants with < 24 mCH if they have CHD, HS-CHD, Neuromuscular disease (NMD), Chronic pulmonary disease (CPD), Pulmonary Hypertension (PHT), Congenital Diaphragmatic Hernia (CDH), Severe Combined Immunodeficiency (SCI), Pharmacological Immunodepression (PID), AIDS	



Different European guidelines on the use of palivizumab in infants with CHD

Country*	1st year	2nd year
Russia	HS-CHD, not operated or partially corrected, regardless of wGA, in the presence of: <ul style="list-style-type: none"> • functional class II-IV heart failure (NYHA), requiring medical treatment • moderate or severe pulmonary hypertension (pulmonary artery pressure \geq 40 mm Hg according to echocardiography results) 	
Serbia	HS-CHD	Not recommended
Slovakia	HS-CHD	
Slovenia	HS-CHD, pulmonary hypertension or cardiomyopathy	HS-CHD (until complete surgical correction)
Spain	1. CHD: <ol style="list-style-type: none"> a. Non corrected, Haemodynamically significant b. Partially corrected (palliative intervention), Haemodynamically significant c. Residual lesions post-correction, Haemodynamically significant d. Corrected with severe pulmonary complications, mechanical ventilation prolonged e. Corrected, post Cardiopulmonary bypass (CPB), in the early postoperative period, Haemodynamically significant 2. Pulmonary Hypertension: primary or secondary, moderate to severe 3. Cardiomyopathies, with medical treatment 4. Arrhythmia: severe, recurrent Haemodynamically significant or with chronic pluri- medication 5. Heart transplant postop or in waiting list. 6. Other CHD not included previously, associated to Down Syndrome, 22q11 del, or immunodeficiency	
Sweden	HS-CHD, pulmonary hypertension, cardiomyopathy (Exclusion: CHD that has been corrected or does not require surgery)	Complicated/palliated CHD can receive prophylaxis (Exclusion: CHD that has been corrected or does not require surgery)
Switzerland	HS-CHD can be indicated	Not recommended
Turkey	HS-CHD and $<$ 24 mCH Infants with cardiomyopathy $<$ 12 mCH that require medical treatment Infants with surgically repaired CHD who continue to need therapy for congestive heart failure and $<$ 12 mCH Infants waiting for transplantation or infants with heart transplant $<$ 12 months of age	Infants with HS-CHD and $<$ 24 mCH
Ukraine	No specific guideline (Palivizumab not available)	
United Kingdom	Acyanotic CHD and \leq 26+0d wGA, \leq 6 mCH \leq 28+0d wGA, \leq 3 mCH \leq 30+0d wGA, \leq 3 mCH \leq 32+0d wGA, \leq 1.5 mCH Cyanotic and acyanotic infants with significant comorbidities	Not recommended

* See list of national guidelines on page 23

See list of abbreviations used on page 19



* Guidelines by countries:

Austria	Austrian Society of Children's and Adolescents' Health (ÖGKJ), 2008
Belgium	Belgian Society for Neonatology, National Institute for Sickness and Disability Insurance (RIZIV), 2006
Bosnia	Neonatal Society in Bosnia and Herzegovina, 2016
Bulgaria	Bulgarian Neonatology Society
Croatia	Croatian RSV Working Group, Croatian Paediatric Society , Croatian Society for Neonatology and Neonatal Intensive Medicine
Cyprus	Cyprus Society of Perinatal Medicine
Czech Republic	Czech Neonatology Society, 2014, Czech Society of Paediatric Cardiology (for CHD), 2009, Czech Society of Paediatric Pulmonology (for special populations), 2018
Denmark	Danish Neonatology Society, 2018
Estonia	Estonian Paediatric Association
Finland	AAP guideline 2014 is used (information provided by Oulu University Hospital)
France	French Neonatal Society (SFN), 2007
Germany	German Society of Paediatric Infectious Diseases (DGPI), 2018
Greece	Hellenic Neonatal Society
Hungary	Hungarian Society of Perinatology, Ministry of Human Resources, 2013
Ireland	Irish Neonatal Society, Neonatal Clinical Advisory Group of the Royal College of Physicians of Ireland
Italy	Italian Society of Neonatology (SIN), 2015
Latvia	Latvian Society of Neonatology, Latvian Paediatric Association, 2015
Lithuania	Lithuanian Neonatology Association
Macedonia	No guideline, palivizumab not available (confirmed by University Hospital Skopje)
Malta	Palivizumab Committee of Mater Dei Hospital, Malta, 2018
Montenegro	(Confirmed by) Institute of Children's Disease
Netherlands	Dutch Society of Paediatrics (NVK), 2005
Norway	Norwegian Pediatric Association ("Norsk barnelegeforening"), 2014
Poland	Polish Neonatal Society
Portugal	Portugese Society of Neonatology, Associação Portuguesa de Enfermagem Pediátrica e Neonatal, General Directorate of Health, 2015
Russia	The Union of Paediatricians of Russia, 2015
Serbia	Institute of Public Health and Ministry of Health, in cooperation with Serbian Perinatal and Neonatal Society, 2018
Slovakia	Slovak Paediatric Society, Ministry of Health in cooperation with the Pediatric Neonatal Society, 2013
Slovenia	Slovene Paediatric Association, Advisory Group of the Slovene Ministry of Health, 2005
Spain	Spanish National Society of Neonatology, 2019
Sweden	Swedish Medical Products Agency, 2015
Switzerland	Swiss Society of Neonatology
Turkey	Turkish Neonatal Society, 2018
Ukraine	No guideline, palivizumab not available (confirmed by Association of Neonatologists of Ukraine)
UK	British Association of Perinatal Medicine (BAPM), UK Joint Committee on Vaccination and Immunisation (JCVI), UK National Health Service (NHS), 2015
Macedonia	No guideline, palivizumab not available (confirmed by University Hospital Skopje)





5. Diagnosis

5.1. Diagnostic tests

Usually an RSV infection is diagnosed by physical examination. The cold-like symptoms may include a runny nose, decrease in appetite, breathing difficulties, coughing, sneezing, fever (typically low-grade), diffuse rales (a rattling sound in the lungs) and wheezing (a whistling sound in the lungs) caused by inflammation. As the majority of lower respiratory tract infections in the first years of life is caused by RSV during RSV season and there is no causative treatment available, a diagnostic test is usually not carried out. Sometimes tests are done to confirm the diagnosis retrospectively, mainly for surveillance and research purposes, and for cohorting hospitalised children.

There are different tests on the market, mainly:

- Tests using polymerase chain reaction (PCR) can deliver the most exact results in a short amount of time
- Immunochromatographic tests can deliver results within hours but are not very reliable
- Viral culture is a safe but very time-consuming method and has lost importance due to the availability of newer tools²

5.2. When to bring an ill infant to a paediatrician

If an infant shows typical signs of a cold, it should be taken to the paediatrician. This is particularly true if the infant is at high risk because it is born preterm and/or has additional underlying medical conditions. Typical signs of a cold include: runny nose, slight fever, sneezing or coughing, irritability, red eyes, lack of appetite, having trouble sleeping or staying asleep, or difficulty with feeding due to a stuffy nose.

5.3. Case of emergency: When to take an infant immediately to hospital

A serious infection in small infants can become life-threatening, therefore infants who show any of the following symptoms are classified as emergency cases and should immediately be taken to hospital:

- Apnoea (breathing pauses)
- Infant appears to be seriously unwell
- Severe respiratory problems (for example grunting), marked chest recession, or a respiratory rate of over 70 breaths/minute
- Central cyanosis (bluish or purplish discolouration of the skin due to lack of oxygen)
- Persistent oxygen saturation below 92%¹⁶



Consider referring infants to hospital if they have any of the following symptoms:

- A respiratory rate of > 60 breaths/minute
- Problems with breastfeeding or insufficient oral fluid intake
- Clinical dehydration¹⁶

Take into account additional risk factors:

- Chronic lung disease (including bronchopulmonary dysplasia)
- Haemodynamically significant congenital heart disease
- Young age (< 3 months)
- Preterm birth (particularly < 32 weeks)
- Neuromuscular disorders
- Immunodeficiency¹⁶

Please also take into consideration the general family situation:

- Can the parents look after a very ill child 24/7?
- Do the parents feel confident to look after an ill child at home?
- How far away is a hospital in case of deterioration?¹⁶

6. Treatment in hospital

6.1. Supportive care measures

There are a number of supportive care measures that can alleviate the symptoms of RSV infections and can help support and stabilise the infant. The term supportive care refers to a large set of measures and treatments to prevent, control or relieve symptoms and complications of a disease and to give the patient comfort.



6.1.1. Supplemental oxygen and respiratory support

If an infant is ill and has a persistently low oxygen saturation (<92%), it needs supplemental oxygen.¹⁶ There are various ways to administer oxygen, which method is used depends on whether the infant is able to breathe sufficiently by itself and how much additional oxygen is needed.

If the infant can breathe without assistance, a nasal cannula is the preferred method to administer additional oxygen. A nasal cannula is a soft and thin plastic tube with soft prongs that are easily inserted into the nostrils.



High-flow nasal cannula (HFNC) therapy is able to deliver oxygen at a flow rate of up to 60 litres per minute. In a recent randomised controlled trial, infants receiving high-flow oxygen vs. standard oxygen at hospital admission had a significantly lower risk of escalation of care due to treatment failure.¹⁷

Continuous positive airway pressure, or CPAP (pronounced „C-pap“), is another non-invasive oxygen supplementation method for infants that are not able to breathe well, but do not need mechanical ventilation. The CPAP machine delivers air or oxygen with constant air pressure via tubes with soft nasal prongs or via a small mask that is put over the infant’s nose. The constant air pressure helps to keep the lungs open. CPAP is recommended for infants with bronchiolitis and impending respiratory failure.¹⁶

Finally, a ventilator or breathing machine might be needed if infants cannot breathe at all because they are too weak, too tired or too ill. The ventilator delivers the gas through a tube that is placed in the infant’s windpipe.

There are new approaches to avoid mechanical ventilation, for example nasal intermittent mandatory ventilation (NIMV). NIMV combines non-invasive CPAP with intermittent ventilator inhalations and does not require intubation. This method was recently investigated in a study with a small cohort. It was shown that 86% of the infants suffering from acute respiratory failure (ARF) and treated with NIMV did not require mechanical ventilation.¹⁸

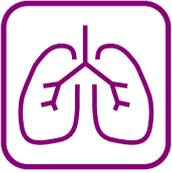


6.1.2. Airway clearance/nasal suctioning

Infants are mainly nasal breathers, so if secretions build up in the nose due to a respiratory infection, nasal bulb suctioning or deep suctioning methods are sometimes used to make breathing easier. However, especially deep suctioning is quite unpleasant and distressing for the infant, it may lengthen the hospital stay¹⁹ and so far there are no evidence-based trials available. Therefore, routine suctioning is not recommended, and upper airway suctioning might be considered only in infants with bronchiolitis, respiratory distress, feeding problems or apnoea caused by upper airway secretions.¹⁶

Another method to mobilise secretions in the lower airways is to apply nebulised saline into the infant’s nose. In clinical trials, regular nebulised saline and nebulised hypertonic saline have been shown to be beneficial, and in a recent study hypertonic saline has been shown to be superior to regular saline droplets.²⁰





6.1.3. Chest physiotherapy

Chest physiotherapy is a method to assist in the clearance of respiratory secretions and improve breathing by manual techniques like percussion, vibration, and gravity. This method is not recommended, unless there are other relevant diseases where clearing of secretions is impaired (e.g. spinal muscular atrophy or severe tracheomalacia).¹⁶



6.1.4. Capillary blood gas testing

It might be necessary to get a capillary blood gas sample from the infant's heel to test adequacy of ventilation. This is recommended in case the respiratory distress is worsening, supplemental oxygen is given by more than 50%, or if there is a risk of respiratory failure. Capillary blood gas testing is not recommended as a routine test in infants with bronchiolitis.¹⁶



6.1.5. Hydration

If an infant is not receiving enough fluid (inadequate oral fluid intake of 50–75% of usual volume) it might rapidly become dehydrated. Signs of dehydration can be a dry mouth and tongue, listlessness, no tears when crying, no wet diapers for three hours or more. If fluids cannot be taken in orally, fluids should be given either by nasogastric tubes (going through the nose into the stomach), or orogastric tubes (going through the mouth into the stomach), or by intravenous fluid replacement.¹⁶



6.1.6. Feeding support

If an infant has trouble breathing and needs oxygen, it might not be able to drink by itself and cannot be breastfed. In this case, it might need to get the necessary calories in by enteral nutrition (via nasogastric or orogastric tubes). Tube feeding is usually unproblematic and infants adjust to it quickly. However, in combination with oxygen supplementation via high-flow nasal cannula there is a small risk of aspiration of the nutritive solution which should be monitored closely.²¹

6.2. Medication

Different drugs have been tested for treatment of RSV infections in randomised controlled trials but did not prove to be effective. They are therefore not routinely recommended for treatment of RSV disease in most guidelines. These medications include ribavirin, bronchodilators, corticosteroids, antibiotics, antipyretics, adrenaline (nebulised), montelukast, and ipratropium bromide.¹⁶



7. Growth and follow-up

7.1. Long-term outcomes

Children who have suffered from a severe RSV infection requiring hospitalisation when they were small, have a higher risk to develop respiratory problems later in life. They should be monitored closely regarding their respiratory function and well-being. It is also advisable taking the child every 6 months to a check-up at a children's pulmonologist, at least for the first 3 years of life, and to continue monitoring lung function and possible pulmonary problems until adulthood.

A systematic review based on data between 1995 and 2015 confirmed that lower respiratory tract infections caused by RSV represent a significant risk factor for respiratory diseases in the first 10 years of life and sometimes well into adolescence and adulthood, like:

- Long-term wheezing
- Asthma
- Impaired lung function⁷

7.2. Some recommendations for children and young adults with lung problems

Smoking:

Active and passive smoking are harmful to every person, but smoking around children and adults with pulmonary problems needs to be avoided completely.

Exercise:

For ill children, exercising has a great potential to improve health and well-being, increase the quality of life, reduce exclusion and promote friendships. Therefore, children who suffer from pulmonary limitations should be encouraged to exercise. Depending on the degree of the pulmonary problems, some rules (and common sense) should be applied to take advantage of the benefits while at the same time avoid overstraining and thus worsening the condition. Parents should also inform school and teachers about the health condition and the lower achievement potential of their child in school sports. Ideally, the reduced abilities in sports are taken into account when giving marks in sports, as to not discourage the child.²²



8. Conclusion and Call to Action

Respiratory syncytial virus (RSV) is the most frequent cause of acute lower respiratory tract infections in infants, associated with significant morbidity in industrialised nations. In particular, preterm infants and infants with bronchopulmonary dysplasia (BPD) and haemodynamically significant congenital heart disease (CHD) have an increased risk of severe RSV infections requiring hospitalisation. RSV infections are one of the most common reasons for hospitalisation and emergency department visits in children under two years.³

The most simple and effective method to prevent RSV infections in infants and young children are simple hygiene and behavioural measures. In addition, RSV prophylaxis with palivizumab has shown to be safe and effective and should be considered in high-risk infants during RSV season.¹²

There are no European-wide guidelines on prevention, prophylaxis, supportive care measures, and follow-up of RSV infections in place, leading to inconsistencies and inequity in Europe.

We therefore call on all stakeholders involved in neonatal and paediatric research and care:

- To educate and train healthcare providers, parent representatives and policy makers about the risks associated with RSV infection, the risk factors for a severe course, and the measures of prevention and prophylaxis to reduce morbidity and hospitalisation in preterm and ill infants
- To develop a European-wide guideline on prevention, prophylaxis, supportive care measures and follow-up of RSV infections in preterm and ill infants, and to implement this European guideline on a national and local level
- To increase research efforts to collect more reliable follow-up data to understand the underlying mechanisms of RSV infections, and why they might cause respiratory problems later in life
- To increase efforts to develop a vaccine against RSV
- To provide accurate and reliable information to parents and families on RSV, including how they can reduce the risk of infection by following simple hygiene and behavioural rules



9. References

1. Broberg EK, Waris M, Johansen K, et al. European Influenza Surveillance Network EIS. Seasonality and geographical spread of respiratory syncytial virus epidemics in 15 European countries, 2010 to 2016. *Eurosurveillance* 2018; 23: 17–00284.
2. Robert Koch Institut. RKI-Ratgeber - Respiratorische Synzytial-Virus-Infektionen (RSV) (Guidebook on RSV infections). https://www.rki.de/DE/Content/Infekt/EpidBull/Merkblaetter/Ratgeber_RSV.html (accessed 28 Nov 2018).
3. Liese J, Forster L. S2k-Leitlinie zur Prophylaxe von schweren Erkrankungen durch Respiratory Syncytial Virus (RSV) bei Risikokindern (German guideline on severe RSV infection prophylaxis in children at risk). Update 2017/2018.
4. Nair H, Nokes DJ, Gessner BD, et al. Global burden of acute lower respiratory infections due to respiratory syncytial virus in young children: a systematic review and meta-analysis. *Lancet* 2010; 375: 1545–55.
5. Shi T, McAllister DA, O'Brien KL, et al. Global, regional, and national disease burden estimates of acute lower respiratory infections due to respiratory syncytial virus in young children in 2015: a systematic review and modelling study. *Lancet* 2017; 390: 946–58.
6. Bont L, Checchia PA, Fauroux B, et al. Defining the Epidemiology and Burden of Severe Respiratory Syncytial Virus Infection Among Infants and Children in Western Countries. *Infectious Diseases and Therapy* 2016; 5: 271–98.
7. Fauroux B, Simões EAF, Checchia PA, et al. The Burden and Long-term Respiratory Morbidity Associated with Respiratory Syncytial Virus Infection in Early Childhood. *Infect Dis Ther* 2017; 6: 173–97.
8. Hasegawa K, Mansbach JM, Bochkov YA, et al. Association of Rhinovirus C Bronchiolitis and Immunoglobulin E Sensitization During Infancy With Development of Recurrent Wheeze. *JAMA Pediatr* 2019; 173(6): 544-552.
9. Furuta M, Sin J, Ng ESW, Wang K. Efficacy and safety of pertussis vaccination for pregnant women – a systematic review of randomised controlled trials and observational studies. *BMC Pregnancy Childbirth* 2017; 17:390.
10. Centers for Disease Control and Prevention (CDC). Tdap during Pregnancy Provides the Best Protection for Mother and Infant. <https://www.cdc.gov/pertussis/pregnant/hcp/pregnant-patients.html> (accessed 15 July 2019).
11. EFCNI. Patient safety and hygiene practice. <https://newborn-health-standards.org/standards/patient-safety-hygiene-practice/overview/> (accessed Feb 22, 2019).
12. IMPact Study Group. Palivizumab, a Humanized Respiratory Syncytial Virus Monoclonal Antibody, Reduces Hospitalization From Respiratory Syncytial Virus Infection in High-risk Infants. *Pediatrics* 1998; 102: 531–7.
13. Feltes TF, Cabalka AK, Meissner HC, et al. Palivizumab prophylaxis reduces hospitalization due to respiratory syncytial virus in young children with hemodynamically significant congenital heart disease. *The Journal of Pediatrics* 2003; 143: 532–40.
14. Committee on Infectious Diseases and Bronchiolitis Guideline Committee. Updated Guidance for Palivizumab Prophylaxis Among Infants and Young Children at Increased Risk of Hospitalization for Respiratory Syncytial Virus Infection. *Pediatrics* 2014; 134: 415–20. (unchanged after review in 2017).
15. Luna MS, Manzoni P, Paes B, et al. Expert consensus on palivizumab use for respiratory syncytial virus in developed countries. *Paediatric Respiratory Reviews* 2020, 33: 35-45.
16. NICE guideline. Bronchiolitis in children: diagnosis and management. 1 June 2015. <https://www.nice.org.uk/guidance/ng9/resources/bronchiolitis-in-children-diagnosis-and-management-pdf-51048523717> (accessed Feb 11, 2019).
17. Franklin D, Babl FE, Schlapbach LJ, et al. A Randomized Trial of High-Flow Oxygen Therapy in Infants with Bronchiolitis. *New England Journal of Medicine* 2018; 378: 1121-1131.
18. Wang BC, Pei T, Lin CB, et al. Clinical characteristics and outcomes associated with nasal intermittent mandatory ventilation in acute pediatric respiratory failure. *World J Crit Care Med* 2018; 7: 46–51.
19. Mussman GM, Parker MW, Statile A, Sucharew H, Brady PW. Suctioning and Length of Stay in Infants Hospitalized With Bronchiolitis. *JAMA Pediatr* 2013; 167: 414–21.
20. Zhang L, Mendoza-Sassi RA, Wainwright C, Klassen TP. Nebulised hypertonic saline solution for acute bronchiolitis in infants. *Cochrane Database of Systematic Reviews* 2017(12).
21. Tracy MC, Cornfield DN. Children With Bronchiolitis on High Flow Nasal Cannula: To Feed or Not Feed, That Is Not the Only Question. *Hospital Pediatrics* 2017; Vol. 7, May 2017.
22. Riner WF, Sellhorst SH. Physical activity and exercise in children with chronic health conditions. *Journal of Sport and Health Science* 2013; 2: 12–20.



10. Appendix

Hygiene measures in hospital

Standard hygiene precautions

The following standard measures are the minimum requirements that should be observed in the care of all patients at all times, and aim to protect healthcare workers and prevent transmission of infectious agents from healthcare worker to patients. These rules should be applied in all patients, regardless of suspected or confirmed infection status.

Hand hygiene

- After touching blood, body fluids, secretions, excretions, and contaminated items
- Immediately before and after any patient contact and after taking off gloves

Use of personal protective equipment

- Gloves: contact with blood, body fluids, secretions, excretions, contaminated items, mucous membranes, and non-intact skin
- Gown: during procedures and patient care activities when skin/clothes might be exposed to body fluids, secretions or excretions
- Mask/eye protection: if splashes or sprays of blood, body fluids, or secretions might occur during procedures and patient care activities

Safe handling of injection equipment

- Needles and syringes are only to be used once
- Limit use of multi-dose vials, and dedicate to a single patient, when possible

Practice safe handling of equipment

- In the patient environment: Potentially contaminated equipment or surfaces
- According to valid facility policy: Environmental cleaning and disinfection

Respiratory hygiene

- Dispose of tissue in no-touch receptacles
- After contact with respiratory secretions practice hand hygiene
- Use mask and maintain spatial separation (approx. 1 metre), if possible



Droplet precautions

To avoid the transmission of infectious organisms like RSV through droplet infections, there are measures to reduce close contact with respiratory secretions via coughing, sneezing, talking, or droplet-inducing procedures.

Droplet precautions include:

- Private room or cohort
- Special air flow is not needed
- Wear mask (surgical or isolation) if working within close range of the patient, if possible
- Put droplet mask on patient when leaving room, if tolerated
- Transport patient only if necessary
- Healthcare professionals to strictly observe respiratory hygiene rules/cough etiquette
- Gown and gloves as part of standard precautions and facility policy

[Source: www.nursingcenter.com/clinical-resources/nursing-pocket-cards/isolation-precautions, downloaded on 03.05.2019]

Letter from an ill baby to family and friends

Sometimes relatives and friends are, understandably, very eager to see the new baby. Especially if the baby is born preterm or ill, they want to help and support the family. However, having many visitors can challenge the baby's immune system. It can become even life threatening if the visitors bring viruses or other germs into the home. Therefore, we developed a letter written in the name of the newborn baby, that parents can send to friends and family:

Dear

My name is and I am very happy that I have wonderful relatives and friends like you! However, at the moment, I am not healthy enough to meet you as I still need to get a lot of rest. So can you please visit me in a few months when I am older and stronger?

Looking forward to seeing you soon, Mom and Dad will let you know when!

Thank you,



How to best wash your hands

<p>Wash your hands - it's easy</p>  <p>EFCNI european foundation for the care of newborn infants</p> <p>NEVEN SUBOTIC STIFTUNG</p>	<p>Wash your hands - it's easy</p> <p>1 Rinse Wet hands under running water.</p> <p>2 Foam Use decent amount of soap.</p> <p>3 Scrub Lather hands completely for about 20-30 sec, also between fingers and fingertips.</p> <p>4 Wash Cleanse hands well under running water.</p> <p>5 Dry Wipe hands thoroughly with clean towel if possible tissue.</p> <p>EFCNI european foundation for the care of newborn infants</p> <p>NEVEN SUBOTIC STIFTUNG</p>	<p>Wash your hands - it's easy</p> <p>1 Rinse Wet hands under running water.</p> <p>2 Foam Use decent amount of soap.</p> <p>3 Scrub Lather hands completely for about 20 seconds, also between fingers and fingertips.</p> <p>4 Wash Cleanse hands well under running water.</p> <p>5 Dry Wipe hands thoroughly with clean towel if possible tissue.</p> <p>EFCNI european foundation for the care of newborn infants</p> <p>NEVEN SUBOTIC STIFTUNG</p>
<p><i>Version for children</i></p>	<p><i>Version for adolescents</i></p>	<p><i>Version for adults</i></p>

Thorough handwashing is the easiest and most efficient way to reduce bacteria and viruses on your hands and reduce the risk to catch or pass on an infection. To create more awareness on washing hands, EFCNI and the Neven Subotic Stiftung have created the campaign "Wash your hands – it's easy". It explains in five easy steps how to wash hands to prevent infections.

You can download the poster at: www.efcni.org/activities/campaigns/wash-your-hands



Hygiene measures at home

- Wash your hands frequently and thoroughly with soap and water for at least 20 seconds, or use a disinfectant
- Keep your nails short and avoid using artificial nails
- Clean frequently touched surfaces with soap and water or disinfectant (e.g. toys, bed rails, tables, smart phones, jewelry)
- Don't share your mug, plate or cutlery with others
- Avoid rubbing your nose or eyes
- Don't kiss high-risk children if you or they show cold-like symptoms. If possible, avoid close interaction with high-risk children altogether if you have cold-like symptoms
- When coughing or sneezing, cover your mouth and nose with a tissue and throw the tissue away. If you don't have a tissue, cough or sneeze into your upper sleeve

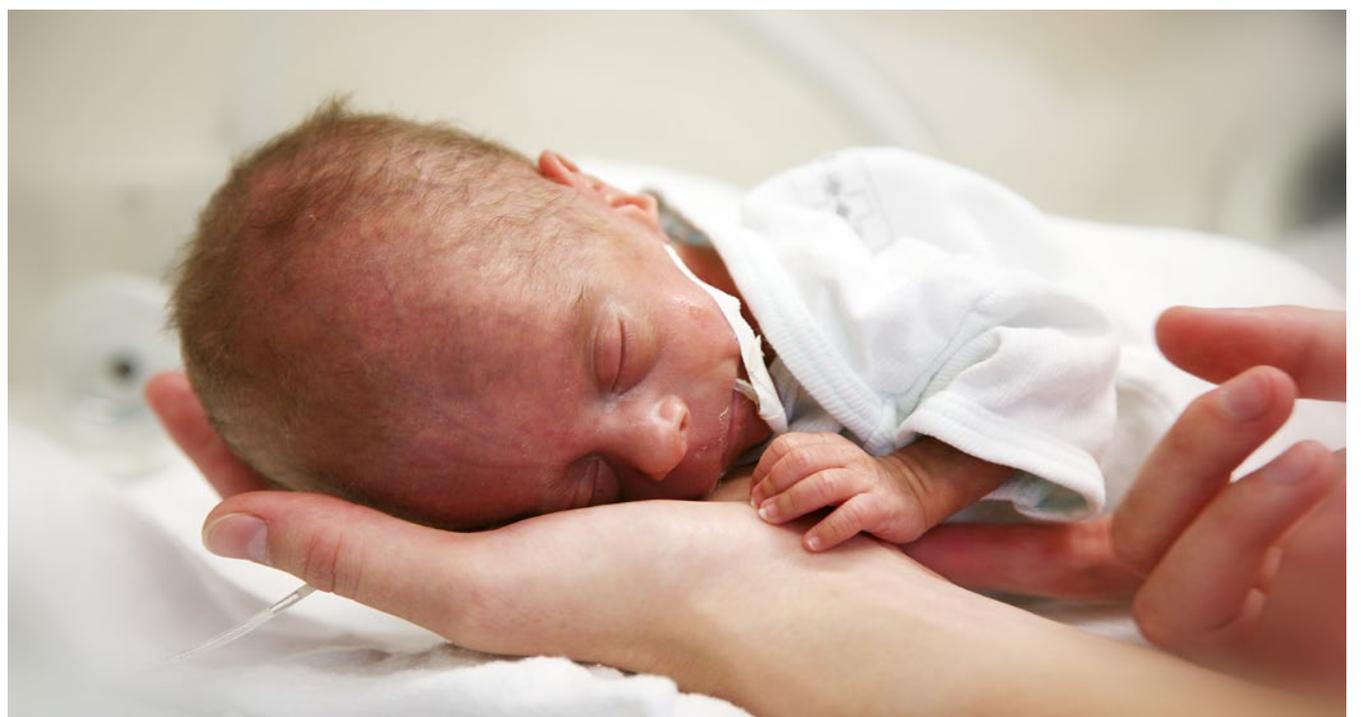
Behavioural measures at home

- Don't smoke at home, in the car, and anywhere near a child. Wash your hands after smoking
- Breastfeeding is crucial, it reduces the risk for infections in general by strengthening the immune system. According to the WHO, (exclusive) breastfeeding is recommended for a minimum of 6 months, if possible
- Keep a distance to small children if you have cold-like symptoms and try to avoid people who have symptoms of common cold
- High-risk children should spend as little time as possible in potentially infectious places, so try to reduce staying in crowded places to a minimum (supermarkets, public transportation, shops etc.)
- If it is possible in the family context, avoid taking siblings of high-risk infants to day care facilities during outbreaks and RSV peak season
- When taking an infant to the doctor's office, take advantage of special timeslots for preterm or vulnerable infants or use separate waiting rooms to prevent transmission of the virus

[Source: www.cdc.gov/rsv/, downloaded on 03.05.2018]



We warmly thank the following **parent organisations** for supporting the position paper on respiratory syncytial virus (RSV) in preterm and ill infants (in alphabetical order):



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*Despeena, born at 24 weeks
weighing 820 grams*



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About EFCNI

The European Foundation for the Care of Newborn Infants (EFCNI) is the first pan-European organisation and network to represent the interests of preterm and newborn infants and their families. It brings together parents, healthcare experts from different disciplines, and scientists with the common goal of improving long-term health of preterm and newborn children. EFCNI's vision is to ensure the best start in life for every baby.

For more information: www.efcni.org

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