

**91****Bronchiolitis in children**

A national clinical guideline

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November 2006

# KEY TO EVIDENCE STATEMENTS AND GRADES OF RECOMMENDATIONS

## LEVELS OF EVIDENCE

- 1<sup>++</sup> High quality meta-analyses, systematic reviews of randomised controlled trials (RCTs), or RCTs with a very low risk of bias
- 1<sup>+</sup> Well conducted meta-analyses, systematic reviews of RCTs, or RCTs with a low risk of bias
- 1<sup>-</sup> Meta-analyses, systematic reviews of RCTs, or RCTs with a high risk of bias
- 2<sup>++</sup> High quality systematic reviews of case control or cohort studies  
High quality case control or cohort studies with a very low risk of confounding or bias and a high probability that the relationship is causal
- 2<sup>+</sup> Well conducted case control or cohort studies with a low risk of confounding or bias and a moderate probability that the relationship is causal
- 2<sup>-</sup> Case control or cohort studies with a high risk of confounding or bias and a significant risk that the relationship is not causal
- 3 Non-analytic studies, eg case reports, case series
- 4 Expert opinion

## GRADES OF RECOMMENDATION

*Note: The grade of recommendation relates to the strength of the evidence on which the recommendation is based. It does not reflect the clinical importance of the recommendation.*

- A** At least one meta-analysis, systematic review of RCTs, or RCT rated as 1<sup>++</sup> and directly applicable to the target population; *or*  
A body of evidence consisting principally of studies rated as 1<sup>+</sup>, directly applicable to the target population, and demonstrating overall consistency of results
- B** A body of evidence including studies rated as 2<sup>++</sup>, directly applicable to the target population, and demonstrating overall consistency of results; *or*  
Extrapolated evidence from studies rated as 1<sup>++</sup> or 1<sup>+</sup>
- C** A body of evidence including studies rated as 2<sup>+</sup>, directly applicable to the target population and demonstrating overall consistency of results; *or*  
Extrapolated evidence from studies rated as 2<sup>++</sup>
- D** Evidence level 3 or 4; *or*  
Extrapolated evidence from studies rated as 2<sup>+</sup>

## GOOD PRACTICE POINTS

- Recommended best practice based on the clinical experience of the guideline development group

Scottish Intercollegiate Guidelines Network

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November 2006

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**Scottish Intercollegiate Guidelines Network**  
**28 Thistle Street, Edinburgh EH2 1EN**

**[www.sign.ac.uk](http://www.sign.ac.uk)**

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# 1 Introduction

## 1.1 BACKGROUND

Bronchiolitis of infancy is a clinically diagnosed respiratory condition presenting with breathing difficulties, cough, poor feeding, irritability and, in the very young, apnoea. These clinical features, together with wheeze and/or crepitations on auscultation combine to make the diagnosis. Bronchiolitis most commonly presents in infants aged three to six months.<sup>1</sup>

Bronchiolitis occurs in association with viral infections (respiratory syncytial virus; RSV, in around 75% of cases)<sup>2</sup> and is seasonal, with peak prevalence in the winter months (November to March) when such viruses are widespread in the community. Re-infection during a single season is possible.

The burden of disease is significant. Around 70% of all infants will be infected with RSV in their first year of life and 22% develop symptomatic disease. Since RSV is associated with only 75% of bronchiolitis cases, it may be estimated that around a third of all infants will develop bronchiolitis (from all viruses) in their first year of life.<sup>3</sup> For Scotland this translates to approximately 15,000 infants.

Around 3% of all infants younger than one year are admitted to hospital with bronchiolitis.<sup>4</sup> Based on Scottish morbidity recording for the years 2001 to 2003 a mean of 1,976 children per year (aged up to 12 months) were admitted to hospital with bronchiolitis as the principal diagnosis.<sup>5</sup>

The rate of admissions to hospital with bronchiolitis has increased over the past 10 years. The reasons for this are not fully understood and are likely to be multifactorial and include improved survival of preterm infants.<sup>4</sup>

In most infants the disease is self limiting, typically lasting between three and seven days. Most infants are managed at home, often with primary care support. Admission to hospital is generally to receive supportive care such as nasal suction, supplemental oxygen or nasogastric tube feeding.

Children with underlying medical problems (prematurity, cardiac disease or underlying respiratory disease) are more susceptible to severe disease and so have higher rates of hospitalisation.<sup>4</sup> In preterm infants less than six months of age, admission rate with acute bronchiolitis is 6.9% with admission to intensive care more frequent in such patients.<sup>4</sup>

In a UK study, the RSV-attributed death rate (measured in infants aged one to 12 months) was 8.4 per 100,000 population.<sup>6</sup>

Twenty percent of infants with bronchiolitis (40-50% of those hospitalised) proceed to a grumbling, sometimes protracted, respiratory syndrome of persistent cough and recurrent viral-induced wheeze.<sup>7</sup> Ongoing symptoms may relate to continuing inflammation and temporary ciliary dysfunction.<sup>8</sup> An association between acute bronchiolitis and later respiratory morbidity is recognised.<sup>9</sup>

## 1.2 NEED FOR A GUIDELINE

There is widespread variation in the management of infants with bronchiolitis both in hospital and, anecdotally, in the community.<sup>10</sup> The guideline aims to reduce the use of unnecessary therapies and investigations, particularly in the acute illness, and to guide referral patterns from primary to secondary and for some, tertiary care.

### 1.3 GUIDELINE REMIT

This guideline provides evidence based recommendations on the prevention, diagnosis, investigation, treatment and management of bronchiolitis. Specific attention has been given to the most appropriate use of diagnostic, referral and prognostic tools, particularly for those in primary care.

The guideline focuses on the clinically diagnosed condition of bronchiolitis in infants less than 12 months of age. This minimises any bias from reporting discrepancies associated with the diagnosis of bronchiolitis above this age. For example, in the USA the term 'bronchiolitis' may be used to describe any wheeze associated with a viral infection in older children, creating the risk that studies on children over twelve months of age may include different disease entities.

As infants with significant comorbidities have increased susceptibility to bronchiolitis beyond twelve months of age, the following specific groups were considered up to 24 months of age:

- those born prematurely ( $\leq 37$  weeks gestational age)
- infants with congenital heart disease (CHD) or underlying respiratory disease.

Most studies of investigations and treatments for bronchiolitis have been conducted in hospitalised infants. In addition, the majority of studies which were identified excluded individuals with significant coexisting conditions. Except where explicitly stated, recommendations apply directly to previously healthy infants.

Bronchiolitis in immunodeficient infants or those with rare ('orphan') lung disease was not considered, nor was preoperative screening for RSV. Specialist intensive care practice was also beyond the scope of the guideline. Virological testing for non-RSV causes of bronchiolitis such as parainfluenza, adenovirus, influenza A and B, metapneumovirus, rhinovirus, enterovirus or *Mycoplasma pneumoniae* is outside the scope of this guideline.

### 1.4 AUDIENCE

This guideline will be of interest to all health professionals in primary and secondary care involved in the management of infants with bronchiolitis including:

- |                                  |                                |
|----------------------------------|--------------------------------|
| ▪ general practitioners (GPs)    | ▪ specialist paediatric nurses |
| ▪ emergency medicine specialists | ▪ paediatric nurses            |
| ▪ general paediatricians         | ▪ infection control team       |
| ▪ respiratory paediatricians     | ▪ health visitors              |
| ▪ neonatologists                 | ▪ practice nurses              |
| ▪ paediatric intensivists        | ▪ paediatric physiotherapists  |
| ▪ public health specialists      | ▪ pharmacists                  |

The guideline will also be of interest to parents and carers as well as to healthcare managers and policy makers.

## 1.5 STATEMENT OF INTENT

This guideline is not intended to be construed or to serve as a standard of care. Standards of care are determined on the basis of all clinical data available for an individual case and are subject to change as scientific knowledge and technology advance and patterns of care evolve. Adherence to guideline recommendations will not ensure a successful outcome in every case, nor should they be construed as including all proper methods of care or excluding other acceptable methods of care aimed at the same results. The ultimate judgement must be made by the appropriate healthcare professional(s) responsible for clinical decisions regarding a particular clinical procedure or treatment plan. This judgement should only be arrived at following discussion of the options with the patient, covering the diagnostic and treatment choices available. It is advised, however, that significant departures from the national guideline or any local guidelines derived from it should be fully documented in the patient's case notes at the time the relevant decision is taken.

## 1.6 REVIEW AND UPDATING

This guideline was issued in 2006 and will be considered for review in three years. Any updates to the guideline in the interim period will be noted on the SIGN website: [www.sign.ac.uk](http://www.sign.ac.uk)

## 2 Diagnosis

### 2.1 CLINICAL DEFINITION

The diagnosis of bronchiolitis is a clinical one based on typical history and findings on physical examination.<sup>11</sup> Clinicians in different countries use different criteria to diagnose acute bronchiolitis.<sup>12</sup>

A consensus guideline from the UK developed using a Delphi panel reported a 90% consensus on the definition of bronchiolitis as 'a seasonal viral illness characterised by fever, nasal discharge and dry, wheezy cough. On examination there are fine inspiratory crackles and/or high pitched expiratory wheeze'.<sup>12</sup>

Bronchiolitis typically has a coryzal phase for two to three days which precedes the onset of other symptoms.<sup>1</sup>

In the first 72 hours of the illness, infants with bronchiolitis may deteriorate clinically before symptom improvement.<sup>1</sup>

A number of other conditions can mimic acute bronchiolitis. Pulmonary causes of bronchiolitis-like symptoms include asthma, pneumonia, congenital lung disease, cystic fibrosis or inhaled foreign body. Non-pulmonary causes include CHD, sepsis or severe metabolic acidosis.<sup>13</sup>

### 2.2 DIAGNOSTIC VALUE OF CLINICAL CHARACTERISTICS

#### 2.2.1 AGE

Bronchiolitis mainly affects infants under two years of age. Ninety percent of cases requiring hospitalisation occur in infants under twelve months of age.<sup>4</sup> Incidence peaks at age three to six months.<sup>1</sup>

No evidence was identified on the value of age as a specific discriminatory feature in the diagnosis of bronchiolitis.

#### 2.2.2 FEVER

Infants with bronchiolitis may have fever or a history of fever.<sup>14-18</sup> High fever is uncommon in bronchiolitis.<sup>1,16</sup> In a prospective study of 90 infants hospitalised with acute bronchiolitis (mean age 4.4 months), only two (2.2%) had a temperature of  $\geq 40^{\circ}\text{C}$ . Twenty eight infants (31%) had fever as defined by a single axillary temperature recording  $> 38^{\circ}\text{C}$  or two successive recordings  $> 37.8^{\circ}\text{C}$  taken four hours apart during the first 24 hours of admission. A high proportion of the febrile infants (71%) had a severe disease course requiring oxygen supplementation.<sup>19</sup>

**D** The absence of fever should not preclude the diagnosis of acute bronchiolitis.

**D** In the presence of high fever (axillary temperature  $\geq 39^{\circ}\text{C}$ ) careful evaluation for other causes should be undertaken before making a diagnosis.

It is unusual for infants with bronchiolitis to appear "toxic". A "toxic" infant who is drowsy, lethargic or irritable, pale, mottled and tachycardic requires immediate treatment. Careful evaluation for other causes should be undertaken before making a diagnosis of bronchiolitis.

2.2.3	RHINORRHOEA	Nasal discharge often precedes the onset of other symptoms such as cough, tachypnoea, respiratory distress and feeding difficulties. <sup>13,14</sup>	4
2.2.4	COUGH	Expert opinion suggests that a dry, wheezy cough is characteristic of bronchiolitis. <sup>12,13</sup> Cough, along with nasal symptoms, is one of the earliest symptoms to occur in bronchiolitis. <sup>17</sup>	4
2.2.5	RESPIRATORY RATE	Increased respiratory rate is an important symptom in lower respiratory tract infection (LRTI) and particularly in bronchiolitis and pneumonia. <sup>1,15,16,18</sup>	3 4
	<b>D</b>	<b>Increased respiratory rate should arouse suspicion of lower respiratory tract infection, particularly bronchiolitis or pneumonia.</b>	
		It is not possible to provide specific definitions of tachypnoea since the range of rates varies by age with rates particularly difficult to interpret in infants less than six months of age. <sup>12</sup> The World Health Organisation cut offs for defining tachypnoea, although widely used, have not been fully validated. <sup>12,18,20</sup>	3 4
2.2.6	POOR FEEDING	Many infants with bronchiolitis have feeding difficulties due to dyspnoea but poor feeding is not essential for the diagnosis of bronchiolitis. Feeding problems are often the reason for hospital admission. <sup>1,14</sup>	4
2.2.7	INCREASED WORK OF BREATHING AND RECESSION	Dyspnoea and subcostal, intercostal and supraclavicular recessions are commonly seen in infants with acute bronchiolitis. <sup>11-14,16</sup>	3 4
		The chest may be visibly hyperinflated in bronchiolitis. <sup>1,13,16</sup> The presence of a hyperinflated chest may help to distinguish bronchiolitis from pneumonia. <sup>16</sup>	3 4
2.2.8	CRACKLES/CREPITATIONS	Fine inspiratory crackles in all lung fields are a common (but not universal) finding in acute bronchiolitis. <sup>1,12,15,16</sup> In the UK, crackles on chest auscultation are regarded as the hallmark of bronchiolitis. Infants with no crackles and only transient early wheezing are usually classified as having viral-induced wheeze rather than bronchiolitis. <sup>14</sup>	3 4
2.2.9	WHEEZE	UK definitions of bronchiolitis describe high pitched expiratory wheeze as a common but not universal examination finding. <sup>1,12,15,18</sup> American definitions of bronchiolitis place much more emphasis on the inclusion of wheeze in the diagnosis. <sup>16</sup> This presents difficulties in extrapolating data from American research.	3 4
2.2.10	APNOEA	Apnoea can be the presenting feature of bronchiolitis, especially in the very young and in premature or low birthweight infants. <sup>13,14,20</sup>	4
2.3	<b>SUMMARY OF DIAGNOSTIC CHARACTERISTICS</b>		
	<b>D</b>	<b>A diagnosis of acute bronchiolitis should be considered in an infant with nasal discharge and a wheezy cough, in the presence of fine inspiratory crackles and/or high pitched expiratory wheeze. Apnoea may be a presenting feature.</b>	

2.4 SEASONALITY

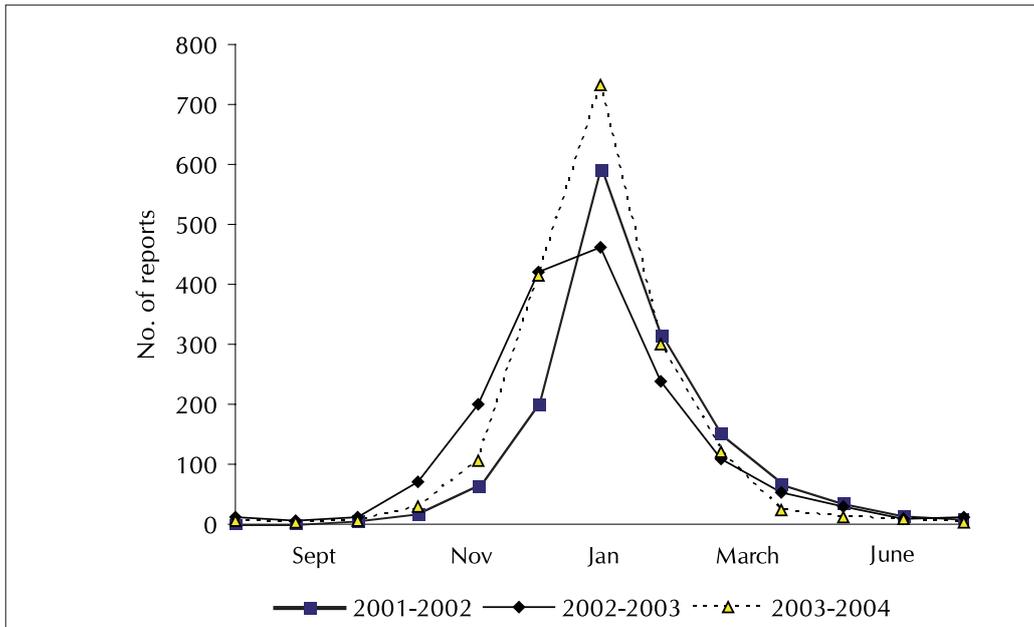
Both bronchiolitis and RSV infection demonstrate winter seasonality in temperate climates.<sup>7</sup> This is less true in other parts of the world,<sup>21</sup> and a recent history of international travel may be significant. In Scotland, RSV infection peaks between November and March (see Figure 1).

4  
3

The generation of epidemiological information is dependent on virological testing and disease surveillance. In Scotland, weekly surveillance information is based on the numbers of laboratory reports to Health Protection Scotland, which come mainly from hospitalised patients.<sup>22</sup>

3

Figure 1: RSV laboratory reports to Health Protection Scotland by four-week period



**D** Healthcare professionals should take seasonality into account when considering the possible diagnosis of acute bronchiolitis.

### 3 Risk factors for severe disease

Almost all studies relating to bronchiolitis are performed on those attending or admitted to hospital. The disease severity status triggering attendance at or admission to hospital will depend on local levels of supportive care provided through both primary and secondary care within the community. Decisions to admit or to discharge from hospital are multifactorial, taking into consideration factors such as comorbidities, geography and the perceived ability of carers to respond appropriately if an infant's condition deteriorates.

#### 3.1 AGE

Younger infants have a higher risk of hospital admission with bronchiolitis than older infants.<sup>23-26</sup> 2+

#### 3.2 SIGNIFICANT COMORBIDITIES

##### 3.2.1 PREMATURITY

Infants born prematurely have a modestly higher rate of RSV-associated hospitalisation compared with full-term healthy babies.<sup>23,25-33</sup> Table 1 presents the results of a study to determine the rates of hospital admission (in children up to two years of age) for RSV infection among infants born at different gestational ages over a ten year period.<sup>27</sup> 2+

Table 1: Association of gestational age with RSV hospital admission rate<sup>27</sup>

Gestational age (weeks)	≤ 28	29-32	33-35	≥ 36
Number of infants observed	168	498	1,133	33,983
RSV hospital admission rate (%)	7	7	4	2
Relative risk of hospital admission (95% Confidence Intervals)	3.6 (2.7 to 4.8)		1.9 (1.4 to 2.6)	1

##### 3.2.2 CONGENITAL HEART DISEASE

In a retrospective observational study of infants born at term, the hospital admission rate for children under three years of age with bronchiolitis was higher for those with congenital heart disease (9.2%) than those with no underlying medical condition (3%).<sup>26</sup> In three further observational studies infants with CHD accounted for 6.4% to 12% of all RSV associated hospital admissions.<sup>28,32,34</sup> 2+  
2-

##### 3.2.3 CHRONIC LUNG DISEASE OF PREMATURITY

A prospective study of the use of healthcare resources in infants with chronic lung disease (CLD) born at 32 weeks gestation or less found that during the first two years after birth 45 infants (19%) had at least one hospital admission for a proven RSV infection and 24 (10%) had at least one admission for probable bronchiolitis.<sup>35</sup> 2+

This increased rate of hospitalisation (with RSV infection) in those with underlying CLD is also shown in five retrospective cohort studies, some of which included full-term infants.<sup>26-28,31,32</sup> 2+  
2-

## 3.2.4 SUMMARY OF EFFECT OF COMORBIDITY

Infants born prematurely or who have congenital heart disease or chronic lung disease are at increased risk of severe RSV disease.

**C Healthcare professionals should be aware of the increased need for hospital admission in infants born at less than 35 weeks gestation and in infants who have congenital heart disease or chronic lung disease of prematurity.**

No evidence was identified on the risk of hospitalisation with bronchiolitis in infants with chronic lung disease not associated with prematurity.

## 3.3 ATOPY

No evidence was identified on personal atopy as a risk factor for severe disease course in bronchiolitis. There is conflicting evidence as to whether a family history of atopy is associated with acute bronchiolitis requiring hospitalisation. In two studies, different markers of atopy demonstrated both association and lack of association with severe disease within the same study.<sup>25,36</sup> A further study demonstrated an association between maternal asthma and less severe hospitalised disease as measured by oxygen saturation and length of stay.<sup>37</sup>

2<sup>+</sup>  
2<sup>+</sup>

## 3.4 SOCIAL FACTORS

## 3.4.1 BREAST FEEDING

In a prospective case control study of infants born at 33-35 weeks gestation or who were less than six months of age at the start of the RSV season, breast feeding for more than two months had a protective effect.<sup>38</sup> There was a greater likelihood of RSV hospitalisation if breast feeding duration was less than two months (odds ratio; OR 3.25, 95% confidence intervals; CI 1.96 to 5.42). In another case control study, breast feeding was associated with a lower risk of RSV hospitalisation in infants under and over six months of age.<sup>39</sup>

2<sup>-</sup>  
2<sup>+</sup>

**C Breast feeding reduces the risk of RSV-related hospitalisation and should be encouraged and supported.**

## 3.4.2 PARENTAL SMOKING

Parental smoking is associated with an increased risk of RSV-related hospitalisation of infants when compared with non-smoking families (with adjusted odds ratios ranging from 1.3 to 3.4 with broad confidence intervals).<sup>23,26,40</sup> There is evidence of a weak association between RSV hospitalisation and smoking in pregnancy.<sup>25,33,40</sup>

2<sup>+</sup>  
2<sup>-</sup>

One study in premature infants found no significant association between hospitalisation for RSV-related LRTI and maternal smoking, although maternal smoking was associated with hospitalisation for any LRTI.<sup>30</sup>

2<sup>-</sup>

**C Healthcare professionals should inform families that parental smoking is associated with increased risk of RSV-related hospitalisation.**

## 3.4.3 NUMBER OF SIBLINGS AND NURSERY OR DAY-CARE ATTENDANCE

Observational studies indicate an association between having siblings at home (particularly of school age or attending day care) and increased risk of hospitalisation of infants with clinically diagnosed bronchiolitis or RSV infection.<sup>23,25,26,28,33,39,41</sup> This effect is seen in infants previously healthy, born prematurely or with CLD.<sup>28</sup>

2<sup>-</sup>  
2<sup>+</sup>

## 3.4.4 SOCIOECONOMIC DEPRIVATION

Only one study was identified that examined the association between severe bronchiolitis and deprivation score. A small case control study in infants under 12 months of age found that the risk of admission with clinically suspected bronchiolitis and with bronchiolitis requiring medical intervention rose with increasing level of deprivation score based on electoral ward of residence.<sup>42</sup>

2+

Overcrowding and fuel poverty are other markers of socioeconomic deprivation. Observational studies show associations between both overcrowding and bedroom sharing and increased risk of hospitalisation with RSV in infants born at term and prematurely.<sup>23,24,33,39</sup> No studies were identified on the influence of domestic heating on incidence or severity of acute bronchiolitis.

2-

## 4 Assessment and referral

### 4.1 ASSESSMENT

#### 4.1.1 SEVERE DISEASE

Previous guidelines identify a number of clinical features of severe disease in bronchiolitis:<sup>12,43</sup>

- poor feeding (<50% of usual fluid intake in preceding 24 hours)
- lethargy
- history of apnoea
- respiratory rate >70/min
- presence of nasal flaring and/or grunting
- severe chest wall recession
- cyanosis.

Risk factors for severe disease are discussed in section 3.

#### 4.1.2 CLINICAL SCORING SYSTEMS

No good quality evidence on the use of formal clinical scoring systems in infants with acute bronchiolitis was identified.

### 4.2 REFERRAL

No good quality studies were identified regarding the effectiveness of indicators for referral from primary to secondary care or for admission to intensive care. Good practice guidance based on the clinical experience of the guideline development group is presented. This takes into account risk factors for, and clinical predictors of, severe disease as well as a previous consensus guideline on breathing difficulty in children, a New Zealand guideline on wheeze and chest infection in children less than one year and the British Thoracic Society guidelines on the management of community acquired pneumonia in childhood.<sup>1,12,44</sup>

☑ Most infants with acute bronchiolitis will have mild disease and can be managed at home with primary care support. Parents/care givers should be given information on how to recognise any deterioration in their infant's condition and asked to bring them back for reassessment should this occur.

☑ Any of the following indications should prompt hospital referral/acute paediatric assessment in an infant with acute bronchiolitis or suspected acute bronchiolitis:

- poor feeding (<50% of usual fluid intake in preceding 24 hours)
- lethargy
- history of apnoea
- respiratory rate >70/min
- presence of nasal flaring and/or grunting
- severe chest wall recession
- cyanosis
- oxygen saturation ≤94%
- uncertainty regarding diagnosis.

Clinicians assessing the need to refer (or review in primary care) should also take account of whether the illness is at an early (and perhaps worsening) stage, or at a later (improving) stage.

- ☑ The threshold for hospital referral should be lowered in patients with significant comorbidities, those less than three months of age or infants born at less than 35 weeks gestation. Geographical factors/transport difficulties and social factors should also be taken into consideration.
- ☑ Indications for high dependency/intensive care unit consultation include:
  - failure to maintain oxygen saturations of greater than 92% with increasing oxygen therapy
  - deteriorating respiratory status with signs of increasing respiratory distress and/or exhaustion
  - recurrent apnoea.

## 5 Investigations

Acute bronchiolitis is a clinical diagnosis. Clinicians assessing infants with possible acute bronchiolitis may perform investigations when diagnostic uncertainty exists or to aid decision making regarding subsequent management. These investigations may include oxygen saturation recording, blood gas analysis, chest X-ray, virological or bacteriological testing, haematology and biochemistry. This section considers the evidence supporting the role of these investigations in the management of an infant with acute bronchiolitis.

### 5.1 OXYGEN SATURATION

In an emergency department study, clinical assessment alone was poor at predicting associated hypoxaemia in infants presenting with a respiratory illness.<sup>45</sup> A survey described how small differences in oxygen saturation level (92% compared to 94%) within the theoretical clinical vignette of an infant with acute bronchiolitis significantly influenced the recommendation of paediatric emergency physicians to admit or discharge patients.<sup>46</sup>

2+  
3

Lower oxygen saturation levels on hospital admission predict more severe disease and longer lengths of stay.<sup>47-49</sup>

2+  
2-

**C Pulse oximetry should be performed in every child who attends hospital with acute bronchiolitis.**

- Infants with oxygen saturation  $\leq 92\%$  require inpatient care.
- Decision making around hospitalisation of infants with oxygen saturations between 92% and 94% should be supported by detailed clinical assessment, consideration of the phase of the illness and take into account social and geographical factors.
- Infants with oxygen saturations  $> 94\%$  in room air may be considered for discharge.

### 5.2 BLOOD GASES

An observational study attempted to correlate clinical respiratory features, arterial blood gases and oxygen saturation with illness severity (measured as the maximum fraction of inspired oxygen;  $FiO_2$ , required during admission). Oxygen saturation and arterial carbon dioxide tension ( $PaCO_2$ ) best predicted the need for high concentration oxygen therapy. Oxygen tension ( $PaO_2$ ) levels were less useful. There is a risk of confounding in the study in that the degree of hypoxaemia or hypercarbia may have influenced both the decision to use oxygen and the concentration used.<sup>50</sup>

2-

- Blood gas analysis (capillary or arterial) is not usually indicated in acute bronchiolitis. It may have a role in the assessment of infants with severe respiratory distress or who are tiring and may be entering respiratory failure. Knowledge of arterialised carbon dioxide values may guide referral to high dependency or intensive care.

### 5.3 CHEST X-RAY

In a systematic review of the use of chest X-ray in acute bronchiolitis it was concluded that, in mild disease, chest X-ray provides no information that is likely to affect treatment.<sup>11</sup>

2+

An observational study identified a range of independent predictive factors for a normal chest X-ray in infants with virologically confirmed RSV attending or admitted to hospital: increased postnatal age in months, larger birth weight, presence of rhinitis, absence of retractions and higher transcutaneously measured oxygen saturation.<sup>51</sup> These studies suggest that chest X-ray need only be performed in selected cases.

3

**C** Chest X-ray should not be performed in infants with typical acute bronchiolitis.

Chest X-ray should be considered in those infants where there is diagnostic uncertainty or an atypical disease course.

#### 5.4 VIROLOGICAL TESTING

Strategies for limiting disease transmission are discussed in section 9.

Rapid virological testing can be of benefit in relation to guiding isolation and allocating patients into cohorts in hospital.<sup>52</sup> Rapid testing for RSV, which can be performed at the point of care in order to facilitate this, has been shown to have acceptable performance in comparison to laboratory based tests despite reduced diagnostic sensitivity.<sup>53,54</sup> A case control study found that rapid diagnosis of respiratory viral infections in infants was cost effective by reducing length of hospital stay, antibiotic use and number of microbiological tests performed compared to a matched group of patients from the previous year who were diagnosed by virus culture.<sup>55</sup>

2+

There may be a reduction in unnecessary interventions associated with knowledge of RSV status.<sup>53,56</sup> In a postal survey, physicians reported that a definitive viral diagnosis was important to patients.<sup>57</sup>

2+  
3

**D** Unless adequate isolation facilities are available, rapid testing for RSV is recommended in infants who require admission to hospital with acute bronchiolitis, in order to guide cohort arrangements.

#### 5.5 BACTERIOLOGICAL TESTING

In a prospective cohort study of 156 previously healthy febrile infants with bronchiolitis, none and 1.9% had bacteraemia or urinary tract infection (UTI) respectively, in comparison with 2.7% and 13.6% of 261 febrile controls.<sup>58</sup> This study concluded that previously healthy febrile infants aged 24 months or younger with bronchiolitis are unlikely to have bacteraemia or UTI.

2+

A cross-sectional study found that 6.5% of febrile infants up to 60 days old with bronchiolitis had a UTI and none had bacteraemia or meningitis in comparison with 10% (UTI), 2.3% (bacteraemia) and 0.8% (meningitis) in febrile non-bronchiolitic infants in the same age range.<sup>59</sup>

3

**C** Routine bacteriological testing (*of blood and urine*) is not indicated in infants with typical acute bronchiolitis. Bacteriological testing of urine should be considered in febrile infants less than 60 days old.

#### 5.6 HAEMATOLOGY

A well conducted systematic review did not identify any studies directly addressing the value of full blood count in the management of infants with bronchiolitis. Extrapolation of data comparing full blood count at baseline in interventional studies suggests that full blood count does not aid diagnosis or guide therapeutic intervention in infants with acute bronchiolitis.<sup>11</sup>

1+

**D** Full blood count is not indicated in assessment and management of infants with typical acute bronchiolitis.

## 5.7 BIOCHEMISTRY

### 5.7.1 UREA AND ELECTROLYTES

No studies were identified on the use of urea and electrolytes (U&E) measurement in infants with acute bronchiolitis. Expert opinion considers that electrolyte disturbances are unlikely unless there is severe disease.<sup>13</sup>

4

**D** Measurement of urea and electrolytes is not indicated in the routine assessment and management of infants with typical acute bronchiolitis but should be considered in those with severe disease.

### 5.7.2 C-REACTIVE PROTEIN

There has been limited investigation into the role of C-reactive protein (CRP) measurement in distinguishing bacterial from viral lower respiratory tract infections. Existing studies are retrospective or of poor quality and do not provide sufficient evidence upon which to base a recommendation in relation to bronchiolitis.<sup>60-62</sup>

2

3

## 6 Treatment

Outcomes examined include short term clinical benefits, development of subsequent chronic respiratory symptoms, attendance at medical services, length of hospital stay and readmissions rate and admission to a paediatric intensive care unit (PICU). Evidence from primary care, accident and emergency (A&E), hospital and PICU environments has been considered. Studies are reported on the basis of their primary outcome measures unless otherwise stated.

### 6.1 ANTIVIRALS

A Cochrane systematic review examined the effectiveness of nebulised ribavirin in infants and children with lower respiratory disease attributable to RSV infection.<sup>63</sup> Many studies in the review excluded children with significant comorbidities. There was a conflict within the review with regard to the acute infection phase. One study, which used a nebulised water placebo, suggested that nebulised ribavirin reduced length of hospital stay and the number of days of mechanical ventilation. Nebulised water, however, may have a detrimental effect on pulmonary mechanics.<sup>64</sup> If this study is excluded, two randomised controlled trials (RCTs) using saline placebo suggest there is no effect in the ribavirin group.

1+

**B** Nebulised ribavirin is not recommended for treatment of acute bronchiolitis in infants.

Three RCTs examined the effect of nebulised ribavirin on chronic respiratory symptoms. All trials were of poor quality with lack of blinding to treatment allocation, no placebo control, short follow up period or very small numbers.<sup>65-67</sup> There is insufficient evidence to make a recommendation on the use of nebulised ribavirin for treatment of long term respiratory symptoms in bronchiolitis.

1+

### 6.2 ANTIBIOTICS

No contemporary studies were identified on the use of antibiotics in infants with acute bronchiolitis. Bacteraemia is infrequent in RSV infection (see section 5.5).

Antibiotic therapy is not recommended in the treatment of acute bronchiolitis in infants.

### 6.3 INHALED BRONCHODILATORS

#### 6.3.1 BETA 2 AGONISTS

In a systematic review of 12 small placebo controlled trials, eight reported no clinical benefit for inhaled beta 2 agonist bronchodilators in infants with acute bronchiolitis. Three studies demonstrated short term (30 to 60 minutes) clinical benefit as measured by various indicators such as clinical scores, respiratory rate, heart rate and oxygen saturation. One study measured a worse clinical outcome in the treatment group. The use of bronchodilators had no effect on rate of hospitalisation or time to hospital discharge. Chronic symptoms and reattendance at hospital were not considered.<sup>68</sup>

1+

**B** Inhaled beta 2 agonist bronchodilators are not recommended for the treatment of acute bronchiolitis in infants.

#### 6.3.2 ANTICHOLINERGICS

Two underpowered studies demonstrate no benefit in the use of nebulised ipratropium in infants with bronchiolitis.<sup>69,70</sup>

1+

Nebulised ipratropium is not recommended for the treatment of acute bronchiolitis in infants.

## 6.4 NEBULISED EPINEPHRINE

In a high quality multicentre RCT, nebulised epinephrine did not affect overall clinical status, oxygen requirement, time to hospital discharge or rate of hospital readmission within one month, for infants hospitalised with acute bronchiolitis.<sup>71</sup> Although additional RCTs were identified, none were of sufficient quality for inclusion.

1<sup>++</sup>

**A Nebulised epinephrine is not recommended for the treatment of acute bronchiolitis in infants.**

## 6.5 ANTI-INFLAMMATORIES

### 6.5.1 INHALED CORTICOSTEROIDS

Two RCTs in infants with bronchiolitis have demonstrated that inhaled corticosteroids have no effect on length of hospital stay, time to becoming asymptomatic or rate of respiratory readmission to hospital within 12 months.<sup>72,73</sup>

1<sup>+</sup>

**A Inhaled corticosteroids are not recommended for the treatment of acute bronchiolitis in infants.**

### 6.5.2 SYSTEMIC CORTICOSTEROIDS

A Cochrane systematic review concluded that oral systemic corticosteroids did not reduce length of hospital stay in previously well infants less than 12 months of age with acute bronchiolitis.<sup>74</sup>

1<sup>++</sup>

**A Oral systemic corticosteroids are not recommended for the treatment of acute bronchiolitis in infants.**

Long term effects of oral corticosteroids were investigated in a small RCT (n = 54) with follow-up at age five years. Oral prednisolone given for the first seven days of acute bronchiolitis did not prevent wheeze or the development of asthma up to a mean age of five years.<sup>75</sup> The applicability of this study is limited by its recruitment of children up to two years of age.

### 6.5.3 LEUKOTRIENE RECEPTOR ANTAGONIST (MONTELUKAST)

Only one study on the use of montelukast in children with bronchiolitis was identified. For children aged three to 36 months (median age nine months) admitted to hospital with acute bronchiolitis/acute wheeze, daily treatment with montelukast for 28 days (starting within seven days of symptom onset) significantly increased the number of symptom free days over a 56 day period (22% v 4% placebo, p=0.015). Day-time (but not night-time) cough scores were reduced.<sup>76</sup> The results of this study cannot be generalised to infants in the UK with bronchiolitis where median age at diagnosis is 4.6 months.<sup>72</sup> There is therefore insufficient evidence on which to base a recommendation.

2<sup>+</sup>

## 6.6 HOSPITAL BASED SUPPLEMENTARY THERAPIES

### 6.6.1 PHYSIOTHERAPY

A Cochrane systematic review examined three RCTs of chest physiotherapy in infants with acute bronchiolitis not undergoing mechanical ventilation, and without comorbidities. Percussion and vibration techniques did not reduce length of hospital stay or oxygen requirements, nor did they improve the clinical severity score.<sup>77</sup>

1<sup>+</sup>

**A Chest physiotherapy using vibration and percussion is not recommended in infants hospitalised with acute bronchiolitis who are not admitted to intensive care.**

## 6.6.2 NASAL SUCTION

There are no clinical trials assessing the benefit of nasal suction in acute bronchiolitis. Expert consensus is that nasal suction may improve respiratory status in infants with bronchiolitis.<sup>43</sup>

4

**D** Nasal suction should be used to clear secretions in infants hospitalised with acute bronchiolitis who exhibit respiratory distress due to nasal blockage.

## 6.6.3 MAINTAINING FLUID BALANCE/HYDRATION

Infants in respiratory distress may have difficulty feeding due to increased work of breathing, nasal secretions and exhaustion. This makes it difficult for them to maintain adequate input and hydration. Common strategies are to commence small frequent feeds, nasogastric or orogastric feeding or intravenous fluids. In a review there was no good quality evidence that rehydration by the nasogastric route is more or less safe than via the intravenous route.<sup>78</sup> Expert opinion considers that nasogastric feeding may be an option where infants are at risk of dehydration.<sup>1</sup>

4

**D** Nasogastric feeding should be considered in infants with acute bronchiolitis who cannot maintain oral intake or hydration.

## 6.6.4 OXYGEN

No studies on the use of oxygen in infants with acute bronchiolitis were identified. The recommendation is based on expert opinion.<sup>79</sup>

4

**D** Infants with oxygen saturation levels  $\leq 92\%$  or who have severe respiratory distress or cyanosis should receive supplemental oxygen by nasal cannulae or facemask.

## 6.6.5 CONTINUOUS POSITIVE AIRWAY PRESSURE AND NEGATIVE PRESSURE VENTILATION

No studies were identified that provided evidence about the location or timing of ventilatory support for infants with acute bronchiolitis.

Early discussion with a paediatric intensive care unit and introduction of respiratory support should be considered in all patients with severe respiratory distress or apnoeas.

## 6.7 HOSPITAL BASED TREATMENT GUIDELINES

Three studies on the effect of treatment guideline implementation on length of hospital stay in infants with acute bronchiolitis were identified. The small numbers included in these studies and significant methodological problems with confounding factors mean that no recommendation can be made.<sup>80-82</sup>

2-3

## 6.8 COMMUNITY BASED SUPPLEMENTARY THERAPIES

No studies were identified on the effectiveness of steam, nasal decongestion, homeopathic remedies or any complementary therapies in the treatment of infants with acute bronchiolitis.

## 7 Symptom duration and hospital discharge

### 7.1 DURATION OF SYMPTOMS FOLLOWING ACUTE BRONCHIOLITIS

In an RCT of inhaled corticosteroid treatment in infants with acute bronchiolitis, time taken for half of the infants in the placebo arm to become asymptomatic for 48 hours was 12 days (95% CI 10 to 16).<sup>72</sup> 2+

Two cohort studies provided information on the duration of symptoms following acute bronchiolitis. The first, employing twice-weekly structured telephone interviews found that the median duration of illness was 12 days (95% CI 11 to 14 days), with 39% of infants reportedly 'not completely well' after 14 days, 18% after 21 days and 9% after 28 days.<sup>83</sup> This study also suggested that subsequent contacts with healthcare professionals may be reduced when parents/carers are fully aware of the potential duration of acute symptoms. The second study further subdivided symptoms and reported median duration of cough was 12 days (interquartile range 8-20 days); wheeze was seven days, difficulty breathing was six days and poor feeding was seven days.<sup>16</sup> 2- 2+

**B** Parents and carers should be informed that, from the onset of acute bronchiolitis, around half of infants without comorbidity are asymptomatic by two weeks but that a small proportion will still have symptoms after four weeks.

Following acute bronchiolitis, ciliary damage persists for 13-17 weeks.<sup>8</sup> 3

### 7.2 HOSPITAL DISCHARGE CRITERIA

#### 7.2.1 OXYGEN SATURATION

Two studies provide evidence that, in infants who attend hospital with bronchiolitis, pulse oximetry has a significant influence on the decision to admit to hospital or to discharge.<sup>84,85</sup> 3

No good quality evidence was identified for specific thresholds on which to base decisions about discharge or whether these should be based on continuous or intermittent oxygen saturation monitoring.

Previous guidelines offer various lower limits for acceptable oxygen saturation levels in air in infants with acute bronchiolitis, ranging from 90-94%. An acceptable duration of desaturation is not defined.<sup>11,12</sup> 4

Infants who have required supplemental oxygen therapy should have oxygen saturation monitoring for a period of 8-12 hours after therapy is discontinued (including a period of sleep) to ensure clinical stability before being considered for discharge.

Infants with oxygen saturations >94% in room air may be considered for discharge.

#### 7.2.2 FEEDING

Although a history of reduced feeding is one of the main factors in deciding whether to admit an infant to hospital, no studies were identified on the use of feeding as an indicator for safe hospital discharge.<sup>86</sup> In hospitalised infants with bronchiolitis, oral feed volumes have been reported as less than half that of well infants.<sup>87</sup>

Hospitalised infants should not be discharged until they can maintain an adequate daily oral intake (>75% of usual intake).

## 8 Chronic symptoms and follow up

### 8.1 CHRONIC SYMPTOMS

An association between acute bronchiolitis and later respiratory morbidity is recognised. The mechanisms for this are poorly understood. There is debate as to whether the primary insult to the lung is the acute bronchiolitic illness, or whether there is prior genetic/environmental predisposition to respiratory morbidity. The severity of acute bronchiolitis may be the best predictor of chronic respiratory symptoms.<sup>88</sup>

4

#### 8.1.1 ONE YEAR

Two small prospective cohort studies confirm high rates of recurrent wheeze episodes in the 12 months following hospitalisation for RSV bronchiolitis.<sup>89,90</sup> A Dutch study (n = 130) reported a recurrent wheeze rate of 61% in those with, compared with 21% in those infants without, signs of airflow limitation at presentation.<sup>89</sup> A German study (n = 126) reported recurrent wheeze in 31% of infants hospitalised with RSV bronchiolitis compared with 3.6% in controls.<sup>89</sup> In extended follow up the Dutch study measured an overall decline in the number of wheeze episodes over three years but with seasonal increases in wheeze episodes in the winter months.<sup>91</sup>

2+

#### 8.1.2 UP TO AGE SIX YEARS

A quantitative review of six case control studies identified wheeze in 40% of children compared with 11% of controls (OR 3.8, 95% CI 1.6 to 9.3, p < 0.001) at five years after hospitalisation with RSV infection.<sup>92</sup> No significant differences between the RSV bronchiolitis group and controls were found regarding a personal history of atopy, a family history of atopy and/or asthma.

2+

#### 8.1.3 UP TO AGE 13 YEARS

Long term morbidity into early adolescence has been studied by two groups who report conflicting results which may relate to differences in patient recruitment, including genetic influences, and study size. The Tucson Children's Respiratory Study which recruited a large cohort of hospitalised and non-hospitalised infants, showed an increase in wheeze up to age 11 but this was no longer significant at age 13 (OR 1.4, 95% CI 0.7 to 2.6, see Table 2). There was no association with allergic sensitisation.<sup>93</sup>

2+

Table 2: Frequent wheeze in children following RSV infection in first three years of life.<sup>93</sup>

	Age 6 (n = 68/669)	Age 8 (n = 56/545)	Age 11 (n = 79/634)	Age 13 (n = 49/469)
Frequent wheeze Adjusted odds ratio* (95% CI)	4.3 (2.2 to 8.7)	1.9 (0.9 to 4.2)	2.4 (1.3 to 4.6)	1.4 (0.7 to 2.6)
* Results adjusted for sex, maternal education, family history of asthma, allergy skin tests at year 6, birthweight, and current maternal smoking.				

In contrast, a small case control study of hospitalised infants with RSV bronchiolitis demonstrated an increase in current asthma/recurrent wheezing (relative risk; RR 5.7, 95% CI 2.6 to 12.5, p < 0.001), allergic rhinoconjunctivitis (RR 2.6, 95% CI 1.4 to 4.7, p = 0.004) and allergic sensitisation at age 13 (serum IgE: RR 1.8, 95% CI 1.1 to 2.9, p = 0.038).<sup>94</sup>

2+

#### 8.1.4 ADULTHOOD

One small cohort study (n = 81) on respiratory morbidity at age 18-20 years, following RSV infection, found that RSV infection in infancy was not a significant risk factor for asthma or bronchial reactivity. In logistic regression adjusted for atopy, there were minor differences for lung function abnormality (one or more abnormal result in flow-volume spirometry; OR 5.27, 95% CI 1.6 to 17.35), indicating that lung function abnormalities may be associated with RSV infection which required hospitalisation in infancy.<sup>95</sup>

2-

## **8.2 REFERRAL TO SECONDARY CARE**

No reliable, valid published evidence was identified that explored when infants should be referred to secondary care because of post-bronchiolitic cough/wheeze.

## **8.3 ROUTINE FOLLOW UP**

No published evidence was identified that explored whether or not routine follow up affected parental anxiety, hospital readmission rates, rates of unplanned primary care contact or attendance at an emergency department.

## 9 Limiting disease transmission

The role of virological testing is discussed in section 5.4

In examining the evidence around reducing disease transmission, a number of characteristics of the RSV virus have been considered in relation to the need for an integrated approach.<sup>96</sup>

RSV:

- is highly infectious
- is transmitted mainly through contagious secretions or via environmental surfaces (skin, cloth and other objects)
- in respiratory droplets produced during coughing or sneezing can spread up to two metres
- enters the body via the mucous membranes of the eyes, nose or mouth
- can survive 6-12 hours on environmental surfaces
- may be transferred on the hands to the eyes or nose
- is destroyed by soap and water/alcohol gel
- may be shed for up to three weeks and longer if a child is immuno-compromised.

4

### 9.1 IN THE COMMUNITY

No studies were identified which examined the effectiveness of measures to reduce bronchiolitis transmission in the community setting.

### 9.2 IN HOSPITAL

Only one contemporary study was identified which examined the effectiveness of infection control measures in RSV transmission.<sup>97</sup> This before and after study measured RSV healthcare associated infection (HAI) rate before and after intervention with an infection control programme based on expert opinion from the Centers for Disease Control and Prevention.<sup>98</sup> The primary outcome of the study was incidence density of RSV HAI and there was no attempt to disentangle the contribution of the various components of the control of infection policy. Implementation of the programme prevented 10 RSV HAIs per season in a 304 bed paediatric hospital. The infection control intervention was also deemed to be cost effective with a cost benefit ratio of 1:6. This is in agreement with a controlled study that compared four infection control strategies in general paediatric wards and found that a regimen including rapid laboratory diagnosis, cohort nursing and the wearing of gowns and gloves for all contacts with RSV infected infants can significantly reduce the risk of RSV HAI.<sup>52</sup>

3  
2+

Recommendations are derived from the key aspects of the interventions implemented in these studies. The use of masks and eye goggles was not investigated.

#### 9.2.1 EDUCATION

**D** Healthcare professionals should be educated about the epidemiology and control of RSV where appropriate.

## 9.2.2 WARD BASED STRATEGIES

- D**
- **Staff should decontaminate their hands** (*with soap and water or alcohol gel*) **before and after caring for patients with viral respiratory symptoms.**
  - **Gloves and plastic aprons** (*or gowns*) **should be used for any direct contact with the patient or their immediate environment.**
  - **Infected patients should be placed in single rooms.** If adequate isolation facilities are unavailable, the allocation of patients into cohorts should be based on laboratory confirmation of infection in all inpatients less than two years of age with respiratory symptoms.
  - **Both service providers and staff should be aware of the risk that those with upper respiratory tract infections pose for high-risk infants.**
  - **Local policies should restrict hospital visiting by those with symptoms of respiratory infections.**
  - **There should be ongoing surveillance by control of infection staff to monitor compliance with infection control procedures.**

# 10 Prophylactic therapies

## 10.1 PALIVIZUMAB

### 10.1.1 CLINICAL EFFECTIVENESS

Palivizumab is a humanised monoclonal RSV antibody licensed for prophylaxis of development of severe pathology arising from an RSV infection. It does not prevent infection.

A well constructed RCT in infants who were born at or less than 35 weeks gestation and six months of age or younger, or children 24 months of age or younger with a clinical diagnosis of bronchopulmonary dysplasia (BPD) and requiring ongoing treatment, examined the effectiveness of five injections of palivizumab (15 mg/kg at 30 day intervals during the winter) in preventing hospitalisation for a respiratory illness with confirmed RSV. Palivizumab reduced RSV hospitalisation in infants with the specific comorbidities (relative RR 55%, absolute RR 5.8%) as described in Table 3. The effect in the BPD group was less than in pre-term infants who did not have BPD.<sup>99</sup>

1++

In a subgroup analysis, there was no clear difference in the effectiveness in infants  $\leq 32$  weeks gestation when compared with those  $> 32$  weeks gestation.<sup>100</sup>

1++

The results of a similar RCT in infants aged less than two years with haemodynamically significant CHD are also shown in Table 3. Palivizumab was effective for prophylaxis of serious RSV disease (as measured by statistically significant reduction in RSV hospitalisation rates).<sup>101</sup> There was no impact on mortality, PICU admission rate or the need for mechanical ventilation. On subgroup analysis, the beneficial effect was only statistically significant in infants with acyanotic heart disease leading to the positive overall results of the study.

1++

Palivizumab was shown to be safe over the short term follow up period (150 days) adopted in each study.

*Table 3: The effectiveness of palivizumab in preventing RSV hospitalisation in specific populations of infants with significant comorbidities.*

Population	Event rate (RSV hospitalisation)		ARR* (95%CI)	RRR* (95%CI)	NNT to prevent one hospitalisation* (95%CI)
	Palivizumab group	Placebo			
IMPACT study population <sup>99</sup> ( $\leq 35$ weeks or BPD) n = 1502	4.8%	10.6%	5.8% (2.8 to 8.8)	54.8% (34 to 69)	18 (11 to 36)
Prematurity <sup>99</sup> ( $\leq 35$ weeks gestation and $\leq 6$ months of age) n = 740	1.8%	8.1%	6.3% (2.7 to 10)	78.1% (52 to 90)	16 (10 to 37)
BPD <sup>99</sup> (and 24 months of age or younger) n = 762	7.9%	12.8%	4.9% (0.3 to 9.6)	38.5% (5 to 60)	21 (10 to 333)
Congenital heart disease <sup>101</sup> n = 1287	5.3%	9.7%	4.4% (1.5 to 7.3)	45.3% (18 to 63)	23 (14 to 67)

\*Calculated using University of Toronto Stats Calculator for Evidence Based Medicine<sup>102</sup>

The clinical benefit of palivizumab in individual infants remains inconclusive. There is evidence that it produces a reduction in RSV associated hospitalisation for routine care in previously premature infants. There is no evidence that it prevents infection and there is no beneficial impact on length of stay (once hospitalised), need for increased oxygen or for mechanical ventilation (see Table 4) or on mortality.<sup>100</sup>

Table 4: RSV Hospital course in the subset of RSV hospitalised subjects<sup>100</sup>

RSV hospital outcome	Measure	Placebo* n = 53	Palivizumab* n = 48
Days of hospitalisation	Total days/subject	5.9	7.6
Days of increased oxygen	Total days/subject	4.8	6.3
Days with lower respiratory infection/ illness (LRI) score $\geq 3$	Total days/subject	4.5	6.2
ICU admission	Yes	15(28%)	13(27%)
	No	38	35
Days ICU stay	Total days/subject	1.2	2.8
Mechanical ventilation	Yes	1(2%)	7(14.6%)
	No	52	41
Days of mechanical ventilation	Total days/subject	0.2	1.7
*Statistical comparison data not available			

Long term effects have not been investigated. The true biological benefit is uncertain and must be balanced against the need to treat a large number of infants. This involves multiple medical contacts during the winter months, parental inconvenience in arranging for and travelling to these appointments and discomfort for the treated infants, in addition to staff time and drug costs.

The consensus-based guidance of the Joint Committee on Vaccination and Immunisation (JCVI), which advises UK health departments, recommends use of palivizumab in high risk groups, as defined by the committee (children under two years of age with chronic lung disease, on home oxygen or who have had prolonged use of oxygen; infants less than six months of age who have left to right shunt haemodynamically significant congenital heart disease and/or pulmonary hypertension; children under two years of age with severe congenital immuno-deficiency).<sup>103</sup>

4

### 10.1.2 COST EFFECTIVENESS

A well conducted systematic review identified seven United Kingdom RSV related cost studies.<sup>104</sup> The studies consistently concluded that the costs of palivizumab prophylaxis were far in excess of any likely savings achieved by decreasing hospital admission rates. One of the studies performed a sensitivity analysis and found that the probability of hospital admission would have to be  $> 31\%$  for palivizumab to be cost effective.<sup>105</sup> The non-societal perspective of most studies was acknowledged.

Another systematic review encompassing UK and non-UK studies reported diverse results ranging from cost savings to considerable incremental costs per hospitalisation avoided. The diversity was attributed to the range of different infant groups, study methods and assumptions and also to the poor quality of some of the studies.<sup>106</sup> In general palivizumab was not cost effective if administered to all infants for whom it was approved.

### 10.1.3 SUMMARY OF USE OF PALIVIZUMB

On a population basis, palivizumab use in preterm infants and patients with congenital heart disease demonstrates benefit although this is unlikely to be cost effective. The potential clinical benefit for an individual patient is limited. Palivizumab prevents hospital admission with RSV for some infants, but it does not decrease length of stay or oxygen requirement for those who are admitted. Trials to date have not directly addressed the use of palivizumab in the highest risk groups of infants (extreme prematurity, complex cardiorespiratory disease).

The guideline development group consider that palivizumab cannot be recommended for routine use in the groups defined by the JCVI as the current evidence suggests that overall clinical benefits in these groups are limited.

Evidence to date is equivocal and no evidence based recommendation can be made.

For some individual patients the degree of respiratory and/or cardiac instability may provide justification for attempting to minimise the effect of RSV disease where the potential for admission to intensive care or death is considered to be extremely high.

The guideline development group consider that palivizumab use may be appropriate in individuals less than 12 months old with significant comorbidity (defined as extreme prematurity, acyanotic congenital heart disease and immune deficiency) where the risk of severe sequelae of RSV disease may be expected to carry significant immediate and long term consequences. Local expert groups should consider cases on an individual basis.

- Routine use of palivizumab is not recommended.
- Palivizumab may be considered for use, on a case by case basis, in infants less than 12 months old with;
  - extreme prematurity
  - acyanotic congenital heart disease
  - congenital or acquired significant orphan lung diseases
  - immune deficiency.
- A local lead specialist should work with the appropriate clinical teams to identify those infants who may benefit from palivizumab.

## 10.2 IMMUNOGLOBULIN

Three RCTs found that RSV hyperimmune globulin (RSVIG) is effective in reducing the incidence of RSV hospitalisations in premature infants and children with bronchopulmonary dysplasia or congenital heart disease.<sup>107-109</sup> RSVIG therapy is not licensed for use in the UK.

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# 11 Information for parents and carers

## 11.1 INFORMATION PROVISION

No studies were identified on the provision of information about bronchiolitis to parents and carers or on the effects this information may have on levels of anxiety and utilisation of healthcare services. General Medical Council guidance states that parents have a right to information about their child's condition, its treatment and its prognosis.<sup>110</sup>

4

**D** Parents and carers should receive information about their child's condition, its treatment and prognosis.

## 11.2 SOURCES OF FURTHER INFORMATION

### British Lung Foundation

73-75 Goswell Road  
London EC1V 7ER

Tel: 08458 50 50 20  
[www.lunguk.org](http://www.lunguk.org)

Baby Breathe Easy groups provide support to parents and carers.

### Contact a Family Scotland

Norton Park  
57 Albion Road  
Edinburgh EH7 5QY

Tel: 0131 475 2608 • Helpline Tel: 0808 808 3555.  
Freephone for parents and families (10am-4pm, weekdays).  
[www.cafamily.org.uk](http://www.cafamily.org.uk)

Contact a Family is a UK-wide charity providing advice, information and support to the parents of all disabled children - no matter what their health condition.

### NHS 24

Tel: 08454 242424  
[www.nhs24.com](http://www.nhs24.com)

Provides health advice and information.

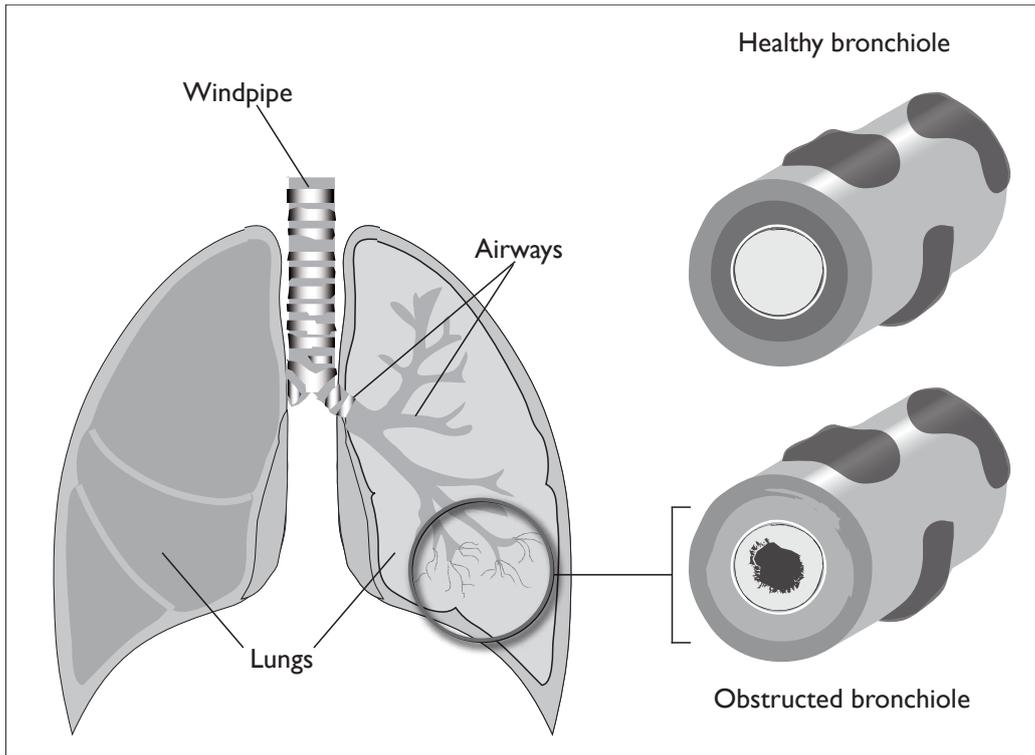
## 11.3 INFORMATION LEAFLET

The following information leaflet for parents and carers has been produced by the guideline development group based on the findings of two small focus groups with a total of seven mothers of infants who had been hospitalised with bronchiolitis. The focus groups, run by an experienced facilitator in March 2005, explored information needs at the time of the illness. The leaflet is also informed by the evidence base as well as by the clinical experience of the multidisciplinary group.

# Information about **bronchiolitis** for parents and carers

## What is bronchiolitis?

Bronchiolitis is when the tiniest air passages in your baby's lungs become swollen. This can make it more difficult for your baby to breathe. Usually, bronchiolitis is caused by a virus called respiratory syncytial virus (known as RSV).



Almost all children will have had an infection caused by RSV by the time they are two. It is most common in the winter months and usually only causes mild 'cold-like' symptoms. Most children get better on their own.

Some babies, especially very young ones, can have difficulty with breathing or feeding and may need to go to hospital.

## Can I prevent bronchiolitis?

No. The virus that causes bronchiolitis in babies also causes coughs and colds in older children and adults so it is very difficult to prevent.

## What are the symptoms?

- Bronchiolitis starts like a simple cold. Your baby may have a runny nose and sometimes a temperature and a cough.
- After a few days your baby's cough may become worse.
- Your baby's breathing may be faster than normal and it may become noisy. He or she may need to make more effort to breathe.

- Sometimes, in very young babies, bronchiolitis may cause them to have brief pauses in their breathing.
- As breathing becomes more difficult, your baby may not be able to take the usual amount of milk by breast or bottle. You may notice fewer wet nappies than usual.
- Your baby may be sick after feeding and become irritable.

### How can I help my baby?

- If feeding is difficult, try breastfeeding more often or offering smaller bottle feeds more often.
- If your baby has a temperature, you can give him or her paracetamol (for example, Calpol or Disprol). You must follow the instructions that come with the paracetamol carefully. If you are not sure, ask your community pharmacist if paracetamol is suitable for your baby, and what dose you should give.
- If your baby is already taking any medicines or inhalers, you should carry on using these. If you find it difficult to get your baby to take them, ask your doctor for advice.
- Bronchiolitis is caused by a virus so antibiotics won't help.

Make sure your baby is not exposed to tobacco smoke. Passive smoking can seriously damage your baby's health. It makes breathing problems like bronchiolitis worse.

### How long does bronchiolitis last?

- Most babies with bronchiolitis get better within about two weeks. They may still have a cough for a few more weeks.
- Your baby can go back to nursery or daycare as soon as he or she is well enough (that is feeding normally and with no difficulty breathing).
- There is usually no need to see your doctor if your baby is recovering well. If you are worried about your baby's progress, discuss this with your doctor or health visitor.

### When should I get advice?

Contact your GP if :

- you are worried about your baby;
- your baby is having difficulty breathing;
- your baby is taking less than half his or her usual feeds over two to three feeds, or has no wet nappy for 12 hours;
- your baby has a high temperature; or
- your baby seems very tired or irritable.

## Dial 999 for an ambulance if:

**Your baby is having a lot of difficulty breathing and is pale or sweaty;**

**Your baby's tongue and lips are turning blue; or**

**There are long pauses in your baby's breathing.**

What will happen if I have to take my baby to hospital?

- At hospital, a doctor or nurse will examine your baby.
- The doctor or nurse will check your baby's breathing using a special machine called a pulse oximeter. This is a light-probe which will usually be wrapped around your baby's finger or toe. It measures the oxygen in your baby's blood, and helps doctors and nurses to assess your baby's breathing.
- If your baby needs oxygen, it will be given through fine tubes into the nose or through a mask.
- If your baby needs help to breathe or feed, he or she may need to stay in hospital.
- You will be able to stay with your baby while he or she is in hospital.
- Your baby will probably only need to stay in hospital for a few days. You will be able to take your baby home when he or she is able to feed and doesn't need oxygen any more.
- To confirm the cause of the bronchiolitis, some of the mucous from your baby's nose may be tested for RSV. In hospital, it is important to separate babies with and without the virus to stop the virus spreading.
- You will need to clean your hands with alcohol gel or wash and dry them carefully before and after caring for your baby.
- Visitors may be restricted to prevent the spread of infection.
- If your baby needs help with feeding, he or she may be given milk through a feeding tube. This is a small plastic tube which is passed through your baby's nose or mouth and down into his or her stomach. It is kept in place by taping the tube to your baby's cheek. The tube will be removed when your baby is able to feed again.
- Some babies may need to be given fluids through a drip to make sure they are getting enough fluids.
- A few babies become seriously ill and need to go into intensive care (perhaps in a different hospital) for specialist help with their breathing.

## After leaving hospital

Remember, you can ask your GP or health visitor for advice or contact them if you become worried about your baby.

## Will it happen again?

Your baby is not likely to get bronchiolitis again, although occasionally it can happen.

## Are there any long-term effects?

Your baby may still have a cough and remain chesty and wheezy for some time but this will settle down gradually.

Bronchiolitis does not usually cause long-term breathing problems.

## Useful contacts

### **NHS 24**

Tel: 08454 242424 • [www.nhs24.com](http://www.nhs24.com)

Provides health advice and information.

## 12 Implementation and audit

### 12.1 LOCAL IMPLEMENTATION

Implementation of national clinical guidelines is the responsibility of each NHS Board and is an essential part of clinical governance. It is acknowledged that every Board cannot implement every guideline immediately on publication, but mechanisms should be in place to ensure that the care provided is reviewed against the guideline recommendations and the reasons for any differences assessed and, where appropriate, addressed. These discussions should involve both clinical staff and management. Local arrangements may then be made to implement the national guideline in individual hospitals, units and practices, and to monitor compliance. This may be done by a variety of means including patient-specific reminders, continuing education and training, and clinical audit.

### 12.2 RESOURCE IMPLICATIONS

It is likely that implementation of the guideline recommendations will result in decreased use of unnecessary diagnostic studies, decreased use of medications (including palivizumab) and a reduction in the use of physiotherapy in infants with bronchiolitis. These factors need to be balanced against the introduction of rapid RSV testing in those centres which do not currently have this facility.

### 12.3 KEY POINTS FOR AUDIT

- Number of emergency referrals from primary care
- admissions rate following attendance at accident and emergency
- percentage of infants given chest X-ray
- use of drug therapies
- palivizumab use
- use of chest physiotherapy
- number of centres with access to rapid RSV testing facilities
- urinary tract infection in those aged <60 days with bronchiolitis
- length of hospital stay
- healthcare associated infection rates
- use of isolation facilities
- re-attendance rates following hospital discharge
- readmission rates.

### 12.4 RECOMMENDATIONS FOR RESEARCH

- Prospective study examining prevalence of bronchiolitis in primary care and current treatment practice in the community
- repeat study of incidence of UTI in infants with bronchiolitis compared with standard hospital cohort
- large placebo controlled RCTs on ipratropium and montelukast
- prospective study of effects of systemic corticosteroids on long term respiratory outcomes
- systematic review of the prognostic factors for hospital admission to identify the most appropriate infants to be treated with palivizumab<sup>105</sup>
- study of the value of oxygen saturation measurement at initial assessment as an independent predictor of need for hospital admission
- prospective investigation into the role of C-reactive protein measurement in distinguishing bacterial from viral lower respiratory tract infections
- assessment of value of the stage of the illness in predicting possible worsening before recovery as a means of guiding decisions to admit to hospital

- evaluation of when to stop oxygen therapy and how soon after cessation it is safe to discharge infants from in-patient care
- investigation of the risks and benefits of nasogastric fluids compared with intravenous fluids
- investigation of whether the use of oxygen therapy at borderline saturation levels is effective in reducing duration of illness or improving long term outcome
- robust studies around effectiveness of infection control measures
- further economic studies into palivizumab
- study of the range of non-RSV viruses in bronchiolitis and their healthcare associated transmission rates
- definition of characteristics most likely to identify those who may have future respiratory symptoms
- assessment of value of planned follow up of hospitalised infants on resource use outcomes
- assessment of the duration of post-bronchiolitic wheeze/cough which should be considered an indication for referral to secondary care
- study of effectiveness of parent/carer information leaflets.

## 13 Development of the guideline

### 13.1 INTRODUCTION

SIGN is a collaborative network of clinicians, other healthcare professionals and patient organisations and is part of NHS Quality Improvement Scotland. SIGN guidelines are developed by multidisciplinary groups of practising clinicians using a standard methodology based on a systematic review of the evidence. Further details about SIGN and the guideline development methodology are contained in “SIGN 50: A Guideline Developer’s Handbook”, available at [www.sign.ac.uk](http://www.sign.ac.uk)

### 13.2 THE GUIDELINE DEVELOPMENT GROUP

Dr Steve Cunningham (Chair)	<i>Consultant Respiratory Paediatrician, Royal Hospital for Sick Children, Edinburgh</i>
Dr Peter W Fowlie (Secretary)	<i>Consultant Paediatrician, Ninewells Hospital, Dundee</i>
Dr Jack Beattie	<i>Consultant Paediatrician, Royal Hospital for Sick Children, Glasgow</i>
Dr Richard Brooker	<i>Consultant Paediatrician, Royal Aberdeen Children’s Hospital</i>
Dr Donna Corrigan	<i>Consultant Paediatrician, Wishaw General Hospital</i>
Dr Jonathan Coutts	<i>Consultant Paediatrician, Royal Hospital for Sick Children, Glasgow</i>
Ms Sue Danby	<i>Nursing Sister, Paediatrics, Royal Aberdeen Children’s Hospital</i>
Ms Elaine Dhouieb	<i>Senior Respiratory Physiotherapist, Royal Hospital for Sick Children, Edinburgh</i>
Ms Jeanette Fitzgerald	<i>Senior Paediatric Nurse, Ninewells Hospital, Dundee</i>
Ms June Grant	<i>Pharmacist, Princess Royal Maternity Hospital, Glasgow</i>
Dr Nick Hallam	<i>Consultant Virologist, Royal Infirmary of Edinburgh</i>
Ms Mareth Irvine	<i>Lay Representative, Dumfries and Galloway</i>
Ms Pamela Joannidis	<i>Senior Nurse, Infection Control, Royal Hospital for Sick Children, Glasgow</i>
Dr Andrew MacIntyre	<i>Consultant in Paediatric Intensive Care Medicine, Royal Hospital for Sick Children, Glasgow</i>
Dr Peter Mackie	<i>Consultant Clinical Scientist (Virology), Aberdeen Royal Infirmary</i>
Dr Jillian McFadzean	<i>Consultant in Anaesthesia and Intensive Care, Royal Hospital for Sick Children, Edinburgh</i>
Dr Maeve McPhillips	<i>Consultant Paediatric Radiologist, Royal Hospital for Sick Children, Edinburgh</i>
Dr Angela Oglesby	<i>Consultant in Accident and Emergency, Royal Hospital for Sick Children, Edinburgh</i>
Dr Ronald Seiler	<i>Retired General Practitioner, Edinburgh</i>
Ms Ailsa Stein	<i>Information Officer, SIGN</i>
Dr Caroline Stimpson	<i>General Practitioner and Clinical Assistant in Accident and Emergency, Edinburgh</i>
Dr Lorna Thompson	<i>Programme Manager, SIGN</i>
Ms Moira Walls	<i>Case Manager, Neonatal Unit, Ninewells Hospital, Dundee</i>
Dr Louise Wilson	<i>Specialist Registrar in Public Health, NHS Lanarkshire</i>
Dr Alan Woodley	<i>General Practitioner, Dundee</i>

The membership of the guideline development group was confirmed following consultation with the member organisations of SIGN. All members of the guideline development group made declarations of interest and further details of these are available on request from the SIGN Executive. Guideline development and literature review expertise, support and facilitation were provided by the SIGN Executive.

### 13.3 SYSTEMATIC LITERATURE REVIEW

The evidence base for this guideline was synthesised in accordance with SIGN methodology. A systematic literature review was carried out using an explicit search strategy devised by the SIGN Information Officer in collaboration with members of the guideline development group. Literature searches were initially conducted in Medline, Embase, Cinahl and the Cochrane Library, using the year range 2000-2005. The main searches were supplemented by material identified by individual members of the development group. All selected papers were evaluated using standard methodological checklists. The Medline version of the main search strategies can be found on the SIGN website.

### 13.4 CONSULTATION AND PEER REVIEW

#### 13.4.1 NATIONAL OPEN MEETING

A national open meeting is the main consultative phase of SIGN guideline development, at which the guideline development group present its draft recommendations for the first time. The national open meeting for this guideline was held on 9th December 2005 and was attended by 150 representatives of all the key specialties relevant to the guideline. The draft guideline was also available on the SIGN website for a limited period at this stage to allow those unable to attend the meeting to contribute to the development of the guideline.

#### 13.4.2 SPECIALIST REVIEW

This guideline was also reviewed in draft form by the following independent expert referees, who were asked to comment primarily on the comprehensiveness and accuracy of interpretation of the evidence base supporting the recommendations in the guideline. SIGN is very grateful to all of these experts for their contribution to the guideline.

Dr Laurence Abernethy	<i>Consultant Paediatric Radiologist, Royal Liverpool Children's Hospital</i>
Dr Tom Beattie	<i>Consultant in Paediatric Emergency Medicine, Royal Hospital for Sick Children, Edinburgh</i>
Ms Emma Dear	<i>Physiotherapist, Ninewells Hospital, Dundee</i>
Dr Anne Devenny	<i>Consultant Respiratory Paediatrician, Royal Hospital for Sick Children, Glasgow</i>
Dr Martin Donaghy	<i>Consultant in Public Health, Health Protection Scotland</i>
Dr George Farmer	<i>Consultant Paediatrician, Raigmore Hospital, Inverness</i>
Ms Hazel Fisher	<i>Senior Clinical Pharmacist, Wishaw General Hospital</i>
Dr Julie Freeman	<i>Consultant in Paediatric Intensive Care, Royal Hospital for Sick Children, Edinburgh</i>
Dr Neil Gibson	<i>Consultant Respiratory Paediatrician, Royal Hospital for Sick Children, Glasgow</i>
Professor Colin A Graham	<i>Associate Professor, Accident and Emergency Medicine Academic Unit, Chinese University of Hong Kong</i>
Dr Rosie Hague	<i>Consultant in Paediatric Infectious Diseases and Immunology, Royal Hospital for Sick Children, Glasgow</i>
Ms Louise Holliday	<i>Clinical Educator, Royal Aberdeen Children's Hospital</i>
Dr Julian Legg	<i>Consultant Respiratory Paediatrician, Southampton General Hospital</i>
Dr Paul Leonard	<i>Locum Consultant, Royal Hospital for Sick Children, Edinburgh</i>

Professor Warren Lenny	<i>Professor of Respiratory Child Health, Keele University</i>
Dr Una MacFadyen	<i>Consultant Paediatrician, Stirling Royal Infirmary</i>
Ms Lynsay McAuley	<i>Paediatric Pharmacist, Wishaw General Hospital</i>
Professor Neil McIntosh	<i>Professor of Child and Life Health, Royal Hospital for Sick Children, Edinburgh</i>
Dr Mike McKean	<i>Consultant Respiratory Paediatrician, Royal Victoria Infirmary, Newcastle Upon Tyne</i>
Dr Pamela J Molyneaux	<i>Consultant Virologist, Aberdeen Royal Infirmary</i>
Dr Somnath Mukhopadhyay	<i>Consultant Paediatrician, Ninewells Hospital, Dundee</i>
Ms S Ammani Prasad	<i>Research Physiotherapist, Great Ormond Street Hospital for Children, London</i>
Dr Rob Primhak	<i>Consultant Respiratory Paediatrician, The Children's Hospital, Sheffield</i>
Mr Neil Richardson	<i>Pharmacist, Royal Hospital for Sick Children, Edinburgh</i>
Dr Margrid Schindler	<i>Consultant Senior Lecturer in Paediatric Intensive Care, Bristol Royal Hospital for Children, Avon</i>
Dr Rajendran Shyam	<i>Specialist Paediatric Registrar, Royal Victoria Infirmary, Newcastle Upon Tyne</i>
Dr Charles Skeoch	<i>Consultant in Neonatal Intensive Care, Princess Royal Maternity Hospital, Glasgow</i>
Dr Iain Small	<i>General Practitioner, Links Terrace Health Centre, Peterhead</i>
Dr Ben Stenson	<i>Consultant in Neonatology, Royal Infirmary of Edinburgh</i>
Mrs Sue Stobie	<i>Medicines Management Pharmacist, Royal Edinburgh Hospital</i>
Dr Robert Tasker	<i>Consultant in Paediatrics, Addenbrooke's Hospital, Cambridge</i>
Mr Steve Tomlin	<i>Principal Paediatric Pharmacist, Guy's Hospital, London</i>
Dr Tom Turner	<i>Neonatology Consultant, Queen Mothers Hospital, Glasgow</i>
Dr Clair Wainwright	<i>Paediatric Respiratory Specialist, Royal Children's Hospital, Brisbane, Australia</i>
Mr James Wallace	<i>Director of Pharmacy Services, Yorkhill Hospital, Glasgow</i>
Dr Peter Weller	<i>Consultant Paediatrician in Respiratory Medicine – Retired, Birmingham</i>
Dr Craig Williams	<i>Consultant Microbiologist, Yorkhill Hospital, Glasgow</i>
Dr Job Van Woensel	<i>Pediatric-Intensivist, Emma Children's Hospital, Amsterdam</i>

#### 13.4.3 SIGN EDITORIAL GROUP

As a final quality control check, the guideline is reviewed by an editorial group comprising the relevant specialty representatives on SIGN Council to ensure that the specialist reviewers' comments have been addressed adequately and that any risk of bias in the guideline development process as a whole has been minimised. The editorial group for this guideline was as follows.

Dr Bernard Higgins	<i>Royal College of Physicians of London</i>
Professor Gordon Lowe	<i>Chair of SIGN; Co-Editor</i>
Professor Chris Kelnar	<i>Royal College of Paediatrics and Child Health, Vice Chair of SIGN</i>
Ms Anne Matthew	<i>Royal College of Midwives</i>
Mrs Fiona McMillan	<i>Royal Pharmaceutical Society of Great Britain (Scottish Dept)</i>
Dr Safia Qureshi	<i>SIGN Programme Director; Co-Editor</i>
Dr Bill Reith	<i>Royal College of General Practitioners</i>
Dr Sara Twaddle	<i>Director of SIGN; Co-Editor</i>

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Dr Jim Beattie	<i>Consultant Paediatrician, Royal Hospital for Sick Children, Glasgow</i>
Ms Carol Prentice	<i>Lay Representative</i>
Dr Alison Ting	<i>Specialist Registrar in Respiratory Medicine, Royal Hospital for Sick Children, Edinburgh</i>
Mrs Jenni Washington	<i>Information Officer, SIGN</i>
Dr Sarah Wheeler	<i>Project Development Officer, Health Rights Information Scotland, Scottish Consumer Council</i>

# Abbreviations

<b>A&amp;E</b>	Accident and emergency
<b>ARR</b>	Absolute risk reduction
<b>BPD</b>	Bronchopulmonary dysplasia
<b>CI</b>	Confidence interval
<b>CHD</b>	Congenital heart disease
<b>CLD</b>	Chronic lung disease
<b>CRP</b>	C-reactive protein
<b>FiO<sub>2</sub></b>	Fraction of inspired oxygen (%)
<b>GP</b>	General practitioner
<b>HAI</b>	Healthcare associated infection
<b>ICU</b>	Intensive care unit
<b>JCVI</b>	Joint Committee on Vaccination and Immunisation
<b>LRI</b>	Lower respiratory illness/infection
<b>LRTI</b>	Lower respiratory tract infection
<b>NNT</b>	Number needed to treat
<b>OR</b>	Odds ratio
<b>PaCO<sub>2</sub></b>	Partial pressure of arterial carbon dioxide
<b>PaO<sub>2</sub></b>	Partial pressure of arterial oxygen
<b>PICU</b>	Paediatric intensive care unit
<b>RCT</b>	Randomised controlled trial
<b>RR</b>	Relative risk
<b>RRR</b>	Relative risk reduction
<b>RSV</b>	Respiratory syncytial virus
<b>RSVIG</b>	Respiratory syncytial virus hyperimmune globulin
<b>U&amp;E</b>	Urea and electrolytes
<b>UK</b>	United Kingdom
<b>USA</b>	United States of America
<b>UTI</b>	Urinary tract infection

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## **i** Information about bronchiolitis for parents and carers

### What is bronchiolitis?

Bronchiolitis is when the tiniest air passages in your baby's lungs become swollen. This can make it more difficult for your baby to breathe. Usually, bronchiolitis is caused by a virus called respiratory syncytial virus (known as RSV).

Almost all children will have had an infection caused by RSV by the time they are two. It is most common in the winter months and usually only causes mild 'cold-like' symptoms. Most children get better on their own.

Some babies, especially very young ones, can have difficulty with breathing or feeding and may need to go to hospital.

### Can I prevent bronchiolitis?

No. The virus that causes bronchiolitis in babies also causes coughs and colds in older children and adults so it is very difficult to prevent.

### What are the symptoms?

- Bronchiolitis starts like a simple cold. Your baby may have a runny nose and sometimes a temperature and a cough.
- After a few days your baby's cough may become worse.
- Your baby's breathing may be faster than normal and it may become noisy. He or she may need to make more effort to breathe.
- Sometimes, in very young babies, bronchiolitis may cause them to have brief pauses in their breathing.
- As breathing becomes more difficult, your baby may not be able to take the usual amount of milk by breast or bottle. You may notice fewer wet nappies than usual.
- Your baby may be sick after feeding and become irritable.

### How can I help my baby?

- If feeding is difficult, try breastfeeding more often or offering smaller bottle feeds more often.
- If your baby has a temperature, you can give him or her paracetamol (for example, Calpol or Disprol). You must follow the instructions that come with the paracetamol carefully. If you are not sure, ask your community pharmacist if paracetamol is suitable for your baby, and what dose you should give.
- If your baby is already taking any medicines or inhalers, you should carry on using these. If you find it difficult to get your baby to take them, ask your doctor for advice.
- Bronchiolitis is caused by a virus so antibiotics won't help.

Make sure your baby is not exposed to tobacco smoke. Passive smoking can seriously damage your baby's health. It makes breathing problems like bronchiolitis worse.

### How long does bronchiolitis last?

- Most babies with bronchiolitis get better within about two weeks. They may still have a cough for a few more weeks.
- Your baby can go back to nursery or daycare as soon as he or she is well enough (that is feeding normally and with no difficulty breathing).
- There is usually no need to see your doctor if your baby is recovering well. If you are worried about your baby's progress, discuss this with your doctor or health visitor.

### When should I get advice?

Contact your GP if :

- you are worried about your baby;
- your baby is having difficulty breathing;
- your baby is taking less than half his or her usual feeds over two to three feeds, or has no wet nappy for 12 hours;
- your baby has a high temperature; or
- your baby seems very tired or irritable.

### Dial 999 for an ambulance if:

Your baby is having a lot of difficulty breathing and is pale or sweaty;

Your baby's tongue and lips are turning blue; or

There are long pauses in your baby's breathing.

### What will happen if I have to take my baby to hospital?

- At hospital, a doctor or nurse will examine your baby.
- The doctor or nurse will check your baby's breathing using a special machine called a pulse oximeter. This is a light-probe which will usually be wrapped around your baby's finger or toe. It measures the oxygen in your baby's blood, and helps doctors and nurses to assess your baby's breathing.
- If your baby needs oxygen, it will be given through fine tubes into the nose or through a mask.
- If your baby needs help to breathe or feed, he or she may need to stay in hospital.
- You will be able to stay with your baby while he or she is in hospital.

- Your baby will probably only need to stay in hospital for a few days. You will be able to take your baby home when he or she is able to feed and doesn't need oxygen any more.

- To confirm the cause of the bronchiolitis, some of the mucus from your baby's nose may be tested for RSV. In hospital, it is important to separate babies with and without the virus to stop the virus spreading.
- You will need to clean your hands with alcohol gel or wash and dry them carefully before and after caring for your baby.
- Visitors may be restricted to prevent the spread of infection.
- If your baby needs help with feeding, he or she may be given milk through a feeding tube. This is a small plastic tube which is passed through your baby's nose or mouth and down into his or her stomach. It is kept in place by taping the tube to your baby's cheek. The tube will be removed when your baby is able to feed again.
- Some babies may need to be given fluids through a drip to make sure they are getting enough fluids.
- A few babies become seriously ill and need to go into intensive care (perhaps in a different hospital) for specialist help with their breathing.

### After leaving hospital

Remember, you can ask your GP or health visitor for advice or contact them if you become worried about your baby.

### Will it happen again?

Your baby is not likely to get bronchiolitis again, although occasionally it can happen.

### Are there any long-term effects?

Your baby may still have a cough and remain chesty and wheezy for some time but this will settle down gradually.

Bronchiolitis does not usually cause long-term breathing problems.

### Useful contacts

#### NHS 24

Phone: 08454 242424 • [www.nhs24.com](http://www.nhs24.com)  
Provides health advice and information.