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ORIGINAL ARTICLE

Australasian bronchiolitis guideline

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Aim: Bronchiolitis is the most common lower respiratory tract disorder in infants aged less than 12 months, and research has demonstrated that there is substantial variation in practice patterns despite treatment being well defined. In order to align and improve the consistency of the management of bronchiolitis, an evidence-based guideline was developed for the Australasian population.

Methods: The guideline development committee included representation from emergency and paediatric specialty medical and nursing personnel in addition to geographical representation across Australia and New Zealand – rural, remote and metropolitan. Formulation of the guideline included identification of population, intervention, comparator, outcomes and time questions and was associated with an extensive literature search from 2000 to 2015. Evidence was summarised and graded using the National Health and Medical Research Council and Grading of Recommendations Assessment, Development and Evaluation methodology, and consensus within the guideline group was sought using nominal group technique principles to formulate the clinical practice recommendations. The guideline was reviewed and endorsed by key paediatric health bodies.

Results: The guideline consists of a usable clinical interface for bedside functionality supported by evidence summary and tables. The Grading of Recommendations Assessment, Development and Evaluation and National Health and Medical Research Council processes provided a systematic and transparent process to review and assess the literature, resulting in a guideline that is relevant to the management of bronchiolitis in the Australasian setting.

Conclusion: This is the first robust Australasian acute paediatric guideline and provides clear guidance for the management of the vast majority of patients seen in Australasian emergency departments and general paediatric wards with bronchiolitis.

Key words: bronchiolitis; guideline; management; paediatric; respiratory.

What is already known on this topic

1 Bronchiolitis is the most common reason for infants <1 year of age to be admitted to hospital.
2 Wide variation in the management of bronchiolitis exists across Australia and New Zealand, with up to 48% of infants admitted into hospital receiving treatment for which there is high quality (Cochrane-level) evidence of no benefit.
3 To date, there have been no high-quality acute paediatric guidelines developed across Australia and New Zealand.

What this paper adds

1 This is the first high-quality acute paediatric guideline developed for use across Australia and New Zealand.
2 A total of 33 questions related to the core management of infants with bronchiolitis were assessed according to Grading of Recommendations Assessment, Development and Evaluation and National Health and Medical Research Council strength-of-evidence guidelines.
3 Thirty research questions were also identified for future research.

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Bronchiolitis is the most common lower respiratory tract disorder in infants less than 12 months of age.[1,2] Each year, approximately 13 500 Australian infants with bronchiolitis are admitted to hospital, accounting for 56% of all admissions to hospital for infants.[3] In New Zealand, 3–7% of all infants require hospital admission with bronchiolitis with those living in the most deprived socio-economic areas, Maori and Pacific infants, having increased rates.[4]

While evidence-supported treatment is focussed on therapies to ensure hydration and respiratory support,[5,6] substantial practice variations remain in Australasian hospitals.[7] For example, up to 48% of infants admitted to hospitals in Australasia receive treatment for which there is Cochrane-level evidence of no benefit.[8] Although high-quality international clinical practice guidelines for bronchiolitis exist from the USA and the UK,[9,10] they do not take into account the latest evidence or the Australian and New Zealand context in terms of health-care systems and epidemiology.[11] Thus, we determined a need for a robust, locally applicable guideline to summarise the latest evidence and provide a practical guide for clinicians in Australia and New Zealand.

To address this important high-volume condition, we undertook a systematic literature review followed by the development of the guideline. The systematic review of the literature used the National Health and Medical Research Council (NHMRC) strength of recommendations classification system[12] and Grading of Recommendations Assessment, Development and Evaluation (GRADE) methodology[13](Table 1), with wide stakeholder consultation. The resulting guideline is the first Australasian acute care paediatric guideline to be developed to this robust standard.

Methods

The Guideline Steering Committee comprised five members (paediatric emergency medicine physicians (SR Dalziel, E Oakley, ML Borland), a regional paediatrician (E Cotterell) and a paediatric nurse (S O'Brien)) from the Paediatric Research in Emergency Departments International Collaborative (PREDICT) executive committee. PREDICT is Australasia's acute paediatric research network and includes members from over 30 hospitals, including all Australasian tertiary paediatric hospitals.[14] Invitations were then sent to all Australasian paediatric hospitals, relevant medical and nursing professional societies and colleges and identified local content experts, asking for nominations to join the Guideline Development Committee (GDC), which finally comprised 22 individuals, including general paediatricians, paediatric respiratory physicians, paediatric and general emergency medicine physicians, paediatric intensive care physicians, paediatric nurse practitioners and paediatric and emergency nurses from metropolitan and non-metropolitan centres in New Zealand and Australia (representing seven of the eight states and territories). The process was funded by an NHMRC Centre of Research Excellence grant (GNT 1058560) as a key knowledge translation priority, and the full Guideline methodology has been described elsewhere.[15]

Scope

The guideline specifically addressed care in both the emergency department (ED) and on general wards for the management of bronchiolitis in order to influence the majority of patients who present to hospital with bronchiolitis. It specifically excluded management in primary care and intensive care units (ICU) as ward-based hospitalisation is the primary determinant of health-care expenditure for bronchiolitis,[16] and only a small proportion of patients admitted to hospital with bronchiolitis require ICU management.[17]

Aim

This study aimed to develop an evidence-based clinical practice guideline for infants presenting to and hospitalised in Australasia.

Target audience

Staff working in Australasian EDs and general paediatric wards areas were the target audience.

Process

The GDC identified 33 key clinical questions in the patient, intervention, comparison, outcome, time format relevant to the management of bronchiolitis (Table 2).

A literature search was performed, with the assistance of a medical information specialist, from 1 January 2000 to 17 December 2015, of the following electronic databases: Ovid MEDLINE, Ovid Embase, PubMed, Cumulative Index to Nursing and Allied Health Literature, Cochrane Review library and Cochrane Database of Systematic Reviews (Appendix I). This was to identify appropriate literature for the clinical questions. Following removal of duplicates, each title and abstract was reviewed by one of the five members of the steering committee for possible inclusion. The resulting manuscripts were then sourced and made available to members of the GDC.

The evidence was summarised in NHMRC and GRADE tables, with clinical recommendations based on NHMRC[12] and GRADE methodology[13](Table 1). Where possible, for those clinical questions involving interventions, the evidence used to make recommendations was based on systematic reviews and randomised controlled trials.

All recommendations and evidence tables were reviewed by the GDC, and consensus was sought using nominal group technique principles.

A draft guideline was produced consisting of both a bedside version and a full guideline including the evidence tables. The draft was circulated to all Australasian tertiary paediatric hospitals, medical and nursing professional societies and colleges and identified local content experts for wide consultation. All feedback was reviewed by the GDC, with only minor adjustments required for the final guideline.

Results

The literature search identified 12 535 manuscripts, of which 8722 were assessed for possible inclusion in the guideline after initial review of the titles and abstracts (Appendix II).

Five evidence-based recommendations were made with regard to diagnosis and 28 with regard to management of infants

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Table 1 National Health and Medical Research Council (NHMRC) strength of recommendation definitions and Grading of Recommendations Assessment, Development and Evaluation (GRADE) quality of evidence definitions used in the guideline process to make a final recommendation

NHMRC strength of recommendation definitions[3]	
A	Body of evidence can be trusted to guide practice
B	Body of evidence can be trusted to guide practice in most situations
C	Body of evidence provides some support for recommendation(s) but care should be taken in its application
D	Body of evidence is weak and recommendation must be applied with caution
GRADE quality of evidence definitions[9]	
High quality	Further research is very unlikely to change our confidence in the estimate of effect
Moderate quality	Further research is likely to have an important impact on our confidence in the estimate of effect and may change the estimate
Low quality	Further research is very likely to have an important impact on our confidence in the estimate of effect and is likely to change the estimate
Very low quality	Any estimate of effect is very uncertain

presenting, and admitted, to hospital with bronchiolitis (Table 3). These have been formatted into a bedside resource for staff (Tables 4 and 5).

Key recommendations for practice change in the guideline include:

Routine investigations

Routine testing of urine or blood is not recommended for the management of infants with bronchiolitis (Table 3, recommendation 4).[10,18–25] However, both retrospective and prospective cohort studies of infants with bronchiolitis have shown an increased risk of concurrent urinary tract infections in infants aged younger than 2 months of age.[20] Based on this evidence, the final recommendations in the guideline state that, in infants younger than 2 months of age with bronchiolitis, with a fever and clinical uncertainty, clinicians may consider collecting a urine sample for microscopy, culture and sensitivity looking for the presence of a urinary tract infection (Table 3, recommendation 4).

Viral testing and patient cohorting

A systematic review of 82 studies, with heterogeneity of study design and outcome, demonstrated a lack of evidence for any clinical benefit from routine viral testing.[18] Based on this evidence, the final recommendations state that routine use of viral testing is not recommended for any clinically relevant end-points, including cohorting of bronchiolitis patients (Table 3, recommendation 5). Further research is recommended to determine if patient cohorting based on virological results has an added advantage over routine contact precautions in reducing hospital transmission.

Salbutamol

Data regarding the administration of beta-2 agonists, such as salbutamol (with the exclusion of adrenaline), in infants with bronchiolitis come from one Cochrane Systematic Review[26] and three systematic reviews and guidelines.[10,27,28] There is high-level evidence (NHMRC A, GRADE strong) demonstrating no benefit of beta-2 agonists in infants with bronchiolitis for the outcomes of admission to hospital, oxygen saturation or length of stay. Furthermore, there is low-quality evidence of adverse events due to the use of beta-2 agonists in bronchiolitis. The evidence is consistent across all ages in the first 12 months of life, with a sensitivity analysis showing no significant subgroup effect in the cohort over 6 months of age.[26]

Based on this evidence, the final recommendations in the guideline do not recommend routine use of beta-2 agonists (Table 3, recommendation 8).

Nebulised adrenaline

Data regarding the administration of adrenaline/epinephrine in infants with bronchiolitis come from one Cochrane Systematic Review[29] and two systematic reviews and guidelines[27,28] and a recent high-quality RCT.[30]

Evidence from the Cochrane Systematic Review[28] and the recent high-quality RCT[30] does not suggest that administering adrenaline/epinephrine in inpatients with bronchiolitis changes hospital length of stay or readmission rates.

Based on this evidence, the final recommendations in the guideline do not recommend the routine use of nebulised adrenaline (Table 3, recommendation 9).

Hypertonic saline

Data regarding the administration of nebulised hypertonic saline in infants with bronchiolitis are based on one Cochrane Systematic Review (11 RCTs),[31] a further nine additional RCTs[32–40] and five subsequent systematic reviews/meta-analyses.[41–45] Infants admitted to hospital with bronchiolitis and administered nebulised hypertonic saline have a reduced length of stay of 0.45 days (95% confidence interval = −0.74 to −0.14 days; 15 studies, n = 1922). However, there is considerable heterogeneity in this overall result (I^2 = 78%). Removal of two studies with an overall length of stay considerably longer than current clinical practice in Australia and New Zealand, and with a primary outcome definition considerably different than that used locally for discharge (no respiratory signs or symptoms for 12 h), partially explains the heterogeneity and results in a pooled estimate, suggesting no effect. Furthermore, analysis restricted to the four largest trials, all at lower risk of bias, again suggests no benefit.[43]

While there is weak evidence of reduced admission rates following the use of nebulised hypertonic saline, there is heterogeneity in the treatment regimens used and a suggestion that one to two dose regimens are ineffective. The routine use of nebulised hypertonic

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Table 2 Patient, intervention, comparison, outcome, time questions relevant to the management of bronchiolitis addressed in the guideline

No.	Question
1	In infants presenting to hospital what factors in history and physical examination contribute to a differential diagnosis of bronchiolitis?
2	In infants presenting to hospital with bronchiolitis, what are the risk factors for admission or severe disease (e.g. prolonged length of hospital stay, intensive care unit admission and death)?
3	In infants presenting to hospital or hospitalised with bronchiolitis, does performing a CXR beneficially change medical management or clinically relevant end-points?
4	In infants presenting to hospital or hospitalised with bronchiolitis, does performing laboratory tests (blood and/or urine) beneficially change medical management or clinically relevant end-points?
5	In infants presenting to hospital or hospitalised with bronchiolitis, does performing virological investigations beneficially change medical management or clinically relevant end-points?
6	For infants presenting to hospital or hospitalised with bronchiolitis, does use of a bronchiolitis scoring system beneficially change medical management or clinically relevant end-points?
7	For infants presenting to hospital or hospitalised with bronchiolitis, what criteria should be used for safe discharge?
8a	(i) In infants presenting to hospital or hospitalised with bronchiolitis, does administration of beta-2 agonists (nebulisation, aerosol, oral or IV) improve clinically relevant end-points? (ii) In older infants presenting to hospital or hospitalised with bronchiolitis, does administration of beta-2 agonists (nebulisation, aerosol, oral or IV) improve clinically relevant end-points?
8b	(i) In infants presenting to hospital or hospitalised with bronchiolitis, with a personal or family history of atopy, does administration of beta-2 agonists (nebulisation, aerosol, oral or IV) improve clinically relevant end-points? (ii) In older infants presenting to hospital or hospitalised with bronchiolitis, with a second or subsequent episode/s of bronchiolitis or wheeze, does administration of beta-2 agonists (nebulisation, aerosol, oral or IV) improve clinically relevant end-points?
9	In infants presenting to hospital or hospitalised with bronchiolitis, does administration of adrenaline/epinephrine (nebulisation, IM or IV) improve clinically relevant end-points?
10	In infants presenting to hospital or hospitalised with bronchiolitis, does administration of nebulised hypertonic saline improve clinically relevant end-points?
11a	In infants presenting to hospital or hospitalised with bronchiolitis, does administration of systemic or local glucocorticoids (nebulisation, oral, IM or IV) improve clinically relevant end-points?
11b	In infants presenting to hospital or hospitalised with bronchiolitis, with a positive response to beta-2 agonists, does administration of systemic or local glucocorticoids (nebulisation, oral, IM or IV) improve clinically relevant end-points?
11c	In infants presenting to hospital or hospitalised with bronchiolitis, does administration of the combination of systemic or local glucocorticoids (nebulisation, oral, IM or IV) and adrenaline improve clinically relevant end-points?
12a	In infants presenting to hospital or hospitalised with bronchiolitis, does administration of supplemental oxygen improve clinically relevant end-points?
12b	In infants presenting to hospital or hospitalised with bronchiolitis, what level of oxygen saturation should lead to commencement or discontinuation of supplemental oxygen to improve clinically relevant end-points?
13	In infants hospitalised with bronchiolitis does continuous monitoring of pulse oximetry beneficially change medical management or clinically relevant end-points?
14	In infants hospitalised with bronchiolitis does the use of heated humidified high flow oxygen, or air, via nasal cannula improve clinically relevant end-points?
15	In infants hospitalised with bronchiolitis, does chest physiotherapy improve clinically relevant end-points?
16a	In infants hospitalised with bronchiolitis, does suctioning of the nose or naso pharynx improve clinically relevant end-points?
16b	In infants hospitalised with bronchiolitis, does deep suctioning in comparison to superficial suctioning beneficially improve clinically relevant end-points?
17	In infants hospitalised with bronchiolitis, does the use of nasal saline drops improve clinically relevant end-points?
18	In infants hospitalised with bronchiolitis, does the use of bubble CPAP improve clinically relevant end-points?
19	In infants hospitalised with bronchiolitis, is provision of home oxygen a safe alternative for management?
20a	In infants presenting to hospital or hospitalised with bronchiolitis, does the use of antibiotic medication improve clinically relevant end-points?
20b	In infants presenting to hospital or hospitalised with bronchiolitis, does the use azithromycin medication improve clinically relevant end-points?
20c	In infants presenting to hospital or hospitalised with bronchiolitis, does the use of antibiotic medication in infants who are at risk of developing bronchiectasis, improve clinically relevant end-points?
21a	In infants presenting to hospital or hospitalised with bronchiolitis, does the use of non-oral hydration improve clinically relevant end-points?
21b	In infants presenting to hospital or hospitalised with bronchiolitis, what forms of non-oral hydration improve clinically relevant end-points
21c	In infants presenting to hospital or hospitalised with bronchiolitis, does limiting the volume of non-oral hydration impact on clinical relevant end-points?
22	In infants presenting to hospital or hospitalised with bronchiolitis, does infection control practices improve clinically relevant end-points?

CPAP, continuous positive airway pressure; CXR, chest X-ray; IM, intramuscular; IV, intravenous.

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Table 3 Evidence-based recommendations for bronchiolitis management

Diagnosis

1 Infants can be diagnosed with bronchiolitis if they have an upper respiratory tract infection followed by onset of respiratory distress with fever and one or more of: cough, tachypnoea, retractions and diffuse crackles or wheeze on auscultation (NHMRC: C, GRADE: Weak)

2 Clinicians should consider as risk factors for more serious illness: gestational age less than 37 weeks; chronological age at presentation less than 10 weeks; exposure to cigarette smoke; breast feeding for less than 2 months; failure to thrive; having chronic lung disease; having chronic heart and/or chronic neurological conditions; and being Indigenous ethnicity, and should take these into account when managing infants with bronchiolitis (NHMRC: C, GRADE: Conditional)

3 Routine CXR is not recommended as it does not improve management in infants presenting with simple bronchiolitis and may lead to treatments of no benefit (NHMRC: D, GRADE: Conditional)

4 There is no role for blood tests in managing infants presenting to hospital and hospitalised with bronchiolitis. Routine bacteriological testing of blood and urine is not recommended (NHMRC: D, GRADE: Conditional)

In infants younger than 2 months of age presenting to hospital or hospitalised with bronchiolitis with a temperature over 38°, there is a low risk of urinary tract infection (UTI). If clinical uncertainty exists, clinicians may consider collecting a urine sample for microscopy, culture and sensitivity, looking for the concurrent presence of UTI

5 In infants with bronchiolitis, routine use of viral testing is not recommended for any clinically relevant endpoints, including cohorting of bronchiolitis patients (NHMRC: C, GRADE: Conditional)

Management

6 For infants presenting to hospital or hospitalised with bronchiolitis, there is insufficient evidence to recommend the use of a scoring system to predict need for admission or hospital length of stay (NHMRC: D, GRADE: Weak)

7 Oxygen saturations, adequacy of feeding, age (infants younger than 8 weeks) and lack of social support should be considered at the time of discharge as a risk for representation. There is insufficient evidence to recommend absolute discharge criteria for infants attending the ED or hospitalised with bronchiolitis (NHMRC: Practice point, GRADE: Weak)

8a Do not administer beta-2 agonists to infants, less than or equal to 12 months of age, presenting to hospital or hospitalised with bronchiolitis (NHMRC: A, GRADE: Strong)

8b Do not administer beta-2 agonists to infants, less than or equal to 12 months of age, presenting to hospital or hospitalised with bronchiolitis, with a personal or family history of atopy (NHMRC: D, GRADE: Weak)

9 Do not administer adrenaline/epinephrine to infants presenting to hospital or hospitalised with bronchiolitis (NHMRC: B, GRADE: Strong)

10 Do not administer nebulised hypertonic saline in infants presenting to hospital or hospitalised with bronchiolitis (NHMRC: D, GRADE: Conditional)

11a Do not administer systemic or local glucocorticoids to infants presenting to hospital or hospitalised with bronchiolitis (NHMRC: B, GRADE: Strong)

11b Do not administer systemic or local glucocorticoids to infants presenting to hospital or hospitalised with bronchiolitis, with a positive response to beta-2 agonists (NHMRC: D, GRADE: Weak)

11c Do not administer a combination of systemic or local glucocorticoids and adrenaline/epinephrine to infants presenting to hospital or hospitalised with bronchiolitis (NHMRC: D, GRADE: Weak)

12a Consider the use of supplemental oxygen in the treatment of hypoxic (oxygen saturations less than 92%) infants with bronchiolitis (NHMRC: C, GRADE: Conditional)

12b In uncomplicated bronchiolitis, oxygen supplementation should be commenced if the oxygen saturation level is sustained at a level less than 92%. At oxygen saturation levels of 92% or greater, oxygen therapy should be discontinued (NHMRC: C, GRADE: Conditional)

13 Routine use of continuous pulse oximetry is not required for medical management of non-hypoxic (saturations greater than or equal to 92%) infants not receiving oxygen or stable infants receiving oxygen (NHMRC: C, GRADE: Conditional)

14 High-flow nasal cannulae oxygen in bronchiolitis can be considered in the inpatient setting on infants with bronchiolitis with hypoxia (oxygen saturations less than 92%). Its use in children without hypoxia should be limited to the RCT setting only (NHMRC: C, GRADE: Conditional)

15 Chest physiotherapy is not recommended for routine use in infants with bronchiolitis (NHMRC: B, GRADE: Strong)

16a Nasal suction is not recommended as routine practice in the management of infants with bronchiolitis. Superficial nasal suction may be considered in those with moderate disease to assist feeding (NHMRC: D, GRADE: Conditional)

16b Deep nasal suction for the management of bronchiolitis is not recommended (NHMRC: D, GRADE: Conditional)

17 Routine nasal saline drops are not recommended. Trial of intermittent saline drops may be considered at time of feeding (NHMRC: Practice point, GRADE: Weak)

18 Nasal CPAP therapy for infants with bronchiolitis may be considered for the management of infants (NHMRC: C, GRADE: Conditional)

19 After a period of observation, infants at low risk for severe bronchiolitis can be considered for discharge on home oxygen as part of an organised 'home oxygen program', which has clear 'return to hospital' advice (NHMRC: C, GRADE: Conditional)

20a Do not use antibiotics to treat infants with bronchiolitis (NHMRC: B, GRADE: Conditional)

20b Do not use azithromycin for treatment of infants admitted to hospital with bronchiolitis (NHMRC: B, GRADE: Conditional)

20c Do not use azithromycin for treatment of infants admitted to hospital with bronchiolitis who are at risk of developing bronchiectasis (NHMRC: C, GRADE: Conditional)

21a Supplemental hydration is recommended for infants who cannot maintain hydration orally (NHMRC: Practice point, GRADE: Weak)

21b Both NG and IV routes are acceptable means for non-oral hydration in infants admitted to hospital with bronchiolitis (NHMRC: B, GRADE: Strong)

(*Continues*)

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Table 3 (Continued)

21c There is insufficient evidence to recommend a specific proportion of maintenance fluid. There is a risk of fluid overload; therefore, judicious and vigilant use of hydration fluid and regular clinical review are recommended. Isotonic fluid is recommended (NHMRC: Practice point, GRADE: Weak)
22 Hand hygiene is the most effective intervention to reduce hospital-acquired infections and is recommended. There is inadequate evidence for benefits in cohorting infants with bronchiolitis (NHMRC: D, GRADE: Weak)

CPAP, continuous positive airway pressure; CXR, chest X-ray; ED, emergency department; GRADE, Grading of Recommendations Assessment, Development and Evaluation; IV, intravenous; NG, nasogastric; NHMRC, National Health and Medical Research Council; RCT, randomised controlled trial.

Table 4 Bedside bronchiolitis assessment aid

	Initial assessment		
	Mild	Moderate	Severe
Behaviour	Normal	Some/Intermittent irritability	Increasing irritability and/or lethargy, fatigue
Respiratory rate	Normal–mild tachypnoea	Increased respiratory rate	Marked increase or decrease in respiratory rate
Use of accessory muscles	Nil to mild chest wall retraction	Moderate chest wall retractions, tracheal tug, nasal flaring	Marked chest wall retractions, marked tracheal tug, marked nasal flaring
Oxygen saturation/ Oxygen requirement	O_2 saturations greater than 92% (in room air)	O_2 saturations 90–92% (in room air)	O_2 saturations less than 90% (in room air), hypoxaemia, may not be corrected by O_2
Apnoeic episodes	None	May have brief apnoea	May have increasingly frequent or prolonged apnoea
Feeding	Normal	May have difficulty with feeding or reduced feeding	Reluctant or unable to feed

This table is meant to provide guidance in order to stratify severity. The more symptoms the infant has in the mod–severe categories, the more likely they are to develop severe disease.

saline in the ED to reduce admissions is not supported by the current evidence, and nebulised hypertonic saline should only be used in infants with bronchiolitis as part of an RCT.

Based on this evidence, the final recommendations in the guideline do not recommend routine use of nebulised hypertonic saline (Table 3, recommendation 10).

Glucocorticoids

Data regarding the administration of glucocorticoids in infants with bronchiolitis come from one Cochrane Systematic Rreview,[46] three subsequent systematic reviews and guidelines[10,27,28] and two further RCTs.[47,48] Infants with bronchiolitis administered glucocorticoids do not have reduced rates of hospitalisation or differences in length of stay.

Based on this evidence, the final recommendations in the guideline do not recommend routine use of glucocorticoids (Table 3, recommendation 11).

Antibiotics

Two Cochrane Systematic Reviews[49,50] and a single RCT of 40 infants[51] show no benefit of antibiotics for treating bronchiolitis in terms of hospital length of stay and hospital readmission rates[49] or persisting symptoms.[50] The risk of secondary bacterial infection in bronchiolitis is very low, and there is potential harm from antibiotics use because of adverse reactions and increased antibiotic resistance.

Based on this evidence, the final recommendations in the guideline do not recommend routine use of antibiotics (Table 3, recommendation 20).

Oxygen and respiratory support

The benefit of supplemental oxygen therapy has not been specifically studied; rather, there are assumptions about the benefits of oxygen based on first principles and observational studies. Studies have predominantly investigated the duration of oxygen administration and feeding difficulties as a gauge of effectiveness.[28,52–54] There is no evidence of the benefit of oxygen in children without hypoxia and low-level evidence that maintaining an oxygen saturation of more than 91% prolongs length of stay.[28,52–58] The absolute oxygen saturation at which to commence supplemental oxygen therapy has ranged in studies from 90 to 94%. To date, no RCTs have reported long-term neurodevelopmental outcomes in babies with bronchiolitis. Due to the lack of this long-term evidence on the safety with oxygen saturation targets of less than

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Table 5 Bedside bronchiolitis management aid

	Initial management		
	Mild	Moderate	Severe
Likelihood of admission	Suitable for discharge	Likely admission, may be able to be discharged after a period of observation	Requires admission and consider need for transfer to an appropriate children's facility/ PICU
	Consider risk factors	Management should be discussed with a local senior physician	Threshold for referral is determined by local escalation policies but should be early
Observations: Vital signs (respiratory rate, heart rate, O_2 saturations, temperature)	Adequate assessment in ED prior to discharge (minimum of two recorded measurements or every 4 h as per local hospital guidelines and EWT)	Hourly – dependent on condition (as per local hospital guidelines and EWT)	Hourly with continuous cardiorespiratory (including oximetry) monitoring and close nursing observation – dependent on condition (as per local hospital guidelines and EWT)
Hydration/Nutrition	Small frequent feeds	If not feeding adequately (less than 50% over 12 h), administer NG or IV hydration	If not feeding adequately (less than 50% over 12 h), or unable to feed, administer NG or IV hydration
Oxygen saturation/Oxygen requirement	Nil requirement	Administer O_2 to maintain saturations greater than or equal to 92%	Administer O_2 to maintain saturations greater than or equal to 92%
Respiratory support		Consider HFNC if a trial of NPO_2 is ineffective	Consider HFNC or CPAP
Disposition/Escalation	Consider further medical review if early in the illness and any risk factors are present or if child develops increasing severity after discharge	Decision to admit should be supported by clinical assessment, social and geographical factors and phase of illness	Consider escalation if severity does not improve. Consider ICU review/admission or transfer to local centre with paediatric HDU/ICU capacity if: (i) severity does not improve; (ii) persistent desaturations; (iii) significant or recurrent apnoea's associated with desaturations
Parental education	Provide advice on the expected course of illness and when to return (worsening symptoms and inability to feed adequately)	Provide advice on the expected course of illness and when to return (worsening symptoms and inability to feed adequately)	Provide advice on the expected course of illness
	Provide parent information sheet	Provide parent information sheet	Provide parent information sheet

The main treatment of bronchiolitis is supportive. This involves ensuring appropriate oxygenation and fluid intake. CPAP, continuous positive airway pressure; ED, emergency department; EWT, early warning tool; HDU, high-dependency unit; HFNC, heated humidified high-flow oxygen/air via nasal cannulae; ICU, intensive care unit; IV, intravenous; NG, nasogastric; NPO_2, nasal prong oxygen; PICU, paediatric intensive care unit.

92%, the GDC recommends commencing oxygen therapy below this level (Table 3, recommendation 12).

For the outcome of admission to hospital, there is moderate evidence that oxygen saturation levels affects the decision to admit independent of other factors, including signs of respiratory distress.[28,57,58] For the important outcome of readmission, oxygen level saturations do not affect readmissions to hospital.[52,57,58]

A prospective observational study[59] with moderate-quality evidence demonstrates that continuous monitoring of pulse oximetry increases hospital length of stay (Table 3, recommendation 13).

There have been limited studies on high flow, humidified nasal cannula oxygen in children with bronchiolitis during inpatient stay outside of the ICU,[60] and all provide low- to very low-level evidence for the benefit of humidified nasal cannula oxygen (Table 3, recommendation 14). Larger RCTs are pending.

Discussion

Clinical guidelines are a familiar tool in the Australasian health-care setting, and there is broad agreement to create joint national emergency medicine guidelines.[61] Guidelines can contribute to health care becoming more consistent, efficient and based on scientific evidence.[62] In order to provide robust recommendations, guidelines should be informed by a systematic review and critical appraisal of the literature.[63] We present the first such project for an acute paediatric condition in an Australasian setting, and in doing so, we have made 31 key recommendations for the diagnosis and management of infants presenting to and admitted into hospital with bronchiolitis (Table 3). These recommendations are evidence based with a clear link to the strength of the evidence behind each recommendation.

Bronchiolitis is the most common reason for infants to be admitted into hospital in Australia and New Zealand and throughout the developed world.[9,10] Despite the frequency of the presentation, and a literature review of over 12 000 titles, it is somewhat disappointing that only 5 recommendations were rated GRADE 'strong', 16 rated 'conditional' and 10 rated 'weak'. There is a strong evidence base that intravenous and nasogastric routes are suitable for non-oral rehydration; there is also strong evidence for not administering beta-2 agonists, adrenaline,

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glucocorticoids and physiotherapy. Yet even amongst these interventions, the evidence base is rated 'weak' for a number of the subgroups. A notable evidence gap is the possible synergy between glucocorticoids and adrenaline, which is a high priority for a definitive RCT.[64] The evidence gaps identified by the systematic review and critical appraisal will be useful for setting out the agenda for bronchiolitis research.

A key strength of the guideline is that it has been undertaken by a multidisciplinary team with a clear understanding of the local challenges of clinical practice. Furthermore, members came from predominantly emergency and general paediatric backgrounds, the two craft groups most closely involved with bronchiolitis management. This will ensure the relevance of the bedside guidance to local clinicians (Appendix III). In addition, the evidence recommendations have used both an international appraisal tool (GRADE)[65] as well as a local standard (NHMRC),[12] again ensuring local relevance.

The final recommendations are broadly consistent with the American Academy of Paediatrics[9] evidence-based recommendations, undertaken a few years prior, and those from the National Institute of Clinical Excellence[10] in the UK, undertaken at the same time as the Australasian guideline. All three guidelines strongly recommend against the use of beta-2 agonists, adrenaline and glucocorticoids. Different oxygen limits (90 vs. 92 vs. 94%) remain recommended in the literature and require further research.

A strength of our process for developing this guideline was the use of nominal group principles and confidential voting using a Likert scale to ascertain consensus for each recommendation and practice point.[66,67] A median score of seven was set as consensus of agreement.[67] The structure for the draft guideline was agreed on by all members of the GDC. Formal feedback was sought from consultations with stakeholders, which included clinical leads of general paediatrics and EDs at Australian and New Zealand tertiary paediatric hospitals, consumers and Australian and New Zealand professional medical and nursing colleges, to ensure relevance of the final guideline to the Australasian emergency and paediatric ward setting. The professional colleges all provided written approval of the guideline and agreement to use this information in the dissemination, increasing the validity of this as a clinical tool.

The guideline does have a number of limitations. First, bronchiolitis is a clinical diagnosis. As such, the experience of the individual clinician is likely to have a key role in terms of their confidence in subsequently following the recommended management. Second, while the American Academy of Paediatrics definition of bronchiolitis includes infants up to 2 years of age, the large RCTs conducted within North America often restrict inclusion criteria to the first episode of wheezing in an infant.[64,68] In contrast, the large RCTs conducted in Australasia include up to 30% of infants with a second or subsequent episode of bronchiolitis.[69,70] Finally, the guideline specifically excluded intensive care patients, and the recommendations need to be interpreted with caution in this population.

Conclusion

This is the first robust Australasian acute paediatric guideline on bronchiolitis. It provides clear guidance for the management of patients seen in Australasian EDs and general paediatric wards with bronchiolitis. The future challenge is to translate and maintain this knowledge into everyday clinical practice.

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References

1 Martinez FD. Respiratory syncytial virus bronchiolitis and the pathogenesis of childhood asthma. *Pediatr. Infect. Dis. J.* 2003; **22** (2 Suppl.): S76–82.
2 Wohl MEB, Chernick V. State of the art: Bronchiolitis. *Am. Rev. Respir. Dis.* 1978; **118**: 759–81.
3 Roche P, Lambert S, Spencer J. Surveillance of viral pathogens in Australia: Respiratory syncytial virus. *Commun. Dis. Intell. Q. Rep.* 2003; **27**: 117–22.
4 Craig E, Anderson P, Jackson C. *The Health Status of Children and Young People in Auckland DHB*. Auckland: New Zealand Child and Youth Epidemiology Service; 2008.
5 Davison C, Ventre KM, Luchetti M, Randolph AG. Efficacy of interventions for bronchiolitis in critically ill infants: A systematic review and meta-analysis. *Pediatr. Crit. Care Med.* 2004; **5**: 482–9.
6 Smyth RL, Openshaw PJM. Bronchiolitis. *Lancet* 2006; **368**: 312–22.
7 Babl FE, Sheriff N, Neutze J, Borland M, Oakley E. Bronchiolitis management in pediatric emergency departments in Australia and New Zealand: A PREDICT study. *Pediatr. Emerg. Care* 2008; **24**: 656–8.
8 Oakley E, Brys T, Borland M, Neutze J, Dalziel S. Medication use in infants admitted with bronchiolitis at 7 Australian and New Zealand centres. *Acad. Emerg. Med.* 2014; **21** (Suppl. 1): S5–327.

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9 American Academy of Pediatrics Subcommittee on Diagnosis and Management of Bronchiolitis. Diagnosis and management of bronchiolitis. *Pediatrics* 2006; **118**: 1774–93.
10 Ricci V, Delgado Nunes V, Murphy MS, Cunningham S; on behalf of the Guideline Development Group and Technical Team. Bronchiolitis in children: Summary of NICE guidance. *BMJ* 2015; **350**: h2305.
11 Australian Indigenous Health Info Net. *Review of Respiratory Disease Among Indigenous Peoples.* Mt Lawley: Edith Cowan University; 2005. Available from: http://www.healthinfonet.ecu.edu.au/chronic-conditions/respiratory/reviews/our-review [accessed 8 June 2016].
12 National Health and Medical Research Council. *NHMRC: Additional Levels of Evidence and Grades for Recommendations for Developers of Guidelines*. Canberra: The Council; 2009.
13 Guyatt GH, Oxman AD, Vist GE *et al*. GRADE: An emerging consensus on rating quality of evidence and strength of recommendations. *BMJ* 2008; **336**: 924–6.
14 Babl FE, Borland ML, Ngo P *et al*. Paediatric Research in Emergency Departments International Collaborative (PREDICT): First steps towards the development of an Australian and New Zealand research network. *Emerg. Med. Australas.* 2006; **18**: 143–7.
15 O'Brien S, Wilson S, Gill FJ *et al*. The management of children with bronchiolitis in the Australasian hospital setting: Development of a clinical practice guideline. *BMC Med. Res. Methodol.* 2018; **18**: 22.
16 Al-Shehri MA, Sadeq A, Quli K. Bronchiolitis in Abha, Southwest Saudi Arabia: Viral etiology and predictors for hospital admission. *West Afr. J. Med.* 2005; **24**: 299–304.
17 Somech R, Tal G, Gilad E, Mandelberg A, Tal A, Dalal I. Epidemiologic, socioeconomic, and clinical factors associated with severity of respiratory syncytial virus infection in previously healthy infants. *Clin. Pediatr.* 2006; **45**: 621–7.
18 Bordley WC, Viswanathan M, King VJ *et al*. Diagnosis and testing in bronchiolitis: A systematic review. *Arch. Pediatr. Adolesc. Med.* 2004; **158**: 119–26.
19 Dayan PS, Roskind CG, Levine DA, Kuppermann N. Controversies in the management of children with bronchiolitis. *Clin. Pediatr. Emerg. Med.* 2004; **5**: 41–53.
20 Elkhunovich MA, Wang VJ. Assessing the utility of urine culture testing in febrile infants 2–12 months of age with bronchiolitis. *Pediatr. Emerg. Care* 2012; **28**: 1093.
21 Fares M, Mourad S, Rajab M, Rifai N. The use of C-reactive protein in predicting bacterial co-infection in children with bronchiolitis. *N. Am. J. Med. Sci.* 2011; **3**: 152–6.
22 Laham JL, Breheny PJ, Gardner BM, Bada H. Procalcitonin to predict bacterial coinfection in infants with acute bronchiolitis: A preliminary analysis. *Pediatr. Emerg. Care* 2014; **30**: 11–5.
23 Luu R, DeWitt PE, Reiter PD, Dobyns EL, Kaufman J. Hyponatremia in children with bronchiolitis admitted to the pediatric intensive care unit is associated with worse outcomes. *J. Pediatr.* 2013; **163**: 1652–6.e1.
24 Ralston S, Hill V, Waters A. Occult serious bacterial infection in infants younger than 60 to 90 days with bronchiolitis: A systematic review. *Arch. Pediatr. Adolesc. Med.* 2011; **165**: 951–6.
25 Titus MO, Wright SW. Prevalence of serious bacterial infections in febrile infants with respiratory syncytial virus infection. *Pediatrics* 2003; **112**: 282–4.
26 Gadomski AM, Scribani MB. Bronchodilators for bronchiolitis. *Cochrane Database Syst. Rev.* 2014: 6: CD001266.
27 Baraldi E, Lanari M, Manzoni P *et al*. Inter-society consensus document on treatment and prevention of bronchiolitis in newborns and infants. *Ital. J. Pediatr.* 2014; **40**: 65.
28 Ralston SL, Lieberthal AS, Meissner HC *et al*. Clinical practice guideline: The diagnosis, management, and prevention of bronchiolitis. *Pediatrics* 2014; **134**: e1474–502.
29 Hartling L, Bialy LM, Vandermeer B *et al*. Epinephrine for bronchiolitis. *Cochrane Database Syst. Rev.* 2011: 6: CD003123.
30 Skjerven HO, Hunderi JO, Brugmann-Pieper SK *et al*. Racemic adrenaline and inhalation strategies in acute bronchiolitis. *N. Engl. J. Med.* 2013; **368**: 2286–93.
31 Zhang L, Mendoza-Sassi RA, Wainwright C, Klassen TP. Nebulised hypertonic saline solution for acute bronchiolitis in infants. *Cochrane Database Syst. Rev.* 2013; 7: CD006458.
32 Everard ML, Hind D, Ugonna K *et al*. SABRE: A multicentre randomised control trial of nebulised hypertonic saline in infants hospitalised with acute bronchiolitis. *Thorax* 2014; **69**: 1105–12.
33 Florin TA, Shaw KN, Kittick M, Yakscoe S, Zorc JJ. Nebulized hypertonic saline for bronchiolitis in the emergency department: A randomized clinical trial. *JAMA Pediatr.* 2014; **168**: 664–70.
34 Jacobs JD, Foster M, Wan J, Pershad J. 7% Hypertonic saline in acute bronchiolitis: A randomized controlled trial. *Pediatrics* 2014; **133**: e8–13.
35 Khanal A, Sharma A, Basnet S, Sharma PR, Gami FC. Nebulised hypertonic saline (3%) among children with mild to moderately severe bronchiolitis – A double blind randomized controlled trial. *BMC Pediatr.* 2015; **15**: 115.
36 Ojha AR, Mathema S, Sah S, Aryal UR. A comparative study on use of 3% saline versus 0.9% saline nebulization in children with bronchiolitis. *J. Nepal Health Res. Counc.* 2014; **12**: 39–43.
37 Sharma BS, Gupta MK, Rafik SP. Hypertonic (3%) saline vs 0.93% saline nebulization for acute viral bronchiolitis: A randomized controlled trial. *Indian Pediatr.* 2013; **50**: 743–7.
38 Silver AH, Esteban-Cruciani N, Azzarone G *et al*. 3% Hypertonic saline versus normal saline in inpatient bronchiolitis: A randomized controlled trial. *Pediatrics* 2015; **136**: 1036–43.
39 Teunissen J, Hochs AHJ, Vaessen-Verberne A *et al*. The effect of 3% and 6% hypertonic saline in viral bronchiolitis: A randomised controlled trial. *Eur. Respir. J.* 2014; **44**: 913–21.
40 Wu S, Baker C, Lang ME *et al*. Nebulized hypertonic saline for bronchiolitis: A randomized clinical trial. *JAMA Pediatr.* 2014; **168**: 657–63.
41 Badgett RG, Vindhyal M, Stirnaman JT, Gibson CM, Halaby R. A living systematic review of nebulized hypertonic saline for acute bronchiolitis in infants. *JAMA Pediatr.* 2015; **169**: 788–9.
42 Chen YJ, Lee WL, Wang CM, Chou HH. Nebulized hypertonic saline treatment reduces both rate and duration of hospitalization for acute bronchiolitis in infants: An updated meta-Analysis. *Pediatr. Neonatol.* 2014; **55**: 431–8.
43 Maguire C, Cantrill H, Hind D, Bradburn M, Everard ML. Hypertonic saline (HS) for acute bronchiolitis: Systematic review and meta-analysis. *BMC Pulm. Med.* 2015; **15**: 148.
44 Mitchell MD, Schast AP, Umscheid CA. Nebulized hypertonic saline treatment for infants with bronchiolitis (structured abstract). *Health Technol. Assess. Database.* 2013; http://onlinelibrary.wiley.com/o/cochrane/clhta/articles/HTA-32013000424/frame.html [accessed 8 June 2016].
45 Zhang L, Mendoza-Sassi RA, Klassen TP, Wainwright C. Nebulized hypertonic saline for acute bronchiolitis: A systematic review. *Pediatrics* 2015; **136**: 687–701.
46 Fernandes RM, Bialy LM, Vandermeer B *et al*. Glucocorticoids for acute viral bronchiolitis in infants and young children. *Cochrane Database Syst. Rev.* 2013; 6: CD004878.
47 Alansari K, Sakran M, Davidson BL, Ibrahim K, Alrefai M, Zakaria I. Oral dexamethasone for bronchiolitis: A randomized trial. *Pediatrics* 2013; **132**: e810–6.
48 Jartti T, Nieminen R, Vuorinen T *et al*. Short- and long-term efficacy of prednisolone for first acute rhinovirus-induced wheezing episode. *J. Allergy Clin. Immunol.* 2015; **135**: 691–8.e9.
49 Farley R, Spurling GK, Eriksson L, Del Mar CB. Antibiotics for bronchiolitis in children under two years of age. *Cochrane Database Syst. Rev.* 2014; 10: CD005189.

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50 McCallum GB, Morris PS, Chang AB. Antibiotics for persistent cough or wheeze following acute bronchiolitis in children. *Cochrane Database Syst. Rev.* 2012; 12: CD009834.
51 Beigelman A, Isaacson-Schmid M, Sajol G, Baty J, Rodriguez OM, Leege E. Randomized trial to evaluate azithromycin's effects on serum and upper airway IL-8 levels and recurrent wheezing in infants with respiratory syncytial virus bronchiolitis. *J. Allergy Clin. Immunol.* 2015; **135**: 1171–8.e1.
52 Cunningham S, McMurray A. Observational study of two oxygen saturation targets for discharge in bronchiolitis. *Arch. Dis. Child.* 2012; **97**: 361–3.
53 Mitchell MD, Schast AP, Umscheid CA. Oxygen saturation discharge thresholds for infants admitted with bronchiolitis (structured abstract). *Health Technol. Assess. Database.* 2013; http://onlinelibrary.wiley.com/o/cochrane/clhta/articles/HTA-32013000425/frame.html [accessed 8 June 2016].
54 Unger S, Cunningham S. Effect of oxygen supplementation on length of stay for infants hospitalized with acute viral bronchiolitis. *Pediatrics* 2008; **121**: 470–5.
55 Choi J, Claudius I. Decrease in emergency department length of stay as a result of triage pulse oximetry. *Pediatr. Emerg. Care* 2006; **22**: 412–4.
56 Hendaus MA, Jomha FA, Alhammadi AH. Pulse oximetry in bronchiolitis: Is it needed? *Ther. Clin. Risk Manag.* 2015; **11**: 1573–8.
57 Schroeder AR, Marmor AK, Pantell RH, Newman TB. Impact of pulse oximetry and oxygen therapy on length of stay in bronchiolitis hospitalizations. *Arch. Pediatr. Adolesc. Med.* 2004; **158**: 527–30.
58 Schuh S, Freedman S, Coates A *et al*. Effect of oximetry on hospitalization in bronchiolitis: A randomized clinical trial. *JAMA* 2014; **312**: 712–8.
59 Kaditis AG, Katsouli G, Malakasioti G, Kaffe K, Gemou-Engesaeth V, Alexopoulos EI. Infants with viral bronchiolitis demonstrate two distinct patterns of nocturnal oxyhaemoglobin desaturation. *Acta Paediatr.* 2015; **104**: e106–11.
60 Beggs S, Wong ZH, Kaul S, Ogden KJ, Walters JA. High-flow nasal cannula therapy for infants with bronchiolitis. *Cochrane Database Syst. Rev.* 2014; 1: CD009609.
61 Dalton S, Babl FE. Paediatric emergency guidelines: Could one size fit all? *Emerg. Med. Australas.* 2009; **21**: 67–70.
62 Woolf SH, Grol R, Hutchinson A, Eccles M, Grimshaw J. Clinical guidelines: Potential benefits, limitations, and harms of clinical guidelines. *BMJ* 1999; **318**: 527–30.
63 Graham R, Mancher M, Wolman DM, Greenfield S, Steinberg E, eds. *Clinical Practice Guidelines We Can Trust*. Washington, DC: National Academies Press; 2011.
64 Plint AC, Johnson DW, Patel H *et al*. Epinephrine and dexamethasone in children with bronchiolitis. *N. Engl. J. Med.* 2009; **360**: 2079–89.
65 Guyatt G, Oxman AD, Akl EA *et al*. GRADE guidelines: 1. Introduction-GRADE evidence profiles and summary of findings tables. *J. Clin. Epidemiol.* 2011; **64**: 383–94.
66 James D, Warren-Forward H. Research methods for formal consensus development. *Nurse Res.* 2015; **22**: 35–40.
67 Rolls KD, Elliott D. Using consensus methods to develop clinical practice guidelines for intensive care: The intensive care collaborative project. *Aust. Crit. Care* 2008; **21**: 200–15.
68 Corneli HM, Zorc JJ, Mahajan P *et al*. A multicenter, randomized, controlled trial of dexamethasone for bronchiolitis. *N. Engl. J. Med.* 2007; **357**: 331–9.
69 Franklin D, Dalziel S, Schlapbach LJ *et al*. Early high flow nasal cannula therapy in bronchiolitis, a prospective randomised control trial (protocol): A Paediatric Acute Respiratory Intervention Study (PARIS). *BMC Pediatr.* 2015; **15**: 183.
70 Oakley E, Borland M, Neutze J *et al*. Nasogastric hydration versus intravenous hydration for infants with bronchiolitis: A randomised trial. *Lancet Respir. Med.* 2013; **1**: 113–20.

Appendix I

Australasian Bronchiolitis Guideline – Literature search strategy

Data Sources	MEDLINE (OvidSP); EMBASE (OvidSP); PubMed; The Cochrane Library; CINAHL(EBSCO)
MeSH terms (MEDLINE OvidSP)	**Population** bronchiolitis/ bronchiolitis, viral/ respiratory syncytial viruses/ respiratory syncytial virus, human/ respiratory syncytial virus infections/ **AND** **Intervention/Area of interest** natural history/ epidemiology/ exp 'reproducibility of results'/ 'severity of illness index'/ diagnosis, differential/ physical examination/ exp auscultation/ blood pressure determination/ exp palpation/ percussion/ pulse/ exp vital signs/ exp *respiratory tract infections/ risk factors/ 'length of stay'/ patient admission/ patient discharge/ exp intensive care units, pediatric/ respiratory care units/ morbidity/ prevalence/ exp mortality/ exp diagnostic imaging/ radiography, thoracic/ exp hematologic tests/ urinalysis/ nasal lavage fluid/ emergency service, hospital/ asthma/ or hypersensitivity, immediate/ exp albuterol/ad, tu epinephrine/ad,tu bronchodilator agents/ad, tu steroids/ad, tu exp cholinergic antagonists/ or receptors, adrenergic, beta-2/ exp anti-inflammatory agents/ exp adrenal cortex hormones/ leukotriene antagonists/ saline solution, hypertonic/ad, tu exp aerosols/ exp sodium chloride/ exp 'nebulizers and vaporizers'/ exp oxygen inhalation therapy/ *oxygen/ad, st exp oximetry/

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Appendix I. continued

	home care services/ home care services, hospital-based/ exp blood gas analysis/ continuous positive airway pressure/ positive pressure respiration/ positive end respiratory pressure/ exp physical therapy modalities/ physical therapy specialty/ exp physiotherapy/ suction/ administration, intranasal/ exp fluid therapy/ rehydration solutions/ enteral feeding/ parenteral feeding/ intubation, gastrointestinal/ exp bacterial infections/ exp otitis media/ exp meningitis/ exp *antibacterial agents/tu exp sepsis/ exp urinary tract infections/ tracheitis/ infection control/ exp primary prevention/ patient isolation/
Keywords (PubMed/ Cochrane Library)	**Population** (bronchiolit* OR wheez* OR (Respiratory Syncytial Virus*) OR rsv **AND** **Intervention/Area of interest** history OR epidemiolog* OR 'severity of illness' OR 'disease severity' OR scoring system* OR diagnosis OR physical exam* OR auscultation OR 'blood pressure' OR palpation* OR percussion OR pulse OR vital sign* OR Respiratory Tract Infection* OR risk factor* OR 'length of stay' OR admission OR discharge OR 'intensive care' OR ICU OR 'respiratory care' OR morbidit* OR prevalence OR mortalit* OR 'diagnostic imaging' OR ((chest OR thorac*) AND (x-ray* OR xray* OR 'X-ray' OR radiograph*)) OR ((hematolog* OR haematolog* OR blood OR virolog* OR urine) AND (test OR tests OR exam* OR investigation*)) OR urinalys* OR 'nasal lavage' OR ((nose OR nasal) AND (mucosa OR mucus)) OR emergency department* OR asthma* OR atopy OR atopic OR hypersensitiv* OR salbutamol OR albuterol OR ventolin OR levalbuterol OR adrenalin* OR epinephrin* OR beta2 adrenergic* OR beta2 agonist* OR ics OR corticosteroid* OR cortico steroid*OR cortico-steroid* OR glucocorticoid* OR gluco corticoid* OR gluco-corticoid* OR montelukast OR bronchodilat* OR steroid OR steroids OR cholinergic antagonist* OR cholinergic receptor* OR anti inflammatory agent* OR adrenal cortex hormone* OR leukotriene antagonist* OR leukotriene receptor* OR 'hypertonic saline' OR (('sodium chloride' OR saline) AND (nebuliz* OR nebulis* OR vaporiz* OR vaporis* OR aerosol* OR intranasal OR 'intra nasal' OR intra-nasal OR nasal)) OR oxygen OR 'home oxygen' OR ((oximetry OR oximeter*) AND ('reproducibility of results' OR reliability OR validity OR function* OR technical specification* OR percutaneous measurement* OR blood gas analys*)) OR CPAP OR 'continuous positive airway pressure' OR 'positive pressure respiration' OR 'positive end respiratory pressure' OR supplementa* oxygen OR 'oxygen saturation' OR oxygen therap* OR oxygen treatment* OR physical therap* OR physiotherap* OR ((nasal* OR nose OR naso) AND (suction* OR toilet OR irrigation)) OR suction* OR saline drop* OR 'nasal saline' OR 'intranasal saline' OR deep suction* OR ((non oral OR oral) AND (feed* OR hydration OR fluid* OR solution* OR therap*)) OR azithromycin OR fluid therap* OR intravenous infusion* OR 'non oral' OR rehydrat* OR 'enteric feeding' OR 'parenteral nutrition' OR 'parenteral feeding' OR 'enteral nutrition' OR oral* administ* OR bacterial infection* OR 'otitis media' OR meningitis OR antibacterial agent* OR anti-bacterial agent* OR anti bacterial agent* OR antimicrobial agent* OR anti-microbial agent* OR anti microbial agent* OR antibiotic* OR sepsis OR septic OR urinary tract infection* OR tracheitis OR serious bacterial infection* OR 'infection control' OR 'primary prevention' OR isolation OR 'patient care'
Search dates	The following databases were searched on the 17th December 2015 for references back to 1 January 2000: Medline (Ovid), Embase (Ovid) and The Cochrane Library. Ebsco Host Cinahl was searched back to 2000 for studies relating to chest physiotherapy and bronchiolitis only. PubMed was searched back to 2013 to capture E-pubs not available in Medline and back to 2000 to capture journals not indexed in Medline.
Other information sources checked	Reference lists of included studies were searched to identify additional relevant papers (i.e. snowballing references)
Inclusion criteria	(Publication type = clinical trial, all or clinical trial, phase i or clinical trial, phase ii or clinical trial, phase iii or clinical trial, phase iv or clinical trial or controlled clinical trial or guideline or meta analysis or practice guideline or randomized controlled trial or 'review' or systematic reviews) or exp evidence-based medicine/ English language

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Appendix I. continued

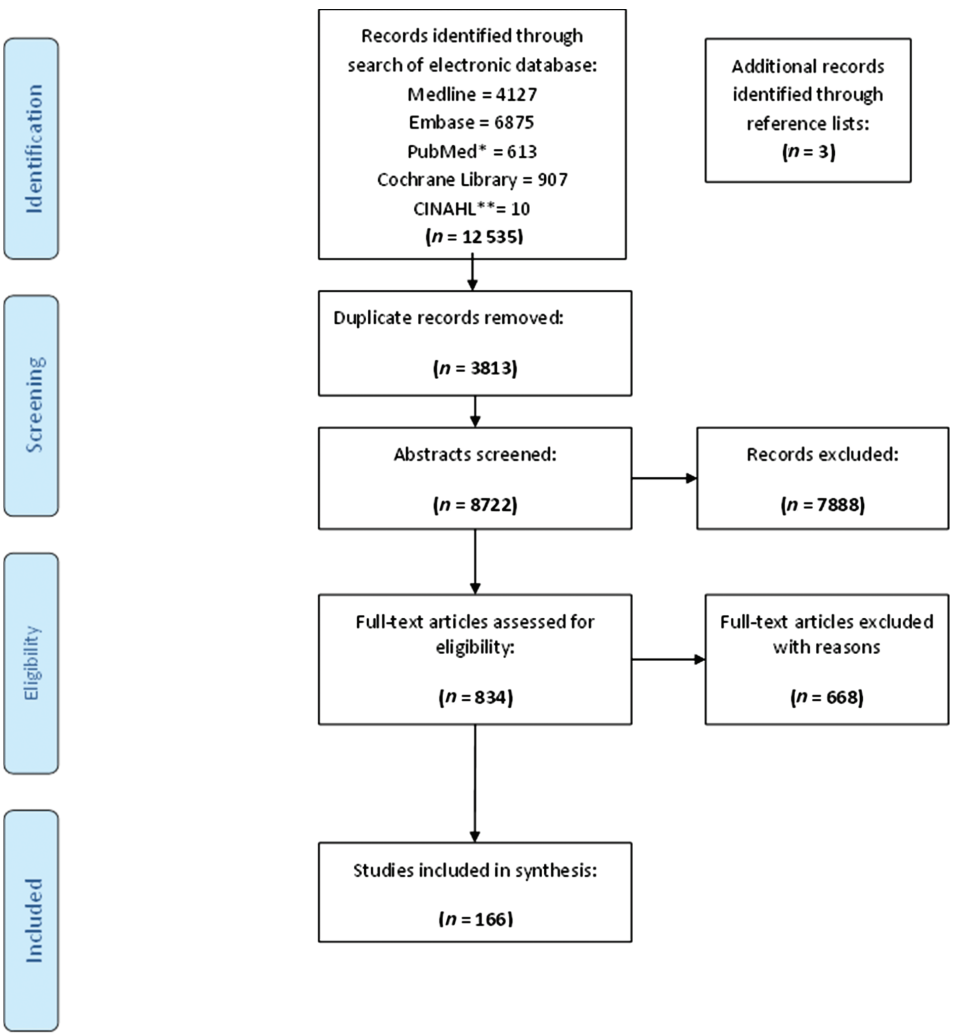
	Year = '2000–current' age limit = ('newborn infant (birth to 1 month)' or 'infant (1 to 23 months)') or infant* or newborn* or neonat* or babies or baby
Exclusion criteria	(Publication type = case reports or comment or editorial or letter) or exp bronchiolitis obliterans/ or bronchiolitis obliterans

Appendix II

Australasian Bronchiolitis Guideline Prisma Diagram

*PubMed was searched back to 2013 to capture E-pubs not available in Medline and back to 2000 to capture journals not indexed in Medline

**CINAHL was searched for studies relating to chest physiotherapy and bronchiolitis only



Appendix III

Australasian Bronchiolitis Bedside Clinical Guideline

http://www.predict.org.au/download/Australasian-bronchiolitis-bedside-clinical-guideline.pdf

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