



Paediatric Research in Emergency Departments International Collaborative

AUSTRALASIAN BRONCHIOLITIS GUIDELINE



ACKNOWLEDGEMENTS

The Australasian Bronchiolitis Guideline has been developed by the Paediatric Research in Emergency Departments International Collaborative (PREDICT) research network. The project was funded by a National Health and Medical Research Council Centre of Research Excellence grant for paediatric emergency medicine (GNT1058560) administered by the Murdoch Childrens Research Institute.

A Guideline Advisory Group was initially established from PREDICT and convened a multidisciplinary Guideline Development Committee with expert knowledge and skills within the fields of Emergency and Paediatric Medicine. This multidisciplinary Development Committee complement the skills and knowledge of the Guideline Advisory Group. This ensured stakeholder engagement and representation from specific specialty areas to ensure broad relevance of the guideline.

GUIDELINE ADVISORY GROUP

Associate Professor Meredith Borland Associate Professor Elizabeth Cotterell Dr Stuart Dalziel Associate Professor Edward Oakley Ms Sharon O'Brien

MULTIDISCIPLINARY GUIDELINE DEVELOPMENT COMMITTEE

Dr David Armstrong Associate Professor Franz Babl Dr Paul Bauert Dr Christine Brabyn Dr Lydia Garside Ms Libby Haskell Dr David Levitt Ms Nicola McKay Dr Jocelyn Neutze Associate Professor Andreas Schibler Dr Kam Sinn Dr Janine Spencer Ms Helen Stevens Dr David Thomas Dr Michael Zhang

PREDICT would like to acknowledge the input and feedback provided in the consultation phase by stakeholders to ensure relevance of the final guideline to the Australasian emergency and paediatric ward setting. Formal feedback was received from: Australasian College for Emergency Medicine, The Australian Paediatric Society, The Royal Australasian College of Physicians, South Island Alliance Child Health Service, Children's Healthcare Australasia, Australian College of Emergency Nursing Ltd, The Australian College of Children and Young People's Nurses, College of Child and Youth Nurses New Zealand, College of Emergency Nurses New Zealand, Family Advisory Committee Royal Children's Hospital Melbourne, New South Wales Office of Kids and Families, New South Wales Paediatric Clinical Nurse Consultant Group, Paediatric Department Christchurch Hospital, Paediatric Respiratory Department Starship Children's Health, Royal New Zealand College of Urgent Care, Professor Innes Asher, Associate Professor Simon Craig, Dr Joshua Osowicki, Dr Arjun Rao, Associate Professor Mike Starr and Dr Emma Tavender. PREDICT would also like to acknowledge the support and assistance provided by Ms Catherine Wilson, PREDICT Research Network Co-ordinator.

CONTENTS

Summary1
Purpose/aim1
Diagnosis1
Features1
Risk factors for more serious illness1
Initial Assessment2
Initial Management3
Investigations4
Management4
Ongoing management4
Discharge planning and community-based management5
Education (parent/care-giver)5
Safety initiatives5
Clinical recommendations6
Diagnosis6
Management7
Methodology9
PICOt Questions
Clinical recommendations evidence summaries
GRADE & NHMRC Evidence tables22
Research recommendations121
References
Disclaimer130

SUMMARY

PURPOSE/AIM

This guideline has been developed to provide an evidence-based clinical framework for the management of infants (0–12 months) with bronchiolitis treated in Australasian emergency departments (EDs) or general paediatric wards. Application of these guidelines for children over 12 months may be relevant but there is less diagnostic certainty in the 12–24 month age group.

(All references to age within this guideline refer to chronological age unless stated otherwise.)

DIAGNOSIS

Viral bronchiolitis is a clinical diagnosis, based on typical history and examination. Peak severity is usually at around day two to three of the illness with resolution over 7–10 days. The cough may persist for weeks. Bronchiolitis most commonly occurs in the winter months, but can be seen all year round.

FEATURES

Bronchiolitis typically begins with an acute upper respiratory tract infection followed by onset of respiratory distress and fever and one or more of:

- Cough
- Tachypnoea
- Retractions
- Widespread crackles or wheeze

Bronchiolitis is usually self-limiting, often requiring no treatment or interventions.

RISK FACTORS FOR MORE SERIOUS ILLNESS

- Gestational age less than 37 weeks
- Chronological age at presentation less than 10 weeks
- Post-natal exposure to cigarette smoke
- Breast fed for less than two months
- Failure to thrive
- Chronic lung disease
- Congenital heart disease
- Chronic neurological conditions
- Indigenous ethnicity

Infants with any of these risk factors are more likely to deteriorate rapidly and require escalation of care. Consider hospital admission even if presenting early in illness with mild symptoms.

INITIAL ASSESSMENT

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.

	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	O₂ saturations greater than 92% (in room air)	O₂ saturations 90 – 92% (in room air)	O2 saturations less than 90% (in room air) Hypoxemia, may not be corrected by O2
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

INITIAL MANAGEMENT

The main treatment of bronchiolitis is supportive. This involves ensuring appropriate oxygenation and fluid intake.

	MILD	MODERATE	SEVERE
Likelihood of admission	Suitable for discharge Consider risk factors	Likely admission, may be able to be discharged after a period of observation Management should be discussed with a local senior physician	Requires admission and consider need for transfer to an appropriate children's facility/PICU Threshold for referral is determined by local escalation policies but should be early
Observations Vital signs (respiratory rate, heart rate, O ₂ saturation, temperature)	Adequate assessment in ED prior to discharge (minimum of two recorded measurements or every four hours 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 hours), administer NG or IV hydration	If not feeding adequately (less than 50% over 12 hours), or unable to feed, administer NG or IV hydration
Oxygen saturation/oxygen requirement	Nil requirement	Administer O2 to maintain saturations greater than or equal to 92%	Administer O₂ 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: • Severity does not improve • Persistent desaturations • Significant or recurrent apnoeas 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

PICU = paediatric intensive care unit, EWT = early warning tool, NG = nasogastric, IV = intravenous, NPO₂ = nasal prong oxygen, HFNC = heated humidified high flow oxygen/air via nasal cannulae, CPAP = continuous positive airway pressure, HDU = high dependency unit.

INVESTIGATIONS

In most infants presenting to hospital and/or hospitalised with bronchiolitis, no investigations are required.

Chest X-ray (CXR)

• Is not routinely indicated in infants presenting with bronchiolitis and may lead to unnecessary treatment with antibiotics with subsequent risk of adverse events

Blood tests (including full blood count (FBC), blood cultures)

• Have no role in management

Virological testing (nasopharyngeal swab or aspirate)

• Has no role in management of individual patients

Urine microscopy and culture

• May be considered to identify urinary tract infection if a temperature over 38 degrees in an infant less than two months of age with bronchiolitis

MANAGEMENT

Respiratory support

- Oxygen therapy should be instituted when oxygen saturations are persistently less than 92%
- It is appreciated that infants with bronchiolitis will have brief episodes of mild/moderate desaturations to levels less than 92%. These brief desaturations are not a reason to commence oxygen therapy.
- Oxygen should be discontinued when oxygen saturations are persistently greater than or equal to 92%.
- Heated humidified high flow oxygen/air via nasal cannulae (HFNC) can be considered in the presence of hypoxia (oxygen saturation less than 92%) and moderate to severe recessions. Its use in infants without hypoxia should be limited to the randomised controlled trial (RCT) setting only

Monitoring

- Observations as per local hospital guidelines and Early Warning Tools (EWTs)
- Continuous oximetry should not be routinely used to dictate medical management unless disease is severe

Hydration/nutrition

- When non-oral hydration is required either intravenous (IV) or nasogastric (NG) hydration are appropriate
- If IV fluid is used it should be isotonic (0.9% Sodium Chloride with Glucose or similar)
- The ideal volume of IV or NG fluids required to maintain hydration remains unknown; between 60% to 100% of maintenance fluid is an appropriate volume to initiate

Medication

- Beta 2 agonists Do not administer beta 2 agonists (including those with a personal or family history of atopy)
- Corticosteroids Do not administer systemic or local glucocorticoids (nebulised, oral, intramuscular (IM) or IV)
- Adrenaline Do not administer adrenaline (nebulised, IM or IV) except in peri-arrest or arrest situation
- Hypertonic Saline Do not administer nebulised hypertonic saline
- Antibiotics Including Azithromycin are not indicated in bronchiolitis
- Antivirals Are not indicated

Nasal suction

- Nasal suction is not routinely recommended. Superficial nasal suction may be considered in those with moderate disease to assist feeding
- Nasal saline drops may be considered at time of feeding

Chest physiotherapy

Is not indicated

ONGOING MANAGEMENT

• HFNC or Nasal CPAP therapy may be considered in the appropriate ward setting

DISCHARGE PLANNING AND COMMUNITY-BASED MANAGEMENT

- Infants can be discharged when oxygen saturations are greater than or equal to 92% and feeding is adequate
- Infants younger than 8 weeks of age are at an increased risk of representation
- Discharge on home oxygen can be considered after a period of observation in selected infants as per local policies, if appropriate community short term oxygen therapy is available
- Follow-up and review as per local practice

EDUCATION (PARENT/CARE-GIVER)

- A Bronchiolitis Parent Information Sheet should be provided
- Parents should be educated about the illness, the expected progression and when and where to seek further medical care

SAFETY INITIATIVES

- Use simple infection control practices such as hand washing
- Cohorting of infants (based on virological testing) has not been shown to improve outcomes

To download this summary only, please see the *Bedside Clinical Guideline* at: http://www.predict.org.au/download/Australasian-bronchiolitis-bedside-clinical-guideline.pdf

CLINICAL RECOMMENDATIONS

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 two months; failure to thrive; having chronic lung disease; having chronic heart and/or chronic neurological conditions; 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 less than two months of age presenting to hospital or hospitalised with bronchiolitis with a temperature over 38 degrees, 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 end-points, 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 eight 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)

MANAGEMENT

14. High Flow Nasal Cannulae Oxygen (HFNC) 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)

(NHMRG: 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)

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 is and regular clinical review is 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)

METHODOLOGY

The aim of this project was to formulate an evidence-based, clinical practice guideline for infants with bronchiolitis presenting to, and admitted into Australasian hospitals.

The scope was to examine the evidence for the diagnosis and management for the purpose of improving health outcomes. The guideline addresses the emergency department and general ward management of bronchiolitis, recognising that in order to influence management for the majority of patients who present to hospital with bronchiolitis, these two areas are critical to in-hospital management. Management in primary care and in intensive care units is excluded (as only a small proportion of patients admitted to hospital with bronchiolitis require intensive care management) (1). The guideline excludes public health prevention as this is outside the scope of Australasian hospital based care.

The Australasian Bronchiolitis Guideline has been developed utilising both the Grading of Recommendations Assessment, Development and Evaluation (GRADE) methodology (2) and the National Health and Medical Research Council (NHMRC) Grading System methodology (3). A Guideline Development Committee was formed comprising of 22 individuals including; General Paediatricians, Paediatric Respiratory Physicians, Paediatric Emergency Medicine Physicians, Emergency Physicians, Paediatric Intensive Care Physicians, Paediatric Nurse Practitioners, Paediatric Nurses, and Emergency Nurses from a mixture of metropolitan and non-metropolitan centres, from both New Zealand and Australia (including representatives from seven of the eight States and Territories). The Guideline Development Committee conducted a face-to-face meeting in which guideline methodology was agreed on, current State and Tertiary Children's Hospitals Bronchiolitis guidelines (4-7) were reviewed and 33 key PICOt guestions relevant to the management of bronchiolitis were formulated.

An evidence search from 1 January 2000 to 1 May 2015 was conducted of the following electronic databases: Ovid Medline, Ovid Embase, PubMed, Cinahl, Cochrane Review library and Cochrane Database of Systematic Reviews (CDSR) (search strategy available in appendix). One of five members of the Guideline Development Committee reviewed the title and abstracts of the 7955 titles identified in the literature search. Articles relevant to 33 PICOt questions and the proposed guideline were included. Where screening by title and abstract was insufficient to make a decision as to relevance, a copy of the complete article was sourced and reviewed. Selected articles were then divided into the relevant PICOt question groups. If a high-quality Cochrane systematic review relevant to the PICOt question existed only systematic reviews and RCTs subsequent to the year of the documented search date in the Cochrane systematic review were included.

Two members of the Guideline Development Committee independently reviewed articles relevant to each PICOt question utilising the GRADE (2) and NHMRC Grading System (3) to assess methodological quality, data synthesis and development of recommendations. The GRADE system entails an assessment of the quality of a body of evidence for each individual outcome, including consideration of within-study risk of bias (methodological quality), directness of evidence, heterogeneity, precision of effect estimates and risk of publication bias. The GRADE method is recognised internationally as a reliable method of reviewing the quality of evidence and is a structured process for developing and presenting evidence summaries for systematic reviews. The process is transparent and includes comprehensive criteria for downgrading and upgrading quality of evidence ratings for the development of recommendations (2). The NHMRC process is Australian specific and addresses the evidence to support clinical questions such as intervention, diagnosis, prognosis, aetiology and screening which are specifically related to guideline development (3). The NHMRC process for evidence review includes rating the five key components of the 'body of evidence' for each recommendation. These components are: the evidence base, in terms of the number of studies, level of evidence and quality of studies (risk of bias), consistency of the study results, potential clinical impact of the proposed recommendation, generalisability of the body of evidence to the target population and the applicability of the body of evidence to the Australian healthcare context (8). Any disagreements that arose between the first two reviewers were resolved through discussion with a third reviewer. Evidence tables and summaries of evidence were prepared for each PICOt question.

Where possible the evidence presented in these guidelines is based on systematic reviews and RCTs. Where there was only low quality indirect supportive evidence, clinical care statements outlining current accepted practise points were included.

A draft guideline, and the recommendations and evidence tables for the 33 PICOt was reviewed by the Guideline Development Committee. Consensus was sought using nominal group technique principles to formulate the clinical practice recommendations and practice points for the draft guideline. A second literature search was performed on the 17th of December 2015 of the same electronic databases, using the same search strategy, to identify any subsequent literature at the time of the draft guideline development (7 months since initial search). A further 764 articles were identified and these were reviewed utilising the same process as used for the first literature search.

The draft guideline was sent to key stakeholders within Australia and New Zealand. Feedback was incorporated into the final guideline.

А	Body of evidence can be trusted to guide practice
В	Body of evidence can be trusted to guide practice in most situations
с	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

NHMRC STRENGTH OF RECOMMENDATION DEFINITIONS (3)

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

PICOt QUESTIONS

NUMBER	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 (ICU) 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 Beta2 Agonists (nebulisation, aerosol, oral or IV) improve clinically relevant end-points?
8a. ii)	In older infants presenting to hospital or hospitalised with bronchiolitis, does administration of Beta2 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 Beta2 Agonists (nebulisation, aerosol, oral or IV) improve clinically relevant end-points?
8b. 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 Beta2 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 Beta2 Agonists, does administration of systemic or local glucocorticoids (nebulisation, oral, IM or IV) improve clinically relevant end-points?

NUMBER	QUESTION
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 practises improve clinically relevant end-points?

CLINICAL RECOMMENDATIONS EVIDENCE SUMMARIES

1. Infants can be diagnosed with bronchiolitis if they have an upper respiratory tract infection followed by onset of respiratory distress with fever, and some of: cough, tachypnoea, retractions and diffuse crackles or wheeze on auscultation.

Strength of recommendation:

С

NHMRC

GRADE WEAK

A systematic review and guideline (10) and two prospective observational studies (11, 12) provide recent evidence for the clinical features that make the diagnosis of bronchiolitis likely. The major factors which were predictive were fever, cough, tachypnoea, retractions and wheeze. Other major international guidelines support the clinical diagnosis of bronchiolitis (10, 13).

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 two months; failure to thrive; having chronic lung disease; having chronic heart and/or neurological conditions; being an indigenous infant, and should take these into account when managing infants with bronchiolitis.

Strength of recommendation:

NHMRC C

GRADE CONDITIONAL

Twenty-two observational studies and two matched case control studies (14-37) provided a diverse patient population and methods, but provide consistent outcomes highlighting chronological age, breast feeding for less than 2 months, poor nutrition, exposure to tobacco smoke, and existing lung disease as being risk factors for more severe bronchiolitis. Two observational studies identify indigenous infants of Australia and New Zealand as being at higher risk (16, 22).

3. Routine CXR is not recommended as it does not improve management in infants presenting with bronchiolitis, and may lead to treatments of no benefit.

Strength of recommendation:

NHMRC D GRADE CONDITIONAL Key data on the clinical utility of CXR in infants presenting to or admitted to hospital with bronchiolitis comes from two systematic reviews (Bordley et al (38), including 13 RCTs and three prospective observational studies; Williams et al (39), including five prospective observational studies, one cohort study and two retrospective studies); a systematic review and guideline (10); a qualitative review of the literature (40); two prospective observational studies (41, 42), with Yong et al (42) also including an economic evaluation. Despite the heterogeneity of the studies, outcomes consistently confirm that CXR is not of clinical value in typical bronchiolitis, adds cost, and increases the risk of unnecessary antibiotic use.

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.

In infants less than two months of age presenting to hospital or hospitalised with bronchiolitis with a temperature over 38 degrees, there is a low risk of UTI. If clinical uncertainty exists clinicians may consider collecting a urine sample for microscopy, culture and sensitivity looking for the concurrent presence of UTI.

Strength of recommendation:

NHMRC D

GRADE CONDITIONAL

A systematic review (38) (which assessed 82 studies) found that studies did not define clear indications for testing or the impact of testing on patient outcomes. A systematic review and guideline (10) found no utility in routine testing. Studies assessing the utility of blood tests in infants with bronchiolitis (38, 43-45) have assessed a variety of markers with none demonstrating clinical benefit.

Studies assessing the incidence of UTI in infants hospitalised with bronchiolitis included a systematic review of infants less than 90 days of age with bronchiolitis (46) including 11 studies (six prospective and five retrospective) and a prospective cohort study of infants with bronchiolitis between 2 and 12months of age (47). The incidence of UTI in infants under 90 days was 3.3% and those aged 2 to 12 months was 2% (48). All studies excluded infants who were severely unwell.

5. In infants with bronchiolitis, routine use of viral testing is not recommended for any clinically relevant end-points, including cohorting of bronchiolitis patients.

Strength of recommendation:

NHMRC

С GRADE CONDITIONAL

Data was obtained from one systematic review (38) which included 82 trials (17 were primary articles on diagnosis of bronchiolitis and 65 were reports of treatment or prevention trials); one systematic review and guideline (10); one controlled clinical trial; and nine prospective observational studies (18, 49-57). The viral panels used were not consistent. There is non-uniformity of study design and outcomes, few studies look at clinical outcomes and where they did, there is lack of evidence of any benefit to clinically relevant outcomes, and routine viral testing cannot be recommended.

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.

Strength of recommendation:

NHMRC D

GRADE WEAK

The evidence is based on eight prospective observational cohort studies and two cross sectional observational studies (58-64) which were conducted using a variety of scoring systems (including Kristjansson Respiratory Score, modified Wood's Clinical Asthma Score (M-WCAS) and Tal severity Score, modified Tal, Respiratory Distress Assessment Instrument (RDAI) and the Children's Hospital of Wisconsin Respiratory Score (CHWRS) in addition to the use of specific identified clinical parameters as a scoring system). Limitations to the studies included low number of patients, single centre based studies, unique clinical settings and varied use/comparison of multiple scoring systems across the eight studies. Outcome measures were most often inter-rater reliability, with only a few clinically relevant outcomes used. None of the studies showed benefit for any clinically relevant outcomes (such as need for admission, length of hospital stay, need for ICU admission and representation after discharge from the ED).

7. Oxygen saturations, adequacy of feeding, age (infants younger than eight weeks), and 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.

Strength of recommendation:

NHMRC	PRACTICE POINT
GRADE	WEAK

The evidence base for discharge criteria comes from three systematic reviews and guidelines (10, 65, 66) and two multi-centre prospective observational studies (67, 68) involving over 3000 infants. There is insufficient evidence to determine absolute criteria for safe discharge from hospital or the ED, of infants with bronchiolitis, but recommend oxygen saturations and adequacy of feeding are the most important criteria.

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.

Strength of recommendation: NHMRC А 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.

Strength of recommendation: NHMRC D GRADE WEAK

Data regarding the administration of beta 2 agonists (with the exclusion of adrenaline) in infants presenting to hospital or hospitalised with bronchiolitis comes from one Cochrane systematic review (69) (30 RCTs, n=1992) and three systematic reviews and guidelines (10, 13, 65). Subsequent to the meta-analysis there has been one further small RCT (70) (n = 56) which does not change the findings of the meta-analysis.

Infants with bronchiolitis administered beta 2 agonists do not have any change in rate of hospitalisation (11.9% in beta 2 agonist group vs. 15.9% in placebo group, Odds ratio (OR) 0.75, 95% confidence interval (CI) 0.46 to 1.21, n=710), length of stay (mean difference (MD) 0.06 days,

95% CI -0.27 days to 0.39 days, n=349), or oxygen saturation (MD -0.43%, 95% CI -0.92% to 0.06%, n=1,242). Administration of beta 2 agonists results in a statistical improvement in short term clinical severity scores (standard MD (SMD) -0.30, 95% CI -0.54 to -0.05, n=1,086). However, this marginal change is not associated with any clinically relevant improvement.

Administration of beta 2 agonists in RCTs resulted in the following adverse events tachycardia, hypertension, decreased oxygen saturation, flushing, hyperactivity, prolonged cough, and tremor.

There is no good quality evidence evaluating the effect of beta 2 agonists in infants with bronchiolitis and a personal or family history of atopy. Given the high quality (NHMRC A, GRADE strong) recommendation not to use beta 2 agonists in infants presenting to or hospitalised with bronchiolitis, beta 2 agonists should only be used in infants with a personal or family history of atopy as part of an RCT.

Previously trials of beta 2 agonists have been suggested as a clinical option. However, given the high level of evidence (NHMRC A, GRADE strong) demonstrating no benefit of beta 2 agonists in infants presenting to or hospitalised with bronchiolitis, and that there is no well-established way to determine an "objective method of response" to beta 2 agonists in bronchiolitis, this option is no longer recommended. Although it is true that a small subset of children with bronchiolitis may have reversible airway obstruction resulting from smooth muscle constriction, attempts to define a subgroup of responders have not been successful to date. If a clinical trial of bronchodilators is undertaken, clinicians should note that the variability of the disease process, the host's airway, and the clinical assessments, particularly scoring, would limit the clinician's ability to observe a clinically relevant response to bronchodilators (13).

The sensitivity analysis of the Cochrane systematic review showed no significant subgroup effect in studies involving inpatients versus outpatients (infants in the outpatient studies tended to be older). Limiting the analysis to infants aged less than or equal to 12 months did not improve heterogeneity. Furthermore, infants less than or equal to 12 months of age are included in the Cochrane systematic meta-analysis for the critical outcomes of rate of hospitalisation and length of stay. A smaller under-powered Cochrane systematic metaanalysis (71) (eight studies, n=281) of short acting beta 2 agonists for recurrent wheeze in children under two years of age has also found that there is no current clinical benefit.

The high quality (NHMRC A, GRADE strong) recommendation not to use beta 2 agonists in infants presenting to or hospitalised with bronchiolitis should be extended to infants less than or equal to 12 months of age.

9. Do not administer adrenaline/epinephrine to infants presenting to hospital or hospitalised with bronchiolitis.

Strength of recommendation:

NHMRC B GRADE STRONG

Data regarding the administration of adrenaline/ epinephrine in infants presenting to hospital or hospitalised with bronchiolitis comes from one Cochrane systematic review (72) (19 RCTs, n=2,256) and two systematic reviews and guidelines (13, 65). Subsequent to the Cochrane systematic review there have been three further RCTs comparing adrenaline/epinephrine to a nasal decongestant or beta-2-agonists (Livni et al (73), n=65; Modaressi et al (74), n=40; Simsek-Kiper et al (75), n=75), or to placebo in ambulatory (Sarrell et al (76), n=330) and inpatient settings (Skjerven et al (77), n=404), that have not changed the findings of the meta-analysis.

Infants with bronchiolitis administered adrenaline/ epinephrine in ambulatory settings have a significant reduction in rate of hospitalisation within the first 24 hours after initiation of treatment (risk ratio (RR) 0.67, 95% CI 0.50 to 0.89, n=995). However this is not the case when only trials at low risk of bias are analysed (RR 0.77, 95% CI 0.56 to 1.07, n=842), in the most recent study (Sarrell et al (76), n=330), or when hospitalization is analysed over the first seven days after initiating treatment (RR 0.81, 95% CI 0.63 to 1.03, n=875).

Evidence from the Cochrane meta-analysis and the recent high quality RCT (Skjerven et al (77), n=404) do not suggest that administering adrenaline/epinephrine in inpatients with bronchiolitis changes hospital length of stay or readmission rates. Administration of adrenaline/epinephrine in RCTs resulted in the adverse events of tachycardia, hypertension, pallor, vomiting and tremor.

10. Do not administer nebulised hypertonic saline in infants presenting to hospital or hospitalised with bronchiolitis.

Strength of recommendation:

NHMRC

D GRADE CONDITIONAL

Data regarding the administration of nebulised hypertonic saline in infants presenting to hospital or hospitalised with bronchiolitis is based on one Cochrane systematic review of 11 RCTs (78) and a further nine additional RCTs (79-87). Subsequent to the Cochrane systematic review there have been three further systematic reviews (88-90) and the newer trials have been included in an updated systematic review by the Cochrane authors (91) and a live metaanalysis (92).

Infants admitted to hospital with bronchiolitis and administered nebulised hypertonic saline have a reduced length of stay of 0.45 of a day (95% CI -0.74 to -0.14 days; 15 studies, n=1,922). However there is considerable heterogeneity in this overall result (I2=78%). Removal of two studies with 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 in Australia and New Zealand for discharge (no respiratory signs or symptoms for 12 hours), 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 (89). A number of studies included in the meta-analysis also appear to be unbalanced with regards to duration of illness prior to treatment in the hypertonic saline arms.

Infants presenting to hospital with bronchiolitis and administered nebulised hypertonic saline in the ED have a reduced admission rate into hospital of 20% (RR 0.80, 95% CI 0.67 to 0.96; 7 RCTs, n=951). The seven RCTs reporting this outcome included a range of regimens, strengths and added medications. Furthermore, subgroup analysis suggests that nebulised hypertonic saline is not effective in the studies using just one to two doses compared with those using three or more (one to two doses RR 0.93, 95% CI 0.73 to 1.20, 4 RCTs, n=358; three or more doses RR 0.67, 95% CI 0.52 to 0.87, 3

RCTs, n=593; p value for subgroup comparison = 0.07).

In infants receiving nebulised hypertonic saline there appears to be no increased risk of adverse events or change in readmission rates following discharge from EDs.

Evidence from the largest individual studies, and from the meta-analysis, does not consistently provide evidence of improved length of stay following the use of nebulised hypertonic saline. 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. Given the lack of long term effect of nebulised hypertonic saline on length of stay the routine use of nebulised hypertonic saline in the ED to reduce admissions is not supported by the current evidence base and nebulised hypertonic saline should only be used in infants with bronchiolitis as part of an RCT.

11a. Do not administer systemic or local glucocorticoids to infants presenting to hospital or hospitalised with bronchiolitis.

Strength of recommendation:		
NHMRC	В	
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.

Strength of recommendation: 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.

Strength of recommendation:

NHMRC	D
GRADE	WEAK

Data regarding the administration of systemic or local glucocorticoids (nebulisation, oral, IM or IV) in infants presenting to hospital or hospitalised with bronchiolitis comes from one Cochrane systematic review (Fernandes et al (93),17 RCTs, n=2,596) and three systematic reviews and guidelines (10, 13, 65). Subsequent to the Cochrane systematic review there have been two further RCTs (Alansari et al (94), n=200; Jartti et al (95), n=79).

Infants with bronchiolitis administered glucocorticoids do not have different rates of hospitalisation (day one RR 0.92, 95% Cl 0.78 to 1.08, n=1,762; day seven RR 0.86, 95% Cl 0.70 to 1.06, n=1,530) or clinically significant differences in length of stay (mean difference -0.18, 95% Cl -0.39 to 0.04, n=633).

There is no good quality evidence evaluating the effect of glucocorticoids in infants with bronchiolitis and a positive response to beta 2 agonists. Furthermore there is no good quality evidence evaluating the effect of glucocorticoids in infants with a personal or family history of atopy. Given the high quality (NHMRC B, GRADE strong) recommendation not to use glucocorticoids in infants presenting to or hospitalised with bronchiolitis, glucocorticoids should only be used in infants with a positive response to beta 2 agonists as part of an RCT.

Adrenaline/epinephrine is not recommended for use in infants presenting to or hospitalised with bronchiolitis (NHMRC B, GRADE strong). This recommendation is based on one Cochrane systematic review (Hartling et al (72), 19 RCTs, n=2,256), three systematic reviews and guidelines (10, 13, 65) and seven subsequent RCTs (73-77, 96, 97).

Evidence for the administration of the combination of glucocorticoids and adrenaline/epinephrine in infants presenting to or hospitalised with bronchiolitis comes from a single multi-centre RCT conducted in eight EDs in Canada (Plint et al (98), n=800). This trial compared adrenaline and high dose dexamethasone in a factorial design. Admission rates in unadjusted analysis suggested a possible benefit in the combination arm (adrenaline/epinephrine and glucocorticoid admission on day of enrolment (RR 0.65, 95% Cl 0.41 to 1.04; day 7 RR 0.65, 95% Cl 0.45 to 0.95). However when adjusted for multiple comparisons in the factorial design this was no longer significant (adrenaline/epinephrine and glucocorticoid admission on day of enrolment RR 0.65, 95% Cl 0.37 to 1.15; day 7 RR 0.65, 95% Cl 0.41 to 1.03).

Given the evidence base for the single interventions, and the exploratory nature of the findings in the Plint trial (98) combination treatment with glucocorticoids and adrenaline/epinephrine should only be used in infants with bronchiolitis as part of an RCT.

12a. Consider the use of supplemental oxygen in the treatment of hypoxic (oxygen saturations less than 92%) infants with bronchiolitis.

Strength of recommendation:

NHMRC	С
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 greater than or equal to 92%, oxygen therapy should be discontinued.

Strength of recommendation:

NHMRC C GRADE CONDITIONAL

In evaluating the effect of oxygen administration for infants with bronchiolitis the evidence is based on a systematic review (99), a systematic review and guideline (13), a prospective observational case series of 68 infants(100) and a retrospective observational cohort study of 127 infants (101). There was low to very low level evidence for the use supplemental oxygen although the evidence based guideline formed a weak recommendation based on low level evidence and reasoning from first principles (13). There was no evidence of the effect of oxygen therapy on readmission to hospital or on feeding difficulties. There is no evidence of the benefit of oxygen in children without hypoxia.

The benefit of supplemental oxygen therapy has not been specifically studied - rather there is an assumption about the benefits of oxygen and the observational studies have principally looked at length of time of administration and feeding difficulties as a gauge of effectiveness. Therefore oxygen therapy is based on practice by first principles and low to very low-grade evidence. The evidence is applicable to the Australian and New Zealand setting.

The evidence relating to the role of oxygen saturations in patient management is based on two systematic reviews (99, 102), a systematic review and guideline (13) and two RCTs of 828 infants (103, 104). Additional evidence is from a prospective observational case series of 68 infants (100) and three retrospective observational studies (101, 105, 106). The absolute level of oxygen saturation for supplemental oxygen therapy to commence with the threshold has ranged in these studies from 90 - 94%. For the critical outcome of admission to hospital there is moderate evidence that oxygen saturation levels affects the decision to admit independently of other factors including signs of respiratory distress.

For the critical outcome of length of stay in hospital there is low level evidence that oxygen saturation targets prolong length of stay with a target of less than 92% established as a need for commencement of oxygen supplementation.

For the important outcome of readmission there is high level evidence that oxygen level saturations do not affect readmissions to hospital.

For the important outcome of feeding difficulties there is very low evidence for the impact of oxygen saturation targets.

To date, neither of the RCTs have reported long-term neurodevelopmental outcomes.

13. Routine use of continuous pulse oximetry is not required for medical management of nonhypoxic (saturations greater than or equal to 92%) infants not receiving oxygen, or stable infants receiving oxygen.

Strength of recommendation:

NHMRC C GRADE CONDITIONAL

The evidence is based on two high quality evidence reviews (13, 99). In addition, there was one randomised, double-blind, parallel-group trial (104) involving 213 infants, one randomised, parallel-group, superiority clinical trial (107) of 161 infants to either continuous vs. intermittent pulse oximetry and one prospective observational study (100) of 68 patients evaluating discharge oxygen saturation levels. A further three retrospective studies (101, 105, 106) involved 439 infants.

For the critical outcome of length of stay there is moderate evidence that continuous monitoring of pulse oximetry increases hospital length of stay. A prospective observational study (108) subjects with bronchiolitis demonstrated significantly lower nocturnal baseline SpO2 than control infants without lung disease or upper airway obstruction on admission which recovered during hospitalisation. For the critical outcome threshold for discharge oxygen saturations there is low quality evidence on the comparative effect of different discharge oxygen saturation thresholds. For the critical outcome frequency of nocturnal desaturations there is very low quality evidence to indicate that the frequency of nocturnal desaturations prolongs length of stay. For the important outcome of feeding there is very low quality evidence that the disease course or hospital length of stay is altered by maintaining feeding. For the important outcome of cost there was no evidence of reduced cost savings in those infants admitted with bronchiolitis on continuous oximetry monitoring.

14. HFNC in bronchiolitis can be considered in the inpatient setting in children with bronchiolitis with hypoxia (oxygen saturations less than 92%). Its use in children without hypoxia should be limited to the RCT setting only.

Strength of recommendation:

NHMRC	С
GRADE	CONDITIONAL

There have been limited studies on HFNC in children with bronchiolitis during inpatient stay outside of the paediatric ICU (PICU). A Cochrane systematic review (109) one systematic review and guideline (13), one RCT (110), two prospective studies (111, 112), four non-systematic reviews (113-116) and one retrospective cohort review (117) all provide low to very low level evidence for the benefit of HFNC. A prospective interventional study of 14 infants with bronchiolitis demonstrates reduction in work of breathing receiving HFNC (118).

There are insufficient studies and patients investigated to recommend HFNC as a standard therapy in a general paediatric unit.

For the critical outcome of length of stay in hospital there is low quality evidence that HFNC oxygen improves length of stay in hospital.

For the critical outcome for rate of PICU admission there is low quality evidence that HFNC oxygen reduces PICU admission rates.

For the important outcome of adverse events there is very low evidence that HFNC oxygen is safe.

For the important outcome of cost there is very low evidence that oxygen administered via HFNC may reduce overall health care cost, with the potential to reduce patient transfers both between hospitals and to the PICU.

15. Chest physiotherapy is not recommended for routine use in infants with bronchiolitis.

Strength of recommendation:

NHMRC

GRADE STRONG

В

There is one Cochrane systematic review (119) with nine clinical trials including 891 patients on the topic. In addition there is one low quality RCT (120) two prospective clinical trials (121, 122) and three observational trials (123-125) of very low quality and one systematic review and guideline (10). For the critical outcome of change in severity status of bronchiolitis there is moderate evidence that physiotherapy does not alter severity. For the critical outcome of time to recovery/ clinical stability there is high quality evidence that physiotherapy does not improve recovery or stability. For the critical outcome of oxygen saturation levels there is very low level evidence of physiotherapy improving this outcome. For the important outcome of duration of oxygen supplementation there is high quality evidence that duration is not altered by physiotherapy. For the important outcome of length of hospital stay there is high level evidence that length of stay is not altered by physiotherapy. For the important outcome of complications of therapy there is high-level evidence of minimal adverse effects resulting from physiotherapy. For the important outcome of heart rate variability there is very low level evidence that heart rate variability is modified by physiotherapy.

16a. Nasal suction is not recommended as routine practice in the management of infants with bronchiolitis. Superficial suction may be considered to assist with feeding.

Strength of recommendation:

NHMRC D GRADE CONDITIONAL

16b. Deep nasal suction for the management of bronchiolitis is not recommended.

Strength of recommendation:

NHMRC	D
GRADE	CONDITIONAL

There is only one retrospective comparative study (125) of 740 patients examining suction types and frequency. Three non-systematic reviews or guidelines refer to the use of suction but without provision of references and are rated very low. For the critical outcome of length of hospital stay there is low level evidence that the use of deep nasal suction increases length of hospital stay while non-invasive frequent suction may decrease length of stay. There was low level evidence for the important outcome of increased adverse events.

17. Routine nasal saline drops are not recommended. Trial of intermittent saline drops may be considered at time of feeding.

Strength of	of recommendation:
NHMRC	PRACTICE POINT

GRADE WEAK

There is no Cochrane review. Two RCTs use administration of nasal saline as the control therapy in chest physiotherapy techniques (120) or phenylephrine nasal drops (126). A guideline (127) and a review article (128) recommend nasal saline as a practice point. Nasal saline drops have not been demonstrated to improve outcomes in bronchiolitis but may be considered for use particularly prior to feeding (breast or bottle). No evidence is available to demonstrate benefit or harm.

18. Nasal CPAP therapy for infants with bronchiolitis may be considered for the management of infants.

Strength of recommendation:

NHMRC C GRADE CONDITIONAL

One Cochrane systematic review (129) analysed two RCTs with a total of 50 patients with low level of evidence and high risk of biases. Relevant clinical outcomes, such as intubation rates, were addressed and a trend towards reduction in intubations was shown. A recent prospective observational study (130) of low quality evaluated general paediatric ward administration of nCPAP. A retrospective study (131) of very low quality compared HFNC to nCPAP

in the ICU setting only. Two recent systematic reviews (116, 132) analysed the use of nCPAP for bronchiolitis. All studies are inconsistent as they evaluated different populations (PICU vs. ward) and interventions (HFNC, nCPAP). There was no evidence for the effect of nCPAP on the important outcome of duration of ED length of stay.

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.

Strength of recommendation:

NHMRC C

GRADE CONDITIONAL

There have been no systematic reviews on this question. The evidence is based on two RCTs of 136 infants both with methodological flaws. One trial (133) was stopped before the enrolment of the desired number of patients in their sample-size calculation was achieved and one trial (134) had very low numbers to compare the two groups in terms of evaluating the cost savings plus the patients were recruited over a single bronchiolitis season. Additional evidence comes from one prospective observational study (135) one retrospective comparative study (136) and three retrospective chart reviews (137-139). For the critical outcome of length of stay in hospital there is very low quality evidence of a reduced length of stay in those treated with home oxygen therapy and there is very low evidence for the critical outcome of the total length of oxygen therapy. For the important outcome of cost savings there is very low quality evidence of reduced costs in those treated with home oxygen therapy. For the critical outcome of readmission within seven days there is very low quality evidence of a reduced readmission rate in those treated with home oxygen therapy. For the important outcome of adverse events there is very low quality evidence of no increase in adverse events in those treated with home oxygen therapy. All studies have had exclusions of infants with factors that place them at risk of severe disease and the evidence to date has indicated no increased risk of harm in infants treated. However, the studies have been underpowered or only observational with risk of imprecision and inconsistency. The true effect on harm has not been established.

20a. Do not use antibiotics to treat infants with bronchiolitis.

Strength of recommendation:

NHMRC	В
GRADE	CONDITIONAL
20b. Do no	t use azithromycin for treatment of infants

Strength of recommendation:

admitted to hospital with bronchiolitis.

NHMRC	В
GRADE	CONDITIONAL

20c. Do not use azithromycin for treatment of infants admitted to hospital with bronchiolitis who are at risk of developing bronchiectasis.

Strength of recommendation:

NHMRC C GRADE CONDITIONAL

Two Cochrane systematic reviews (140, 141) and a single RCT of 40 infants (142) showed no benefit of antibiotics for treating bronchiolitis, in terms of hospital length of stay and hospital readmission rates (140) or persisting symptoms (141). The risk of secondary bacterial infection in bronchiolitis is very low and there is potential harm of antibiotics use from adverse reactions and increased antibiotic resistance.

One Cochrane systematic review containing three RCTS (140) shows that there is no difference in length of stay, PICU admission, or symptom resolution for those treated with azithromycin versus placebo for infants hospitalised with bronchiolitis.

There is low quality evidence (140) that there is no difference in length of stay, PICU admission, or symptom resolution for those treated with azithromycin versus placebo for infants hospitalised with bronchiolitis.

One RCT of azithromycin versus placebo, once a week for three weeks, in 219 indigenous infants enrolled in Australia and New Zealand found no difference in length of hospital stay, symptoms at 21 days, adverse events or readmission rates at six months (143). There are no reports on bronchiectasis as an outcome.

21a. Supplemental hydration is recommended for infants who cannot maintain hydration orally.

Strength of recommendation:

NHMRC	PRACTICE POINT
GRADE	WEAK

A Cochrane systematic review(144) of benefit versus harm from advice to increase fluid intake for treating acute respiratory infections was unable to identify any evidence from RCTs in the primary care or outpatient setting.

21b. Both NG and IV routes are acceptable means for non-oral hydration in infants admitted to hospital with bronchiolitis.

Strength of recommendation:

NHMRC

GRADE STRONG

R

A large RCT(145) of 759 infants showed no difference in mean length of stay for infants with bronchiolitis treated with IV hydration vs. NG feeds; however there was a higher likelihood of success of first insertion of NG tubes versus IV cannulae.

21c. There is insufficient evidence to recommend a specific proportion of maintenance fluid. There is a risk of fluid overload and judicious and vigilant use of hydration fluid is recommended. Isotonic fluid is recommended.

Strength of recommendation:

NHMRC PRACTICE POINT

GRADE WEAK

Serious concerns about risk of hyponatraemia in moderate bronchiolitis (146) have prompted caution about use of hypotonic IV fluids in infants with bronchiolitis. Regimens of fluid volumes, from restricted to liberal, have been used with little evidence supporting their use.

22. Hand hygiene is the most effective intervention to reduce hospital acquired infections and is recommended. There is inadequate evidence for the benefits of cohorting bronchiolitic patients.

Strength of recommendation:

NHMRC B GRADE WEAK

The current evidence is derived from observational studies (147-150). No RCT on containing common viral infections such as RSV by different infection control practices in ED or general paediatric ward setting is available. The Cochrane systematic review (151) on this topic focuses on different pandemic viral infections affecting a range of population in a variety of settings. This evidence could be extrapolated as indirect evidence for infants with bronchiolitis secondary to common respiratory viral infections for the outcome of nosocomial infection rates.

GRADE & NHMRC EVIDENCE TABLES

	RADE Eviden		inar y					
	Considered Judgem	ent - Streng	th of recom	mendation				
Question 1: In infants presenting to hospital bronchiolitis?	what factors in the h	istory and p	hysical exar	nination co		_		
1. Outcome measures:		portance of outcome making a decision						
	HIGH	HIGH MOD LOW V. LOW Critical						
O1 Diagnosis of bronchiolitis			x		х			
O2 Sensitivity and specificity			x		х			
2. Is there is insufficient evidence to a	make a recommenda	tion?						
Evidence statement A systematic review and guideline and two prospe bronchiolitis likely. The major factors which were clinical diagnosis of bronchiolitis. Major guidelines all suggest a clinical picture of br	e predictive were fever	, tachypnoea,	, retractions a	and wheeze.	Other major in	ternational guide		
3. What benefit will the proposed inte			vidence for t	ne predictive		chinear midnigs.		
Evidence statement						Ouality	of evidence	
The combination of cough, wheeze and retraction	ns demonstrate RSV po	ositive broncl	hiolitis (as op	posed to bro	onchiolitis from			
other viruses) with a sensitivity of 0.8.						I	LOW	
Judging the benefits in context The evidence is applicable and generalizable to th	o Now Zooland and A	setualiza hool	the activities of					
4. What harm might the proposed int			ui settiligs.					
Evidence statement						Quality of e	vidence	
Single observational study with limited numbers.						- •	AY LOW	
Judging the harms in context						•		
Risks of missing diagnosis of other serious condit	tions such as cardiac fa	ilure remains	, but evidenc	e for other c	linical or test fe	atures for diagno	ses these in thi	
Risks of missing diagnosis of other serious condit context are missing.		ilure remains	, but evidenc	e for other c	linical or test fe	atures for diagno	ses these in this	
Risks of missing diagnosis of other serious condit context are missing. 5. What is the likely balance between		ilure remains	, but evidenc	e for other c	linical or test fe	-		
Risks of missing diagnosis of other serious condit context are missing.	good and harm?				linical or test fe	O quality	verall of evidence	
Risks of missing diagnosis of other serious condit context are missing. 5. What is the likely balance between Evidence statement Clinical diagnosis is reasonably accurate but award Judging the balance of benefits and harms in	good and harm? eness of differential dia context	gnoses needs	s to be maint	ained.		O quality VER	verall of evidence Y LOW	
Risks of missing diagnosis of other serious condit context are missing. 5. What is the likely balance between Evidence statement Clinical diagnosis is reasonably accurate but award Judging the balance of benefits and harms in Given the wealth of clinical experience within the	good and harm? eness of differential dia context	gnoses needs	s to be maint	ained.		O quality VER	verall of evidence Y LOW	
Risks of missing diagnosis of other serious condit context are missing. 5. What is the likely balance between Evidence statement Clinical diagnosis is reasonably accurate but aware Judging the balance of benefits and harms in Given the wealth of clinical experience within the to be made around consensus of opinion.	good and harm? eness of differential dia context e bronchiolitis working	gnoses needs party, I am c	s to be maint	ained.		O quality VER gnosis of bronchi	verall of evidence Y LOW	
Risks of missing diagnosis of other serious condit context are missing. 5. What is the likely balance between Evidence statement Clinical diagnosis is reasonably accurate but award Judging the balance of benefits and harms in Given the wealth of clinical experience within the to be made around consensus of opinion. Benefits clearly outweigh harms	good and harm? eness of differential dia context e bronchiolitis working Recommend	gnoses needs party, I am c	s to be maint	ained.		O quality o VER gnosis of bronchi STRONG	verall of evidence Y LOW iolitis will be ab	
Risks of missing diagnosis of other serious condit context are missing. 5. What is the likely balance between Evidence statement Clinical diagnosis is reasonably accurate but award Judging the balance of benefits and harms in Given the wealth of clinical experience within the to be made around consensus of opinion. Benefits clearly outweigh harms Benefits probably outweigh harms	good and harm? eness of differential dia context e bronchiolitis working Recommend Consider	gnoses needs party, I am c	s to be maint confident tha	ained. t clear guidel	ines around dia;	o quality VER gnosis of bronchi STRONG CONDITIO	verall of evidence Y LOW iolitis will be ab	
Risks of missing diagnosis of other serious condit context are missing. 5. What is the likely balance between Evidence statement Clinical diagnosis is reasonably accurate but award Judging the balance of benefits and harms in Given the wealth of clinical experience within the to be made around consensus of opinion. Benefits clearly outweigh harms Benefits probably outweigh harms Not known	good and harm? eness of differential dia context e bronchiolitis working Recommend	gnoses needs party, I am c	s to be maint confident tha	ained. t clear guidel	ines around dia;	O quality o VER gnosis of bronchi STRONG	verall of evidence Y LOW iolitis will be ab	
Risks of missing diagnosis of other serious condit context are missing. 5. What is the likely balance between Evidence statement Clinical diagnosis is reasonably accurate but award Judging the balance of benefits and harms in Given the wealth of clinical experience within the to be made around consensus of opinion. Benefits clearly outweigh harms Benefits probably outweigh harms Not known Benefits probably don't outweigh harms	good and harm? eness of differential dia context e bronchiolitis working Recommend Consider	party, I am c	s to be maint confident tha	ained. t clear guidel	ines around dia;	o quality VER gnosis of bronchi STRONG CONDITIO	verall of evidence Y LOW iolitis will be ab	
Risks of missing diagnosis of other serious condit context are missing. 5. What is the likely balance between Evidence statement Clinical diagnosis is reasonably accurate but award Judging the balance of benefits and harms in Given the wealth of clinical experience within the to be made around consensus of opinion. Benefits clearly outweigh harms Benefits probably outweigh harms Not known Benefits probably don't outweigh harms	good and harm? eness of differential dia context bronchiolitis working Recommend Consider Make a reco	party, I am c	s to be maint confident tha	ained. t clear guidel	ines around dia;	o quality VER gnosis of bronchi STRONG CONDITIO WEAK	verall of evidence Y LOW iolitis will be ab	
Risks of missing diagnosis of other serious condit context are missing. 5. What is the likely balance between Evidence statement Clinical diagnosis is reasonably accurate but award Judging the balance of benefits and harms in Given the wealth of clinical experience within the to be made around consensus of opinion. Benefits clearly outweigh harms Benefits probably outweigh harms Not known Benefits probably don't outweigh harms Harms probably outweigh benefits	good and harm? eness of differential dia context e bronchiolitis working Recommend Consider Make a reco Consider aga	gnoses needs party, I am c I pommendatio	s to be maint confident tha	ained. t clear guidel	ines around dia;	o quality VER gnosis of bronchi STRONG CONDITIO WEAK CONDITIO	verall of evidence Y LOW iolitis will be ab	
Risks of missing diagnosis of other serious condit context are missing. 5. What is the likely balance between Evidence statement Clinical diagnosis is reasonably accurate but award Judging the balance of benefits and harms in Given the wealth of clinical experience within the to be made around consensus of opinion. Benefits clearly outweigh harms Benefits probably outweigh harms Not known Benefits probably don't outweigh harms Harms probably outweigh benefits Benefits clearly don't outweigh harms	good and harm? eness of differential dia context bronchiolitis working Recommend Consider Make a reco	gnoses needs party, I am c I pommendatio	s to be maint confident tha	ained. t clear guidel	ines around dia;	o quality VER gnosis of bronchi STRONG CONDITIO WEAK	verall of evidence Y LOW iolitis will be ab	
Risks of missing diagnosis of other serious condit context are missing. 5. What is the likely balance between Evidence statement Clinical diagnosis is reasonably accurate but award Judging the balance of benefits and harms in Given the wealth of clinical experience within the to be made around consensus of opinion. Benefits clearly outweigh harms Benefits probably outweigh harms Not known Benefits probably don't outweigh harms Harms probably outweigh benefits Benefits clearly don't outweigh harms	good and harm? eness of differential dia context bronchiolitis working Recommend Consider Make a reco Consider aga Recommend	gnoses needs party, I am c l ommendatio iinst against	s to be maint confident tha	ained. t clear guidel ch (see 8 b	ines around dia;	o quality VER gnosis of bronchi STRONG CONDITIO WEAK CONDITIO	verall of evidence Y LOW iolitis will be ab	
Risks of missing diagnosis of other serious condit context are missing. 5. What is the likely balance between Evidence statement Clinical diagnosis is reasonably accurate but award Judging the balance of benefits and harms in Given the wealth of clinical experience within the to be made around consensus of opinion. Benefits clearly outweigh harms Benefits probably outweigh harms Benefits probably outweigh harms Harms probably don't outweigh harms Harms clearly don't outweigh harms Harms clearly outweigh benefits 6. Is the intervention/action impleme Summary statement	good and harm? eness of differential dia context bronchiolitis working Recommend Consider Make a reco Consider aga Recommend entable in the New Z	gnoses needs party, I am c l ommendatio iinst against	s to be maint confident tha	ained. t clear guidel ch (see 8 b	ines around dia;	o quality VER gnosis of bronchi STRONG CONDITIO WEAK CONDITIO	verall of evidence Y LOW iolitis will be at	
Risks of missing diagnosis of other serious condit context are missing. 5. What is the likely balance between Evidence statement Clinical diagnosis is reasonably accurate but award Judging the balance of benefits and harms in Given the wealth of clinical experience within the to be made around consensus of opinion. Benefits clearly outweigh harms Benefits probably outweigh harms Benefits probably don't outweigh harms Harms probably don't outweigh harms Harms clearly outweigh benefits Benefits clearly outweigh benefit	good and harm? eness of differential dia context bronchiolitis working Recommend Consider Make a reco Consider aga Recommend entable in the New Z	gnoses needs party, I am c ommendatio iinst against ealand and	s to be maint confident tha on for resear Australian c	ained. t clear guidel ch (see 8 bo	ines around dia;	o quality VER gnosis of bronchi STRONG CONDITIO WEAK CONDITIO	verall of evidence Y LOW iolitis will be ab	
Risks of missing diagnosis of other serious condit context are missing. 5. What is the likely balance between Evidence statement Clinical diagnosis is reasonably accurate but award ludging the balance of benefits and harms in Given the wealth of clinical experience within the to be made around consensus of opinion. Benefits clearly outweigh harms Benefits probably outweigh harms Not known Benefits probably don't outweigh harms Harms probably outweigh benefits Benefits clearly don't outweigh harms Harms clearly outweigh benefits 6. Is the intervention/action implement Summary statement This evidence is directly transferrable to the Austra Yes	good and harm? eness of differential dia context bronchiolitis working Recommend Consider Make a reco Consider aga Recommend entable in the New Z	ignoses needs party, I am c i ommendatio iinst against ealand and Rec	s to be maint confident tha on for resear Australian c	ained. t clear guidel ch (see 8 bo context?	ines around dia	o quality VER gnosis of bronchi STRONG CONDITIO WEAK CONDITIO	verall of evidence Y LOW iolitis will be at	
Risks of missing diagnosis of other serious condit context are missing. 5. What is the likely balance between Evidence statement Clinical diagnosis is reasonably accurate but award fudging the balance of benefits and harms in Given the wealth of clinical experience within the to be made around consensus of opinion. Benefits clearly outweigh harms Benefits probably outweigh harms Benefits probably outweigh harms Harms probably don't outweigh harms Harms clearly outweigh benefits Benefits clearly transferrable to the Austr Yes Not known	good and harm? eness of differential dia context bronchiolitis working Recommend Consider Make a reco Consider aga Recommend entable in the New Z	gnoses needs party, I am c i ommendatio iinst against ealand and Cor	s to be maint confident tha on for resear Australian c commend/c	ained. t clear guidel ch (see 8 bo context?	ines around dia, elow)	o quality VER gnosis of bronchi STRONG CONDITIO WEAK CONDITIO	verall of evidence Y LOW iolitis will be at	
Risks of missing diagnosis of other serious condit context are missing. 5. What is the likely balance between Evidence statement Clinical diagnosis is reasonably accurate but award Judging the balance of benefits and harms in Given the wealth of clinical experience within the to be made around consensus of opinion. Benefits clearly outweigh harms Benefits probably outweigh harms Mot known Benefits clearly don't outweigh harms Harms probably outweigh benefits Benefits clearly don't outweigh harms Harms clearly outweigh benefits 6. Is the intervention/action impleme Summary statement This evidence is directly transferrable to the Austr Yes Not known	good and harm? eness of differential dia context bronchiolitis working Recommend Consider Make a reco Consider aga Recommend entable in the New Z	gnoses needs party, I am c i ommendatio iinst against ealand and Cor	s to be maint confident tha on for resear Australian c	ained. t clear guidel ch (see 8 bo context?	ines around dia, elow)	o quality VER gnosis of bronchi STRONG CONDITIO WEAK CONDITIO	verall of evidence Y LOW iolitis will be at	
Risks of missing diagnosis of other serious condit context are missing. 5. What is the likely balance between Evidence statement Clinical diagnosis is reasonably accurate but award Judging the balance of benefits and harms in Given the wealth of clinical experience within the to be made around consensus of opinion. Benefits clearly outweigh harms Benefits probably outweigh harms Mot known Benefits clearly outweigh benefits Benefits clearly don't outweigh harms Harms clearly outweigh benefits 6. Is the intervention/action implement Summary statement This evidence is directly transferrable to the Austr Yes Not known	good and harm? eness of differential dia context bronchiolitis working Recommend Consider Make a reco Consider aga Recommend entable in the New Z	gnoses needs party, I am c i ommendatio iinst against ealand and Cor	s to be maint confident tha on for resear Australian c commend/c	ained. t clear guidel ch (see 8 bo context?	ines around dia, elow)	o quality VER gnosis of bronchi STRONG CONDITIO WEAK CONDITIO	verall of evidence Y LOW iolitis will be al	
Risks of missing diagnosis of other serious condit context are missing. 5. What is the likely balance between Evidence statement Clinical diagnosis is reasonably accurate but award Judging the balance of benefits and harms in Given the wealth of clinical experience within the to be made around consensus of opinion. Benefits clearly outweigh harms Benefits probably outweigh harms Not known Benefits clearly don't outweigh harms Harms probably don't outweigh harms Harms clearly outweigh benefits 6. Is the intervention/action implement Summary statement This evidence is directly transferrable to the Austr Yes Not known No 7. Final recommendation Infants can be diagnosed with bronchiolitis if	good and harm? eness of differential dia context bronchiolitis working Recommend Consider Make a reco Consider aga Recommend entable in the New Z ralasian population.	ignoses needs party, I am c i ommendatio inst against ealand and Rec Con Rec	s to be maint confident tha on for resear Australian c commend/c commend/cc ract infectio	ained. t clear guidel ch (see 8 bo context? consider mic evaluation mic again m	ines around dia, elow) elow) st Strength of rec	o quality VER gnosis of bronchi STRONG CONDITIO WEAK CONDITIO	verall of evidence Y LOW iolitis will be at	
Risks of missing diagnosis of other serious condit context are missing. 5. What is the likely balance between Evidence statement Clinical diagnosis is reasonably accurate but award Judging the balance of benefits and harms in Given the wealth of clinical experience within the to be made around consensus of opinion. Benefits clearly outweigh harms Benefits probably outweigh harms Mot known Benefits clearly don't outweigh harms Harms probably don't outweigh harms Harms clearly outweigh benefits Benefits clearly don't outweigh harms Harms clearly outweigh benefits 6. Is the intervention/action implement Summary statement This evidence is directly transferrable to the Austr Yes Not known No 7. Final recommendation Infants can be diagnosed with bronchiolitis if followed by onset of respiratory distress with	good and harm? eness of differential dia context bronchiolitis working Recommend Consider Ake a reco Consider aga Recommend entable in the New Z ralasian population. f they have an upper a fever, and one or more	ignoses needs party, I am c i ommendatio inst against ealand and Rec Con Rec	s to be maint confident tha on for resear Australian c commend/c commend/cc ract infectio	ained. t clear guidel ch (see 8 bo context? consider mic evaluation mic evaluation mic evaluation	ines around dia, elow) elow) st Strength of rec STRONG	o quality VER gnosis of bronchi STRONG CONDITIO WEAK CONDITIO STRONG	verall of evidence Y LOW iolitis will be ab	
Risks of missing diagnosis of other serious condit context are missing. 5. What is the likely balance between Evidence statement Clinical diagnosis is reasonably accurate but award Judging the balance of benefits and harms in Given the wealth of clinical experience within the to be made around consensus of opinion. Benefits clearly outweigh harms Benefits probably outweigh harms Not known Benefits clearly don't outweigh harms Harms probably don't outweigh harms Harms clearly outweigh benefits 6. Is the intervention/action implement Summary statement This evidence is directly transferrable to the Austr Yes Not known No 7. Final recommendation Infants can be diagnosed with bronchiolitis if	good and harm? eness of differential dia context bronchiolitis working Recommend Consider Ake a reco Consider aga Recommend entable in the New Z ralasian population. f they have an upper a fever, and one or more	ignoses needs party, I am c i ommendatio inst against ealand and Rec Con Rec	s to be maint confident tha on for resear Australian c commend/c commend/cc ract infectio	ained. t clear guidel ch (see 8 bo context? consider mic evaluation mic evaluation mic evaluation mic evaluation	ines around dia, elow) elow) st Strength of rec	o quality VER gnosis of bronchi STRONG CONDITIO WEAK CONDITIO STRONG	verall of evidence Y LOW iolitis will be ab	

Question 1.

NHMRC Evidence Summary

Question 1: In infants p	resenting to hosp	ital what factors in the histor	y and ph	ysical examination	Evidence table ref:		
contribute to a differential	diagnosis of bron	chiolitis.			Amat 2014, Corneli 2012, Drolia 2009,		
					Durani 2008, McLellan 2014, Ralston		
1 E 1 1 () (· · · · · · · · · · · · · · · · · · ·	1 . 1 . 6 1	1		2014, Ricci 2015 (10-13, 21, 152, 153).		
1. Evidence base (number of studies, level of evidence and risk of bias in the included studies)							
A systematic review and guid			А		studies with a low risk of bias, or several		
provide recent evidence for			21	Level II studies with			
		re predictive were fever, cough,	В	One or two Level II studies with a low risk of bias, or SR/sev			
tachypnoea, retractions and support the clinical diagnosis		or international guidelines		Level III studies with	studies with a low risk of bias or Level I or		
Major guidelines all suggest a		pronchiolitis but cite no	С	II studies with mode:			
supportive evidence for the					Level I to III studies/SRs with a high		
			D	risk of bias	, 8		
2. Consistency (if only one sta	udy was available, rank	this component as 'not applicable')					
		· · · · ·					
			А	All studies consistent			
			В	Most studies consiste	ent and inconsistency can be explained		
				Some inconsistency	reflecting genuine uncertainty around		
			С	question	0.0.		
			D	Evidence is not cons	istent		
			NA	Not applicable (one	e study only)		
3. Clinical impact (indicate is not be determined)	if the study results varied	d according to some unknown factor (no	t simply stu	ly quality or sample size) a	nd thus the clinical impact of the intervention could		
Well conducted prospective	study		А	Very large			
			В	Substantial			
			С	Moderate			
			D	Slight/Restricted			
4. Generalisability (how well	does the body of evident	ce match the population and clinical sett	ings being to	ő			
Evidence in children under 3			A		neralisable to target population		
under one year of age.		, 8			eneralisable to target population with		
			В	some caveats			
			С	Evidence not directly	generalisable to target population but could		
			0	be sensibly applied			
			D	Evidence not directly	y generalisable to target population and hard		
-				to judge whether sen			
	·	e Australian/New Zealand healthcare	context in t	5	5 5 5 7		
Studies were undertaken in t Australia and New Zealand		lence is applicable to children in	А	Evidence directly app healthcare context	plicable to Australian/New Zealand		
			В		e to Australian/New Zealand healthcare		
				context with few ca	pplicable to Australian/New Zealand		
			С	healthcare context wi			
			D		able to Australian/New Zealand healthcare		
			D	context			
Other factors (indicate here an recommendation)	ny other factors that you	took into account when assessing the et	vidence base	(for example, issues that m	ight cause the group to downgrade or upgrade the		
EVIDENCE STATEMEN	NT MATRIX (summ	narise the development group's synthesis	of the evider	ace relating to the key quest	ion, taking all the above factors into account)		
Component	Rating	Description					
1. Evidence base	D	Level IV studies or Level I to I	II studies/	SRs with a high risk of	f bias		
2. Consistency	NA	Not applicable (one study or		ÿ			
3. Clinical Impact	С	Moderate	••				
4. Generalisability	В	Evidence directly generalisable	to target r	onulation with some c	aveats		

5. Applicability B Evidence applicable to Australian/New Zealand healthcare context with few caveats

EVIDENCE STATEMENT

There is one prospective cohort study from USA assessing clinical predictors of RSV bronchiolitis infection in infants and children less than 36 months of age. One hundred and ninety seven patients were admitted to hospital with suspected RSV infection – all had viral testing. They identified cough, fever, wheeze, and retractions as independent predictors.

Major guidelines all suggest a clinical picture of bronchiolitis but site no supportive evidence for the predictive value of these clinical findings.

RECOMMENDATION (What recommendation(s) does		OVERALL GRADE OF RECOMMENDATION			
the guideline development group draw from this evidence? Use	A Body of evidence can be trusted to guide practice				
action statements where possible)	В	Body of evidence can be trusted to guide practice in most situation	S		
	С	Body of evidence provides some support for recommendation	is(s) but care		
Infants can be diagnosed with bronchiolitis if they	C	should be taken in its application			
have an upper respiratory tract infection followed	D	Body of evidence is weak and recommendation must be applied wi	th caution		
by onset of respiratory distress with fever, and one					
or more of: cough, tachypnoea, retractions and	PP	Practice Point			
diffuse crackles or wheeze on auscultation.					
UNRESOLVED ISSUES (If needed, keep a note of specific i	ssues that ar	ise when each recommendation is formulated and that require follow up)			
Further research should concentrate on risk factors for ot	her conditi	ions that may masquerade as bronchiolitis including immunodeficiency	v, congenital lung		
disease and cardiac anomalies.					
IMPLEMENTATION OF RECOMMENDATION	(Please india	cate yes or no to the following questions. Where the answer is yes, please provide exp	blanatory information		
about this. This information will be used to develop the implementation	tion plan for	the guidelines)			
Will this recommendation result in changes in usual care?			YES		
			NO		
Are there any resource implications associated with imple	menting th	is recommendation?	YES		
			NO		
Will the implementation of this recommendation require	changes in	the way care is currently organised?	YES		
			NO		
Are the guideline development group aware of any barrier	rs to impler	mentation of this recommendation?	YES		
			NO		

Question 2.

GRADE Evidence Summary

Consid	dered Judgem	ent - Stre	ngth of recom	mendatio	n			
Question 2: In infants presenting to hospital with br hospital stay, ICU admission, death)?	onchiolitis, w	hat are th	e risk factors	for admiss			0 0	
1. Outcome measures:		Quality	of evidence		nportance of out n making a deci			
	HIGH	MOD	LOW	Critical	Important	Not Important		
O1 Admission to hospital			X			X		
O2 Admission to ICU			Х		Х			
O3 Prolonged hospital length of stay			Х			Х		
O ₄ Death			Х		Х			
2. Is there sufficient evidence to make a reco	ommendation	?					•	
Evidence statement: Twenty two observational studies and two matched case Two observational studies included indigenous Australiar smoke exposure, chronological age at presentation) with supporting each risk factor, but findings were consistent. 3. What benefit will the proposed intervention	ns and New Ze diverse inclusio Significant inco	alanders. Non criteria on sistency	Many studies fo and outcomes.	cussed on Despite th	individual risk fac e number of stud	ctors (e.g. premati	urity, cigarette a few studies	
	ni/ action nav					0 15	<u> </u>	
Evidence statement Gestational age less than 37 weeks; chronological age at p	presentation les	s than 10 ·	weeks; postnata	l exposure	to cigarette	Quanty	of evidence	
smoke; breast feeding for less than two months; failure to should all be considered as risk factors for more serious i		of indigen	ous origin; havi	ng chronic	lung disease	I	LOW	
Judging the benefits in context Benefit of ensuring clinicians think about the management	nt more careful	lv in those	thought to be	at high risk	No harms in an	nlving this		
4. What harm might the proposed intervention			thought to be	at ingii iisi		piying tins.		
Evidence statement						Quality	of evidence	
Clinicians should consider the presence of any of the risk	factors when a	making ma	anagement deci	sions in int	ants with			
bronchiolitis. Judging the harms in context						1	LOW	
No harms.								
5. What is the likely balance between good a	ind harm?							
Evidence statement Reducing discharge of infants likely to deteriorate must b	e weighed again	nst the risk	xs of inpatient l	nospital sta	у.	quality	verall of evidence LOW	
Judging the balance of benefits and harms in contex	t					•		
Benefits clearly outweigh harms	Recommend	l				STRONG		
Benefits probably outweigh harms	Consider					CONDITIONAL		
Not known	Make a recor	mmendati	on for research	(see 8 belo	ow)	WEAK		
Benefits probably don't outweigh harms						0.01 10 100		
Harms probably outweigh benefits	Consider aga	unst				CONDITIO	ONAL	
Benefits clearly don't outweigh harms						07770 00 1 0		
Harms clearly outweigh benefits	Recommend	l against				STRONG		
6. Is the intervention/action implementable	in the New Z	ealand ar	nd Australian o	context?				
Summary statement								
Implementable in Australia and New Zealand. Yes			D 1 /					
			Recommend/					
Not known			Consider econo					
No		1	Recommend/co	msider aga	mist			
7. Final recommendation	1 1 1	• •			0, 1, 6			
Clinicians should consider; gestational age less than 37 we 10 weeks; postnatal exposure to cigarette smoke; breas thrive; having chronic lung disease; being an indigenous and should take these into account when managing infant	st feeding for infant all as ris	less than sk factors	two months; f	ailure to	Strength of re STRONG CONDITION WEAK	commendation		
8. Recommendations for research								
Large cohort studies are needed to define the relative risk	of particular f	actors and	to define subp	opulations	with increased ris	sk or other risk fa	ctors.	

Question 2: Question 2: In infants presenting to hospital with bronchiolitis for admission or severe disease (e.g. prolonged hospital stay, ICU admission	Evidence table ref: Al-Sheri 2005, Alvarez 2013, Bailey 2009 Bradley 2005, Brand 2012, Chan 2002, Chatzimichael 2007, Corneli 2012, Craig 2008, Damore2008, DiFranza 2012, Figueras 2004, Garcia 2010, Gouyon 20 Hasegawa 2015, Helfrich 2015, Holman 2003, Marlais 2011, Papoff 2011, Sala 2015, Somech 2006, Stagliano 2015, Trefny 2000, Voets 2006 (14-37).				
1. Evidence base (number of studies, level of evidence and risk of bias in the included studies,)				
Twenty two observational studies and two matched case control studies provided a diverse patient population and methods, but provide consistent outcomes. Two observational studies included indigenous Australians and New Zealanders. Many studies focussed on individual risk factors (e.g. prematurity,	A B	Level II studies with	I studies with a low risk of bias, or SR/several		
cigarette smoke exposure, chronological age at presentation) with diverse inclusion criteria and outcomes. Despite the number of studies there are only a	С		II studies with a low risk of bias or Level I or		
few studies supporting each risk factor, but most findings were consistent. Significant inconsistency was demonstrated in the role of RSV infection as a risk factor.	D	Level IV studies o risk of bias	r Level I to III studies/SRs with a high		
2. Consistency (if only one study was available, rank this component as 'not applicable')					
Some inconsistency in outcome measures and patient populations making comparison across studies difficult.	А	All studies consister	nt		
	В	Most studies consis	tent and inconsistency can be explained		
	С	Some inconsistency, reflecting genuine uncertainty around question			
	D	Evidence is not consistent			
	NA	Not applicable (one	study only)		
3. Clinical impact (indicate if the study results varied according to some unknown factor (not not be determined)	simply stud	ly quality or sample size)	and thus the clinical impact of the intervention could		
Risk factors for more severe disease in bronchiolitis are elucidated and will help clinicians make informed decisions.	А	Very large			
	В	Substantial			
	С	Moderate			
	D	Slight/Restricted			
4. Generalisability (how well does the body of evidence match the population and clinical setti	ings being ta	rgeted by the guideline?)			
Should be generalisable but study populations were heterogeneous.	А		eneralisable to target population		
	В	caveats	eneralisable to target population with some		
	С	could be sensibly			
	D	to judge whether se			
5. Applicability (is the body of evidence relevant to the Australian/New Zealand healthcare	context in to	erms of health services / c	lelivery of care and cultural factors?)		
	А	healthcare context	oplicable to Australian/New Zealand		
	В	context with few c			
	С	healthcare context v			
	D	Evidence not applicable to Australian/New Zealand healthcare context			

Component	Rating	Description					
1. Evidence base	D	Level	IV studies o	or Level I to III studies/SRs with a high risk of bias			
2. Consistency	С	Some	inconsisten	cy, reflecting genuine uncertainty around question			
3. Clinical Impact	С	Moder	ate				
 Generalisability 	С	Evider	nce not dire	ctly generalisable to target population but could be sensibly applied			
5. Applicability	В	Evider	ice applical	ble to Australian/New Zealand healthcare context with few caveats			
settings and should guide I	practice with consider	ation to l			and New Zealand		
RECOMMENDATION				OVERALL GRADE OF RECOMMENDATION			
the guideline development group action statements where possible		Use	А	Body of evidence can be trusted to guide practice			
unon sidiemenis where possible	<i>\$</i>)		В	Body of evidence can be trusted to guide practice in most situation			
Clinicians should consider; gestational age less than 37 weeks; chronological age at presentation			С	Body of evidence provides some support for recommendation should be taken in its application			
less than 10 weeks; post			D	Body of evidence is weak and recommendation must be applied with	ith caution		
smoke; breast feeding for failure to thrive; having of being an indigenous infa more serious illness and account when managing bronchiolitis.	chronic lung disease ant all as risk factors should take these in	e; s for	рр	Practice Point			
UNRESOLVED ISSUE	S (If needed, keep a note	of specific i	ssues that ari	ise when each recommendation is formulated and that require follow up)			
about this. This information we Will this recommendation Currently little adrenaline/	ill be used to develop the a result in changes in u	<i>implementa</i> sual care?	tion plan for	ate yes or no to the following questions. Where the answer is yes, please provide ex the guidelines) Australia and New Zealand, this is in contrast to North American	planatory information YES NO		
practice.							
Are there any resource implications associated with implementing this recommendation?				is recommendation?	YES		
the there any resource imp					NO		
file there any resource inf							
	f this recommendatio	n require	changes in	the way care is currently organised?	YES		
	f this recommendatio	n require	changes in	the way care is currently organised?	YES NO		
Will the implementation o		Ŷ		the way care is currently organised? mentation of this recommendation?			

Question 3.	FRADE E	vidence	Summa	ary			
	Considere	d Judgmen	t - Strength	of recommer	ndation		
Question 3: In infants presenting to hospita medical management or clinically relevant e		sed with bro	onchiolitis,	does perform	ning CXR b	eneficially ch	ange
1. Outcome measures:	ortance of outo	comein making a decision					
	HIGH	MOD	LOW	V. LOW	Critical	Importan	t Not Important
O1 Diagnostic accuracy				x	x		
O2 Cost savings (without compromise of							
diagnostic accuracy of alternate diagnoses)				X		X	
O3 Indicator for administration of antibiotics				X	X		
O4 Readmission				X		X	
2. Is there is insufficient evidence to	make a reco	ommendatio	n?				
Key data on the clinical utility of CXR in infants including 13 RCTs and three prospective observ retrospective studies); a systematic review and gy Yong et al (42) also including an economic evalu value in typical bronchiolitis, adds cost and incre 3. What benefit will the proposed int	ational studies udeline (10); a ation. Despi ases the risk o	s; Williams en a qualitative r ite the hetero of unnecessar	t al (39), inclu eview of the geneity of th	uding five pros literature (40) le studies, outo	spective obs); two prosp	ervational stud ective observat	ies, one cohort study and two ional studies (41, 42), with a that CXR is not of clinical
Evidence statement For the critical outcome of diagnostic accuracy,	the r e is low a	uality eviden	ce of a reduc	red length of s	stav in those	natients who	Quality of evidence
receive a CXR.	unere is io ii q	unity eviden		ieu iengui or e	ay in alooe	putiento uno	VERY LOW
For the important outcome of cost saving, evide	nce of low au	ality indicate	s that avoidi	ng CXR saves	money		
For the important outcome on indication for ad	Ŷ					propests CXR is	
not useful in confirming the diagnosis of bronch				* *	nee that sug	556515 07111 15	
Judging the benefits in context The evidence is applicable and generalisable to the	ne New Zeala	nd and Aust	ralian health	settings			
4. What harm might the proposed in				settings.			
Evidence statement							Quality of evidence
For the important outcome of readmission rate who had a CXR taken.	there is low	quality evide	ence of impr	oved diagnost	ic accuracy	in the infants	VERY LOW
Judging the harms in context							I
Evidence to date indicates no direct increased ris the majority of studies have only been in mild on							
5. What is the likely balance between			s, and so the	lisk ill severer	iy unwen nn.		
Evidence statement						0	verall quality of evidence
Harms are likely to outweigh benefits. Judging the balance of benefits and harms in	contoxt						VERY LOW
	T						
Benefits clearly outweigh harms	Recomme						STRONG
Benefits probably outweigh harms	Consider						CONDITIONAL
Not known	Make a re	ecommendati	on for resear	rch (see 8 belo	ow)		WEAK
Benefits probably don't outweigh harms	Consider	r against					CONDITIONAL
Harms probably outweigh benefits							
Benefits clearly don't outweigh harms Harms clearly outweigh benefits	Recomme	end against					STRONG
		N 7	1		++)		
6. Is the intervention/action implem	ientable in th	ne mew Zea	iand and At	ustranan cont	lext?		
Summary statement The evidence is implementable in Australia and	New Zealand						
Yes			Recomm	nend/conside	er		
Not known				economic eva			
No			Recomme	end/consider :	against		
7. Final recommendation							
Routine CXR does not improve management in to treatments of no benefit.	infants preser	nting with sir	nple bronchi	olitis, and may	-	Strength of re STRONG CONDITION WEAK	commendation
Recommendation for research							
Studies on children with more severe bronchioli	tis are needed	to define the	e role of CXI	R in this popu	lation.		

Question 3. NHMRC Evidence Sur	nmary	,				
Question 3. In infants presenting to hospital or hospitalised with bronchiolitis, does performing CXR Evidence table ref: beneficially change medical management or clinically relevant end-points? Bordley 2004, Caiulo 2011, Farah 2 Kern 2001, Kneyber 2001, Offer 20 Quintero 2007, Ricci 2015, Schuh 2 Williams 2012, Yong 2009 (10, 38-4) 158).						
1. Evidence base (number of studies, level of evidence and risk of bias in the incl	uded stud	ies)				
Key data on the clinical utility of CXR in infants presenting to or admitted to	А		I studies with a low risk of bias, or several			
hospital with bronchiolitis comes from two systematic reviews (Bordley et al (38), including 13 RCTs and three prospective studies; Williams et al (39),		Level II studies with One or two Level II	a low risk of bias studies with a low risk of bias, or SR/several			
including five prospective observational studies, one cohort study and two	В	Level III studies wit	h a low risk of bias			
retrospective studies); a systematic review and guideline (10); a qualitative review of the literature (40); two prospective observational studies (41, 42), with	С	One or two Level II II studies with mode	I studies with a low risk of bias or Level I or erate risk of bias			
Yong et al (42) also including an economic evaluation. Despite the heterogeneity of the studies, outcomes consistently confirm that CXR is not of clinical value in typical bronchiolitis, adds cost and increases the risk of unnecessary antibiotic use.	D	Level IV studies or Level I to III studies/SRs with a high risk of bias				
2. Consistency (if only one study was available, rank this component as 'not appli	icable')					
Evidence regarding the use of CXRs is not consistent, due to the heterogeneity of the studies.	А	All studies consisten	ıt			
Outcomes from Bordley et al (38) suggests that in mild disease, CXRs offer no information that is likely to affect treatment and should not routinely be	В	Most studies consistent and inconsistency can be explained				
performed. Data from two studies (41, 42) demonstrate that CXRs may lead to the use of	С	Some inconsistency, reflecting genuine uncertainty around question				
antibiotics. Therefore more likely to be inappropriate use than to improve clinical outcomes and insufficient data exists to show that CXR films reliably distinguish between viral and bacterial disease or predict severity of disease.	D	Evidence is not co	nsistent			
Yong et al (42) concludes that for infants with typical bronchiolitis, omitting radiography is cost saving without compromising diagnostic accuracy of alternate diagnoses and of associated pneumonia.	NA	Not applicable (one study only)				
Schuh et al (41) suggests that radiographs in children with typical bronchiolitis						
have limited value in children without severe distress or significant hypoxia. 3. Clinical impact (indicate if the study results varied according to some unknown factor (not simply study quality or sample size) and thus the clinical						
of the intervention could not be determined) That radiographs in children with typical bronchiolitis have no proven value in A Very large						
children with bronchiolitis outside the ICU setting, and may lead to treatments						
that are of no benefit.	В	Substantial				
	С	Moderate				
	D	Slight/Restricted				
4. Generalisability (how well does the body of evidence match the population an	d clinical s	0 0 0				
Studies were conducted in a number of countries including the USA, Canada, Europe and Israel using populations that are directly generalizable to patients	Α	Evidence directly	generalisable to target population			
with bronchiolitis seen in Australia and New Zealand.	В	Evidence directly ge caveats	neralisable to target population with some			
	С	Evidence not directl be sensibly applied	ce not directly generalisable to target population but could ibly applied			
	D	Evidence not directl to judge whether ser	y generalisable to target population and hard nsible to apply			

						<u> </u>		
•• • •	y of evidence relevant to	o the Australi	ian/New Zealan	id healthcar	e context in terms of health services / delivery of care an	1d cultural		
factors?)					Eniderra director continution According (Norm Zoole			
The results are applicable to the Australian and New Zealand health care context with few caveats.			А	Evidence directly applicable to Australian/New Zeala healthcare context	na			
				В	Evidence applicable to Australian/New Zealand healthcar context with few caveats			
				С	Evidence probably applicable to Australian/New Zeal	land		
				C	healthcare context with some caveats			
					Evidence not applicable to Australian/New Zealand healthcare context			
Other factors (indicate here a	any other factors that you too	k into account	when assessing the	evidence base	(for example, issues that might cause the group to downgrade or up	bgrade the		
recommendation)			0			0		
EVIDENCE STATEME	NT MATRIX (summa	rise the devel	opment group's	synthesis o	f the evidence relating to the key question, taking all the	above		
factors into account)	× ×							
Component	Rating 1	Description						
1. Evidence base	D 1	Level IV stu	dies or Level I	to III stud	ies/SRs with a high risk of bias			
2. Consistency	D 1	Evidence is	not consistent					
3. Clinical Impact	C 1	Moderate						
4. Generalisability			rectly generalis					
5. Applicability	B	Evidence ap	oplicable to Au	stralian/N	ew Zealand healthcare context with few caveats			
Evidence statement	diagnostic accuracy, the	re is low qual	ity evidence of a	reduced le	ngth of stay in those patients who receive a CXR.			
For the chucal outcome of	diagnostic accuracy, the	te is low quai	ity evidence of a	i reduced ie	light of stay in those patients who receive a CAR.			
For the important outcome	of cost saving, evidence	e of low quali	ty suggests that	avoiding C	KR saves money			
For the important outcome diagnosis of bronchiolitis, a				is low qual	ty evidence that suggests CXR is not useful in confirmi	ng the		
RECOMMENDATION the guideline development group d				OVERA	LL GRADE OF RECOMMENDATION			
action statements where possible)		A	Body of	of evidence can be trusted to guide practice				
		В			vidence can be trusted to guide practice in most situations			
Routine CXR does not improve management in Body of				of evidence provides some support for recommendations(s) but care should be				
					in its application			
			Body of	evidence i	idence is weak and recommendation must be applied with caution			
		PI						
UNRESOLVED ISSUES	(If needed, keep a note of s	becific issues the	at arise when each w	recommendati	on is formulated and that require follow up)			
					g questions. Where the answer is yes, please provide explanatory in	formation		
about this. This information will be used to develop the implementation plan for the guidelines)								
Will this recommendation result in changes in usual care?					YES			
Some clinicians are currently using routine CXR.					NO			
Are there any resource implications associated with implementing this recommendation?					YES			
					NO			
Will the implementation of this recommendation require changes in the way care is currently organised?					v organised? YES			
					NO			
Are the guideline development group aware of any barriers to implementation of this recommendation?								
The the Suideane development group aware of any barners to implementation of this recommendation;								
1					NO			

Question 4.

GRADE Evidence Summary

Consi	Considered Judgement - Strength of recommendation							
Question 4: In infants presenting to hospital and hospitalized with bronchiolitis, does performing pathology tests (blood and urine) beneficially								
change medical management or clinically relevant e 1. Outcome measures:	na points.	Quality of	nportance of ou in making a deci	portance of outcome				
	HIGH	MOD	LOW	V. LOW	Critical	Important	Not Important	
O1 Length of stay				x	x		1	
O2 Length of stay in ICU				x		x		
O ₃ Death in ICU				x		x		
O4 Diagnosis of bacterial co-infection				x		x		
O5 Diagnosis of pneumonia				x		x		
O6 Diagnosis of UTI		x				x		
2. Is there is insufficient evidence to make a	recommenda	tion?		1				
Evidence statement Evidence for diagnostic testing comes from a systema indications for testing or the impact of testing on patient Subsequent studies have indicated some risk of UTI in y	outcomes.	(47).	ied 82 studie	es. Bordley e	t al (38) found	l that studies did	not define clear	
3. What benefit will the proposed intervention Evidence statement	on/action hav	e:					of evidence	
There is evidence from two cohort studies, one prospective and one retrospective, demonstrating that in febrile infants with a diagnosis of bronchiolitis, one from 2-12 months of age and the other in infants less than eight weeks (with RSV positive bronchiolitis) that the rate of UTI is 2% and 1.4% respectively. Another study with low evidence rating demonstrated that in febrile infants under 60 days of age with a diagnosis of bronchiolitis, the rate of UTI was 3.3%. There is very low quality and inconsistent evidence that procalcitonin can predict the presence of co-infection in an infant with bronchiolitis. The clinical role of procalcitonin is yet to be defined. With regards to length of stay, there was one study demonstrating that length of stay is not affected by measurement of CRP.							LOW	
Judging the benefits in context This is applicable to infants in Australia and New Zealan								
4. What harm might the proposed interventi	on/action do	r					• •	
Evidence statement Evidence has not suggested any adverse harm in children having a urine sample tested for UTI. There is a theoretical risk there will be false positives and therefore unnecessary antibiotics given. The evidence for doing blood tests to look for co-infection is very low and of unknown clinical importance.							Quality of evidence LOW	
There is pain and discomfort associated with blood tests	and invasive u	rine testing.		*				
Judging the harms in context For otherwise well febrile children with bronchiolitis the	harms of blood	d testing and	urine testing	probably ou	tweigh the ben	efits.		
5. What is the likely balance between good a	and harm?							
Evidence statement It is likely that testing urine in infants with bronchiolitis will not cause any harm, but needs to be confined to the patients at highest risk.							verall of evidence .OW	
Judging the balance of benefits and harms in context The benefits are likely to outweigh the harm								
Benefits clearly outweigh harms	Recommend	1	STRONG					
Benefits probably outweigh harms	Consider					CONDITI	ONAL	
Not known Make a recommendation for research (see 8 below)							WEAK	
Benefits probably don't outweigh harms	Consider a	ainst				CONDITI		
Harms probably outweigh benefits							UINAL	
Benefits clearly don't outweigh harms	Decommond							
Harms clearly outweigh benefits	Recommend against							
6. Is the intervention/action implementable in the New Zealand and Australian context?								
Summary statement								
Yes Recommend/consider								
Not known	for known Consider economic evaluation							
No Recommend/consider against								

7. Final recommendation							
There is no role for blood tests in managing infants presenting to hospital and hospitalised with	Strength of recommendation						
bronchiolitis. Routine bacteriological testing of urine or blood is not indicated. STRONG							
	CONDITIONAL						
In infants less than 2 months of age who are hospitalised or in hospital for bronchiolitis with a WEAK							
temperature over 38 degrees, there is a low risk of UTI. If clinical uncertainty exists clinicians							
may consider collecting a urine sample for microscopy, culture and sensitivity looking for the							
concurrent presence of UTI.							
8. Recommendations for research							

More research needs to look into whether febrile (greater than 38°C) infants (less than or equal to 12 months) with a clear diagnosis of bronchiolitis have a concurrent UTI as this not only has implications for immediate treatment but also for further imaging of the urinary tract.

Research on the clinical role of new markers of bacterial infection is needed to define any role for them in the clinical environment.

Question 4. NHMRC Evidence Summary

Question 4: In infants presenting to hospital and hospitalized with bronchiolitis, does performing Evidence table ref:							
blood tests (blood and urine) beneficially change medical managemen	ically relevant end	Bordley 2004, Dayan 2004, Elkhunovich					
points?			2015, Fares 2011, Laham 2014, Luu 2013,				
		Ralston 2011, Ricci 2015, Titus 2003 (10, 38, 43, 48, 150)					
38, 43-48, 159). 1. Evidence base (number of studies, level of evidence and risk of bias in the included studies)							
Evidence for diagnostic testing comes from a systematic review (38) that	А	A One or more Level I studies with a low risk of bias, or seve					
identified 82 studies. They found that studies did not define clear indications for	11	Level II studies with	*				
testing or the impact of testing on patient outcomes.	В	One or two Level II s	studies with a low risk of bias, or SR/several				
		Level III studies with					
A systematic review and Guideline (10) recommends against routine diagnostic	С		or two Level III studies with a low risk of bias or Level I or				
testing.		II studies with moder	rate risk of bias				
Studies assessing the incidence of UTI in infants hospitalised with bronchiolitis included a systematic review of infants under 90 days of age with bronchiolitis (46) including 11 studies (6 prospective and 5 retrospective) a prospective cohort study of infants with bronchiolitis between 2 and 12 months of age (47).	D	Level IV studies or Level I to III studies/SRs with a high risk of bias					
2. Consistency (if only one study was available, rank this component as 'not appl	icable')						
In the studies looking at urine, different age groups were looked at – less than 60days (48), less than 8 weeks (159) and 2-12 months (47).	А	All studies consistent					
In the studies looking for bacterial co infection using blood tests, one study looked at procalcitonin and one looked CRP, FBC and ESR and therefore no	В	Most studies consistent and inconsistency can be explained					
comment can be made on consistency.	С	Some inconsistency	, reflecting genuine uncertainty around				
		question					
	D	Evidence is not consi	istent				
	NA	Not applicable (one s	study only)				
3. Clinical impact (indicate if the study results varied according to some unknown factor (not simply study quality or sample size) and thus the clinical impact of the intervention could not be determined)							
There is moderate evidence from two cohort studies, one prospective and one retrospective, demonstrating that in febrile children with a diagnosis of	А	Very large					
bronchiolitis, one from 2-12 months of age and the other in infants less than 8 weeks (with RSV positive bronchiolitis) that the rate of UTI is 2% and 1.4%	В	Substantial					
respectively. Another study with low evidence rating demonstrated that in	С	Moderate					
febrile children under 60 days of age with a diagnosis of bronchiolitis, the rate							
of UTI was 3.3%.	D	Slight/Restricted					
There is moderate evidence that blood tests do not impact clinical outcomes		Ŭ					
There is moderate evidence that blood tests do not impact clinical outcomes. 4. Generalisability (how well does the body of evidence match the population and clinical settings being targeted by the guideline?)							
They are mainly applicable to this guideline.	А	Evidence directly gen	neralisable to target population				
		Evidence directly generalisable to target population with some caveats					
		Evidence not directly generalisable to target population but could be sensibly applied					
	D	Evidence not directly to judge whether sense	generalisable to target population and hard sible to apply				

5. Applicability (is the body of evidence relevant to the Australian/New Zealand healthcare context in terms of health services / delivery of care and cultural factors?)							
Study outcomes are applicable in Australia and NZ			А	Evidence directly applicable to Australian/M healthcare context	New Zealand		
				В	Evidence applicable to Australian/New context with few caveats	Zealand healthcare	
					С	Evidence probably applicable to Australian, healthcare context with some caveats	/New Zealand
					D	Evidence not applicable to Australian/New context	v Zealand healthcare
Other factors (indicate here downgrade or upgrade the re		at you to	ook into acco	ount when as	ssessing the	e evidence base (for example, issues that migh	nt cause the group to
In the study designs on meas	suring urines, it is no			y how broncl	hiolitis was	diagnosed and therefore the question arises a	as to whether the
children had a primary diagn	osis of bronchiolitis	or UTI.					
EVIDENCE STATEMEN factors into account)	NT MATRIX (sumn	narise th	ne developm	ent group's s	synthesis of	f the evidence relating to the key question, tak	king all the above
Component	Rating	Descr	ription				
1. Evidence base	D			r Level I to I	III studies/	SRs with a high risk of bias	
2. Consistency	С					ncertainty around question	
3. Clinical Impact	С	Mode	rate		0		
4. Generalisability	В	Evide	nce directly	generalisable	to target p	opulation with some caveats	
5. Applicability	В					are context with few caveats	
Evidence statement There is evidence from two cohort studies, one prospective and one retrospective, demonstrating that in febrile infants with a diagnosis of bronchiolitis, one from 2-12 months of age and the other in infants less than 8 weeks (with RSV positive bronchiolitis) that the rate of UTI is 2% and 1.4% respectively. Another study with low evidence rating demonstrated that in febrile infants under 60 days of age with a diagnosis of bronchiolitis, the rate of UTI was 3.3%. There is no consistency of the evidence relating to blood tests with a systematic review highlighting that there has been no evidence to suggest benefit to clinically relevant outcomes There is very low quality and inconsistent evidence that procalcitonin can predict the presence of co-infection in an infant with bronchiolitis. The clinical role of procalcitonin is yet to be defined. Regarding length of stay, one study demonstrated that length of stay is not affected by measurement of CRP. RECOMMENDATION (Wbat recommendation(s) does the guideline development group draw from this evidence? Use action statements where possible) There is no role for blood tests in managing infants presenting to hospital and hospitalized with bronchiolitis.							
UTI. If clinical uncertainty exists clinicians may consider collecting a urine sample for microscopy, culture and sensitivity looking for the concurrent presence of UTI.					actice Point arise when each recommendation is formulated and that require follow up)		
UNKESULVED ISSUES	(11 needed, keep a no	ne or sp	ectric issues	that arise wi	ien each fe	commendation is formulated and that require	e tonow upj
IMPLEMENTATION OF RECOMMENDATION (Please indicate yes or no to the following questions. Where the answer is yes, please provide							
explanatory information about this. This information will be used to develop the implementation plan for the guidelines)							
Will this recommendation result in changes in usual care?							YES
						NO	
Are there any resource implications associated with implementing this recommen-					dation?		YES
							NO
Will the implementation of this recommendation require changes in the way care					is currently	organised?	YES
							NO
Are the guideline development group aware of any barriers to implementation of t					this recom	mendation?	YES
						NO	
							110

Question 5. GRADE Evidence Summary

	sidered Judgem	,	,					
Question 5. In infants presenting to hospital or ho	-	bronchioliti	is, does perf	orming vire	ological investi	gations benefici	ally change	
nedical management or clinically relevant end-point of the second	intsr	Quality of		nportance of out n making a deci				
	HIGH	MOD	LOW	V. LOW	Critical	Important	Not Important	
O1 Hospital Admission			X		X			
O2 Hospital Length of stay			Х			Х		
O3 ICU admission			X		Х			
O ₄ Death			N/A		X			
2. Is there is insufficient evidence to make	a recommenda	ition?						
Evidence statement Systematic review (38) reviewed 82 trials (17 reports on bronchiolitis and found no clear indications for testing study results at 12 hours does not influence clinical care panels and outcomes with inconsistent results about th and outcome measures but studies consistently show la virus (RSV). A systematic review and guideline (10) rec	nor impact on cl e over knowledge e influence of RS ck of influence o ommends agains	linical outcor e at four wee SV on disease on clinician n t routine vira	nes. An RCT ks. Eight pro e severity or h nanagement, o	(56) has sul ospective ob ospital leng	osequently show servational stud th of stay. There	n that clinician kr ies have looked at is heterogeneity	nowledge of viral a variety of viral of study design	
3. What benefit will the proposed intervent	tion/action hav	e?						
Evidence statement: No clinical benefit has been demonstrated.							of evidence LOW	
Judging the benefits in context Cost savings and reduction in discomfort. 4. What harm might the proposed interven	tion/action do	>						
Evidence statement	action do	•				Quality of e	vidence	
Potential for hospital acquired infection.							LOW	
Judging the harms in context No evidence of increased hospital acquired infections,	and simple mean	s to limit so	ead exist					
5. What is the likely balance between good	1	is to mint spi	eact chist.					
Evidence statement Benefits of limiting viral testing outweigh harms.						quality	verall of evidence .OW	
Judging the balance of benefits and harms in conte	ext							
Benefits clearly outweigh harms	Recommend	1				STRONG	STRONG	
Benefits probably outweigh harms	Consider					CONDITIONAL		
Not known	Make a reco	mmendation	for research	(see 8 below	v)	WEAK	WEAK	
Benefits probably don't outweigh harms	— Consider a	rainet				CONDITI	ONAI	
Harms probably outweigh benefits	Consider a	gailist				CONDIN	OTTAL	
Benefits clearly don't outweigh harms	Recommend	l against				STRONG		
Harms clearly outweigh benefits		Ũ						
6. Is the intervention/action implementab	le in the New Z	Lealand and	Australian o	context?				
Summary statement Fully implementable in Australia and New Zealand.								
Yes			commend/o					
	Not known Consider economic evaluation							
No Final common dation		Ke	commend/co	onsider agair	1Sť			
7. Final recommendation		a da d C		I	Stars 1			
In infants with bronchiolitis, routine use of viral testing is not recommended for any clinically relevant end-points, including cohorting of bronchiolitis patients. STRONG CONDITIONA WEAK								
8. Recommendations for research								
Research to determine if patient cohorting on virologic	al results improv	es hospital tr	ransmission n	nore than ap	propriate conta	ct precautions is v	warranted.	

Question 5.		NHMRC Evidence Su	mmar	у					
virological investigations	beneficially chan	al or hospitalised with bronchio ge medical management or clini	Evidence table ref: Bamberger 2012, Baumer 2007, Bordley 2004, Brand 2012, Friedman 2003, Garcia- Garcia 2006, Huijskens 2012, Mackie 2001, Mansbach 2012, Nascimento 2010, Ralston 2014, Ricart 2013, Ricci 2015, Wishaupt 2011, Yu 2010 (10, 13, 18, 38, 49-57, 66, 160)						
1. Evidence base (number of	f studies, level of evider	nce and risk of bias in the included studie.	s)						
Systematic review (38) revie			А		studies with a low risk of bias, or several				
		r testing nor impact on clinical vn that clinician knowledge of		Level II studies with One or two Level II	a low risk of bias studies with a low risk of bias, or SR/several				
viral study results at 12 hour	rs does not influend	e clinical care over knowledge at	В	Level III studies with	h a low risk of bias				
		udies have looked at a variety of sults about the influence of RSV	С		II studies with a low risk of bias or Level moderate risk of bias				
1	tal length of stay. A nagement, or impre	ll have consistently shown lack	D	Level IV studies or Level I to III studies/SRs with a high risk of bias					
1 0, (,	e, rank this component as 'not appl	icable')						
Results are not consistent ar	,								
consistent.	,		А	All studies consisten	t				
			В	Most studies consiste	ent and inconsistency can be explained				
			С	Some inconsistency, reflecting genuine uncertainty around question					
			D	Evidence is not consistent					
			NA	Not applicable (one	study only)				
3. Clinical impact (indicate of the intervention could not		s varied according to some unknow	n factor (not simply study quality	y or sample size) and thus the clinical impact				
Varied results and in consist			А	Very large					
			В	Substantial					
			C	Moderate					
			D	Slight/Restricted					
4. Generalisability (how w	ell does the body o	f evidence match the population ar	nd clinical	settings being targeted	by the guideline?)				
Population consistent with	Australasian popula	tion.	А	Evidence directly generalisable to target population					
			В	Evidence directly generalisable to target population with some caveats					
			С		y generalisable to target population but could				
			D	Evidence not directly generalisable to target population and hard					
5 Applicability (is the hade	of anidom co relevant to	the Australian/New Zealand healthcare		to judge whether sen	11 ?				
Applicable.	oj evidence relevani lo l	ne Austratian/ iNew Zeatana heatthcare	context in		plicable to Australian/New Zealand				
Applicable.			А	healthcare context	•				
			В	Evidence applicable context with few ca	le to Australian/New Zealand healthcare				
			С	Evidence probably a	pplicable to Australian/New Zealand				
				healthcare context w Evidence not applic	able to Australian/New Zealand healthcare				
		· · · · · · · · · · · · · · · · · · ·	D	context					
Other factors (indicate here a recommendation)	my other factors that y	ou look into account when assessing the e	vidence basi	e (for example, issues that n	night cause the group to downgrade or upgrade the				
EVIDENCE STATEME	NT MATRIX (sur	nmarise the development group's s	synthesis o	of the evidence relating	to the key question, taking all the above				
Component	Rating	Description							
1. Evidence base 2. Consistency	C C	One or two Level III studies w Some inconsistency, reflecting			r II studies with moderate risk of bias tion				
3. Clinical Impact	C	Moderate	t	acana ques					
4. Generalisability	B	Evidence directly generalisable							
5. Applicability Evidence statement	В	Evidence applicable to Austral	ian/New	Zealand healthcare con	text with few caveats				
	viral testing does no	ot improve or change clinical care,	and incon	sistent about the link to	o severity of disease, so cannot recommend				

RECOMMENDATION (What recommendation(s) does	OVER	ALL GRADE OF RECOMMENDATION						
the guideline development group draw from this evidence? Use	А	A Body of evidence can be trusted to guide practice						
action statements where possible)	В	Body of evidence can be trusted to guide practice in most situations						
In infants with bronchiolitis, routine use of viral	С	ndations(s) but care						
testing is not recommended for any clinically	D	Body of evidence is weak and recommendation must be applied with caution						
relevant end-points, including cohorting of bronchiolitis patients.	РР	Practice Point						
UNRESOLVED ISSUES (If needed, keep a note of specific	UNRESOLVED ISSUES (If needed, keep a note of specific issues that arise when each recommendation is formulated and that require follow up)							
explanatory information about this. This information wi	ll be used t	ndicate yes or no to the following questions. Where the answer is to develop the implementation plan for the guidelines)	s yes, please provide					
Will this recommendation result in changes in usual care	:?		YES					
A number of sites currently undertake viral testing.			NO					
Are there any resource implications associated with impl			YES					
Test resource savings if implemented. Increased resource	ce usage if	increased hospital transmission and infection.	NO					
Will the implementation of this recommendation require	e changes i	n the way care is currently organised?	YES					
Varies according to site.			NO					
Are the guideline development group aware of any barrie			YES					
Cohorting practices exist in some sites based on the resu	ult of viral	testing.	NO					

Question 6.

Consid	dered Judgem	ient - Streng	gth of recom	mendatior	l				
Question 6: For infants presenting to hospital or hospital	ised with bron	chiolitis, doe	s use of a bro	onchiolitis s	coring system be	eneficially change	medical		
management or clinically relevant end-points?					Ir	nportance of out	come		
1. Outcome measures:		Quality of	evidence	V.		n making a deci	sion		
	HIGH	MOD	LOW	Important	Not Important				
O1 Length of stay				X		Х			
O2 Inter rater Agreement				х		Х			
O ₃ Score Reliability				х		Х			
O ₄ Useful Predictor				х		Х			
2. Is there is insufficient evidence to make a	recommenda	tion?							
The evidence is based on eight prospective observational scoring systems (including Kristjansson Respiratory Score Respiratory Distress Assessment Instrument (RDAI) and identified clinical parameters as a scoring system). Limita settings and varied use/comparison of multiple scoring sy 3. What benefit will the proposed intervention Evidence statement For the important outcome of score reliability, there is le of two scoring systems for the assessment of severity in h	e, modified Wo the Children's tions to the stu ystems across t on/action hav	ood's Clinical Hospital of adies include he 8 studies. e?	Asthma Sco Wisconsin R d low numbe	re (M-WCA espiratory S r of patient	and Tal Seve core (CHWRS) s; single centre b	rity Score, modifie in addition to the ased studies, unic Quality	ed Tal, use of specific ue clinical of evidence		
of two scoring systems for the assessment of severity in bronchiolitis. VERY LOW For the important outcome of useful predictor, there is low quality evidence from two studies which demonstrates a correlation between score and severity of illness. Judging the benefits in context									
4. What harm might the proposed interventi	on/action do	?							
Evidence statement For the important outcome of score reliability there is low admission or escalation of care. Application of these score					requiring	Quality of e	vidence RY LOW		
Judging the harms in context Due to minimal evidence, there are no indicators that a sp and observations when assessing, admitting or dischargin 5. What is the likely balance between good a	g a child from					l recording of oxy	gen saturation		
	inu nann:								
Evidence statement The benefits are not likely to outweigh the harm.						quality	Overall quality of evidence VERY LOW		
Judging the balance of benefits and harms in contex Until further studies are conducted, the use of a scoring s		t change me	dical manage	ment or clir	ically relevant e	adnoints			
	Recommend	8	anour munugo.	inclut of chi	ically relevant e	STRONG			
Benefits probably outweigh harms	Consider					CONDITIO	ONAL		
Not known	Make a rec	ommendati	on for resea	rch (see 8 l	pelow)	WEAK			
Benefits probably don't outweigh harms									
Harms probably outweigh benefits	Consider ag	ainst				CONDITIO	ONAL		
Benefits clearly don't outweigh harms									
Harms clearly outweigh benefits	Recommend	l against	STRONG						
6. Is the intervention/action implementable	in the New Z	ealand and	Australian o	context?					
Summary statement Current Bronchiolitis scoring systems do not change med	lical manageme	0	2	1	oints.				
Yes Recommend/consider									
	Not known Consider economic evaluation No Recommend/consider against								
No 7 Final manufaction		Ке	commend/co	msider agai	ust				
7. Final recommendation 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. Strength of recommendation STRONG CONDITIONAL									
8. Recommendations for research					WEAK				
Further research is needed to derive and validate a bronch populations, and that has significance for patient centred		system for in	nfants diagno	sed with br	onchiolitis that i	s generalisable for	r different		

Question	Đ.

NHMRC Evidence Summary

Question 6: For infants presenting to hospital or hospitalised with bronchi	,		Evidence table ref:		
bronchiolitis scoring system beneficially change medical management or c	elevant end-	Chin 2004, Destino 2012, Duarte-Dorado			
points?			2013, Fernandes 2015, Gajdos 2009, Liu 2004, McCallum 2013, Mosalli 2015, Shete		
			2014, Walsh 2006 (58-64, 161-163).		
1. Evidence base (number of studies, level of evidence and risk of bias in the inc	luded stud	ies)	· · · · ·		
Eight prospective observational cohort studies enrolling a total of 594 children					
enrolled and two cross sectional observational studies which enrolled 282	А		I studies with a low risk of bias, or several		
children.	11	Level II studies with	a low risk of bias		
All studies are rated low or unclear for risk of bias.		One or two Level II	studies with a low risk of bias, or SR/several		
All studies are rated low of unclear for fisk of blas.	В	Level III studies with			
	С	One or two Level II	I studies with a low risk of bias or Level I or		
	C	II studies with mode			
	D	Level IV studies or risk of bias	: Level I to III studies/SRs with a high		
		risk of blas			
2. Consistency (if only one study was available, rank this component as 'not appl	licable')	1			
Evidence is inconsistent: There were eight different scoring systems used in the literature:	А	All studies consisten	t		
incluture.					
1. Chin et al (58) - Kristjansson Respiratory Score to Wang Respiratory	В	Most studies consist	ent and inconsistency can be explained		
Score					
 Destino et al (59) - Resp Distress Assessment Instrument and Children's Hospital of Wisconsin Respiratory Score in Bronchiolitis 	С		reflecting genuine uncertainty around		
3. Duarte-Dorado et al (60) - Modified Woods Clinical Asthma Score	0	question			
(M-WCAS) and the Tal et al Severity Score	-	D • 1	•		
4. Liu et al (61) - Clinical Parameters used for score were respiratory	D	Evidence is not co	nsistent		
rate, retractions, dyspnoea and auscultation					
 Modified Resp Distress Assessment Instrument (RDAI) McCallum et al (62) - Comparison of Tal and Modified Tal Scoring 					
5. McCalum et al (62) - Companson of Tai and Modified Tai Scomig Systems	NA	Not applicable (one	study only per topic/tool)		
 Walsh et al (64) - assessment tool used – work of breathing, 		rtot applicable (olie	orady only per topic, tool,		
dehydration and tachycardia					
8. Shete et al (63) - Modified Tal's score and oxygen saturation					
3. Clinical impact (indicate if the study results varied according to some unknow of the intervention could not be determined)	n factor (1	not simply study quality	y or sample size) and thus the clinical impact		
Outcomes of studies concluded that RDAI score may serve as a guide to	А	Very large			
clinician in recognizing categories of patients who may require general or					
intensive care.	В	Substantial			
The Tal and mTal scoring systems were found to be reliable for research and	С	Moderate			
clinical practice in one study.					
Further evaluation is needed to ensure validity and consistency of the other					
scoring systems used in these studies.		Slight/Restricted			
	D				
Regarding predicting admission (59) the CHWRS had a sensitivity of 0.65 and					
specificity of 0.65, while the RDAI is not predictive of disposition. There is a correlation between oxygen saturations and Tals score.					
4. Generalisability (how well does the body of evidence match the population ar	nd clinical	settings being targeted	by the guideline?)		
The studies were conducted in a number of countries using populations that are	Α		generalisable to target population		
directly generalisable to patients with bronchiolitis seen in Australia and New			neralisable to target population with some		
Zealand. One study was conducted in the Northern Territory of Australia and	В	caveats	~ * *		
therefore relative and reflective of the indigenous population present in	С		y generalisable to target population but could		
Australia and New Zealand.		be sensibly applied	y generalisable to target population and hard		
	D	to judge whether ser			
5. Applicability (is the body of evidence relevant to the Australian/New Zealand	l healthcar	e context in terms of h	ealth services / delivery of care and cultural		
factors?)					
The results are probably applicable to the Australian/New Zealand healthcare	1.	Evidence directly an	plicable to Australian/New Zealand		
context.	А	healthcare context	-		
	В		to Australian/New Zealand healthcare		
		context with few cav	yeats y applicable to Australian/New Zealand		
	С	healthcare context			
	D		cable to Australian/New Zealand healthcare		
Other factors (indicate here any other factors that you took into account when assessing the en		context	· 1, ,1 ,. 1 1 · · ·		
Under factors (inducate here any other factors that you took into account when assessing the en-	maence hase	(for example, issues that n	night cause the group to downgrade or upgrade the		

Component	Rating	Desc	ription				
1. Evidence base	D			or Level I to III studies/SRs with a high risk of			
2. Consistency	D		ence is not				
3. Clinical Impact	D		/Restricted				
4. Generalisability	А			y generalisable to target population			
5. Applicability Evidence statement:	С	Evide	nce probab	bly applicable to Australian/New Zealand healthcare contex	t with some caveats		
Australia and New Zeal RECOMMENDATIO does the guideline devel evidence? Use action sta	DN (What recommend lopment group draw fr atements where possibl	om this le)	A B	OVERALL GRADE OF RECOMMEND Body of evidence can be trusted to guide practice Body of evidence can be trusted to guide practice in mo Body of evidence provides some support for recommer	st situations		
For infants presenting			С	taken in its application			
with bronchiolitis, there is insufficient evidence to recommend the use of a scoring system to predict need for admission or hospital length of stay.			D	Body of evidence is weak and recommendation must be applied with caution			
			РР	Practice Point			
				es that arise when each recommendation is formulated and t	hat require follow up)		
Studies compared a range	ge of different scoring	systems, a	nd the opti	mal scoring system is still to be determined.			
				dicate yes or no to the following questions. Where the answ	er is yes, please provide		
Will this recommendation				o develop the implementation plan for the guidelines)	YES		
will this recommendate	on result in changes in	usual care					
					NO		
Are there any resource i	implications associated	with impl	ementing tl	his recommendation?	YES		
					NO		
Will the implementation	n of this recommendati	on require	changes in	the way care is currently organised?	YES		
					NO		

Question 7.

Cons	idered Judgem	ent - Streng	th of recom	mendation			
Question 7: For infants presenting to hospital or he	ospitalised with	n bronchioli	tis, what cri	teria should	be used for saf	e discharge?	
1. Outcome measures:		Quality of		ortance of outcome making a decision			
	HIGH	MOD	LOW	V. LOW	Critical	Important	Not Important
Length of Stay				X	X		
Readmission				X	Х		
2. Is there is insufficient evidence to make	a recommenda	tion?					
Evidence statement The evidence is based on two prospective cohort studie	s (67, 68) condu	cted in over	30 United Sta	ates EDs and	l hospitals and 3	Guidelines (10,	65, 66).
3. What benefit will the proposed intervent	ion/action have	e?					
Evidence statement Quality of evidence For the critical outcome of length of stay there is low quality evidence of identified criteria that should be used for safe VERY LOW For the critical outcome of readmission rate, there is low quality evidence that supports an increase or decrease in the readmission rate of children who have been discharged from hospital with a diagnosis of bronchiolitis using a specific VERY LOW							
discharge criterion.	,		-8		8P		
Judging the benefits in context The evidence is applicable and generalisable to the New	Zealand and Au	ıstralian heal	th settings.				
4. What harm might the proposed intervent			0				
Evidence statement	· 1 · 1.	· 1			·C 1. 1	Quality	of evidence
For the important outcome of readmission rate there criteria which would lead to a reduced length of stay.	is low quality	evidence tha	t supports t	ne use of sp	becific discharge	VER	Y LOW
Judging the harms in context							
5. What is the likely balance between good	and harm?						
Evidence statement The benefits are not likely to outweigh the harm.						quality o	verall of evidence Y LOW
Judging the balance of benefits and harms in conte Benefits clearly outweigh harms.	xt						
Benefits clearly outweigh harms	Recommend	l				STRONG	
Benefits probably outweigh harms	Consider					CONDITIONAL	
Not known	Make a reco	ommendatio	on for resear	ch (see 8 b	elow)	WEAK	
Benefits probably don't outweigh harms	Consider aga	ainst				CONDITIO	DNAL
Harms probably outweigh benefits	00000000000						
Benefits clearly don't outweigh harms	Recommend	against				STRONG	
Harms clearly outweigh benefits		0				oniono	
6. Is the intervention/action implementabl	e in the New Z	ealand and	Australian c	context?			
Summary statement							
Yes Recommend/consider							
Not known Consider economic evaluation							
No		Ree	commend/co	onsider again	st		
7. Final recommendation							
	Oxygen saturations, adequacy of feeding, age (infants younger than 8 weeks), and social support should be considered at the time of discharge as a risk for representation. There is insufficient evidence to recommend absolute discharge griegie for infants attending the ED, or hegoitalised with branchicities CONDITIONAL						
	uie ED, or	nospitalised	with bronchie		WEAK		
8. Recommendations for research		, ,				,	
Research on outcomes of infants with differing levels of	t oxygen saturati	ons and dura	tion of adequ	uate teeding	at the time of dis	charge.	

Question 7.		NHMRC Evidence Su	mmar	у				
For infants presenting to safe discharge?	hospital or hospi	talised with bronchiolitis, what c	riteria sh	ould be used for	Evidence table ref: Baraldi 2014, Baumer 2007, Mansbach 2008, Mansbach 2015, Ricci 2015 (10, 65-68).			
	cohort studies con				e age of two years who were seen in ED or			
All studies are rated low or	0		А	One or more Level I Level II studies with	studies with a low risk of bias, or several a low risk of bias			
			В		studies with a low risk of bias, or SR/several			
			С	One or two Level III studies with a low risk of bias or Level I or II studies with moderate risk of bias				
			D	Level IV studies or risk of bias	Level I to III studies/SRs with a high			
2. Consistency (if only one	e study was availabl	e, rank this component as 'not appl	licable')					
Evidence is inconsistent.			А	All studies consisten	t			
			В	Most studies consiste	ent and inconsistency can be explained			
			С	Some inconsistency, question	reflecting genuine uncertainty around			
			D	Evidence is not consistent				
			NA	Not applicable (one study only per topic/tool)				
of the intervention could no	ot be determined)		vn factor (not simply study quality	y or sample size) and thus the clinical impact			
Outcomes of studies conclu what criteria should be used	ided there is insuff	icient data to demonstrate clearly	А	Very large				
What effectia should be ever	TIOI sare ciocining-		В	Substantial				
			С	Moderate				
			D	Slight/Restricted				
4. Generalisability (how w	ell does the body o	of evidence match the population ar	nd clinical	settings being targeted	by the guideline?)			
		populations that are directly	Α		generalisable to target population			
generalisable to patients wit Zealand.	h bronchiolitis who	o are seen in Australia and New	В	caveats	neralisable to target population with some			
			С	Evidence not directly generalisable to target population but cou be sensibly applied				
			D	Evidence not directly generalisable to target population and hard to judge whether sensible to apply				
5. Applicability (is the bod factors?)	ly of evidence relev	ant to the Australian/New Zealand	d healthcar	re context in terms of h	ealth services / delivery of care and cultural			
	plicable to the Aus	tralian/New Zealand healthcare	А	Evidence directly app healthcare context	plicable to Australian/New Zealand			
			В		to Australian/New Zealand healthcare reats			
			С	Evidence probably	applicable to Australian/New Zealand			
			D	healthcare context with some caveats Evidence not applicable to Australian/New Zealand healthcare				
		that you took into account when a	ssessing th	context ne evidence base (for ex	ample, issues that might cause the group to			
downgrade or upgrade the t	ecommendation)							
EVIDENCE STATEME	NT MATRIX (still	nmarise the development group's synthesis	s of the evide	ence relating to the key quest	tion, taking all the above factors into account)			
Component	Rating	Description						
1. Evidence base	D	Level IV studies or Level I to 1	III studies	/SRs with a high risk of	f			
2. Consistency	N/A	Not applicable (one study only	per topic	:/tool)				
3. Clinical Impact 4. Generalisability	D A	Slight/Restricted Evidence directly generalisable	to target	nonvittion				
5. Applicability	C				hcare context with some caveats			
Evidence statement:	3	=						
	nt evidence of ben	efits to infants with bronchiolitis.						
The evidence is generalisable	le to Australia and	New Zealand.						

The evidence is generalisable to Australia and New Zealand.

RECOMMENDATION (What recommendation(s) does	OVERAL	L GRADE OF RECOMMENDATION						
the guideline development group draw from this evidence? Use	А	A Body of evidence can be trusted to guide practice						
action statements where possible)	В	Body of evidence can be trusted to guide practice in most situations						
	С	Body of evidence provides some support for recommendations(s) b	out care should be					
Oxygen saturations, adequacy of feeding, age	C	taken in its application						
(infants younger than 8 weeks), and social support	D	Body of evidence is weak and recommendation must be applied with	h caution					
should be considered at the time of discharge as a								
risk for representation. There is insufficient								
evidence to recommend absolute discharge	PP	Practice Point						
criteria for infants attending the ED, or								
hospitalised with bronchiolitis.								
UNRESOLVED ISSUES (If needed, keep a note of specific issues that arise when each recommendation is formulated and that require follow up)								
		cate yes or no to the following questions. Where the answer is yes, ple	ase provide					
explanatory information about this. This information will	be used to a	develop the implementation plan for the guidelines)						
Will this recommendation result in changes in usual care	1		YES					
			NO					
Are there any resource implications associated with imple	ementing this	s recommendation?	YES					
			NO					
Will the implementation of this recommendation require	changes in t	he way care is currently organised?	YES					
			NO					
Are the guideline development group aware of any barrie	rs to implen	nentation of this recommendation?	YES					
Knowledge base			NO					

Question 8a. i) GRADE Evidence Summary

Consid	lered Judgem	ent - Streng	th of recom	mendation			
Question 8a i): In infants presenting to hospital or h oral or IV) improve clinically relevant end-points?	ospitalised w	ith bronchio	olitis, does a	dministrat	ion of beta 2 ag	gonists (nebulisa	tion, aerosol,
1. Outcome measures:		Quality of	evidence			nportance of out in making a deci	
	HIGH	MOD	LOW	V. LOW	Critical	Important	Not Important
O1 Rate of hospitalisation	X				X		
O2 Length of stay	X				X		
O3 Rate of readmission				X		X	
O4 Adverse outcomes			X			Х	
2. Is there sufficient evidence to make a reco	mmendation	?					I
Evidence statement The evidence is based predominantly on one systematic r inpatient, 10 outpatient, and 9 mixed inpatient/outpatient change the findings of the review. 3. What benefit will the proposed intervention	t studies (69).	Subsequently					
	n/ action nav	er				0.15	c · 1
Evidence statement For the critical outcomes of rate of hospitalisation and lea affect rate of hospitalisation or length of stay.	ngth of stay the	ere is high qu	uality evidenc	e that beta 2	2 agonists do no	ot	of evidence IIGH
Judging the benefits in context There is a high quality of evidence that routine use of bet benefit.	č		t of infants v	vith bronchi	olitis is not asso	ociated with any cl	inically relevant
4. What harm might the proposed intervention	on/action do	?					
Evidence statement For the important outcome of rate of readmission no evid	dence was avai	lable.				Quality	of evidence
Reporting of adverse effects in the RCTs were exclusively found in the study groups receiving beta 2 agonists and included LOW the following adverse events: tachycardia, hypertension, decreased oxygen saturation, flushing, hyperactivity, prolonged							
cough, and tremor. Furthermore, adverse effects of beta 2 Judging the harms in context While the majority of the adverse events associated with 1 the treatment of infants with bronchiolitis, beta 2 agonists 5. What is the likely balance between good a	oeta 2 agonist u s should not be	ise are self-li	miting, given	the lack of	evidence to sup		ta 2 agonists for
Evidence statement The lack of benefits clearly doesn't outweigh the harms.						quality	verall of evidence
Judging the balance of benefits and harms in context	t					Н	IGH
Benefits clearly outweigh harms	Recommend	1				STRONG	
Benefits probably outweigh harms	Consider					CONDITIO	DNAL
Not known	Make a recor	mmendation	for research	(see 8 below	v)	WEAK	
Benefits probably don't outweigh harms	Consider aga	ainst				CONDITIO	DNAL
Harms probably outweigh benefits	Ŭ						
Benefits clearly don't outweigh harms	Recommen	d against				STRONG	
Harms clearly outweigh benefits							
6. Is the intervention/action implementable	in the New Z	ealand and	Australian o	context?			
Summary statement Studies were conducted internationally (USA, Canada, UF generalizable to patients with bronchiolitis seen in Austra							
Yes		Re	commend/	consider			
Not known Consider economic evaluation							
No		Ree	commend/co	onsider again	ıst		
7. Final recommendation		1					
Do not administer beta 2 agonists to infants presenting to	o hospital or ho	ospitalised wi	th bronchiol	itis.	Strength of re STRONG CONDITION WEAK	commendation	
8. Recommendations for research				I			

Previous studies should be reviewed to clarify rates of readmission in infants administered beta 2 agonists and discharged home.

Question 8a. i)	Ν	IHMRC Evidence Su	mmary	/					
Question 8a i): In infants presenting to hospital or hospitalised with bronchiolitis, does administration Evidence table ref: of beta 2 Agonists (nebulisation, aerosol, oral or IV) improve clinically relevant end-points? Baraldi 2014, Gadomski 2014 Ralston 2014, Ricci 2015 (10 70).									
1. Evidence base (number of	studies, level of evidence	and risk of bias in the included studies	ſ		,				
One systematic review conta nine mixed inpatient/outpat		npatient, 10 outpatient, and ng 1992 infants (Level I). Most	Α		I studies with a low risk of bias, or dies with a low risk of bias				
	ear for risk of bias; s	ensitivity analysis restricted to	В	One or two Level II studies with a low risk of bias, or SR/several Level III studies with a low risk of bias					
Subsequently there has been	one additional RCT	of 56 infants which did not	С	One or two Level III II studies with mode:	studies with a low risk of bias or Level I or rate risk of bias				
alter the previous findings.			D	Level IV studies or Level I to III studies/SRs with a high risk of bias					
2. Consistency (if only one sta	udy was available, rank	this component as 'not applicable')							
Evidence is consistent that b hospitalisation rates or lengt	0	0	А	All studies consistent	t				
There is considerable hetero oxygenation and clinical seve	· · ·		В	Most studies consis	stent and inconsistency can be explained				
	on levels are not rep	orted at consistent times, and a	С	Some inconsistency, reflecting genuine uncertainty around question					
			D	Evidence is not consistent					
			NA	Not applicable (one study only)					
3. Clinical impact (indicate if the study results varied according to some unknown factor (not simply study quality or sample size) and thus the clinical impact of the intervention could not be determined)									
		onists do not have any change	А	Very large					
in rate of hospitalisation (OF 0.06 days, 95% CI -0.27 days		to 1.21), length of stay (MD ygen saturation (MD -0.43%,	В	Substantial					
95% CI -0.92% to 0.06%). A			С	Moderate					
statistical improvement in short term clinical severity scores (SMD -0.30, 95% CI -0.54 to -0.05). However, this marginal change is not associated with any clinically relevant improvement. Administration of beta 2 agonists results in the following adverse events: tachycardia, hypertension, decreased oxygen saturation, flushing, hyperactivity, prolonged cough, and tremor.				Slight/Restricted					
· · ·	• • •	e match the population and clinical sett	ings being to	argeted by the guideline?)					
Studies were completed in a			A Evidence directly generalisable to target population						
Australia, Turkey, France, Sa	udi Arabia, Egypt, C	Chile and Tunisia) using	В	Evidence directly generalisable to target population with					
	generalisable to patie	ents with bronchiolitis seen in		some caveats					
Australia and New Zealand.			С	Evidence not directly generalisable to target population but coul be sensibly applied					
No studies have been done s Aboriginal infants who do ha			D	Evidence not directly generalisable to target population and hard to judge whether sensible to apply					
5. Applicability (is the body of	f evidence relevant to the	e Australian/New Zealand healthcare	context in t	erms of health services / de	livery of care and cultural factors?)				
The results are directly appli- context. Beta 2 agonists are a			Α	Evidence directly a healthcare context	pplicable to Australian/New Zealand				
			В	context with few cav					
			С	healthcare context w					
			D	Evidence not applicable to Australian/New Zealand healthcare context					
recommendation)				· -	ight cause the group to downgrade or upgrade the				
	1		of the evider	nce relating to the key quest	tion, taking all the above factors into account)				
Component 1. Evidence base	Rating A	Description One or more Level I studies wi	ith a low •	isk of bias or several I	evel II studies with a low risk of bias				
2. Consistency	В	Most studies consistent and inc			ever if studies with a fow fisk Of Dias				
3. Clinical Impact	B	Substantial	stroutent	,					
4. Generalisability	В	Evidence directly generalisable	to target r	population with some c	aveats				
5. Applicability	А	Evidence applicable to Australi		-					
Evidence statement									
There is clear evidence of no	clinically relevant b	enefits to infants with bronchiolit	tis adminis	stered beta 2 agonists.					

RECOMMENDATION (What recommendation(s) does		OVERALL GRADE OF RECOMMENDATION	
the guideline development group draw from this evidence? Use	Α	Body of evidence can be trusted to guide practice	
action statements where possible)	В	Body of evidence can be trusted to guide practice in most situations	3
Do not administer beta 2 agonists to infants	С	Body of evidence provides some support for recommendations(s) b taken in its application	out care should be
presenting to hospital or hospitalised with	D	Body of evidence is weak and recommendation must be applied with	th caution
bronchiolitis.	РР	Practice Point	
UNRESOLVED ISSUES (If needed, keep a note of specific a	issues that ar	ise when each recommendation is formulated and that require follow up)	
about this. This information will be used to develop the implementa	tion plan for	the guidelines)	
Will this recommendation result in changes in usual care? There is no evidence that the use of bronchodilators is ef beta agonists therapy are done in this population and pot	fective in t	<i>the guidelines)</i> reating first time wheezing infants with bronchiolitis. Often trials of ment risks outweighs the body of evidence that suggests that beta	YES NO
Will this recommendation result in changes in usual care? There is no evidence that the use of bronchodilators is ef beta agonists therapy are done in this population and pot agonist use in bronchiolitis is not useful.	fective in t ential treat	reating first time wheezing infants with bronchiolitis. Often trials of ment risks outweighs the body of evidence that suggests that beta	_
Will this recommendation result in changes in usual care? There is no evidence that the use of bronchodilators is ef beta agonists therapy are done in this population and pot gonist use in bronchiolitis is not useful.	fective in t ential treat	reating first time wheezing infants with bronchiolitis. Often trials of ment risks outweighs the body of evidence that suggests that beta	NO
Will this recommendation result in changes in usual care? There is no evidence that the use of bronchodilators is ef beta agonists therapy are done in this population and pot agonist use in bronchiolitis is not useful. Are there any resource implications associated with imple	fective in te ential treate ementing th	reating first time wheezing infants with bronchiolitis. Often trials of ment risks outweighs the body of evidence that suggests that beta his recommendation?	NO YES
Will this recommendation result in changes in usual care? There is no evidence that the use of bronchodilators is ef beta agonists therapy are done in this population and pot agonist use in bronchiolitis is not useful. Are there any resource implications associated with imple	fective in te ential treate ementing th	reating first time wheezing infants with bronchiolitis. Often trials of ment risks outweighs the body of evidence that suggests that beta his recommendation?	NO YES NO
Will this recommendation result in changes in usual care? There is no evidence that the use of bronchodilators is ef	fective in t ential treatu menting th changes in	reating first time wheezing infants with bronchiolitis. Often trials of ment risks outweighs the body of evidence that suggests that beta his recommendation? the way care is currently organised?	NO YES NO YES

Γ

GRADE Evidence Summary

Considered Judgement - Strength of recommendation

1. Outcome measures:	HIGH MOD LOW V. Critical			Importance of outcome in making a decision			
	HIGH	MOD	LOW	V. LOW	Critical	Important	Not Important
O1 Rate of hospitalisation	X				Х		
O2 Length of stay	X				Х		
O3 Rate of readmission				X		Х	
O ₄ Adverse outcomes			X			Х	
Evidence statement: The evidence is based predominantly on one systematic and 10 outpatient studies (69). Subsect The sensitivity analysis of the Cochrane systematic	quently there has been or	ne additional i	RCT of 56 in	nfants (70) w	hich does not c	hange the finding	s of the review
The evidence is based predominantly on one systematic and 10 outpatient studies (69). Subsection	quently there has been or atic meta-analysis showed miting the analysis to infa	ne additional d no significa ants aged less	RCT of 56 in nt subgroup s than or equ	nfants (70) w effect in stud al to 12 mon	hich does not c dies involving ir ths did not imp	hange the finding patients vs. outp prove heterogenei	s of the review atients (infants ty. Furthermor
The evidence is based predominantly on one systematic and 10 outpatient studies (69). Subsect The sensitivity analysis of the Cochrane systematic in the outpatient studies tended to be older). Lift infants less than or equal to 12 months of age at length of stay. A smaller under-powered Cochrane systematic in children under two years of age has also found to	uently there has been or atic meta-analysis showed miting the analysis to infa re included in the Cochra meta-analysis (Chavasse that there is no current c	d no significa ants aged less ane systemati et al (71), 8 st linical benefit	RCT of 56 in nt subgroup s than or equ c meta-analy tudies, n=28	nfants (70) w effect in stud al to 12 mon rsis for the cr	hich does not c dies involving ir ths did not imp itical outcomes	hange the finding patients vs. outp prove heterogenei of rate of hospita	ts of the review atients (infants ty. Furthermor ulisation and
The evidence is based predominantly on one systinpatient and 10 outpatient studies (69). Subsect The sensitivity analysis of the Cochrane systema in the outpatient studies tended to be older). Lin infants less than or equal to 12 months of age as length of stay. A smaller under-powered Cochrane systematic r children under two years of age has also found to	uently there has been or atic meta-analysis showed miting the analysis to infa re included in the Cochra meta-analysis (Chavasse that there is no current c	d no significa ants aged less ane systemati et al (71), 8 st linical benefit	RCT of 56 in nt subgroup s than or equ c meta-analy tudies, n=28	nfants (70) w effect in stud al to 12 mon rsis for the cr	hich does not c dies involving ir ths did not imp itical outcomes	hange the finding npatients vs. outp rrove heterogenei of rate of hospitz nists for recurren	ts of the review atients (infants ty. Furthermor ulisation and

There is a high quality of evidence that routine use of beta 2 agonists in the treatment of infants with bronchiolitis is not associated with any clinically relevant benefit.

4. What harm might the proposed intervention/action do?

Evidence statement

Evidence statement	Quality of evidence
For the important outcome of rate of readmission no evidence was available.	LOW
Reporting of adverse effects in the RCTs were exclusively found in the study groups receiving beta 2 agonists and included	
the following adverse events: tachycardia, hypertension, decreased oxygen saturation, flushing, hyperactivity, prolonged	
cough, and tremor. Furthermore, adverse effects of beta 2 agonists are generally well described in the literature.	
Judging the harms in context	

While the majority of the adverse events associated with beta 2 agonist use are self-limiting, given the lack of evidence to support the use of beta 2 agonists for the treatment of infants with bronchiolitis, beta 2 agonists should not be routinely used in the treatment of infants with bronchiolitis.

5. What is the likely balance between good and harm?

Evidence statement	Overall quality of evidence
The lack of benefits clearly doesn't outweigh the harms.	HIGH
Judging the balance of benefits and harms in context	

Benefits clearly outweigh harms	Recommend	STRONG
Benefits probably outweigh harms	Consider	CONDITIONAL
Not known	Make a recommendation for research (see 8 below)	WEAK
Benefits probably don't outweigh harms	Consider against	CONDITIONAL
Harms probably outweigh benefits		CONDITIONAL
Benefits clearly don't outweigh harms	Recommend against	STRONG
Harms clearly outweigh benefits	Recommend against	5110100
6. Is the intervention/action implementable	in the New Zealand and Australian context?	

Summary statement

Studies were conducted internationally (USA, Canada, UK, Australia, Turkey, France, Saudi Arabia, Egypt, Chile and Tunisia) in populations that are generalizable to patients with bronchiolitis seen in Australia and New Zealand. Beta 2 agonists are widely used and available in Australia and New Zealand. Infants less than or equal to 12 months of age are included in the Cochrane systematic meta-analysis for the critical outcomes of rate of hospitalisation and length of stay.

Yes	Recommend/consider
Not known	Consider economic evaluation
No	Recommend/consider against

7. Final recommendation	
Do not administer beta 2 agonists to infants, less than or equal to 12 months of age, presenting to	Strength of recommendation
hospital or hospitalised with bronchiolitis.	STRONG
	CONDITIONAL
	WEAK
8. Recommendations for research	
Previous studies should be reviewed to clarify the effects of beta 2 agonists in infants aged between 6 and 1	2 months of age.

Question 8a. ii) NHMRC Evidence Summary

Question 8a ii): In older infants presenting to hospital or hospitalised with a administration of beta 2 Agonists (nebulisation, aerosol, oral or IV) improve points?			Evidence table ref: Baraldi 2014, Chavasse 2002, Gadomski 2014, Kose 2014, Ralston 2014, Ricci 2015 (10, 13, 65, 69-71).
1. Evidence base (number of studies, level of evidence and risk of bias in the included studies,)		
One systematic review containing 30 RCTs (11 inpatient, 10 outpatient, and nine mixed inpatient/outpatient settings) involving 1992 infants (Level I). Most	A	several Level II stu	I studies with a low risk of bias, or dies with a low risk of bias
studies are rated low or unclear for risk of bias; sensitivity analysis restricted to those studies of low risk of bias confirmed the results.	В	Level III studies with	
Subsequently there has been one additional RCT of 56 infants which did not alter the previous findings.	С	One or two Level III II studies with mode	I studies with a low risk of bias or Level I or rate risk of bias
A smaller under-powered Cochrane systematic meta-analysis (Chavasse et al (71), eight studies, n=281) of short acting beta 2 agonists for recurrent wheeze in children under two years of age has also found that there is no current clinical benefit.	D	Level IV studies or I bias	Level I to III studies/SRs with a high risk of
2. Consistency (if only one study was available, rank this component as 'not applicable')			
Evidence is consistent that beta 2 agonists are not associated with changes to hospitalisation rates or length of stay, with low levels of heterogeneity.	А	All studies consisten	t
There is considerable heterogeneity in meta-analysis of the outcomes of oxygenation and clinical severity scores. Both may represent measurement	В	Most studies consi	stent and inconsistency can be explained
differences in that oxygenation levels are not reported at consistent times, and a number of clinical severity scores are used.	С	Some inconsistency, question	reflecting genuine uncertainty around
The sensitivity analysis of the Cochrane systematic meta-analysis showed no significant subgroup effect in studies involving inpatients vs. outpatients (infants	D	Evidence is not cons	istent
in the outpatient studies tended to be older). Limiting the analysis to infants aged less than or equal to 12 months did not improve heterogeneity. Furthermore, infants less than or equal to 12 months of age are included in the Cochrane systematic meta-analysis for the critical outcomes of rate of hospitalisation and length of stay.	NA	Not applicable (one	
3. Clinical impact (indicate if the study results varied according to some unknown factor (not not be determined)	simply stua	ly quality or sample size) a	ind thus the clinical impact of the intervention could
Infants with bronchiolitis administered beta 2 agonists do not have any change	А	Very large	
in rate of hospitalisation (OR 0.75, 95% CI 0.46 to 1.21), length of stay (MD 0.06 days, 95% CI -0.27 days to 0.39 days), or oxygen saturation (MD -0.43%,	В	Substantial	
95% CI -0.92% to 0.06%). Administration of beta 2 agonists results in a statistical improvement in short term clinical severity scores (SMD -0.30, 95%	С	Moderate	
CI -0.54 to -0.05). However, this marginal change is not associated with any clinically relevant improvement. Administration of beta 2 agonists results in the following adverse events: tachycardia, hypertension, decreased oxygen saturation, flushing, hyperactivity, prolonged cough, and tremor.	D	Slight/Restricted	

4. Generalisability (how well	l does the body of evidend	e match t	he population a	and clinical set	tings being t	argeted by the guideline?)	
Studies were completed in a	wide range of count	ries (US	A, Canada, U	JK,	А	Evidence directly generalisable to target popu	lation
Australia, Turkey, France, Sa populations that are directly					В	Evidence directly generalisable to target I some caveats	
Australia and New Zealand.					С	Evidence not directly generalisable to target p be sensibly applied	opulation but could
No studies have been done a Aboriginal infants who do h					D	Evidence not directly generalisable to target p to judge whether sensible to apply	opulation and hard
5. Applicability (is the body of	of evidence relevant to the	e Australi	ian/New Zeald	and healthcare	context in i	terms of health services / delivery of care and cultural fac	tors?)
The results are directly appli context. Beta 2 agonists are					Α	Evidence directly applicable to Australian healthcare context	/New Zealand
					В	Evidence applicable to Australian/New Zeala context with few caveats	ind healthcare
					С	Evidence probably applicable to Australian/N healthcare context with some caveats	Jew Zealand
					D	Evidence not applicable to Australian/New 2 context	Zealand healthcare
Other factors (indicate here a recommendation)	ny other factors that you	took into	account when	assessing the e	vidence base	(for example, issues that might cause the group to downs	grade or upgrade the
EVIDENCE STATEMEN	NT MATRIX (summ	arise the	development gro	oup's synthesis	of the evide	nce relating to the key question, taking all the above fact	ors into account)
Component	Rating	Desc	ription				
1. Evidence base	А	One o	or more Leve	l I studies w	ith a low r	isk of bias, or several Level II studies with a low	risk of bias
2. Consistency	В	Most	studies consi	stent and in	consistenc	y can be explained	
3. Clinical Impact	В	Subst	antial				
4. Generalisability	В	Evide	nce directly g	generalisable	to target	population with some caveats	
5. Applicability	А	Evide	nce applicabl	le to Austral	ian/New 2	Zealand healthcare context	
Evidence statement							
There is clear evidence of no			o infants with	h bronchioli		~	
RECOMMENDATION						LL GRADE OF RECOMMENDATION	
the guideline development group a	lraw from this evidence?	Use	A			can be trusted to guide practice	
action statements where possible)			В			n be trusted to guide practice in most situations	
Do not administer beta 2	agonists to infants,	less	С	Body of e taken in it	-	rovides some support for recommendations(s) b on	ut care should be
than or equal to 12 month		g to	D	Body of e	vidence is	weak and recommendation must be applied wit	h caution
hospital or hospitalised w	ith bronchiolitis.		PP	Practice P	oint		
UNRESOLVED ISSUES	(If needed, keep a note of	of specific	issues that aris	e when each re	commendati	on is formulated and that require follow up)	
					the followin	g questions. Where the answer is yes, please provide exp.	lanatory information
about this. This information will Will this recommendation re				je guidelines)			YES
	0			in treating	first time	wheezing infants with bronchiolitis.	
						reatment risks and the body of evidence	NO
-	onist use in bronch	iolitis i	s not useful.	Previous r	esearch i	n Australasia shows that a considerable	
Are there any resource impli		-		5		"Fl.	YES
The there any resource impli	callons associated w	pi	emenang une	, recomment	Gattolli		
							NO
Will the implementation of	this recommendation	n require	changes in the	he way care	15 currentl	y organised?	YES
							NO
Are the guideline developme	ent group aware of a	ny barrie	ers to implem	entation of	this recorr	nmendation?	YES
							NO

Question 8b. i) GRADE Evidence Summary

Cons	idered Judgem	nent - Streng	gth of recom	mendation			
Question 8b i): In infants presenting to hospital or	-			-	r family history	of atopy, does	administration
of beta 2 agonists (nebulisation, aerosol, oral or IV) 1. Outcome measures:	improve clinic	cally relevan Quality of	-	s?	Im	portance of out	tcome
1. Outcome measures:		Quanty of	evidence		iı	n making a deci	
	HIGH	MOD	LOW	V. LOW	Critical	Important	Not Important
O1 Rate of hospitalisation				Х	Х		
O2 Length of stay				X	X		
O3 Rate of readmission				X		Х	
O ₄ Adverse outcomes			X			X	
2. Is there sufficient evidence to make a rec	ommendation	?		1			
Evidence statement							
In the Gadomski et al (69) review none of the 30 RCTs	· ·		dence for be	ta 2 agonist	use in infants pro	esenting to hospi	tal or
hospitalised with bronchiolitis with a personal or family 3. What benefit will the proposed interventi							
	on/ action hav	er				Oralita	- f: 1
Evidence statement There is no specific evidence for this subgroup. In gene	eral. for infants	with bronch	iolitis for the	e critical out	comes of rate of		of evidence
hospitalisation and length of stay there is high quality							RY LOW
length of stay.							
Judging the benefits in context There is no randomised controlled evidence of benefit f	or this subgrou	D.					
4. What harm might the proposed intervent							
Evidence statement						Quality of e	vidence
For the important outcome of rate of readmission no ev	idence was avai	lable.					
Reporting of adverse effects in general studies of beta 2	agonists vs. pla	cebo we r e ex	clusively fou	nd in the stu	dy groups	1	LOW
receiving beta 2 agonists and included the following adv						-	
flushing, hyperactivity, prolonged cough, and tremor. Fu	irthermore, adv	erse effects o	of beta 2 agor	nists are gene	erally well		
described in the literature.							
Judging the harms in context While the majority of the adverse events associated with	beta 2 agonistu	use a r e self-li	miting given	the lack of	evidence to supr	ort the use of be	ta 2 agonists for
the treatment of infants with bronchiolitis, beta 2 agonis							
history of atopy.							
5. What is the likely balance between good	and harm?						
Evidence statement There is no good evidence to support the trial of beta 2	econiste in infe	nto with none	anal an famil	r history of	toar	_	verall of evidence
There is no good evidence to support the that of beta 2	agoinsts in inta	ins with pers		y instory or a	atopy.		Y LOW
Judging the balance of benefits and harms in conte	xt						
Benefits clearly outweigh harms	Recommend	1				STRONG	
Benefits probably outweigh harms	Consider					CONDITIO	ONAL
Not known	-	mmendation	for research	(see 8 below	<i>a</i>)	WEAK	
Benefits probably don't outweigh harms	Marce a reco	minendation	ior researen	(see o belov	•)	W LAIR	
Harms probably outweigh benefits	Consider ag	ainst				CONDITIO	ONAL
1 . 0							
Benefits clearly don't outweigh harms Harms clearly outweigh benefits	Recommend	lagainst				STRONG	
Framis clearly outweigh benefits		8					
6. Is the intervention/action implementable	e in the New Z	Lealand and	Australian o	context?			
Summary statement	and N== 7	and					
Beta 2 agonists are widely used and available in Australia Yes	and New Zeal		commend/	consider			
Not known			nsider econo		011		
No			commend/co				
		Ке		msider agair	151		
7. Final recommendation							
Do not administer beta 2 agonists to infants presenting a personal or family history of atopy.	to hospital or h	ospitalised w	1th bronchiol	-	Strength of reco STRONG	ommendation	
a personal or family instory of atopy.					CONDITIONA	L	
					WEAK		
8. Recommendations for research							
Studies of the use of beta 2 agonists in infants presenting	g to hospital or	hospitalised	with bronchi	olitis and a p	personal or famil	y history of atop	y are needed.

Question 8b. i) **NHMRC Evidence Summary** Question 8b i): In infants presenting to hospital or hospitalised with bronchiolitis, with a personal or Evidence table ref: family history of atopy, does administration of Beta 2 agonists (nebulisation, aerosol, oral or IV) Baraldi 2014, Gadomski 2014, Ralston improve clinically relevant end-points? 2014, Ricci 2015 (10, 13, 65, 69). 1. Evidence base (number of studies, level of evidence and risk of bias in the included studies) No studies have addressed this question. One or more Level I studies with a low risk of bias, or several А Level II studies with a low risk of bias One or two Level II studies with a low risk of bias, or SR/several В Level III studies with a low risk of bias One or two Level III studies with a low risk of bias or Level I or С II studies with moderate risk of bias Level IV studies or Level I to III studies/SRs with a high D risk of bias 2. Consistency (if only one study was available, rank this component as 'not applicable') А All studies consistent В Most studies consistent and inconsistency can be explained Some inconsistency, reflecting genuine uncertainty around С question D Evidence is not consistent NA Not applicable (one study only) 3. Clinical impact (indicate if the study results varied according to some unknown factor (not simply study quality or sample size) and thus the clinical impact of the intervention could not be determined) А Very large В Substantial С Moderate D Slight/Restricted 4. Generalisability (how well does the body of evidence match the population and clinical settings being targeted by the guideline?) Evidence directly generalisable to target population А Evidence directly generalisable to target population with some В caveats Evidence not directly generalisable to target population but could С be sensibly applied Evidence not directly generalisable to target population and D hard to judge whether sensible to apply 5. Applicability (is the body of evidence relevant to the Australian/New Zealand healthcare context in terms of health services / delivery of care and cultural factors?) Evidence directly applicable to Australian/New Zealand А healthcare context Evidence applicable to Australian/New Zealand healthcare В context with few caveats Evidence probably applicable to Australian/New Zealand С healthcare context with some caveats Evidence not applicable to Australian/New Zealand D healthcare context

Other factors (indicate here any other factors that you took into account when assessing the evidence base (for example, issues that might cause the group to downgrade or upgrade the recommendation)

There is no good quality evidence evaluating the effect of beta 2 agonists in infants with bronchiolitis and a personnel or family history of atopy.

Previously trials of beta 2 agonists have been suggested as a clinical option. However, given the high level of evidence (NHMRC A, GRADE strong) demonstrating no benefit of beta 2 agonists in infants presenting to or hospitalised with bronchiolitis, and that there is no well-established way to determine an "objective method of response" to beta 2 agonists in bronchiolitis, this option is no longer recommended. Although it is true that a small subset of children with bronchiolitis may have reversible airway obstruction resulting from smooth muscle constriction, attempts to define a subgroup of responders have not been successful to date. If a clinical trial of bronchodilators is undertaken, clinicians should note that the variability of the disease process, the host's airway, and the clinical assessments, particularly scoring, would limit the clinician's ability to observe a clinically relevant response to bronchodilators (13).

Administration of beta 2 agonists has resulted in the following adverse events: tachycardia, hypertension, decreased oxygen saturation, flushing, hyperactivity, prolonged cough, and tremor.

Beta 2 agonists should only be used in infants with a personal or family history of atopy as part of an RCT in order to establish a better evidence base. **EVIDENCE STATEMENT MATRIX** (summarise the development group's synthesis of the evidence relating to the key question, taking all the above factors into account)

	Rating		iption		
1. Evidence base	D	Level	IV studies o	or Level I to III studies/SRs with a high risk of bias	
2. Consistency	NA		LL \	ne study only)	
3. Clinical Impact	D	Slight	/Restricted		
4. Generalisability	D			ectly generalisable to target population and hard to judge whether it is s	sensible to apply
5. Applicability	D	Evider	nce not app	licable to Australian healthcare context	
Evidence statement					
There is no good evider	nce to support the trial	of beta 2 a	gonists in ir	nfants with personal or family history of atopy.	
RECOMMENDATIO	DN (What recommendatio	n(s) does		OVERALL GRADE OF RECOMMENDATION	
the guideline development gr	oup draw from this evidence	e? Use	А	Body of evidence can be trusted to guide practice	
action statements where poss	ible)		В	Body of evidence can be trusted to guide practice in most situations	s
			С	Body of evidence provides some support for recommendations(s) h	out care should be
Do not administer bet	0	s	C	taken in its application	
presenting to hospital	-		D	Body of evidence is weak and recommendation must be appli	ed with caution
bronchiolitis, with a p	ersonal or family his	ory of	РР	Practice Point	
atopy.					
TINDEROLVED TOOL		·· · · · · · · · · · · · · · · · · · ·	issues that ari	ise when each recommendation is formulated and that require follow up)	
UNRESOLVED ISSU	ES (If needed, keep a no.	e of specific i	issues indi uni	se when each recommendation is formatured and that require follow up	
	() 1	515		3 x 3 x/	
IMPLEMENTATION	N OF RECOMMEN	DATION	(Please indic	ate yes or no to the following questions. Where the answer is yes, please provide exp	blanatory information
	N OF RECOMMEN	DATION	(Please indic	ate yes or no to the following questions. Where the answer is yes, please provide exp	blanatory information
IMPLEMENTATION about this. This information	N OF RECOMMEN	DATION implementa	(Please indic tion plan for i	ate yes or no to the following questions. Where the answer is yes, please provide exp	blanatory information YES
IMPLEMENTATION	N OF RECOMMEN	DATION implementa	(Please indic tion plan for i	ate yes or no to the following questions. Where the answer is yes, please provide exp	
IMPLEMENTATION <i>about this. This information</i> Will this recommendation	N OF RECOMMEN a will be used to develop the	DATION implementa	(Please indic tion plan for 1	ate yes or no to the following questions. Where the answer is yes, please provide exp the guidelines)	YES
IMPLEMENTATION <i>about this. This information</i> Will this recommendation	N OF RECOMMEN a will be used to develop the	DATION implementa	(Please indic tion plan for 1	ate yes or no to the following questions. Where the answer is yes, please provide exp the guidelines)	YES NO YES
IMPLEMENTATIO about this. This information Will this recommendation Are there any resource i	N OF RECOMMEN a will be used to develop the on result in changes in mplications associated	DATION <i>implementa</i> usual care? with imple	(Please indic tion plan for i	ate yes or no to the following questions. Where the answer is yes, please provide exp the guidelines) is recommendation?	YES NO YES NO
IMPLEMENTATIO <i>about this. This information</i> Will this recommendation Are there any resource i	N OF RECOMMEN a will be used to develop the on result in changes in mplications associated	DATION <i>implementa</i> usual care? with imple	(Please indic tion plan for i	ate yes or no to the following questions. Where the answer is yes, please provide exp the guidelines)	YES NO YES NO
IMPLEMENTATION about this. This information Will this recommendation Are there any resource in Will the implementation	N OF RECOMMEN a will be used to develop the on result in changes in mplications associated a of this recommendati	DATION implementa usual care? with imple	<i>(Please indiction plan for i pla</i>	ate yes or no to the following questions. Where the answer is yes, please provide exp the guidelines) is recommendation? the way care is currently organised?	YESNOYESNOYESNO
IMPLEMENTATION <i>about this. This information</i> Will this recommendation Are there any resource in Will the implementation	N OF RECOMMEN a will be used to develop the on result in changes in mplications associated a of this recommendati	DATION implementa usual care? with imple	<i>(Please indiction plan for i pla</i>	ate yes or no to the following questions. Where the answer is yes, please provide exp the guidelines) is recommendation?	YES NO YES NO

Question 8b. ii)

	_	-		mendation	anal or family	history of atom	doos
Question 8b ii): In older infants presenting to administration of Beta 2 agonists (nebulisatio					oints?		
1. Outcome measures:		Quality of	evidence			nportance of out n making a deci	
	HIGH	MOD	LOW	V. LOW	Critical	Important	Not Important
O1 Rate of hospitalisation				X	Х		
D ₂ Length of stay				X	Х		
D ₃ Rate of readmission				X		Х	
D ₄ Adverse outcomes			X			Х	
2. Is there sufficient evidence to make	e a recommendation	?					
 hospitalised with bronchiolitis with a personal or i 3. What benefit will the proposed inte Evidence statement There is no specific evidence for this subgroup. I hospitalisation and length of stay there is high q length of stay. Judging the benefits in context There is no randomised controlled evidence of be 4. What harm might the proposed inte Evidence statement For the important outcome of rate of readmission Reporting of adverse effects in general studies of I receiving beta 2 agonists and included the following flushing, hyperactivity, prolonged cough, and tren described in the literature. 	In general, for infants uality evidence that be mefit for this subgroup ervention/action doi n no evidence was avai beta 2 agonists vs. plac ng adverse events: tach	e? with bronchi eta 2 agonist o. ? lable. cebo were exe nycardia, hypo	s do not aff	nd in the stur	dy groups en saturation,	f r VEF	of evidence RY LOW vidence
udging the harms in context While the majority of the adverse events associate							
Iudging the harms in context While the majority of the adverse events associate the treatment of infants with bronchiolitis, beta 2 history of atopy. 5. What is the likely balance between Evidence statement There is no good evidence to support the trial of l	agonists should not be good and harm? beta 2 agonists in infar	e routinely us	ed in the trea	atment of inf	ants with brond	chiolitis, with a period	
udging the harms in context While the majority of the adverse events associate the treatment of infants with bronchiolitis, beta 2 history of atopy. 5. What is the likely balance between Evidence statement There is no good evidence to support the trial of l	agonists should not be good and harm? beta 2 agonists in infar	e routinely us	ed in the trea	atment of inf	ants with brond	chiolitis, with a period	verall of evidence
Judging the harms in context While the majority of the adverse events associate While the majority of the adverse events associate the treatment of infants with bronchiolitis, beta 2 history of atopy. 5. What is the likely balance between Evidence statement There is no good evidence to support the trial of I Judging the balance of benefits and harms in	agonists should not be good and harm? beta 2 agonists in infar	e routinely us	ed in the trea	atment of inf	ants with brond	chiolitis, with a period	verall of evidence
Judging the harms in context While the majority of the adverse events associate While the majority of the adverse events associate while the treatment of infants with bronchiolitis, beta 2 history of atopy. 5. What is the likely balance between Evidence statement There is no good evidence to support the trial of 1 Judging the balance of benefits and harms in Benefits clearly outweigh harms	agonists should not be good and harm? beta 2 agonists in infar context	e routinely us	ed in the trea	atment of inf	ants with brond	chiolitis, with a po Quality VER	ersonal or fami verall of evidence XY LOW
udging the harms in context While the majority of the adverse events associate he treatment of infants with bronchiolitis, beta 2 history of atopy. 5. What is the likely balance between Evidence statement There is no good evidence to support the trial of I udging the balance of benefits and harms in Benefits clearly outweigh harms Benefits probably outweigh harms	agonists should not be good and harm? beta 2 agonists in infar context Recommend Consider	e routinely us	ed in the tree	atment of inf	topy.	chiolitis, with a period of the second secon	verall verall of evidence Y LOW
udging the harms in context While the majority of the adverse events associate he treatment of infants with bronchiolitis, beta 2 history of atopy. 5. What is the likely balance between Evidence statement There is no good evidence to support the trial of I udging the balance of benefits and harms in Benefits clearly outweigh harms Benefits probably outweigh harms Benefits probably don't outweigh harms	agonists should not be good and harm? beta 2 agonists in infar context Recommend Consider	e routinely us	ed in the tree	atment of inf	topy.	Chiolitis, with a period of the second secon	verall of evidence Y LOW
udging the harms in context While the majority of the adverse events associate while the treatment of infants with bronchiolitis, beta 2 history of atopy. 5. What is the likely balance between Evidence statement There is no good evidence to support the trial of 1 udging the balance of benefits and harms in Benefits clearly outweigh harms Benefits probably outweigh harms Benefits probably don't outweigh harms Harms probably outweigh benefits	agonists should not be good and harm? beta 2 agonists in infar context Recommend Consider Make a recom- Consider aga	e routinely us	ed in the tre	atment of inf	topy.	Condition of the second	verall of evidence Y LOW
udging the harms in context While the majority of the adverse events associate he treatment of infants with bronchiolitis, beta 2 history of atopy. 5. What is the likely balance between Evidence statement There is no good evidence to support the trial of I (udging the balance of benefits and harms in Benefits clearly outweigh harms Benefits probably outweigh harms Harms probably outweigh benefits Benefits clearly don't outweigh harms	agonists should not be good and harm? beta 2 agonists in infar context Recommend Consider Make a recommend	e routinely us	ed in the tre	atment of inf	topy.	Conditional Condit	verall of evidence Y LOW
udging the harms in context While the majority of the adverse events associate he treatment of infants with bronchiolitis, beta 2 istory of atopy. 5. What is the likely balance between Evidence statement There is no good evidence to support the trial of 1 udging the balance of benefits and harms in Benefits clearly outweigh harms Aot known Benefits probably don't outweigh harms Harms probably outweigh benefits Benefits clearly don't outweigh harms	agonists should not be good and harm? beta 2 agonists in infar context Recommend Consider Make a recon Consider aga Recommend	e routinely us the swith person mmendation ainst l against	ed in the tree	y history of <i>a</i> (see 8 below	topy.	Condition of the second	verall of evidence Y LOW
udging the harms in context While the majority of the adverse events associate he treatment of infants with bronchiolitis, beta 2 history of atopy. 5. What is the likely balance between Evidence statement There is no good evidence to support the trial of 1 udging the balance of benefits and harms in Benefits clearly outweigh harms Benefits probably outweigh harms Harms probably outweigh benefits Benefits clearly don't outweigh harms Harms clearly outweigh benefits Benefits clearly outweigh benefits Benefits clearly don't outweigh harms Harms probably outweigh benefits Benefits clearly don't outweigh harms Harms clearly outweigh benefits Benefits at 2 agonists are widely used and available in And a	agonists should not be good and harm? beta 2 agonists in infar context Recommend Consider Make a recor Consider aga Recommend entable in the New Z	e routinely us nts with perso nts with perso nts addition nts nts nts nts nts nts nts nts nts nt	ed in the tree	y history of a (see 8 below	topy.	Condition of the second	verall of evidence Y LOW
udging the harms in context While the majority of the adverse events associate he treatment of infants with bronchiolitis, beta 2 history of atopy. 5. What is the likely balance between Evidence statement There is no good evidence to support the trial of 1 udging the balance of benefits and harms in Benefits clearly outweigh harms Benefits probably outweigh harms Anton N Benefits clearly don't outweigh harms Harms probably outweigh benefits Benefits clearly don't outweigh harms Harms clearly outweigh benefits Benefits clearly don't outweigh harms Harms clearly outweigh benefits Benefits clearly don't outweigh harms Harms clearly outweigh benefits Benefits clearly outweigh benefits Benefits clearly don't outweigh harms Harms clearly outweigh benefits Benefits and harms in the intervention/action implement Beta 2 agonists are widely used and available in Autors	agonists should not be good and harm? beta 2 agonists in infar context Recommend Consider Make a recor Consider aga Recommend entable in the New Z	e routinely us nts with perso nmmendation ainst l against Cealand and and. Re	ed in the tree	atment of inf y history of a (see 8 below context? consider	topy.	Condition of the second	verall of evidence Y LOW
udging the harms in context While the majority of the adverse events associate the treatment of infants with bronchiolitis, beta 2 history of atopy. 5. What is the likely balance between Evidence statement There is no good evidence to support the trial of I Judging the balance of benefits and harms in Benefits clearly outweigh harms Benefits probably outweigh harms Not known Benefits clearly don't outweigh harms Harms probably outweigh benefits Benefits clearly outweigh benefits Benefits clearly outweigh benefits Benefits and harms Harms probably outweigh benefits Benefits clearly don't outweigh harms Harms clearly outweigh benefits Benefits and available in Augustatement Beta 2 agonists are widely used and available in Augustatement Beta 2 agonists are widely used and available in Augustatement Bott known	agonists should not be good and harm? beta 2 agonists in infar context Recommend Consider Make a recor Consider aga Recommend entable in the New Z	e routinely us nts with perso nts with person nts with pe	ed in the tree	y history of a y history of a (see 8 below context? consider mic evaluatio	ants with brond topy.	Condition of the second	verall of evidence Y LOW
udging the harms in context While the majority of the adverse events associate the treatment of infants with bronchiolitis, beta 2 history of atopy. 5. What is the likely balance between Evidence statement There is no good evidence to support the trial of I Judging the balance of benefits and harms in Benefits clearly outweigh harms Benefits probably outweigh harms Mot known Benefits clearly don't outweigh harms Harms probably outweigh benefits Benefits clearly outweigh benefits Benefits agonists are widely used and available in Au Yes Not known No	agonists should not be good and harm? beta 2 agonists in infar context Recommend Consider Make a recor Consider aga Recommend entable in the New Z	e routinely us nts with perso nts with person nts with pe	ed in the tree	atment of inf y history of a (see 8 below context? consider	ants with brond topy.	Condition of the second	verall of evidence Y LOW
Judging the harms in context While the majority of the adverse events associate the treatment of infants with bronchiolitis, beta 2 history of atopy. 5. What is the likely balance between Evidence statement There is no good evidence to support the trial of I Judging the balance of benefits and harms in Benefits clearly outweigh harms Benefits probably outweigh harms Harms probably don't outweigh harms Harms clearly don't outweigh harms	agonists should not be good and harm? beta 2 agonists in infar context Recommend Consider Make a recor Consider agr Recommend entable in the New Z ustralia and New Zeala than or equal to 12 mo	e routinely us ints with perso ints with perso ints with perso ints inst i against i against i against i and. i Rec i Con i Rec i Donths of age, i I	ed in the tree onal or family for research Australian of commend/on sider econo commend/co	y history of a y history of a (see 8 below context? consider mic evaluatio	ints with brond topy.	commendation	verall of evidence Y LOW

Question 8b. ii) NHMRC Evidence Sur	mmary	/	
Question 8b ii): In older infants presenting to hospital or hospitalised personal or family history of atopy, does administration of Beta 2 agonists or IV) improve clinically relevant end-points?		Evidence table ref: Baraldi 2014, Chavasse 2002, Gadomski 2010, Ralston 2014, Ricci 2015 (10, 13, 65, 69, 71).	
1. Evidence base (number of studies, level of evidence and risk of bias in the included studies	r)		
No studies have addressed this question.	А	Level II studies with	
	В	Level III studies with	
	С	studies with a low risk of bias or Level I or rate risk of bias	
	D	Level IV studies or risk of bias	Level I to III studies/SRs with a high
2. Consistency (if only one study was available, rank this component as 'not applicable')			
	А	All studies consistent	:
	В	Most studies consiste	ent and inconsistency can be explained
	С	Some inconsistency, question	reflecting genuine uncertainty around
	D	Evidence is not cons	istent
	NA	Not applicable (one	e study only)
3. Clinical impact (indicate if the study results varied according to some unknown factor (not not be determined)	t simply stu	dy quality or sample size) a	nd thus the clinical impact of the intervention could
	А	Very large	
	В	Substantial	
	С	Moderate	
	D	Slight/Restricted	
4. Generalisability (how well does the body of evidence match the population and clinical settle	ings being t	argeted by the guideline?)	
	А		neralisable to target population
	В	caveats	neralisable to target population with some
	С	Evidence not directly be sensibly applied	generalisable to target population but could
	D		tly generalisable to target population and her sensible to apply
5. Applicability (is the body of evidence relevant to the Australian/New Zealand healthcare	context in t	erms of health services / de	livery of care and cultural factors?)
	А	healthcare context	plicable to Australian/New Zealand
	В	context with few cav	
	С	healthcare context w	
	D	healthcare context	icable to Australian/New Zealand
Other factors (indicate bere any other factors that you took into account when assessing the ev recommendation)	ridence base	(for example, issues that m	ight cause the group to downgrade or upgrade the

There is no good quality evidence evaluating the effect of beta 2 agonists in infants with bronchiolitis and a personnel or family history of atopy.

Previously trials of beta 2 agonists have been suggested as a clinical option. However, given the high level of evidence (NHMRC A, GRADE strong) demonstrating no benefit of beta 2 agonists in infants presenting to or hospitalised with bronchiolitis, and that there is no well-established way to determine an "objective method of response" to beta 2 agonists in bronchiolitis, this option is no longer recommended. Although it is true that a small subset of children with bronchiolitis may have reversible airway obstruction resulting from smooth muscle constriction, attempts to define a subgroup of responders have not been successful to date. If a clinical trial of bronchodilators is undertaken, clinicians should note that the variability of the disease process, the host's airway, and the clinical assessments, particularly scoring, would limit the clinician's ability to observe a clinically relevant response to bronchodilators (13).

Administration of beta 2 agonists has resulted in the following adverse events: tachycardia, hypertension, decreased oxygen saturation, flushing, hyperactivity, prolonged cough, and tremor.

Beta 2 agonists should only be used in infants with a personal or family history of atopy as part of an RCT in order to establish a better evidence base. **EVIDENCE STATEMENT MATRIX** (summarise the development group's synthesis of the evidence relating to the key question, taking all the above factors into account)

Component	Rating	Description						
1. Evidence base	D	Level 1	Level IV studies or Level I to III studies/SRs with a high risk of bias					
2. Consistency	NA	Not af	Not applicable (one study only)					
3. Clinical Impact	D	Slight/	Slight/Restricted					
4. Generalisability	D	Evider	Evidence not directly generalisable to target population and hard to judge whether it is sensible to apply					
5. Applicability	D	Evider	Evidence not applicable to Australian healthcare context					
Evidence statement								
Do not administer beta 2	agonists to infants pres	senting to	hospital or	r hospitalised with bronchiolitis, with a personal or family history of a	topy.			
RECOMMENDATIO	N (What recommendation(s) does		OVERALL GRADE OF RECOMMENDATION				
the guideline development grou	up draw from this evidence?	Use A Body of evidence can be trusted to guide practice						
action statements where possik	ble)		В	Body of evidence can be trusted to guide practice in most situation	15			
				Body of evidence provides some support for recommendations(s) taken in its application	but care should be			
than or equal to 12 months of age, presenting to D Body of evidence is weak and recommendation must be a				Body of evidence is weak and recommendation must be applied w	applied with caution			
hospital or hospitalised with bronchiolitis, with a personal or family history of atopy. Practice Point								
UNRESOLVED ISSUI	ES (If needed, keep a note	of specific i	ssues that ari	se when each recommendation is formulated and that require follow up)				
				ate yes or no to the following questions. Where the answer is yes, please provide ex				
					blanatory information			
	will be used to develop the in	mplementai	tion plan for i					
	will be used to develop the in	mplementai	tion plan for i		blanatory information YES NO			
Will this recommendation	will be used to develop the in n result in changes in us	<i>mplementai</i> sual care?	tion plan for i	the guidelines)	YES			
Will this recommendation	will be used to develop the in n result in changes in us	<i>mplementai</i> sual care?	tion plan for i	the guidelines)	YES NO			
Will this recommendation Are there any resource in	will be used to develop the in n result in changes in us nplications associated w	mplementati sual care? ith imple	<i>tion plan for i</i>	the guidelines)	YES NO YES			
Will this recommendation Are there any resource in	will be used to develop the in n result in changes in us nplications associated w	mplementati sual care? ith imple	<i>tion plan for i</i>	the guidelines)	YES NO YES NO			
Will this recommendation Are there any resource in Will the implementation of	will be used to develop the in n result in changes in us nplications associated w of this recommendation	mplementai sual care? tith imple	tion plan for 1 menting thi changes in	the guidelines)	YES NO YES NO YES			

Question 9.

Con	sidered Judgem	nent - Streng	th of recom	mendation			
Question 9: In infants presenting to hospital or ho	spitalised with	bronchioliti	s, does adm	inistration	of adrenaline/	epinephrine (ne	bulisation, IM
or IV) improve clinically relevant end-points? 9. Outcome measures:		Quality of	-	oortance of outcome making a decision			
	IIICII			V.			Not
	HIGH	MOD	LOW	LOW	Critical	Important	Important
O1 Rate of hospitalisation			x		x		
O2 Length of stay	х				x		
O3 Rate of readmission		x				х	
O4 Adverse outcomes			x			x	
10. Is there sufficient evidence to make a re	commendation	?					
	tion/action hav	findings of th e? idence that In	e review. nfants with t	pronchiolitis	administered	Quality	of evidence
For the critical outcome of rate of hospitalisation there is low quality evidence that Infants with bronchiolitis administered adrenaline/epinephrine in ambulatory settings have a significant reduction in rate of hospitalisation within the first 24 hours after initiation of treatment (RR 0.67, 95% CI 0.50 to 0.89, n=995). However this is not the case when only trials at low risk of bias are analysed (RR 0.77, 95% CI 0.56 to 1.07, n=842), in the most recent study (Sarrell et al (76), n=330), or when hospitalization is analysed over the first seven days after initiating treatment (RR 0.81, 95% CI 0.63 to 1.03, n=875). For the critical outcome of length of stay there is high quality of evidence (mean difference -0.25, 95% CI -0.62 to 0.13, n=696) that adrenaline/epinephrine administration does not affect length of stay.							//HIGH
Judging the benefits in context There is a moderate quality of evidence that routine us consistent clinically relevant benefit. 12. What harm might the proposed interver	e of adrenaline/e	pinephrine ir	the treatme	nt of infants	with bronchioli	tis is not associat	ed with any
Evidence statement		·				Quality	of evidence
For the important outcome of rate of readmission there is moderate quality evidence that adrenaline/epinephrine administration does not affect readmission rate.						IODERATE	
vomiting and tremor. Judging the harms in context While the majority of the adverse events associated wit adrenaline/epinephrine for the treatment of infants with bronchiolitis.							
13. What is the likely balance between good	l and harm?						
Evidence statement						0	verall
The lack of benefits clearly doesn't outweigh the harms	3.						of evidence DERATE
Judging the balance of benefits and harms in cont	ext					MOL	DEKALE
J g g							
Benefits clearly outweigh harms	Recommend	1				STRONG	
Benefits probably outweigh harms	Consider					CONDITIO	ONAL
Not known	Make a reco	mmendation	for research	(see 8 below	r)	WEAK	
Benefits probably don't outweigh harms						000	
Harms probably outweigh benefits	Consider aga	aınst				CONDITIO	JNAL
Benefits clearly don't outweigh harms							
Harms clearly outweigh benefits	Recommen	ıd against				STRONG	
14. Is the intervention/action implementab	le in the New Z	ealand and	Australian	context?			
Summary statement Studies were conducted internationally (USA, Canada, generalizable to patients with bronchiolitis seen in Aus Zealand.							
Yes		Re	commend/	consider			
Not known		Co	nsider econo	mic evaluatio	on		
No	Recommend/consider against						

15. Final recommendation	
Do not administer adrenaline/epinephrine to infants presenting to hospital or hospitalised with	Strength of recommendation
bronchiolitis.	STRONG
	CONDITIONAL
	WEAK
16. Recommendations for research	
Nil.	

Question 9. NHMRC Evidence Summary Question 9: In infants presenting to hospital or hospitalised with bronchiolitis, does administration of Evidence table ref: adrenaline/epinephrine (nebulisation, IM or IV) improve clinically relevant end-points? Baraldi 2014, Hartling 2011, Hartling 2011, Livni 2010, Modaressi 2012, Ralston 2014, Ricci 2015 Sarrell 2010, Simsek-Kiper 2010, Skjerven 2013 (10, 13, 65, 72-76, 164). 1. Evidence base (number of studies, level of evidence and risk of bias in the included studies) One systematic review (Hartling et al (72), 19 studies, n=2,256) (level I). One or more Level I studies with a low risk of bias, or А Subsequent to this there has been three further RCTs comparing several Level II studies with a low risk of bias adrenaline/epinephrine to a nasal decongestant or beta-2-agonists (Livni et al One or two Level II studies with a low risk of bias, or SR/several в (73), n=65, Modaressi et al (74), n=40, Simsek-Kiper et al (75), n=75) or to Level III studies with a low risk of bias placebo in ambulatory (Sarrell et al (76), n=330) and inpatient settings (Skjerven One or two Level III studies with a low risk of bias or Level I or С et al (77), n=404) that have not changed the findings of the meta-analysis. II studies with moderate risk of bias Infants with bronchiolitis administered adrenaline/epinephrine in ambulatory settings have a significant reduction in rate of hospitalisation within the first 24 hours after initiation of treatment (RR 0.67, 95% CI 0.50 to 0.89, n=995). Level IV studies or Level I to III studies/SRs with a high risk of D However this is not the case when only trials at low risk of bias are analysed bias (RR 0.77, 95% CI 0.56 to 1.07, n=842), in the most recent study (Sarrell et al (76), n=330), or when hospitalization is analysed over the first seven days after initiating treatment (RR 0.81, 95% CI 0.63 to 1.03, n=875). 2. Consistency (if only one study was available, rank this component as 'not applicable') There is inconsistency in evidence regarding rate of hospitalisation. А All studies consistent The evidence regarding length of stay, adverse events and readmissions is consistent. В Most studies consistent and inconsistency can be explained Some inconsistency, reflecting genuine uncertainty around С question D Evidence is not consistent NA Not applicable (one study only) 3. Clinical impact (indicate if the study results varied according to some unknown factor (not simply study quality or sample size) and thus the clinical impact of the intervention could not be determined) Evidence regarding hospitalisation discussed above. Evidence from the А Very large Cochrane meta-analysis and the recent high quality RCT (Skjerven et al (77), В Substantial n=404) do not suggest that administering adrenaline/epinephrine in inpatients with bronchiolitis changes hospital length of stay or readmission rates. С Moderate Administration of adrenaline/epinephrine in RCTs resulted in the following D Slight/Restricted adverse events tachycardia, hypertension, pallor, vomiting and tremor. 4. Generalisability (how well does the body of evidence match the population and clinical settings being targeted by the guideline?) Evidence directly generalisable to target population Studies were conducted internationally (USA, Canada, UK, Australia, Norway, А Turkey, Iran, Israel, Jordan, Chile, India, Bangladesh) in populations that are Evidence directly generalisable to target population with В generalizable to patients with bronchiolitis seen in Australia and New Zealand. some caveats Adrenaline/epinephrine is widely used and available in Australia and New Evidence not directly generalisable to target population but could С Zealand. be sensibly applied Evidence not directly generalisable to target population and hard No studies have been done specifically looking at Maori/Pacific Island or D to judge whether sensible to apply Aboriginal infants who do have a high disease burden with bronchiolitis.

5. Applicability (is the body of	f evidence relevant to the	e Australia	n/New Zeal	land healthcare a	context in	terms of health services / delivery of care and cultural fa	ctors?)		
The results are directly appli-	cable to the Australia	an/New	Zealand hea	althcare	Α	n/New Zealand			
context. Adrenaline/epineph	nrine is readily availa	ble in Au	stralia and N	New	A	healthcare context			
Zealand.					В	Evidence applicable to Australian/New Zeal	and healthcare		
				D	context with few caveats				
			С	Evidence probably applicable to Australian/2	Australian/New Zealand				
				C	healthcare context with some caveats				
				D	Evidence not applicable to Australian/New context	Zealand healthcare			
Other factors (indicate here an recommendation)	ny other factors that you	took into	account when	assessing the evi	idence base	(for example, issues that might cause the group to down	grade or upgrade the		
EVIDENCE STATEMEN	NT MATRIX (summ	arise the a	levelopment gr	oup's synthesis o	of the evide	nce relating to the key question, taking all the above fac	tors into account)		
Component	Rating	Descr	iption						
1. Evidence base	А	One of	r more Leve	el I studies wit	th a low 1	isk of bias, or several Level II studies with a low	w risk of bias		
2. Consistency	С	Some	nconsistenc	cy, reflecting g	genuine u	ncertainty around question			
3. Clinical Impact	В	Substa	ntial						
4. Generalisability	В	Evider	nce directly §	generalisable (to target	population with some caveats			
5. Applicability	А	Evider	ice applicab	le to Australia	an/New 2	Zealand healthcare context			
Evidence statement									
There is clear evidence of no	clinically relevant b	enefits to	infants wit	h bronchioliti	is admini	stered beta 2 agonists.			
RECOMMENDATION (What recommendation(.	s) does		(OVERA	LL GRADE OF RECOMMENDATION			
the guideline development group d	raw from this evidence?	Use	А	Body of ev	dy of evidence can be trusted to guide practice				
action statements where possible)			В	Body of ev	vidence	can be trusted to guide practice in most situ	ations		
			С	Body of ev	idence pr	ovides some support for recommendations(s) l	out care should be		
Do not administer adrenal			C	taken in its	aken in its application				
infants presenting to hosp	ital or hospitalised	with	D	Body of ev	idence is	weak and recommendation must be applied wi	th caution		
bronchiolitis.			PP	Practice Po	oint				
UNRESOLVED ISSUES	(If needed, keep a note	of specific i	ssues that aris	se when each rec	ommendati	on is formulated and that require follow up)			
					the followin	g questions. Where the answer is yes, please provide exp	slanatory information		
about this. This information will			tion plan for ti	he guidelines)					
Will this recommendation re	0						YES		
-	oinephrine are used i	n clinical	practice in	Australia and	New Ze	aland, this is in contrast to North American	NO		
practice.									
Are there any resource impli	cations associated w	ith imple	menting this	s recommend	lation?		YES		
							NO		
Will the implementation of t	his recommendation	require	changes in t	he way care is	s currentl	y organised?	YES		
*			Ŭ			• ~	NO		
Are the guideline developme	ent group aware of a	ny harrie	es to implem	pentation of t	his recor	mendation?	YES		
The the guideline developine	aware of a	iny barrier	.5 to impicit			interitation:	_		
						NO			

Question 10.

Question 10.	UNADI		e Julilla	iy				
	Consid	lered Judgeme	ent - Strength o	of recommenda	tion			
Question 10: In infants presenting to hos	pital or hos	pitalised with	bronchiolitis,	does administra	ation of nebulised h	ypertonic salin	e improve	
clinically relevant end-points?								
1. Outcome measures:		Quality	of evidence		Importance of o	outcome in mak	ting a decision	
	HIGH	MOD	LOW	V. LOW	Critical	Not Important		
O1 Length of stay				X	X			
O ₂ Admission rate			X		X			
O ₃ Readmission rate			X			Х		
O4 Adverse events			X			X		
2. Is there is insufficient evidence	e to make a	recommendati						
Evidence statement								
The evidence is based on one Cochrane syste there have been three further systematic revia and a live meta-analysis (92). 3. What benefit will the proposed	ews (88-90) a	nd the newer tr	ials have been i					
Evidence statement	interventio	ii/ action nave	•				y of evidence	
nebulised hypertonic saline (mean difference considerable heterogeneity in the overall resu than current clinical practice in Australia and that used in Australia and New Zealand for heterogeneity and results in a pooled estimate lower risk of bias, again suggests no bene unbalanced with regards to duration of illnes. For the critical outcome of admission rate the nebulised hypertonic saline (RR 0.80, 95% C range of regimens, strengths and added med not effective in the studies using just one to 95% CI 0.73 to 1.20, 4 RCTs, n=358; three comparison = 0.07). Judging the benefits in context There are two positive studies with overall le outcome definition considerably different that of these studies partially explains the heterog appear applicable and generalisable to the Au	It (I2=78%). I New Zeala r discharge (i e suggesting i fit (89). A s prior to tree: here is very le I 0.67 to 0.90 ications. Furt to two doses of or more dose ngth of stay e in that used i eneity in the istralian and i	Removal of tw nd, and with a no respiratory s no effect. Furth number of stu atment in the hy ow quality evide 5; 7 RCTs, n=95 thermore, subgr compared with es RR 0.67, 95% considerably lor n Australia and length of stay as New Zealand h	vo studies with o primary outcor signs or sympto idees included ypertonic saline ence of a reduc 51). The seven roup analysis su those using the 6 CI 0.52 to 0.8 mger than currer New Zealand f nalysis and resu	overall length of ne definition cor- oms for 12 hour s restricted to the in the meta-ana arms. ed admission rat RCTs reporting ggests that nebu- ree or more (one 7, 3 RCTs, n=59 nt clinical practice for discharge (no	stay considerably long nsiderably different the rs), partially explains a e four largest trials, all dysis also appear to the in infants treated we this outcome include lised hypertonic saling e to two doses RR 0. 03; p value for subgroup e in Australia and New respiratory signs or s	ger tan the l at be vith d a e is 93, pup w Zealand, and y ymptoms for 12	hours), remova	
4. What harm might the proposed	d interventio	on/action do?						
Evidence statement						Quality of	of evidence	
For the important outcome of readmission a with nebulised hypertonic saline. For the important outcome of adverse event								
nebulised hypertonic saline.	5 111111 15 10	quality evident			ints in those treated w	1,11		
Judging the harms in context Evidence to date indicates no increased risk of and so the risk in severely unwell infants is un		fants treated. H	owever the maj	ority of studies h	nave only been in mile	d or moderately	unwell infants,	
5. What is the likely balance betw		nd harm?						
Evidence statement Evidence from the largest individual studie length of stay following the use of nebuli following the use of hypertonic saline, there dose regimens are ineffective. Given the lack of nebulized hypertonic saline in the ED to r Judging the balance of benefits and harm	s, and from sed hypertor is heterogen of long tern educe admiss	the meta-analy nic saline. Whil neity in the treat n effect of nebu sions is not supp	le there is wea tment regimens ilised hypertoni	k evidence of r used, and a sug c saline on lengt	reduced admission ra ggestion that one to t h of stay the routine	ved qualit ttes VE wo use	Overall y of evidence CRY LOW	
Benefits clearly outweigh harms.								
Benefits clearly outweigh harms	Recommend STRONG							
Benefits probably outweigh harms	Consider					CONDITIO	ONAL	
Not known	Make a ree	commendation	for research (se	e 8 below)		WEAK		
Benefits probably don't outweigh harms	1		<u> </u>	,		1		
Harms probably outweigh benefits	- Consider	against				CONDITI	ONAL	
Benefits clearly don't outweigh harms Harms clearly outweigh benefits Recommend against								

|--|

Summary statement						
Hypertonic saline is readily available in Australia and New Zealand, although use is currently confined to patients with bronchiectasis and cystic fibrosis.						
Yes Recommend/consider						
Not known	Consider economic evaluation	n				
No Recommend/consider against						
7. Final recommendation						
Do not administer nebulised hypertonic saline in infants presenting to hospital or hospitalised with Strength of recommendation						
bronchiolitis.		STRONG				
		CONDITIONAL				
		WEAK				

8. Recommendations for research

Further research is required to determine the optimum strength and frequency of this treatment. Further large multicenter trials are required to confirm the overall benefits of nebulized hypertonic saline in ED settings with regards to effects on admission into hospital. To date, research studies conducted in regard to the use of nebulised hypertonic saline have included a range of regimens, strengths and added medications. Further research is required to determine the optimum strength and frequency of this treatment.

Question 10.

NHMRC Evidence Summary

Question 10: In infants presenting to hospital or hospitalised with bronchio nebulised hypertonic saline improve clinically relevant end-points?	es administration of Evidence table ref: Badgett 2015, Chen 2014, Everard 2014, Florin 2014, Jacobs 2014, Khanal 2015, Maguire 2015, Mitchell 2013, Ojha 2015, Sharma 2013, Silver 2015, Teunissen 2015, Wu 2014, Zhang 2013, Zhang 2015 (78- 92).						
1. Evidence base (number of studies, level of evidence and risk of bias in the included studies)							
The evidence is based on one Cochrane systematic review of 11 RCTs (78) and a further nine additional RCTs (79-87). Subsequent to the Cochrane review there have been three further systematic reviews (88-90) and the newer trials	А	One or more Level I studies with a low risk of bias, or several Level II studies with a low risk of bias					
have included in an updated systematic review by the Cochrane authors (91) and	В	One or two Level II studies with a low risk of bias, or SR/several Level III studies with a low risk of bias					
a live meta-analysis (92).	С	One or two Level III studies with a low risk of bias or Level I or II studies with moderate risk of bias					
Use of hypertonic saline is associated with a reduced length of stay in infants treated with nebulised hypertonic saline (mean difference -0.44 days, 95% CI - 0.74 to -0.14 days; 15 RCTs, n=1,944) and a reduced admission rate (RR 0.80, 95% CI 0.67 to 0.96; 7 RCTs, n=951).	D	Level IV studies or Level I to III studies/SRs with a high risk of bias					
2. Consistency (if only one study was available, rank this component as 'not applicable')							
Studies reporting length of stay have considerable heterogeneity in the overall result (12=78%). Removal of two studies with overall length of stay considerably longer than current clinical practice in Australia and New Zealand,	А	All studies consistent					
and with a primary outcome definition considerably different than that used in Australia and New Zealand for discharge (no respiratory signs or symptoms for 12 hours), partially explains the heterogeneity and results in a pooled estimate	В	Most studies consistent and inconsistency can be explained					
suggesting no effect. Furthermore, analysis restricted to the four largest trials, all at lower risk of bias, again suggests no benefit (89). A number of studies	С	Some inconsistency, reflecting genuine uncertainty around question					
included in the meta-analysis also appear to be unbalanced with regards to duration of illness prior to treatment in the hypertonic saline arms.	D	Evidence is not consistent					
Studies reporting admission rates included a range of regimens, strengths and added medications. Furthermore, subgroup analysis suggests that nebulised hypertonic saline is not effective in the studies using just one to two doses compared with those using three or more (one to two doses RR 0.93, 95% CI 0.73 to 1.20, 4 RCTs, n=358; three or more doses RR 0.67, 95% CI 0.52 to 0.87, 3 RCTs, n=593; p value for subgroup comparison = 0.07).	NA	Not applicable (one study only)					
3. Clinical impact (indicate if the study results varied according to some unknown factor (not not be determined)	t simply stu	dy quality or sample size) and thus the clinical impact of the intervention could					
Length of stay for patients admitted to hospital receiving nebulised hypertonic saline is reduced by 0.45 of a day (95% CI -0.82 to -0.08). Admission rates to	А	Very large					
hospital for patients receiving nebulised hypertonic saline in the ED are reduced	В	Substantial					
by 20% (RR 0.80, 95% CI 0.67 to 0.96). There appears to be no increase in adverse events or change in readmission rates following discharge from EDs.	С	Moderate					
adverse events of change in readmission rates following discharge from EDS.	D	Slight/Restricted					

4. Generalisability (how well	does the body of evidence	match th	e population a	nd clinical sett	ings being t	argeted by the guideline?)			
Studies were conducted inter	Studies were conducted internationally (USA, Canada, UK, Netherlands,					A Evidence directly generalisable to target population			
Turkey, Tunis, Israel, Qatar,	, , ,	· · ·		/	В	Evidence directly generalisable to target p			
populations that are generalizable to patients with bronchiolitis seen in Australia			n Australia		some caveats				
and New Zealand.					С	Evidence not directly generalisable to target population by be sensibly applied			
No studies have been done specifically looking at Maori/Pacific Island or				D	Evidence not directly generalisable to target p	opulation and hard			
Aboriginal infants who do have a high disease burden with bronchiolitis.			t1S.	to judge whether sensible to apply					
					context in i	terms of health services / delivery of care and cultural fact	<i>.</i>		
There are two positive studies with overall length of stay considerably longer than current clinical practice in Australia and New Zealand, and with a primary				А	A Evidence directly applicable to Australian/New Zealan				
outcome definition considera				x 7		healthcare context	11 11		
Zealand for discharge (no res	spiratory signs or syn	nptoms	for 12 hours), removal	В	Evidence applicable to Australian/New Zeala context with few caveats	nd nealthcare		
of these studies partially expl						Evidence probably applicable to Australia	n/New Zealand		
and results in a pooled estimation appear applicable Australian/	00 0				С	healthcare context with some caveats			
saline is readily available in A					D	Evidence not applicable to Australian/New 2	Zealand healthcare		
confined to patients with bro	onchiectasis and cysti	c fibrosi	is.		D	context			
Other factors (indicate here an	y other factors that you i	took into	account when a	assessing the ev	vidence base	(for example, issues that might cause the group to downg	yrade or upgrade the		
recommendation)									
			4 0	oup's synthesis	of the evide.	nce relating to the key question, taking all the above factor	ors into account)		
Component	Rating	Descr	-						
1. Evidence base	D				II studies,	/SRs with a high risk of bias			
2. Consistency	D		nce is not con	nsistent					
3. Clinical Impact	D	0	Restricted	1. 1.1		1.			
4. Generalisability	B			,	0,	population with some caveats			
5. Applicability	С	Evider	ice probably	applicable to	o Australi	an/New Zealand healthcare context with some	caveats		
Evidence statement	mationally (USA Car	ada III	Z Nothoulan	da Turkar 1	Funia Ian	ol Ostan Dhahi India Arcontina Nanal Italy	China) in		
	• •			•		ael, Qatar, Dhabi, India, Argentina, Nepal, Italy, Jealand. Hypertonic saline is readily available in J			
Zealand, although use is curr	-						rustralia and rvew		
RECOMMENDATION (2 1		ui bronenie	,		LL GRADE OF RECOMMENDATION			
the guideline development group dr			А			n be trusted to guide practice			
action statements where possible)	5		В			n be trusted to guide practice in most situations			
* · ·						ovides some support for recommendations(s) by			
Do not administer nebulis	ed hypertonic salin	e in	С		n its application				
infants presenting to hospi	ital or hospitalised	with	D	Body of e	f evidence is weak and recommendation must be applied with caution				
bronchiolitis.			PP	Practice Po					
UNRESOLVED ISSUES	(If needed, keep a note oj	f specific i	ssues that arise	e when each rec	:ommendati	on is formulated and that require follow up)			
			when given i	n the ED rer	mains unc	ertain. Studies used different regimens of nebul	ised hypertonic		
saline, and the optimal regim									
					the followin	g questions. Where the answer is yes, please provide expl	anatory information		
about this. This information will			1 7	e guidelines)			MEG		
Will this recommendation re-	sult in changes in usu	ial care?					YES		
							NO		
Are there any resource implie	cations associated wit	th imple	menting this	recommend	lation?		YES		
							NO		
Will the implementation of the	his recommendation	require	changes in th	he way care i	s currentl	y organised?	YES		
							NO		
Are the guideline developme	nt group aware of an	y barrie	rs to implem	entation of t	his recom	imendation?	YES		
	5 1		I				NO		
L									

Question 11a.

							ticoids
Question 11a: In infants presenting to hospital of (nebulisation, oral, IM or IV) improve clinically			itis, does ad	ministration	n of systemic	or local glucocor	licolus
1. Outcome measures:		Quality of		nportance of out in making a deci			
	HIGH	MOD	LOW	V. LOW	Critical	Important	Not Important
D ₁ Rate of hospitalisation	X				X		
D ₂ Length of stay		X			X		
D ₃ Rate of readmission		X				X	
D ₄ Adverse outcomes			X			X	
2. Is there sufficient evidence to make a	recommendation	?	I	I	I		L
 Evidence statement: The evidence is based predominantly on one Cochra there has been two further RCTs (Alansari et al (94), 3. What benefit will the proposed intervent 	n=200; Jartti et al	(95), n=79).	17 RCTs inv	olving 2,596	infants with b	ronchiolitis (93). S	Subsequently
Evidence statement						Quality	of evidence
For the critical outcome of rate of hospitalisation the	· · ·						
hospitalisation at either one day (RR 0.92 , 95% CI 0 . n=1,530).	/8 to 1.08, n=1,/62	2) or seven da	ays (RR 0.86,	95% CI 0./() to 1.06,	E	IIGH
glucocorticoids effects length of stay (mean differen conducted by Alansari found a significant differ glucocorticoids and those not (favouring shorter le available to allow this to be combined with the ei	ence in geometric ngth of stay with	mean leng glucocorticoi	th of stay b ds). Unfortu	between tho nately publis	se treated wit shed data is no	h ot	
clinical significance. Judging the benefits in context There is a high quality of evidence that routine use o	oids on length of s	tay (-0.18, 95	5% CI -0.39	to 0.04) rem	ains of margin	al	onsistent
clinical significance. Judging the benefits in context There is a high quality of evidence that routine use o clinically relevant benefit.	f glucocorticoids in	tay (-0.18, 95	5% CI -0.39	to 0.04) rem	ains of margin	al	onsistent
 Elinical significance. udging the benefits in context There is a high quality of evidence that routine use of elinically relevant benefit. 4. What harm might the proposed interval 	f glucocorticoids in	tay (-0.18, 95	5% CI -0.39	to 0.04) rem	ains of margin	al pociated with any c	
clinical significance. Judging the benefits in context There is a high quality of evidence that routine use o clinically relevant benefit. 4. What harm might the proposed interv Evidence statement	f glucocorticoids in	tay (-0.18, 95	5% CI -0.39	to 0.04) remain with bronchie	ains of margin	al pociated with any c	onsistent of evidence
Evidence statement For the important outcome of rate of readmission th not affect readmission rate. Administration of glucocorticoids in the RCTs did n glucocorticoids have not been studied, the number o	bids on length of s f glucocorticoids in ention/action do ere is moderate qu ot result in excess a f participants is no	tay (-0.18, 95 the treatment ality evidence dverse event	i% CI -0.39 int of infants we that glucoccoss. However,	to 0.04) rem: with bronchio prticoid admi	ains of margin olitis is not asso nistration does n effects of	al ociated with any c	
 clinical significance. Judging the benefits in context There is a high quality of evidence that routine use of clinically relevant benefit. 4. What harm might the proposed interv Evidence statement For the important outcome of rate of readmission the not affect readmission rate. Administration of glucocorticoids in the RCTs did n glucocorticoids have not been studied, the number of adverse events were not systematically measured 	bids on length of s f glucocorticoids in ention/action do ere is moderate qu ot result in excess a f participants is no	tay (-0.18, 95 the treatment ality evidence dverse event	i% CI -0.39 int of infants we that glucoccoss. However,	to 0.04) rem: with bronchio prticoid admi	ains of margin olitis is not asso nistration does n effects of	al ociated with any c	of evidence
clinical significance. Judging the benefits in context There is a high quality of evidence that routine use of clinically relevant benefit. 4. What harm might the proposed interv Evidence statement For the important outcome of rate of readmission the not affect readmission rate. Administration of glucocorticoids in the RCTs did n glucocorticoids have not been studied, the number of and adverse events were not systematically measured Judging the harms in context While glucocorticoids do not appear to have an excer support the use of glucocorticoids in the treatment of bronchiolitis.	f glucocorticoids in f glucocorticoids in rention/action do ere is moderate qu ot result in excess a f participants is no across the RCTs. ss of short term ad f infants with bron	tay (-0.18, 95 the treatment ality evidence idverse event t adequate for verse events	the long-term	with bronchio prticoid admi the long-tern verse events	ains of margin olitis is not asso nistration does n effects of to be evident nts are unknow	al Deciated with any contract of the second	of evidence DERATE
clinical significance. Judging the benefits in context There is a high quality of evidence that routine use of clinically relevant benefit. 4. What harm might the proposed intervent Evidence statement For the important outcome of rate of readmission the not affect readmission rate. Administration of glucocorticoids in the RCTs did ne glucocorticoids have not been studied, the number of and adverse events were not systematically measured Judging the harms in context While glucocorticoids do not appear to have an excense support the use of glucocorticoids in the treatment of	f glucocorticoids in f glucocorticoids in rention/action do ere is moderate qu ot result in excess a f participants is no across the RCTs. ss of short term ad f infants with bron	tay (-0.18, 95 the treatment ality evidence idverse event t adequate for verse events	the long-term	with bronchio prticoid admi the long-tern verse events	ains of margin olitis is not asso nistration does n effects of to be evident nts are unknow	al Deciated with any contract of the second	of evidence DERATE
clinical significance. Judging the benefits in context There is a high quality of evidence that routine use of clinically relevant benefit. 4. What harm might the proposed intervent Evidence statement For the important outcome of rate of readmission the not affect readmission rate. Administration of glucocorticoids in the RCTs did ne glucocorticoids have not been studied, the number of and adverse events were not systematically measured Judging the harms in context While glucocorticoids do not appear to have an excess support the use of glucocorticoids in the treatment of bronchiolitis.	bids on length of s f glucocorticoids in ention/action do ere is moderate qu ot result in excess a f participants is no across the RCTs. ss of short term ad f infants with bron od and harm?	tay (-0.18, 95 the treatment ality evidence idverse event t adequate for verse events	the long-term	with bronchio prticoid admi the long-tern verse events	ains of margin olitis is not asso nistration does n effects of to be evident nts are unknow	al cociated with any cociated	of evidence DERATE
 Elinical significance. Indging the benefits in context There is a high quality of evidence that routine use of elinically relevant benefit. 4. What harm might the proposed intervent of the important outcome of rate of readmission the not affect readmission rate. Administration of glucocorticoids in the RCTs did n glucocorticoids have not been studied, the number of and adverse events were not systematically measured fudging the harms in context While glucocorticoids do not appear to have an excess support the use of glucocorticoids in the treatment of pronchiolitis. 5. What is the likely balance between go Evidence statement 	bids on length of s f glucocorticoids in ention/action do ere is moderate qu ot result in excess a f participants is no across the RCTs. ss of short term ad f infants with bron od and harm? ms.	tay (-0.18, 95 the treatment ality evidence idverse event t adequate for verse events	the long-term	with bronchio prticoid admi the long-tern verse events	ains of margin olitis is not asso nistration does n effects of to be evident nts are unknow	al cociated with any cociated	of evidence DERATE to of evidence to of infants with verall of evidence
 Elinical significance. fudging the benefits in context There is a high quality of evidence that routine use of Elinically relevant benefit. 4. What harm might the proposed interv Evidence statement For the important outcome of rate of readmission the not affect readmission rate. Administration of glucocorticoids in the RCTs did n glucocorticoids have not been studied, the number of adverse events were not systematically measured fudging the harms in context While glucocorticoids do not appear to have an excemport the use of glucocorticoids in the treatment of pronchiolitis. 5. What is the likely balance between go Evidence statement The lack of benefits clearly doesn't outweigh the harms in context 	bids on length of s f glucocorticoids in ention/action do ere is moderate qu ot result in excess a f participants is no across the RCTs. ss of short term ad f infants with bron od and harm? ms.	tay (-0.18, 95 the treatment ality evidence idverse event t adequate for verse events chiolitis, gluc	the long-term	with bronchio prticoid admi the long-tern verse events	ains of margin olitis is not asso nistration does n effects of to be evident nts are unknow	al cociated with any cociated	of evidence DERATE to of evidence to of infants with verall of evidence
 Elinical significance. fudging the benefits in context There is a high quality of evidence that routine use of Elinically relevant benefit. 4. What harm might the proposed interv Evidence statement For the important outcome of rate of readmission the not affect readmission rate. Administration of glucocorticoids in the RCTs did n glucocorticoids have not been studied, the number of adverse events were not systematically measured udging the harms in context While glucocorticoids do not appear to have an exceupport the use of glucocorticoids in the treatment or oronchiolitis. 5. What is the likely balance between go Evidence statement The lack of benefits clearly doesn't outweigh the harmatic or or adverse of the balance of benefits and harms in context 	bids on length of s f glucocorticoids in rention/action do ere is moderate qu ot result in excess a f participants is no across the RCT's. ss of short term ad f infants with bron od and harm? ms.	tay (-0.18, 95 the treatment ality evidence idverse event t adequate for verse events chiolitis, gluc	the long-term	with bronchio prticoid admi the long-tern verse events	ains of margin olitis is not asso nistration does n effects of to be evident nts are unknow	al peciated with any e Quality MOI vn. Given the lack I in the treatment O quality H	of evidence DERATE c of evidence to of infants with verall of evidence (IGH
 Elinical significance. fudging the benefits in context There is a high quality of evidence that routine use of Elinically relevant benefit. 4. What harm might the proposed interv Evidence statement For the important outcome of rate of readmission the not affect readmission rate. Administration of glucocorticoids in the RCTs did n glucocorticoids have not been studied, the number of adverse events were not systematically measured fudging the harms in context While glucocorticoids do not appear to have an excemport the use of glucocorticoids in the treatment of pronchiolitis. 5. What is the likely balance between go Evidence statement The lack of benefits clearly doesn't outweigh the harms in comparison in the second promotion of the second promotic o	bids on length of s f glucocorticoids in rention/action do ere is moderate qu ot result in excess a f participants is no across the RCT's. ss of short term ad if infants with bron od and harm? ms. ntext Recommend Consider	tay (-0.18, 95 the treatment ality evidence idverse event t adequate for verse events chiolitis, gluc	i% CI -0.39 int of infants we can be addressed as a second structure of the long-term to corticoids second	to 0.04) remains the long-term of term of ter	ains of margin olitis is not asso nistration does n effects of to be evident eroutinely used	al cociated with any cociated	of evidence DERATE c of evidence to of infants with verall of evidence (IGH
 Elinical significance. fudging the benefits in context There is a high quality of evidence that routine use of Elinically relevant benefit. 4. What harm might the proposed interv Evidence statement For the important outcome of rate of readmission the not affect readmission rate. Administration of glucocorticoids in the RCTs did n glucocorticoids have not been studied, the number of adverse events were not systematically measured udging the harms in context While glucocorticoids do not appear to have an excemport the use of glucocorticoids in the treatment or oronchiolitis. 5. What is the likely balance between go Evidence statement The lack of benefits clearly doesn't outweigh the harma in comparison of the balance of benefits and harms in comparison in the sentent of the sentent of the sentent of the sentent of the balance of benefits and harms in comparison is clearly outweigh harms Benefits probably outweigh harms 	bids on length of s f glucocorticoids in rention/action do ere is moderate qu ot result in excess a f participants is no across the RCT's. ss of short term ad f infants with bron od and harm? ms. ntext Recommend Consider Make a reco	tay (-0.18, 95 the treatment ality evidence idverse event t adequate for verse events chiolitis, gluc d mmendation	i% CI -0.39 int of infants we can be addressed as a second structure of the long-term to corticoids second	to 0.04) remains the long-term of term of ter	ains of margin olitis is not asso nistration does n effects of to be evident eroutinely used	al coiated with any constraints of the second secon	of evidence DERATE c of evidence to of infants with verall of evidence (IGH
clinical significance. Judging the benefits in context There is a high quality of evidence that routine use of clinically relevant benefit. 4. What harm might the proposed interv Evidence statement For the important outcome of rate of readmission the not affect readmission rate. Administration of glucocorticoids in the RCTs did n glucocorticoids have not been studied, the number of and adverse events were not systematically measured Judging the harms in context While glucocorticoids do not appear to have an exces support the use of glucocorticoids in the treatment of bronchiolitis. 5. What is the likely balance between go Evidence statement	bids on length of s f glucocorticoids in rention/action do ere is moderate qu ot result in excess a f participants is no across the RCT's. ss of short term ad if infants with bron od and harm? ms. ntext Recommend Consider	tay (-0.18, 95 the treatment ality evidence idverse event t adequate for verse events chiolitis, gluc d mmendation	i% CI -0.39 int of infants we can be addressed as a second structure of the long-term to corticoids second	to 0.04) remains the long-term of term of ter	ains of margin olitis is not asso nistration does n effects of to be evident eroutinely used	al coiated with any constraints of the second secon	of evidence DERATE c of evidence to of infants with verall of evidence (IGH
 clinical significance. Judging the benefits in context There is a high quality of evidence that routine use of clinically relevant benefit. 4. What harm might the proposed interv Evidence statement For the important outcome of rate of readmission the not affect readmission rate. Administration of glucocorticoids in the RCTs did n glucocorticoids have not been studied, the number of and adverse events were not systematically measured Judging the harms in context While glucocorticoids do not appear to have an exceed support the use of glucocorticoids in the treatment of pronchiolitis. 5. What is the likely balance between go Evidence statement The lack of benefits clearly doesn't outweigh the har Benefits probably outweigh harms Not known Benefits probably don't outweigh harms 	bids on length of s f glucocorticoids in rention/action do ere is moderate qu ot result in excess a f participants is no across the RCT's. ss of short term ad f infants with bron od and harm? ms. ntext Recommend Consider Make a reco	tay (-0.18, 95 the treatment ality evidence idverse event t adequate for verse events chiolitis, gluc d mmendation	i% CI -0.39 int of infants we can be addressed as a second structure of the long-term to corticoids second	to 0.04) remains the long-term of term of ter	ains of margin olitis is not asso nistration does n effects of to be evident eroutinely used	al coiated with any constraints of the second secon	of evidence DERATE c of evidence to of infants with verall of evidence (IGH

6. Is the intervention/action implementable in the New Zealand and Australian context?

Summary statement

Studies were conducted internationally (USA, Canada, UK, Belgium, Brazil, Turkey, Israel, Thailand, Mexico, Paraguay) in populations that are generalizable to patients with bronchiolitis seen in Australia and New Zealand. Glucocorticoids are widely used and available in Australia and New Zealand.

Yes	Recommend/consider			
Not known	Consider economic evaluation			
No	Recommend/consider against			
7. Final recommendation				
Do not administer local or systemic glucocorticoids to infants presenting to ho	ospital or hospitalised with	Strength of recommendation		
bronchiolitis.		STRONG		
		CONDITIONAL		
		WEAK		
8. Recommendations for research				

Studies of long-term effects are required.

Question 11a.

NHMRC Evidence Summary

Question 11a: In infants presenting to hospital or hospitalised with bronchiolitis, does administration Evidence table ref:								
of systemic or local glucocorticoids (nebulisation, oral, IM or IV) improve of	relevant end- Alansari 2013, Baraldi 2014, Fernandes							
points?	2013, Jartti 2015, Ralston 2014, Ricci 2015							
	(10, 13, 65, 93-95).							
1. Evidence base (number of studies, level of evidence and risk of bias in the included studies.	s)							
One systematic review (Fernandes et al (93), 17 RCTs, n=2,596) (level I).	One or more Level I studies with a low risk of bias, or							
Subsequent to this there have been two further RCTs (Alansari et al (94),	Α	several Level II studies with a low risk of bias						
n=200; Jartti et al (95), n=79).	В	One or two Level II studies with a low risk of bias, or SR/several						
	Б	Level III studies with a low risk of bias						
	С	One or two Level III studies with a low risk of bias or Level I or						
	C	II studies with moderate risk of bias						
	D	Level IV studies or Level I to III studies/SRs with a high risk						
	D	of bias						
2. Consistency (if only one study was available, rank this component as 'not applicable')								
There is possible inconsistency in evidence regarding length of stay.								
	А	All studies consistent						
The evidence regarding hospitalisations, adverse events and readmissions is		Most studies consistent and inconsistency can be explained						
consistent.	В							
	-							
	C	Some inconsistency, reflecting genuine uncertainty around						
		question						
	D	Evidence is not consistent						
	D	Evidence is not consistent						
	NA	Not applicable (one study only)						
3. Clinical impact (indicate if the study results varied according to some unknown factor (no.	t simply stu	dy quality or sample size) and thus the clinical impact of the intervention could						
not be determined)	15							
	А	Very large						
	В	Substantial						
	С	Moderate						
	D	Slight/Restricted						
4. Generalisability (how well does the body of evidence match the population and clinical set	tings being to	argeted by the guideline?)						
Studies were conducted internationally (USA, Canada, UK, Belgium, Brazil,	А	Evidence directly generalisable to target population						
Turkey, Israel, Thailand, Mexico, Paraguay) in populations that are generalizable	В	Evidence directly generalisable to target population with						
to patients with bronchiolitis seen in Australia and New Zealand.	в	some caveats						
Glucocorticoids are widely used and available in Australia and New Zealand.	С	Evidence not directly generalisable to target population but could						
		be sensibly applied						
No studies have been done specifically looking at Maori/Pacific Island or	D	Evidence not directly generalisable to target population and hard						
Aboriginal infants who do have a high disease burden with bronchiolitis.		to judge whether sensible to apply						

The results are directly applicable to the Australian/New Zealand healthcare				thcare	_ Evi	dence directly applicable to Aus	stralian/New Zealand	
context. Glucocorticoids are readily available in Australia and New Zealand.				A	lthcare context			
				B Evic	dence applicable to Australian/Ne	w Zealand healthcare		
					con	text with few caveats		
					(dence probably applicable to Austr	alian/New Zealand	
					heal	thcare context with some caveats		
					D Evic	dence not applicable to Australian	/New Zealand healthcar	
					cont			
Other factors (indicate here as	ny other factors that you	took into i	account when as	ssessing the evident	e base (for exi	ample, issues that might cause the group	to downgrade or upgrade the	
recommendation)								
EVIDENCE STATEMEN	NT MATRIX (summ	arise the d	evelopment grou	up's synthesis of th	e evidence rela	ting to the key question, taking all the a	bove factors into account)	
Component	Rating	Descri						
1. Evidence base	А	One or	more Level	I studies with a	low risk of	bias, or several Level II studies with	th a low risk of bias	
2. Consistency	С	Some i	nconsistency	, reflecting genu	iine uncertai	inty around question		
3. Clinical Impact	В	Substan						
4. Generalisability	В					ation with some caveats		
5. Applicability	А	Eviden	ce applicable	e to Australian/	New Zealan	d healthcare context		
Evidence statement								
There is clear evidence of no			infants with			0		
RECOMMENDATION (RADE OF RECOMMENDATI	ON	
					Body of evidence can be trusted to guide practice			
action statements where possible)			В			trusted to guide practice in mo		
D			С		-	s some support for recommendation	ons(s) but care should be	
Do not administer local or systemic taken in i				taken in its app				
0		tal or	D	-	ody of evidence is weak and recommendation must be applied with caution			
hospitalised with bronchio			PP	Practice Point				
UNRESOLVED ISSUES	(If needed, keep a note o	f specific is	sues that arise	when each recomm	endation is fo	rmulated and that require follow up)		
					ollowing questi	ions. Where the answer is yes, please pro	vide explanatory information	
about this. This information will			ion plan for the	e guidelines)				
Will this recommendation re	0		A . 1				YES	
There is some use of glucoco	orticoids in clinical pi	ractice in	Australia and	a New Zealand	•		NO	
Are there any resource impli	ications associated wi	th imple	menting this	recommendatio	n?		YES	
							NO	
Will the implementation of t	this recommendation	require o	changes in the	e way care is cu	rrently organ	nised?	YES	
r							NO	
Are the guideline development group aware of any barriers to implementation of			entation of this.	recommend	811011r	YES		
Are the guideline developme	ent group aware of at	ly Darrier	s to impleme				NO	

Question 11b.

Γ

GRADE Evidence Summary

Considered	Judgement - St	rength of rec	commendation

Question 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?										
1. Outcome measures:	Ouality of evidence				nportance of ou n making a dec					
	HIGH	MOD	LOW	V. LOW	Critical	Important	Not Important			
O1 Rate of hospitalisation				Х	X					
O2 Length of stay				X	X					
O3 Rate of readmission				X		X				
O ₄ Adverse outcomes			x			X				
2. Is there sufficient evidence to make a recommendation?										
 Evidence statement In the Fernandes et al (93) review none of the 17 RCTs specifically addresses the evidence for glucocorticoid use in infants presenting to hospital or hospitalised with a positive response to beta 2 agonists, or those with a personal or family history of atopy. 3. What benefit will the proposed intervention/action have? 										
Evidence statement						Quality	of evidence			
There is no specific evidence for this subgroup. In gener hospitalisation and length of stay there is high quality ev	f	VERY LOW								
length of stay.										
Judging the benefits in context There is no randomised controlled evidence of benefit fo	r this suberour	2								
4. What harm might the proposed intervention										
Evidence statement						Quality of e	evidence			
For the important outcome of rate of readmission no evid	dence is availab	ole.								
Administration of glucocorticoids in the RCTs did not result in excess adverse events. However, the long-term effects of glucocorticoids has not been studied, the number of participants is not adequate for very rare adverse events to be evident and adverse events were not systematically measured across the RCTs. Judging the harms in context										
Given the lack of evidence to support the use of glucocor the treatment of infants with bronchiolitis, with a positive 5. What is the likely balance between good a	e response to b			bronchioliti	s, glucocorticoi	ds should not be	routinely used in			
Evidence statement There is no good evidence to support glucocorticoids in i		onchiolitis an	id a positive	response to l	beta 2 agonists.	quality	overall of evidence RY LOW			
Judging the balance of benefits and harms in context	t									
Benefits clearly outweigh harms	Recommend	1				STRONG				
Benefits probably outweigh harms	Consider					CONDITI	CONDITIONAL			
Not known	Make a reco	mmendation	for research	(see 8 below	7)	WEAK				
Benefits probably don't outweigh harms	Consil					CONDUT	ONAL			
Harms probably outweigh benefits	Consider aga	amst				CONDITI	UNAL			
Benefits clearly don't outweigh harms										
Harms clearly outweigh benefits	Recommend against					STRONG				
6. Is the intervention/action implementable	in the New Z	ealand and	Australian o	context?						
Summary statement										
Beta 2 agonists are widely used and available in Australia and New Zealand. Yes Recommend/consider										
Not known Consider economic evaluation										
No Recommend/consider against										
7. Final recommendation				er again						
Do not administer systemic or local glucocorticoids to infants presenting to hospital or hospitalised with bronchiolitis, with a positive response to beta 2 agonists. Strength of recommendation STONG CONDITIONAL										
8. Recommendations for research					WEAK					
Studies of the use of glucocorticoids in infants presenting	to hospital or	hospitalised	with bronch	iolitis and wi	th a positive res	ponse to beta 2 :	agonists are			
needed.	, <u>r</u>	1			1		0			

Question 11b.

NHMRC Evidence Summary

Question 11b: In infants presenting to hospital or hospitalised with be	ronchioli	tis, with a positive Evidence table ref:					
response to beta 2 agonists, does administration of systemic or local glucocorticoids (nebulisation, Baraldi 2014, Fernandes 2013, Gadomski							
oral, IM or IV) improve clinically relevant end-points?	2014, Ralston 2014, Ricci 2015 (10, 13, 65,						
		69, 93).					
1. Evidence base (number of studies, level of evidence and risk of bias in the included studies)							
No studies have addressed this question.	А	One or more Level I studies with a low risk of bias, or several					
	11	Level II studies with a low risk of bias					
	В	One or two Level II studies with a low risk of bias, or SR/several					
		Level III studies with a low risk of bias					
	С	One or two Level III studies with a low risk of bias or Level I or					
		II studies with moderate risk of bias					
	D	Level IV studies or Level I to III studies/SRs with a high					
		risk of bias					
2. Consistency (if only one study was available, rank this component as 'not applicable')	1						
	А	All studies consistent					
	В	Most studies consistent and inconsistency can be explained					
	С	Some inconsistency, reflecting genuine uncertainty around					
		question					
	D	Evidence is not consistent					
	NA	Not applicable (one study only)					
3. Clinical impact (indicate if the study results varied according to some unknown factor (no.	t simply stu	dy auality or sample size) and thus the clinical impact of the intervention could					
not be determined)	15						
	А	Very large					
	В	Substantial					
	С	Moderate					
	D	Slight/Restricted					
4. Generalisability (how well does the body of evidence match the population and clinical set	tings being t	argeted by the guideline?)					
	А	Evidence directly generalisable to target population					
	В	Evidence directly generalisable to target population with some					
		caveats					
	С	Evidence not directly generalisable to target population but could be sensibly applied					
		Evidence not directly generalisable to target population and					
	D	hard to judge whether sensible to apply					
5. Applicability (is the body of evidence relevant to the Australian/New Zealand healthcare	context in 1	erms of health services / delivery of care and cultural factors?)					
	Δ	Evidence directly applicable to Australian/New Zealand					
	А	healthcare context					
	В	Evidence applicable to Australian/New Zealand healthcare					
	Б	context with few caveats					
	С	Evidence probably applicable to Australian/New Zealand healthcare context with some caveats					
		Evidence not applicable to Australian/New Zealand					
	D	healthcare context					
Other factors (indicate here any other factors that you took into account when assessing the en	vidence base	(for example, issues that might cause the group to downgrade or upgrade the					
recommendation) There is no good quality evidence evaluating the effect of glucocorticoids in infan	to with h-	probiolitis and a positive response to both 2 aponists					
There is no good quality evidence evaluating the effect of glucocordColds in infan	is with Dro	nemonus and a positive response to beta 2 agoinsts.					
Previously individual patient trials of beta 2 agonists have been suggested as a clin	ical option	However, given the high level of evidence (NHMRC A GRADE					

Previously individual patient trials of beta 2 agonists have been suggested as a clinical option. However, given the high level of evidence (NHMRC A, GRADE strong) demonstrating no benefit of beta 2 agonists in infants presenting to or hospitalised with bronchiolitis, and that there is no well-established way to determine an "objective method of response" to beta 2 agonists in bronchiolitis, this option is no longer recommended. Although it is true that a small subset of children with bronchiolitis may have reversible airway obstruction resulting from smooth muscle constriction, attempts to define a subgroup of responders have not been successful to date. If a clinical trial of bronchodilators is undertaken, clinicians should note that the variability of the disease process, the host's airway, and the clinical assessments, particularly scoring, would limit the clinician's ability to observe a clinically relevant response to bronchodilators (13).

Component	Rating	Description				
1. Evidence base	D	Level IV studies or Level I to III studies/SRs with a high risk of bias				
2. Consistency	NA	Not applicabl	e (one study only)			
3. Clinical Impact		Slight/Restric				
4. Generalisability		Evidence not directly generalisable to target population and hard to judge whether it is sensible to apply				
5. Applicability	D	Evidence not	applicable to Australian healthcare context			
agonists. RECOMMENDATION	J (What recommendation(s)	does	OVERALL GRADE OF RECOMMEND	×		
the guideline development group						
action statements where possible) B Body of evidence can be trusted to guide practice in most						
Do not administer systemic or local C Body of evidence provides some support for recommend taken in its application				idations(s) but care should be		
glucocorticoids to infants presenting to hospital or D Body of evidence is weak and recommendation must				st be applied with caution		
hospitalised with broncl	hiolitis, with a positive	PF		Practice Point		
response to beta 2 agoni						
UNRESOLVED ISSUE	\mathbf{S} (If needed, keep a note of .	specific issues tha	tt arise when each recommendation is formulated and that require follow u	<i>þ)</i>		
			indicate yes or no to the following questions. Where the answer is yes, plea	se provide explanatory information		
about this. This information n			for the guidelines)	VEC		
Will this recommendation		d care?		YES		
This practice is used by some clinicians.				NO		
Are there any resource implications associated with implementing this recommendation?				YES		
				NO		
	Will the implementation of this recommendation require changes in the way care is currently organised?					
Will the implementation o				NO		
Will the implementation o				NU		
		barriers to im	plementation of this recommendation?	YES		

Question 11c.

GRADE Evidence Summary

Considered Judgement - Strength of recommendation Question 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? Importance of outcome Outcome measures: Quality of evidence 1. in making a decision V. Not HIGH MOD LOW Critical Important LOW Important O1 Rate of hospitalisation x х х х O2 Length of stay Х O3 Rate of readmission х Х Х O4 Adverse outcomes 2 Is there sufficient evidence to make a recommendation? Evidence statement The evidence for the administration of glucocorticoids in bronchiolitis is based on one Cochrane systematic meta-analysis (Fernandes et al (93), 17 RCTs, n=2,596) and three systematic reviews (10, 13, 65). The evidence for the administration of adrenaline in bronchiolitis is based on one Cochrane systematic meta-analysis (Hartling et al (72), 19 RCTs, n=2,256), three systematic reviews (10, 13, 65) and seven subsequent RCTs (73-77, 96, 97). Evidence for the administration of the combination of glucocorticoids and adrenaline comes from a single high quality multi-centre RCT conducted in eight EDs in Canada (Plint et al (98), n=800). This trial compared adrenaline and high dose dexamethasone in a factorial design. What benefit will the proposed intervention/action have? 3. Evidence statement Quality of evidence For the critical outcome of hospitalisation there is low quality evidence in support of the combination of glucocorticoids and LOW adrenaline. Admission rates in unadjusted analysis of the Plint trial (98) suggested a possible benefit in the combination arm (adrenaline and glucocorticoid admission on day of enrolment RR 0.65, 95% CI 0.41 to 1.04; day 7 RR 0.65, 95% CI 0.45 to 0.95). However when adjusted for multiple comparisons in the factorial design this was no longer significant (adrenaline and glucocorticoid admission on day of enrolment RR 0.65, 95% CI 0.37 to 1.15; day 7 RR 0.65, 95% CI 0.41 to 1.03). For the critical outcome of length of stay the combination of glucocorticoids and adrenaline is no better than placebo. Judging the benefits in context Given the evidence base for the single interventions, and the exploratory nature of the finding in the Plint trial (98), combination treatment with glucocorticoids and adrenaline should only be used in infants with bronchiolitis as part of an RCT What harm might the proposed intervention/action do? 4. Evidence statement Quality of evidence For the important outcome of rate of readmission no evidence is available. LOW Adverse events were uncommon and generally self-limiting in the Plint study (98). Judging the harms in context Given the lack of evidence to support the use of glucocorticoids or adrenaline in isolation for the treatment of infants with bronchiolitis, and the exploratory nature of the findings suggesting possible benefit with combination of glucocorticoids and adrenaline, combination treatment of glucocorticoids and adrenaline should not be routinely used in the treatment of infants with bronchiolitis. 5. What is the likely balance between good and harm? Evidence statement Overall There is no good evidence to support the combination of glucocorticoids and adrenaline treatment in infants with quality of evidence LOW bronchiolitis. Judging the balance of benefits and harms in context STRONG Benefits clearly outweigh harms Recommend CONDITIONAL Benefits probably outweigh harms Consider WEAK Not known Make a recommendation for research (see 8 below) Benefits probably don't outweigh harms CONDITIONAL Consider against Harms probably outweigh benefits Benefits clearly don't outweigh harms STRONG Recommend against Harms clearly outweigh benefits Is the intervention/action implementable in the New Zealand and Australian context? 6. Summary statement Glucocorticoids and adrenaline are widely available in Australia and New Zealand, but rarely used in combination. Yes Recommend/consider Not known Consider economic evaluation No Recommend/consider against

Do not administer a combination of systemic or local glucocorticoids and a			
presenting to hospital or hospitalised with bronchiolitis.	STRONG		
	CONDITIONAL		
8. Recommendations for research	WEAK		
Studies of the use of a combination of glucocorticoids and adrenaline in in	ants presenting to	o nospital or nospitalised with brotenonus are needed.	
Question 11c. NHMRC Evidence	Summary		
Question 11c: In infants presenting to hospital or hospitalised with of the combination of systemic or local glucocorticoids (nebulisation improve clinically relevant end-points?		V) and adrenalineBaraldi 2014, Fernandes 2013, Hartling 2011, Livni 2010, Modaressi 2012, Plint 2009, Ralston 2014, Ricci 2015, Sarrell 2010, Simsek-Kiper 2011, Skjerven 2013	
1. Evidence base (number of studies, level of evidence and risk of bias in the include	d studies)	(10, 13, 65, 72-77, 93, 98).	
	,	One or more Level I studies with a low risk of bias, or several	
	А	Level II studies with a low risk of bias	
	В	One or two Level II studies with a low risk of bias, or SR/sever Level III studies with a low risk of bias	
	С	One or two Level III studies with a low risk of bias or Level I or II studies with moderate risk of bias	
	D	Level IV studies or Level I to III studies/SRs with a high risk of bias	
2. Consistency (if only one study was available, rank this component as 'not applica	ble')		
	А	All studies consistent	
	В	Most studies consistent and inconsistency can be explained	
	С	Some inconsistency, reflecting genuine uncertainty around question	
	D	Evidence is not consistent	
	NA	Not applicable (one study only)	
3. Clinical impact (indicate if the study results varied according to some unknown fan not be determined)	ector (not simply stud	y quality or sample size) and thus the clinical impact of the intervention could	
	А	Very large	
	В	Substantial	
	С	Moderate	
	D	Slight/Restricted	
4. Generalisability (how well does the body of evidence match the population and clin	iical settings being ta	rgeted by the guideline?)	
	А	Evidence directly generalisable to target population	
	В	Evidence directly generalisable to target population with some caveats	
	С	Evidence not directly generalisable to target population but coul be sensibly applied	
	D	Evidence not directly generalisable to target population and hard to judge whether sensible to apply	
		rms of health services / delivery of care and cultural factors?)	
5. Applicability (is the body of evidence relevant to the Australian/New Zealand he	althcare context in te		
	Allocare context in te	Evidence directly applicable to Australian/New Zealand healthcare context	
		healthcare context Evidence applicable to Australian/New Zealand healthcare context with few caveats	
5. Applicability (is the body of evidence relevant to the Australian/New Zealand he Single study from Canada.	А	healthcare context Evidence applicable to Australian/New Zealand healthcar	

Other factors (indicate bere any other factors that you took into account when assessing the evidence base (for example, issues that might cause the group to downgrade or upgrade the							
recommendation)							
Given the lack of evidence to support the use of glucocorticoids or adrenaline in isolation for the treatment of infants with bronchiolitis, and the exploratory							
				of glucocorticoids and adrenaline, combination treatment of glucocortic	coids and adrenaline		
should not be routinely used							
EVIDENCE STATEMEN	T MATRIX (summ	earise the a	development g	roup's synthesis of the evidence relating to the key question, taking all the above fact	tors into account)		
Component	Rating	Descr	iption				
1. Evidence base	D			or Level I to III studies/SRs with a high risk of bias			
2. Consistency	NA	Not ap	oplicable				
3. Clinical Impact	В	Substa					
4. Generalisability	В	Evider	nce directly	generalisable to target population with some caveats			
5. Applicability	В	Evider	nce applical	ble to Australian/New Zealand healthcare context with few caveats			
Evidence statement							
Do not administer a combina	ation of systemic or	local glu	cocorticoid	ls and adrenaline to infants presenting to hospital or hospitalised with b	oronchiolitis.		
RECOMMENDATION (<i>V</i>				OVERALL GRADE OF RECOMMENDATION			
the guideline development group draw from this evidence? Use A Body of evidence can be trusted to guide practice							
action statements where possible) B Body of evidence can be trusted to guide practice in most situations							
Body of evidence provides some support for recommendations(s) but care should be							
taken in its application							
local glucocorticoids and adrenaline/epinephrine D Body of evidence is weak and recommendation must be applied with caution							
to infants presenting to hospital or hospitalised PP Practice Point							
with bronchiolitis.							
UNRESOLVED ISSUES (If needed, keep a note of specific issues that arise when each recommendation is formulated and that require follow up)							
IMPLEMENTATION OF RECOMMENDATION (Please indicate yes or no to the following questions. Where the answer is yes, please provide explanatory information							
about this. This information will be used to develop the implementation plan for the guidelines)							
Will this recommendation res	sult in changes in us	ual care?			YES		
	NO						
Are there any resource implic	Are there any resource implications associated with implementing this recommendation? YES						
	NO						
Will the implementation of th	nis recommendation	require	changes in	the way care is currently organised?	YES		
					NO		
Are the guideline development	nt group aware of a	ny barrie	rs to implei	mentation of this recommendation?	YES		
					NO		

Question 12a.

Cons	idered Judgen	nent - Streng	th of recom	mendation			
Question 12a: In infants presenting to hospital or h relevant end-points?	ospitalised wi	th bronchiol	itis, does ad	ministratio	n of suppleme	ental oxygen imp	rove clinically
1. Outcome measures:		Quality of	evidence			nportance of out in making a deci	
	HIGH	MOD	LOW	V. LOW	Critical	Important	Not Important
O1 Admission to hospital			x		x		
O2 Length of stay in hospital			x		x		
O3 Oxygen saturation target			x			х	
O ₄ Feeding difficulties				х		х	
O ₅ Readmission				x		х	
2. Is there is insufficient evidence to make	a recommenda	tion?			•	•	
Evidence statement: The evidence is based on a systematic review (99), an ev observational cohort study (101). There was low - very weak recommendation based on low level evidence and to hospital.	low level evider reasoning from	ice for the us first principl	e supplement	tal oxygen al	though the evic	lence based guide	line formed a
3. What benefit will the proposed interventi	on/action hav	e:				0.15	c :1
Evidence statement:For the critical outcome of admission to hospital there the rate of hospital admission.For the critical outcome of length of stay in hospital hospital length of stay.For the important outcome of oxygen saturation target	there is low gr	ade evidence	that admini	stration of d	oxygen prolong	28 I 75	of evidence .OW
target for supplemental oxygen. Judging the benefits in context	7 1 1 1 4	. 1. 1. 1					
The evidence is applicable and generalisable to the New 4. What harm might the proposed intervent			th settings.				
Evidence statement						Quality of e	vidence
For the important outcome of feeding difficulties there a	s very low grad	e evidence th	at oxygen the	erapy affects	feeding.		RY LOW
Judging the harms in context						ł	
There is little evidence to determine the effect of oxyger 5. What is the likely balance between good	<u>,</u> ,	ding difficult	ies.				
Evidence statement						0	verall
The benefit of supplemental oxygen therapy has not be been made and observational studies have looked at le effectiveness. Judging the balance of benefits and harms in conte:	ngth of time of					s quality	of evidence
Benefits probably outweigh harms.	χι.						
Benefits clearly outweigh harms	Recommend	1				STRONG	
Benefits probably outweigh harms	Consider					CONDITI	ONAL
Not known	Make a reco	mmendation	for research	(see 8 below	r)	WEAK	
Benefits probably don't outweigh harms	Consider ag	ainst				CONDITIO	ONAL
Harms probably outweigh benefits							
Benefits clearly don't outweigh harms	Recommend	l against				STRONG	
Harms clearly outweigh benefits		/1	A				
6. Is the intervention/action implementable	e in the New Z	lealand and	Australian C	context?			
Summary statement Oxygen therapy has been based on practice by first p. Zealand setting.	rinciples and lo	w to very lo	w grade evid	lence. The e	widence is app	licable to the Au	stralian and New
Yes		Re	commend/c	consider			
Not known		Со	nsider econor	mic evaluatio	on		
No		Ree	commend/co	onsider again	st		

7. Final recommendation	
Consider the use of supplemental oxygen in the treatment of hypoxic (saturations less than 92%) infants with bronchiolitis.	Strength of recommendation
	Conditional

8. Recommendations for research

Large randomised controlled studies with pre-defined indications and protocols for supplemental oxygen are required to determine the effect on hospital admission, length of stay, oxygen saturation targets and effect on feeding difficulties.

Question 12a.

Question 12a: In infants presenting to hospital or hospitalised with bronchi of supplemental oxygen improve clinically relevant end-points?	iolitis, do	es administration	Evidence table ref: Cunningham 2012, Mitchell 2013, Ralston
of suppremental oxygen improve clinically relevant end-points:			2014, Unger 2008 (13, 99-101).
1. Evidence base (number of studies, level of evidence and risk of bias in the included studies)		
One systematic review (Level I study) with a high risk of bias and one evidence	А		I studies with a low risk of bias, or several
based guideline (Level I study) with a moderate risk of bias. There have been no RCTs.		Level II studies with One or two Level II	a low risk of bias studies with a low risk of bias, or SR/several
	В	Level III studies with	h a low risk of bias
There has been one prospective observational case series of 68 infants (Level IV) and one retrospective observational cohort study of 102 infants (Level IV).	С		II studies with a low risk of bias or Level moderate risk of bias
All studies are rated moderate for risk of bias.	D		Level I to III studies/SRs with a high risk of
	D	bias	
2. Consistency (if only one study was available, rank this component as 'not applicable')	r	Γ	
All studies recommend the use of supplemental oxygen but there is no direct comparison with withholding therapy. Outcomes have been limited to length of stay in hospital and oxygen saturation targets with limited evaluation of other	А	All studies consisten	t
outcomes including no evidence for readmission.	В	Most studies consist	ent and inconsistency can be explained
	С	Some inconsistency, question	reflecting genuine uncertainty around
	D	Evidence is not con	nsistent
	NA	Not applicable (one	study only)
3. Clinical impact (indicate if the study results varied according to some unknown factor (not not be determined)	t simply stud	ly quality or sample size) a	and thus the clinical impact of the intervention could
The use of supplemental oxygen therapy on increasing admission rate and prolonging admissions has not been evaluated. The impact on these parameters	А	Very large	
has significant impact on wellbeing of infants as well as cost implications for	В	Substantial	
health services.	С	Moderate	
	D	Slight/Restricted	
4. Generalisability (how well does the body of evidence match the population and clinical sette	ings being to	argeted by the guideline?)	
Current limited evidence has been obtained from similar health systems and can	А		neralisable to target population
be generalised to Australian and New Zealand setting.	в		generalisable to target population with
		some caveats	y generalisable to target population but could
	С	be sensibly applied	, generalisable to unget population but could
	D		y generalisable to target population and hard
5. Applicability (is the body of evidence relevant to the Australian/New Zealand healthcare	context in t		nsible to apply elivery of care and cultural factors?)
Relevant to Australian and New Zealand setting.			applicable to Australian/New Zealand
Recvant to Australian and New Zealand setting.	Α	healthcare context	
	В	Evidence applicable context with few cav	to Australian/New Zealand healthcare reats
	С	Evidence probably a healthcare context w	pplicable to Australian/New Zealand
	D	Evidence not applic	cable to Australian/New Zealand healthcare
Other factors (indicate here any other factors that you took into account when assessing the er	idence hase	context (for example, issues that n	night cause the group to downgrade or upgrade the
recommendation)		yo, arampio, issues intel m	ing a compare the group to complete of approace the
Administration of oxygen is used by reason of first principles.			

Component	Rating	Desci	ription		
1. Evidence base	С	One o	or two Lev	rel III studies with a low risk of bias or Level I or II studies with n	noderate risk of bias
2. Consistency	D	Evide	nce is not	consistent	
3. Clinical Impact	С	Mode	rate		
4. Generalisability	В	Evide	nce direct	ly generalisable to target population with some caveats	
5. Applicability	А	Evide	nce direct	ly applicable to Australian/New Zealand healthcare context	
saturation targets, or eff	ect on feeding difficu	ulties.	t principle	es and there is weak evidence for its effect on hospital admission,	
RECOMMENDATIC	,			OVERALL GRADE OF RECOMMENDATI	ON
the guideline development gro	1 5	ence? Use	А	Body of evidence can be trusted to guide practice	
action statements where poss	ible)		В	Body of evidence can be trusted to guide practice in most sit	
Consider the use of su			С	Body of evidence provides some support for recommend should be taken in its application	dations(s) but care
treatment of hypoxic (s less than	D	Body of evidence is weak and recommendation must be appl	lied with caution
92%) infants with bror	nchiolitis.		PP	Practice Point	
Consistent definition of Process of weaning the	oxygen saturation ta oxygen therapy N OF RECOMME	nrget demons	strating hy (<i>Please int</i>	urise when each recommendation is formulated and that require follow up) poxia and need for administration of oxygen dicate yes or no to the following questions. Where the answer is yes, please pro-	vide explanatory information
Will this recommendation				, 100 Summers)	YES
The practice of startin	0			ed.	NO
Are there any resource is	mplications associate	ed with imple	ementing	this recommendation?	YES
	×		Ũ		NO
Will the implementation	of this recommendation	ation require	changes i	n the way care is currently organised?	YES
					NO
		of our bourio	re to impl	ementation of this recommendation?	YES
Are the guideline develo Nurse led commencer		•	· ·		115

Question 12b.

GRADE Evidence Summary

Considered Judgement - Strength of recommendation

Question 12b: In infants presenting to hospital or ho or discontinuation of supplemental oxygen to improv	-			vel of oxyge	n saturation s	hould lead to co	mmencement
1. Outcome measures:		Quality of	evidence			nportance of out n making a deci	
	HIGH	MOD	LOW	V. LOW	Critical	Important	Not Important
O1 Admission to hospital		x			х		
O2 Length of stay in hospital			X		X		
O3 Oxygen saturation target		х			х		
O4 Feeding difficulties			x			х	
O5 Readmission to hospital		х				Х	
2. Is there is insufficient evidence to make a	recommenda	tion?			•		
The evidence relates to the role of saturations in patient n RCTs (103, 104). Additional evidence was from a prospe							
3. What benefit will the proposed intervention			ies (100) and	unce redosj		tional studies (10	, 103, 100).
Evidence statement						Quality	of evidence
For the critical outcome of admission to hospital there is	moderate evid	ence that lov	ver oxygen s	aturation lev	els increases th		
rate of admission independently of other factors.						MOI	DERATE
For the critical outcome of length of stay in hospital the	e is low level e	vidence that	lower oxyge	n saturations	s prolong lengtl	h	
of stay.							
For the critical outcome of oxygen saturation target	there is mod	erate eviden	ice in uncor	nplicated bi	onchiolitis tha	t	
saturations less than 92% is an acceptable absolute target				1			
Judging the benefits in context	Coolord and Au	studion hoal	the pattings				
The evidence is applicable and generalisable to the New 2 4. What harm might the proposed intervention			in settings.				
Evidence statement	•					Quality of e	vidence
For the important outcome of readmission there is	high level evi	dence that	oxygen level	saturations	do not affec	-	
readmissions to hospital.						MOI	DERATE
For the important outcome of feeding difficulties the	e is very low	evidence fo	or the impac	t of oxygen	saturations of	n	
resolution.	2			.0			
Judging the harms in context Oxygen saturation targets less than 92% do not impact or	, and uning food	ing difficulti	oo ou acadamic	viene			
5. What is the likely balance between good a	0		es of feading	5510115.			
Evidence statement:						0	verall
The harms probably outweigh the benefits.							of evidence
Judging the balance of benefits and harms in context						MOD	DERATE
Not known	L						
Benefits clearly outweigh harms	Recommend					STRONG	
Benefits probably outweigh harms	Consider					CONDITIO	ONAL
Not known	Make a recor	nmendation	for research	(see 8 below)	WEAK	
Benefits probably don't outweigh harms	Consider ag	ainst				CONDITI	ONAL
Harms probably outweigh benefits		,					
Benefits clearly don't outweigh harms	Recommend	against				STRONG	
Harms clearly outweigh benefits	iteeoimiteite	uguillot				omorio	
6. Is the intervention/action implementable	in the New Z	ealand and	Australian c	ontext?			
Summary statement Oxygen saturation level has been demonstrated to infl discontinued has been established less than 92%.	uence admissio	on and lengt	h of stay. T	'he level at	which oxygen	therapy should o	commence or be
Yes		Ree	commend/c	onsider			
Not known		Cor	nsider econor	nic evaluatio	n		
No		Rec	commend/co	nsider again	st		

7. Final recommendation	
In uncomplicated bronchiolitis oxygen supplementation should be commenced if the oxygen saturation	Strength of recommendation
level is sustained at a level less than 92%. At oxygen saturation levels of 92% or greater oxygen therapy	STRONG
should be discontinued.	CONDITIONAL
	WEAK
8. Recommendations for research	
Further randomised controlled studies are needed to confirm the level of oxygen saturations to establish ox	ygen therapy.
The effect of sustained hypoxia on long term development needs to be measured.	

Further research is needed in determining an appropriate oxygen saturation level at which to consider discharge of an infant from hospital with bronchiolitis.

Question 12b.

Question 12b: In infants presenting to hospital or hospitalised with broncl		
saturation should lead to commencement or discontinuation of supple clinically relevant end-points?	emental (Cunningham 2012, Cunningham 2015, Hendaus 2015,
chineary relevant end-points:		Mitchell 2013, Ralston 2014, Schroder
		2004, Schuh 2014, Unger 2008 (13, 99-
		106).
1. Evidence base (number of studies, level of evidence and risk of bias in the included studies	5)	
The evidence relates to the role of saturations in patient management and is	А	One or more Level I studies with a low risk of bias, or several
based on two systematic reviews (99, 102), an evidence based guideline (13) and	11	Level II studies with a low risk of bias
two RCTs (103, 104). Additional evidence was from a prospective	В	One or two Level II studies with a low risk of bias, or
observational case series (100) and three retrospective observational studies (101, 105, 106). Recent RCTs have established the absolute level of oxygen		SR/several Level III studies with a low risk of bias One or two Level III studies with a low risk of bias or Level I or
saturation for oxygen therapy to commence or be discontinued.	С	Il studies with moderate risk of bias
		Level IV studies or Level I to III studies/SRs with a high risk of
	D	bias
2. Consistency (if only one study was available, rank this component as 'not applicable')		
Two Level II RCTs relating to question and moderate to high grade evidence	А	All studies consistent
based systematic reviews demonstrating limited evidence addressing the question.	11	
	В	Most studies consistent and inconsistency can be explained
	С	Some inconsistency, reflecting genuine uncertainty around
		question
	D	Evidence is not consistent
	NA	Not applicable (one study only)
 Clinical impact (indicate if the study results varied according to some unknown factor (non not be determined) 	t simply stu	ly quality or sample size) and thus the clinical impact of the intervention could
Saturations measurement will modify current practice	А	Very large
	В	Substantial
	С	Moderate
	D	Slight/Restricted
4. Generalisability (how well does the body of evidence match the population and clinical set	tings being to	argeted by the guideline?)
	А	Evidence directly generalisable to target population
	В	Evidence directly generalisable to target population with some caveats
	С	Evidence not directly generalisable to target population but
	Ŭ	could be sensibly applied
	D	Evidence not directly generalisable to target population and hard
		to judge whether sensible to apply
5. Applicability (is the body of evidence relevant to the Australian/New Zealand healthcare	context in t	
	А	Evidence directly applicable to Australian/New Zealand healthcare context
	В	Evidence applicable to Australian/New Zealand healthcare context with few caveats
	С	Evidence probably applicable to Australian/New Zealand
		healthcare context with some caveats
	D	Evidence not applicable to Australian/New Zealand healthcare
	1	context

	ere any other factors that y	ou took into	account when	a assessing the evidence base (for example, issues that might cause the group to down	grade or upgrade the
recommendation)	dress the question of	ovvicon cat	unation love	l for commencing or discontinuing oxygen supplementation	
					11 .1 .1
factors into account)	MENT MATRIX (su	nmarise th	ie developn	nent group's synthesis of the evidence relating to the key question, takin	ng all the above
Component	Rating	Descr	iption		
1. Evidence base	В	One o	r two Level	II studies with a low risk of bias, or SR/several Level III studies with	a low risk of bias
2. Consistency	В	Most	studies cons	sistent and inconsistency can be explained	
3. Clinical Impact	В	Substa	intial		
4. Generalisability	С	Evide	nce not dire	ectly generalisable to target population but could be sensibly applied	
5. Applicability	С	Evide	nce probabl	y applicable to Australian/New Zealand healthcare context with some	caveats
Evidence statement:					
of other factors.	-			evidence that lower oxygen saturation levels increases the rate of adm el evidence that lower oxygen saturations prolong length of stay.	ission independently
For the critical outcome	of oxygen saturation t	arget there	e is moderat	e evidence in uncomplicated bronchiolitis that saturations less than 92	% is an acceptable
target for supplemental	oxygen				
RECOMMENDATIC	N (What recommendatio	n(s) does		OVERALL GRADE OF RECOMMENDATION	
the guideline development gro		e? Use	А	Body of evidence can be trusted to guide practice	
action statements where possi	ible)		В	Body of evidence can be trusted to guide practice in most situations	
In uncomplicated bro	nchiolitis oxygen		С	Body of evidence provides some support for recommendation should be taken in its application	s(s) but care
supplementation shou			D	Body of evidence is weak and recommendation must be applied with	th caution
oxygen saturation leve					
than 92%. At oxygen s			PP	Practice Point	
greater oxygen therap					
				ise when each recommendation is formulated and that require follow up)	1
				rate yes or no to the following questions. Where the answer is yes, please provide exp	planatory information
about this. This information				the guidetines)	YES
Will this recommendation				andian discharge for infants with bronchislitis	
				earlier discharge for infants with bronchiolitis	NO
Are there any resource in			ementing th	is recommendation?	YES
Reduced health care c	osts relating to inpat	ient care			NO
Will the implementation	of this recommendati	on require	changes in	the way care is currently organised?	YES
_		-		tion levels to determine admission to hospital and discharge	NO
from care					
Are the guideline develo	pment group aware of	any barrie	rs to impler	nentation of this recommendation?	YES
					NO

Question 13.

Considered	Judgement -	Strength	of recommen	dation			
Question 13: In infants hospitalised with bronchiolitis doe clinically relevant end-points.	es continuous	s monitor	ing of pulse or	kimetry ben		-	- -
1. Outcome measures:		Quality	of evidence		-	ortance of out making a decis	
	HIGH	MOL	D LOW	V. LOW	Critical	Important	Not Importan t
O1 Length of stay in hospital		x			x		
O2 Thresholds for discharge oxygen saturations			x			х	
O3 Frequency of nocturnal desaturations				х		х	
O4 Maintenance of feeding				x		х	
O5 Cost savings				x			x
2. Is there is insufficient evidence to make a recor	nmendation?			•			•
The evidence is based on a systematic review and two high qua searches involving Medline, EMBASE and Cochrane. In additi randomised, parallel-group, superiority clinical trial of 161 infar patients evaluating discharge oxygen saturation levels. A furthe 3. What benefit will the proposed intervention/ac	ion, there was its to continuo er three retrosp	one rando ous vs inter	mised, double- rmittent pulse o	blind, paralle eximetry and	el-group trial inv	volving 213 infa	nts, one
Evidence statement:						Quality	of evidence
For the critical outcome of length of stay there is moderate q not reduce hospital length of stay in non-hypoxic (saturations g For the critical outcome of threshold for discharge oxygen sat different discharge oxygen saturations thresholds. For the critical outcome frequency of nocturnal desaturations	reater than or urations, there	equal to 9 is low qu	2%) infants. ality evidence o	on the comp	arative effect of	f	ERATE
nocturnal desaturations influences length of stay. Judging the benefits in context The evidence is applicable and can be generalised to all acute he settings.		ties caring	g for bronchioli	tic infants in	the New Zeala	nd and Australi	an health
4. What harm might the proposed intervention/ac	ction do?						
Evidence statement For the important outcome of maintenance of feeding there affect feeding during the course of the disease.	is ve r y low qu	ality evid	ence that conti	nuous moni	toring does no	Quality of	evidence
For the important outcome of cost there was no evidence of r continuous oximetry monitoring.	educed cost sa	wings in th	hose infants ad	mitted with	bronchiolitis or		YLOW
Judging the harms in context							
5. What is the likely balance between good and ha	ırm:						
Evidence statement The current evidence does not support continuous pulse oxime	etry monitoring	<i>z</i> .				quality of	erall f evidence DW
Judging the balance of benefits and harms in context Not Known							
Benefits clearly outweigh harms	Recommen	ıd				STRONG	
Benefits probably outweigh harms	Consider					CONDIT	ONAL
Not known	Make a reco	ommenda	tion for researc	h (see 8 belo	ow)	WEAK	
Benefits probably don't outweigh harms	Consider	agingt				CONTRAT	IONAL
Harms probably outweigh benefits	Consider a	gamst				CONDIT	
Benefits clearly don't outweigh harms	Recommen	d against				STRONG	
Harms clearly outweigh benefits	Recommen	di agailist				SIROINO	
6. Is the intervention/action implementable in the	e New Zealan	id and Au	istralian conte	xt?			
Summary statement The benefit of continuous pulse oximetry in bronchiolitis has n Yes	ot been establi		requires additic Recommend/		to support its i	coutine use in al	settings.
Not known			Consider econo		on		
No			Recommend/co				
			acconnicitu/ 0	monor again	101		

7. Final recommendation	
Routine use of continuous 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.	Strength of recommendation STRONG CONDITIONAL WEAK
8. Recommendations for research	
Randomised controlled studies are needed to establish use of continuous oximetry in the setting of hypoxic inf Further studies are needed to determine what effect continuous oximetry monitoring has on time to discharge.	

Question 13. NHMRC Evidence Summary

Question 13: In infants hospitalised with bronchiolitis does continuous	Eviden	ce table ref:
Monitoring of pulse oximetry beneficially change medical management		006, Cunningham 2012, Hendaus 2015, Kaditis 2015,
or clinically relevant end-points.		och 2015, Mitchell 2013, Ralston 2014, Schroeder 2004,
······································		2014, Unger 2008 (13, 99-102, 104-108).
1. Evidence base (number of studies, level of evidence and risk of bias in the included studies)	oonun	,,,,,,,,,,,,,,,,,,,
	-	
One systematic review (level I) and two evidence reviews (level II-a) with moderate to	А	One or more Level I studies with a low risk of bias, or
low risk of bias, one randomised, double-blind, parallel-group trial involving 213		several Level II studies with a low risk of bias
infants (level II) rated low risk of bias, one randomised, parallel-group, superiority	В	One or two Level II studies with a low risk of bias, or
clinical trial of 161 patients (Level II) with low risk of bias and one prospective	D	SR/several Level III studies with a low risk of bias
observational study (level III) with high risk of bias involving 68 infants and three	С	One or two Level III studies with a low risk of bias or
retrospective studies involving 439 infants, (level III-2) with a high risk of bias.	C	Level I or II studies with moderate risk of bias
	D	Level IV studies or Level I to III studies/SRs with a high
	D	risk of bias
2. Consistency (if only one study was available, rank this component as 'not applicable')		
Evidence is inconsistent that in infants hospitalised with bronchiolitis that continuous		
monitoring of pulse oximetry either at admission, at several key points during	А	All studies consistent
admission and during the weaning phase of oxygen beneficially changes medical		Most studies consistent and inconsistency can be
management and/or clinically relevant end-points such as length of stay.	В	explained
		*
	С	Some inconsistency, reflecting genuine uncertainty around
		question
	D	Evidence is not consistent
	D	Evidence is not consistent
	NA	Not applicable (one study only)
2 Clinian linear (in line if the state when with a with a second state (as the state for the state f		in an energy in the set of the internet of the internet in the set
3. Clinical impact (indicate if the study results varied according to some unknown factor (not simply not be determined)	sinay quan	iy or sample size) and thus the cunical impact of the intervention could
Pulse oximetry and oxygen thresholds determines the length of stay in hospital coupled	А	Very large
with the return of feeding, thereby reducing the costs. There is low to moderate clinical	11	very large
evidence on the benefit of continuous oximetry for infants who have been hospitalized	В	Substantial
with bronchiolitis. Adverse events and the effect of low oxygen saturations on the	С	Moderate
patient appear unaffected by continuous vs intermittent oximetry.	D	Slight/Restricted
4. Generalisability (how well does the body of evidence match the population and clinical settings bein	a targeted	In the guideline?)
All studies matched the population and clinical settings and can be generalised to	А	Evidence directly generalisable to target population
Australia and New Zealand; two European studies, two United Kingdom studies, three	В	Evidence directly generalisable to target population
USA studies and one study conducted in Western Australia.		with some caveats
	С	Evidence not directly generalisable to target population
		but could be sensibly applied
	D	Evidence not directly generalisable to target population and hard to judge whether sensible to apply
5. Applicability (is the body of evidence relevant to the Australian/New Zealand healthcare context a	in terms of	
		Evidence directly applicable to Australian/New Zealand
The results are directly applicable to the Australasian Healthcare context.	А	
Oximeters are used in all hospital settings.		healthcare context
	В	Evidence applicable to Australian/New Zealand healthcare context with few caveats
		Evidence probably applicable to Australian/New Zealand
	С	healthcare context with some caveats
	-	Evidence not applicable to Australian/New Zealand
	D	healthcare context
Other factors (indicate here any other factors that you took into account when assessing the evidence h	ase (for exa	
recommendation)		
No direct evidence to address the question of oxygen saturation level.		

Component	Rating	Description	
1. Evidence base	С	One or two Level 1	III studies with a low risk of bias or Level I or
	C	II studies with mod	derate risk of bias
2. Consistency	D	Evidence is not con	nsistent
3. Clinical Impact	С	Slight/Restricted	
4. Generalisability	В	Evidence directly g	eneralisable to target population with some
		caveats	
5. Applicability	В	Evidence applicabl	e to Australian/New Zealand healthcare
	В	context with few ca	aveats
non-hypoxic infants on admission, days of	g that there is no consistent benefit for the use of c n oxygen, discharge or hospital length of stay.		
non-hypoxic infants on admission, days of	n oxygen, discharge or hospital length of stay.		
non-hypoxic infants on admission, days or RECOMMENDATION (What recommend		is OVER A	
non-hypoxic infants on admission, days of RECOMMENDATION (What recommen evidence? Use action statements where possible)	n oxygen, discharge or hospital length of stay. dation(s) does the guideline development group draw from th		ALL GRADE OF RECOMMENDATION Body of evidence can be trusted to guide practice
non-hypoxic infants on admission, days of RECOMMENDATION (What recommen evidence? Use action statements where possible) Routine use of continuous oximetry is	n oxygen, discharge or hospital length of stay. dation(s) does the guideline development group draw from the not required for medical management of non-	is OVERA	ALL GRADE OF RECOMMENDATION Body of evidence can be trusted to guide practice Body of evidence can be trusted to
non-hypoxic infants on admission, days of RECOMMENDATION (What recommen evidence? Use action statements where possible) Routine use of continuous oximetry is hypoxic (saturations greater than or eq	n oxygen, discharge or hospital length of stay. dation(s) does the guideline development group draw from th	is OVERA	ALL GRADE OF RECOMMENDATION Body of evidence can be trusted to guide practice Body of evidence can be trusted to guide practice in most situations
non-hypoxic infants on admission, days of RECOMMENDATION (What recommen evidence? Use action statements where possible) Routine use of continuous oximetry is hypoxic (saturations greater than or eq	n oxygen, discharge or hospital length of stay. dation(s) does the guideline development group draw from the not required for medical management of non-	is OVERA	ALL GRADE OF RECOMMENDATION Body of evidence can be trusted to guide practice Body of evidence can be trusted to guide practice in most situations Body of evidence provides some
non-hypoxic infants on admission, days of RECOMMENDATION (What recommen evidence? Use action statements where possible) Routine use of continuous oximetry is hypoxic (saturations greater than or eq	n oxygen, discharge or hospital length of stay. dation(s) does the guideline development group draw from the not required for medical management of non-	is OVERA	ALL GRADE OF RECOMMENDATION Body of evidence can be trusted to guide practice Body of evidence can be trusted to guide practice in most situations Body of evidence provides some support for recommendations(s)
non-hypoxic infants on admission, days of RECOMMENDATION (What recommen evidence? Use action statements where possible) Routine use of continuous oximetry is hypoxic (saturations greater than or eq	n oxygen, discharge or hospital length of stay. dation(s) does the guideline development group draw from the not required for medical management of non-	is OVERA	ALL GRADE OF RECOMMENDATION Body of evidence can be trusted to guide practice Body of evidence can be trusted to guide practice in most situations Body of evidence provides some support for recommendations(s) but care should be taken in its
non-hypoxic infants on admission, days of RECOMMENDATION (What recommen evidence? Use action statements where possible) Routine use of continuous oximetry is	n oxygen, discharge or hospital length of stay. dation(s) does the guideline development group draw from the not required for medical management of non-	is OVERA	ALL GRADE OF RECOMMENDATION Body of evidence can be trusted to guide practice Body of evidence can be trusted to guide practice in most situations Body of evidence provides some support for recommendations(s)

UNRESOLVED ISSUES (If needed, keep a note of specific issues that arise when each recommendation is form	nulated and that requir	e follow up)
IMPLEMENTATION OF RECOMMENDATION (Please indicate yes or no to the following question	ns. Where the answer is	yes, please provide explanatory information
about this. This information will be used to develop the implementation plan for the guidelines)		
Will this recommendation result in changes in usual care?		YES
Reduce the use of continuous oximetry		NO
Are there any resource implications associated with implementing this recommendation?		YES
Reduce admission length of stay and costs associated		NO
Will the implementation of this recommendation require changes in the way care is currently organi	sed?	YES
Education and guidelines to support change in practice		NO
Are the guideline development group aware of any barriers to implementation of this recommendat	ion?	YES
		NO

PP

Practice Point

Question 14.

	sidered Judgen		0			<u> </u>	
Question 14: In infants hospitalised with bro cannula improve clinically relevant end-poin		es the use	of heated hi	umidified high fl	low oxy	gen, or air, vi	a nasal
1. Outcome measures:		Quali	ity of evidenc	e		Importance o in making a	
	HIGH	MOD	LOW	V. LOW	Cr iti ca 1	Important	Not Important
O1 Length of stay in hospital			x		x		
O2 Rate of PICU admission			X		x		
O3 Adverse Events				х		х	
O4 Cost				Х		х	
2. Is there is insufficient evidence to make There have been limited studies on HFNC in children			atient stay out	side of the PICU. A	Cochrai	ne systematic rev	iew (109), one
 evidence based guideline (13), one RCT (110), two provide low to very low level evidence for the reduction in work of breathing receiving HFNC (118). There are insufficient studies and patients investigated 3. What benefit will the proposed intervention 	benefit of HFN0	C. A prospec IFNC as a st	ctive intervent	ional study of 14 inf	ants wit	h bronchiolitis de	
Evidence statement For the critical outcome of length of stay in hospital th For the critical outcome for rate of PICU admission th Judging the benefits in context	ere is low quality	v evidence th	at HFNC redu	aces PICU admissio	n rates.	ital.	y of evidence LOW
The evidence is applicable and can be generalised to al settings. 4. What harm might the proposed interver			ring for brond	hiolitic infants in th	le New Z	Lealand and Aust	ralian health
4. what nam high the proposed merver		•				Quality o	f evidence
For the important outcome of adverse events there is v For the important outcome of cost there is very low ev	•			e cost ove r all.		-	LOW
Judging the harms in context The evidence is applicable and can be generalised to al Australian health settings.					e New Z	Lealand and	
5. What is the likely balance between good	d and harm?						
Evidence statement The benefits of HFNC therapy probably outweigh har	m.					-	ty of evidence DW
Judging the balance of benefits and harms in cont Benefit probably outweigh harms	ext						
Benefits clearly outweigh harms	Recommend	1				STRONG	
Benefits probably outweigh harms	Consider					CONDITION	AL
Not known	Make a reco	mmendation	n for research	(see 8 below)		WEAK	
Benefits probably don't outweigh harms Harms probably outweigh benefits	— Consider ag	ainst				CONDITION	AL
Benefits clearly don't outweigh harms	Recommend	l against				STRONG	
Harms clearly outweigh benefits 6. Is the intervention/action implementab	lo in the New 7	loaland and	Australian	ontoxt?			
-	ole in the New Z	Lealand and	Australian c	ontext			
Summary statement HFNC in bronchiolitis is feasible therapy in the inpatie	ent setting althou	-			o outweig	gh the harms.	
Yes			ecommend/o				
Not known				mic evaluation			
No		Ro	ecommend/co	onsider against			
7. Final recommendation							
HFNC in bronchiolitis can be considered in the inpatie (oxygen saturations 90-92%). Its use in children withou						STR CONDI	commendatio ONG TIONAL EAK
8. Recommendations for research							
Large RCT comparing HFNC with standard oxygen the PICU setting.	erapy including s	sub groups o	f infants with	hypoxia and respira	tory dist	ress without hype	oxia outside of

Question 14: In infants hospitalised with bronchiolitis does humidified high flow oxygen, or air, via nasal cannula improve end-points?	Evidence table ref: Beggs 2014, Bressan 2013, Bueno Campana 2014, I Dalt 2013, Hanlon 2014, Haq 2014, Kelly 2013, Lee 2013, Mayfield 2014, Pham 2015, Ralston 2014, Sin 2015 (13, 109-118, 165).		
1. Evidence base (number of studies, level of evidence and risk of bias in the included	studies)		
A Cochrane systematic review (109) identified only one RCT with very low quality evidence of benefit. Further RCT (110) provides more	А	One or more Level I studies with a low risk of bias, or several Level II studies with a low risk of bias	
evidence that HFNC is feasible and two prospective (111, 112) and one retrospective study (117) provide further very low level evidence of	В	One or two Level II studies with a low risk of bias, or SR/several Level III studies with a low risk of bias	
possible benefit. A prospective interventional study of 14 infants with bronchiolitis demonstrates reduction in work of breathing receiving HFNC (118). There are four non-systematic reviews (113-116).	С	One or two Level III studies with a low risk of bias or Level I or II studies with moderate risk of bias	
III I (III). Incle ale four non systemate reviews (III) III).	D	Level IV studies or Level I to III studies/SRs with a high risk of bias	
2. Consistency (if only one study was available, rank this component as 'not applicabl	le')	· ·	
The RCT (110) compared HFNC to non-standardised therapy. No studies have compared to routine care.	А	All studies consistent	
	В	Most studies consistent and inconsistency can be explained	
	С	Some inconsistency, reflecting genuine uncertainty around question	
	D	Evidence is not consistent	
	NA	Not applicable (one study only)	
3. Clinical impact (indicate if the study results varied according to some unknown fact not be determined)	tor (not simply study quality o	or sample size) and thus the clinical impact of the intervention could	
HFNC is gaining in popularity despite the paucity of evidence for its	А	Very large	
use. This seems to be driving the uptake of this therapy which is	В	Substantial	
	С	Moderate	
	D	Slight/Restricted	
4. Generalisability (how well does the body of evidence match the population and clinic	cal settings being targeted by i	the guideline?)	
	А	Evidence directly generalisable to target population	
	В	Evidence directly generalisable to target population with some caveats	
	С	Evidence not directly generalisable to target population but could be sensibly applied	
		Evidence not directly generalisable to target population	
	D	and hard to judge whether sensible to apply	
5. Applicability (is the body of evidence relevant to the Australian/New Zealand heal			
5. Applicability (is the body of evidence relevant to the Australian/New Zealand heat		<i>alth services / delivery of care and cultural factors?)</i> Evidence directly applicable to Australian/New Zealand healthcare context	
5. Applicability (is the body of evidence relevant to the Australian/New Zealand heat	lthcare context in terms of hea	alth services / delivery of care and cultural factors?) Evidence directly applicable to Australian/New Zealand healthcare context Evidence applicable to Australian/New Zealand healthcare context with few caveats	
5. Applicability (is the body of evidence relevant to the Australian/New Zealand heat	lthcare context in terms of hea A	alth services / delivery of care and cultural factors?) Evidence directly applicable to Australian/New Zealand healthcare context Evidence applicable to Australian/New Zealand	

Component	Rating	Des	cription			
1. Evidence base	С	One	or two Level III s	tudies with a low risk of bias or Level I or II studies	with moderate risk of bias	
2. Consistency	С	Som	e inconsistency, re	flecting genuine uncertainty around question		
3. Clinical Impact	С	Mod	erate			
4. Generalisability	С	Evid	ence not directly g	generalisable to target population but could be sensil	bly applied	
5. Applicability	С	Evid	ence probably app	blicable to Australian/New Zealand healthcare conte	ext with some caveats	
Evidence statement:						
The benefits of HFNO	C therapy probably o	utweigh ł	arm.			
RECOMMENDATI				OVERALL GRADE OF RECOMMEN	NDATION	
does the guideline developn		is	А	Body of evidence can be trusted to guide pract		
evidence? Use action states	nents where possible)		В	Body of evidence can be trusted to guide pract	tice in most situations	
HFNC in bronchioli		ed in	С	Body of evidence provides some support for should be taken in its application	or recommendations(s) but care	
the inpatient setting			D	Body of evidence is weak and recommendation must be applied with caution		
saturations 90-92%).	bronchiolitis with hypoxia (oxygen saturations 90-92%). Its use in children without hypoxia should be limited to the RCT		РР	Practice Point		
0.	UES (If needed, keep	a note of sp	ecific issues that arise	when each recommendation is formulated and that require fo	llow up)	
UNRESOLVED ISS	ON OF RECOMM	ENDAT	ION (Please indicat	te yes or no to the following questions. Where the answer is ye	* '	
UNRESOLVED ISS IMPLEMENTATIC about this. This informatic	ON OF RECOMM on will be used to develop	ENDAT the imple	ION (Please indicat mentation plan for th	te yes or no to the following questions. Where the answer is ye	s, please provide explanatory informatio	
UNRESOLVED ISS IMPLEMENTATIC about this. This informatic	ON OF RECOMM on will be used to develop	ENDAT the imple	ION (Please indicat mentation plan for th	te yes or no to the following questions. Where the answer is ye	s, please provide explanatory informatio	
UNRESOLVED ISS IMPLEMENTATIC about this. This informati Will this recommendat	ON OF RECOMM on will be used to develop tion result in change	ENDAT the imple s in usual	ION (Please indicat mentation plan for th care?	te yes or no to the following questions. Where the answer is yes	s, please provide explanatory informatio YES NO	
UNRESOLVED ISS IMPLEMENTATIO about this. This information Will this recommendat Are there any resource	ON OF RECOMM on will be used to develop cion result in change implications associa	ENDAT the imple s in usual atted with	ION (<i>Please indicat</i> mentation plan for the care?	te yes or no to the following questions. Where the answer is yes e guidelines) recommendation?	s, please provide explanatory informatio YES NO YES	
UNRESOLVED ISS IMPLEMENTATIC about this. This information Will this recommendat Are there any resource Introduction of HFNO	ON OF RECOMM on will be used to develop cion result in change implications associa	ENDAT the imple s in usual atted with	ION (<i>Please indicat</i> mentation plan for the care?	te yes or no to the following questions. Where the answer is yes	s, please provide explanatory informatio YES NO	
UNRESOLVED ISS IMPLEMENTATIC about this. This informatic Will this recommendat Are there any resource Introduction of HFNO tertiary care.	DN OF RECOMM on will be used to develop ion result in change implications associa C requires special equ	ENDAT to the imple s in usual tted with uipment a	ION (<i>Please indicat</i> mentation plan for th care? implementing this nd training of staf	te yes or no to the following questions. Where the answer is yes e guidelines) recommendation?	s, please provide explanatory informatio YES NO YES	
UNRESOLVED ISS IMPLEMENTATIC about this. This informatic Will this recommendat Are there any resource Introduction of HFNO tertiary care.	DN OF RECOMM on will be used to develop ion result in change implications associa C requires special equ	ENDAT to the imple s in usual tted with uipment a	ION (<i>Please indicat</i> mentation plan for th care? implementing this nd training of staf	te yes or no to the following questions. Where the answer is yes e guidelines) recommendation? ff. Successful implemental may reduce transfers to	s, please provide explanatory informatio YES NO YES NO NO	
UNRESOLVED ISS IMPLEMENTATIC about this. This informatii Will this recommendat Are there any resource Introduction of HFNO tertiary care. Will the implementatio	DN OF RECOMM on will be used to develop tion result in change implications associat c requires special equipment on of this recomment	ENDAT b the imple s in usual ated with alignment a dation rec	ION (Please indicat mentation plan for the care? implementing this nd training of staf quire changes in th	te yes or no to the following questions. Where the answer is yes e guidelines) recommendation? ff. Successful implemental may reduce transfers to	s, please provide explanatory informatio YES NO YES NO YES	

Question 15. **GRADE Evidence Summary** Considered Judgement - Strength of recommendation Question 15: In infants hospitalised with bronchiolitis, does chest physiotherapy improve clinically relevant end-points? 1. Outcome measures: Quality of evidence Importance of outcome in making a decision Not HIGH MOD LOW V. LOW Critical Important Important O1 Change in severity status of bronchiolitis x x х x O2 Time to recovery/clinical stability O3 Oxygen saturation levels Х Х x O4 Duration of oxygen supplementation х O5 Length of Hospital Stay Х Х O6 Complications of therapy Х Х O7 Heart rate variability x x 2. Is there is insufficient evidence to make a recommendation? There is one Cochrane review (119) with nine clinical trials including 891 patients on the topic. In addition there is one low quality RCT (120), two prospective clinical trials (121, 122), three observational trials (123-125) of very low quality, and a further systematic review and guideline (10). 3. What benefit will the proposed intervention/action have? Evidence statement Quality of evidence For the critical outcome of change in severity status of bronchiolitis there is moderate evidence that physiotherapy does HIGH not alter severity. For the critical outcome of time to recovery/clinical stability there is high quality evidence that physiotherapy does not improve recovery or stability. For the critical outcome of oxygen saturation levels there is very low level evidence of physiotherapy affecting oxygen saturation. For the important outcome of duration of oxygen supplementation there is high quality evidence that duration of oxygen supplementation is not altered by physiotherapy. For the important outcome of length of hospital stay there is high level evidence that length of stay is not altered by physiotherapy. Judging the benefits in context The evidence is probably applicable and generalisable to the New Zealand and Australian health settings. What harm might the proposed intervention/action do? Evidence statement Quality of evidence For the important outcome of complications of therapy there is high level evidence of minimal adverse effects resulting MODERATE from physiotherapy. For the important outcome of heart rate variability there is very low level evidence that heart rate variability is modified by physiotherapy. Judging the harms in context The evidence is probably applicable and generalisable to the New Zealand and Australian health settings. What is the likely balance between good and harm? 5. Evidence statement: Overall quality of evidence The benefits are not demonstrated to improve outcomes. HIGH Judging the balance of benefits and harms in context: Benefits clearly don't outweigh harms STRONG Benefits clearly outweigh harms Recommend CONDITIONAL Benefits probably outweigh harms Consider Not known Make a recommendation for research (see 8 below) WEAK Benefits probably don't outweigh harms CONDITIONAL Consider against Harms probably outweigh benefits Benefits clearly don't outweigh harms STRONG Recommend against Harms clearly outweigh benefits Is the intervention/action implementable in the New Zealand and Australian context? 6. Summary statement: The evidence is probably applicable and generalisable to the New Zealand and Australian health settings. Yes Recommend/consider Not known Consider economic evaluation Recommend/consider against No

7. Final recommendation	
Chest physiotherapy is not recommended for routine use in infants with bronchiolitis.	Strength of recommendation
	STRONG
	CONDITIONAL
	WEAK
8. Recommendations for research	
Further research into newer specific techniques to determine the use in specific patient cohorts.	

Question 15. **NHMRC Evidence Summary** Question 15: In infants hospitalised with bronchiolitis, does chest physiotherapy improve Evidence table ref: Figuls 2012, Gomes 2012; Goncalves clinically relevant end-points? 2014, Jacinto 2013, Mussman 2013; Pupin 2009, Remondini 2014, Ricci 2015, Roqué i (10, 119-125). 1. Evidence base (number of studies, level of evidence and risk of bias in the included studies) There is one Cochrane review (119) with nine clinical trials including 891 One or more Level I studies with a low risk of bias, or several А Level II studies with a low risk of bias patients on the topic. In addition there is one low quality RCT (120), two prospective clinical trials (121, 122), three observational trials (123-125) of very One or two Level II studies with a low risk of bias, or В low quality, and a further systematic review and guideline (10). SR/several Level III studies with a low risk of bias One or two Level III studies with a low risk of bias or Level I or С II studies with moderate risk of bias Level IV studies or Level I to III studies/SRs with a high risk of D bias 2. Consistency (if only one study was available, rank this component as 'not applicable') All studies consistent А В Most studies consistent and inconsistency can be explained Some inconsistency, reflecting genuine uncertainty around C question D Evidence is not consistent NA Not applicable (one study only) 3. Clinical impact (indicate if the study results varied according to some unknown factor (not simply study quality or sample size) and thus the clinical impact of the intervention could not be determined) Very large А

в Substantial С Moderate D Slight/Restricted 4. Generalisability (how well does the body of evidence match the population and clinical settings being targeted by the guideline?) Evidence directly generalisable to target population А Evidence directly generalisable to target population with В some caveats Evidence not directly generalisable to target population but could С be sensibly applied Evidence not directly generalisable to target population and hard D to judge whether sensible to apply 5. Applicability (is the body of evidence relevant to the Australian/New Zealand healthcare context in terms of health services / delivery of care and cultural factors?) Evidence directly applicable to Australian/New Zealand А healthcare context Evidence applicable to Australian/New Zealand healthcare В context with few caveats Evidence probably applicable to Australian/New Zealand С healthcare context with some caveats Evidence not applicable to Australian/New Zealand healthcare D context Other factors (indicate here any other factors that you took into account when assessing the evidence base (for example, issues that might cause the group to downgrade or upgrade the recommendation)

Component	Rating	Descr	iption				
1. Evidence base	B		1	el II studies with a low risk of bias, or SR/several Level III studie	es with a low risk of bias		
2. Consistency	B			sistent and inconsistency can be explained	es with a low lisk of blas		
3. Clinical Impact	C	Moder		sistent and meonsistency can be explained			
4. Generalisability	B		Evidence directly generalisable to target population with some caveats				
5. Applicability	С		Evidence probably applicable to Australian/New Zealand healthcare context with some caveats				
Evidence statement:			1				
The benefits of chest pl	nysiotherapy are not	demonstrated	l to improv	ve outcomes.			
RECOMMENDATIO			Ŷ	OVERALL GRADE OF RECOMMENDAT	ION		
the guideline development gr	oup draw from this evid	lence? Use	А	Body of evidence can be trusted to guide practice			
action statements where poss	rible)		В	Body of evidence can be trusted to guide practice in me	ost situations		
			С	Body of evidence provides some support for recommendations(s) but care should			
Chest physiotherapy i			C	taken in its application			
routine use in infants	with bronchiolitis.		D	Body of evidence is weak and recommendation must be applied with caution			
			PP	Practice Point			
	12 1	515		rise when each recommendation is formulated and that require follow up)			
				icate yes or no to the following questions. Where the answer is yes, please pre	wide explanatory information		
about this. This information	1	1	1 3	the guidelines)			
Will this recommendation	on result in changes	in usual care?			YES		
					NO		
Are there any resource i	mplications associat	ted with imple	menting th	is recommendation?	YES		
					NO		
		lation require	changes in	the way care is currently organised?	YES		
Will the implementation	n of this recommend						
Will the implementation	n of this recommend	iudon require			NO		
κ.		1	rs to imple	mentation of this recommendation?	NO YES		

Question 16a.

С	onsidered Judgem	nent - Streng	th of recom	mendatior	l		
Question 16a: In infants hospitalised with brond	chiolitis, does suc			aso pharyn	-	cally relevant en nportance of out	-
1. Outcome measures:		Quality of	evidence		n making a deci		
	HIGH	MOD	LOW	V. LOW	Critical	Important	Not Important
O1 Length of Stay in hospital			x		x		
O ₂ Adverse events				x		x	
2. Is there is insufficient evidence to ma	ke a recommenda	ition?					
There is only one retrospective comparative study (1	25) of 740 patients	examining b	oth suction t	ype and suc	tion frequency. '	Three non-system	atic reviews or
guidelines refer to suction but without provision of a			7.				
3. What benefit will the proposed interve	ention/action hav	re?					
Evidence statement						Quality	of evidence
For the critical outcome of length of stay in hospi	tal there is modera	te level evide	ence that dee	ep nasal suc	tioning increase	s I	.OW
length of stay but frequent non-invasive superficial s	uctioning decreases	s length of sta	ay.				
Judging the benefits in context							
The evidence is applicable and generalisable to the N			th settings.				
4. What harm might the proposed interv	ention/action do	:					
Evidence statement							of evidence
For the important outcome of the occurrence of adv	verse events there is	very low lev	el evidence.			VER	YLOW
Judging the harms in context The evidence is applicable and generalisable to the N	Jew Zealand and A	ustralian heal	th settings				
5. What is the likely balance between go		ustranan near	ui settings.				
Evidence statement The benefits probably don't outweigh harms.							verall of evidence
The benefits probably don't outweigh harms.							OW
Judging the balance of benefits and harms in co	ntext					L	
Benefits probably don't outweigh harms.							
Benefits clearly outweigh harms	Recommend	1				STRONG	
Benefits probably outweigh harms	Consider					CONDITIO	DNAL
Not known	Make a reco	mmendation	for research	(see 8 belo	w)	WEAK	
Benefits probably don't outweigh harms							0.).I.I.
Harms probably outweigh benefits	Consider ag	gainst				CONDITI	UNAL
Benefits clearly don't outweigh harms						07770-001-0	
Harms clearly outweigh benefits	Recommenc	l against				STRONG	
6. Is the intervention/action implement	able in the New Z	Lealand and	Australian o	context?			
Summary statement							
The use of deep suctioning in bronchiolitis appears t	to lengthen hospital	stay while n	on-invasive s	uctioning n	ay decrease leng	gth of stay.	
Yes		Re	commend/o	consider			
Not known		Со	nsider econo	mic evaluat	on		
No		Ree	commend/co	onsider agai	nst		
7. Final recommendation							
Nasal suction is not recommended as routine practic	ce in the manageme	nt of infants	with bronchi	iolitis.	Strength of re	commendation	
Superficial suction may be considered to assist with	feeding.				STRONG		
					CONDITION	NAL	
					WEAK		
8. Recommendations for research							

Question 16a.

improve clinically relevan		pronchiolitis, does suctioning of	of the nose	e or naso pharynx	Evidence table ref: Mussman 2013 (125).
	-	ce and risk of bias in the included studi	ies)		
There is only one clinical tr	ial - retrospective co	mparative trial examining		One or more Level	I studies with a low risk of bias, or several
suctioning techniques and f		1 0	А	Level II studies with	
			В		I studies with a low risk of bias, or SR/severa
				Level III studies wit	
			С	II studies with mode	II studies with a low risk of bias or Level I or erate risk of bias
					r Level I to III studies/SRs with a high
			D	risk of bias	
2. Consistency (if only one s	tudy was available, ran	k this component as 'not applicable')	-		
			А	All studies consister	
			Λ	All studies consister	IL
			В	Most studies consist	tent and inconsistency can be explained
			С	Some inconsistency	, reflecting genuine uncertainty around
				question	
			D	Evidence is not con	sistent
			NA	Not applicable (or	ne study only)
3. Clinical impact (indicate	if the study results vari	ed according to some unknown factor (n	ot simply stu	dy quality or sample size)	and thus the clinical impact of the intervention could
not be determined)			-	Г	
			А	Very large	
			В	Substantial	
			С	Moderate	
			D	Slight/Restricted	
4. Generalisability (how we	Il does the body of evide	nce match the population and clinical se	ttings being t	targeted by the guideline?)	
		* *	A		eneralisable to target population
			В		generalisable to target population with
			D	some caveats	
			С		ly generalisable to target population but could
				be sensibly applied	ly generalisable to target population and hard
			D	to judge whether set	
5. Applicability (is the body	of evidence relevant to t.	he Australian/New Zealand healthcar	e context in t	terms of health services / a	lelivery of care and cultural factors?)
			Δ	Evidence directly ap	pplicable to Australian/New Zealand
			А	healthcare context	
			В		to Australian/New Zealand healthcare
				context with few car	
			С		y applicable to Australian/New Zealand t with some caveats
			-		cable to Australian/New Zealand healthcare
			D	context	
	any other factors that yo	u took into account when assessing the	evidence base	(for example, issues that n	might cause the group to downgrade or upgrade the
recommendation)	NT MATRIX (sum		is of the evide	ence relating to the key que.	stion, taking all the above factors into account)
EVIDENCE STATEME	- ·	Description		/cp :.1 1:1 ::	(1)
EVIDENCE STATEME Component	Rating			/NRC with a bigh melt of	at brac
EVIDENCE STATEME Component 1. Evidence base	D	Level IV studies or Level I to		/ Sits with a high lisk (n blas
EVIDENCE STATEME Component 1. Evidence base 2. Consistency	D NA	Level IV studies or Level I to Not applicable (one study onl		7 SKS with a high lisk (1 0145
EVIDENCE STATEME Component 1. Evidence base 2. Consistency 3. Clinical Impact	D NA D	Level IV studies or Level I to Not applicable (one study onl Slight/Restricted	y)		
EVIDENCE STATEME Component 1. Evidence base 2. Consistency 3. Clinical Impact 4. Generalisability	D NA D B	Level IV studies or Level I to Not applicable (one study onl Slight/Restricted Evidence directly generalisabl	y) e to target j	population with some	caveats
EVIDENCE STATEME Component 1. Evidence base 2. Consistency 3. Clinical Impact	D NA D	Level IV studies or Level I to Not applicable (one study onl Slight/Restricted Evidence directly generalisabl	y) e to target j	population with some	

RECOMMENDATION (What recommendation(s) does		OVERALL GRADE OF RECOMMEN	DATION
the guideline development group draw from this evidence? Use	А	Body of evidence can be trusted to guide practice	
action statements where possible)	В	Body of evidence can be trusted to guide practice in n	nost situations
Nasal suction is not recommended as routine	С	Body of evidence provides some support for recomm taken in its application	endations(s) but care should be
practice in the management of infants with	D	Body of evidence is weak and recommendation m	nust be applied with caution
bronchiolitis. Superficial suction may be considered to assist with feeding.	PP	Practice Point	
UNRESOLVED ISSUES (If needed, keep a note of specific	issues that ar	ise when each recommendation is formulated and that require follow	up)
IMPLEMENTATION OF RECOMMENDATION about this. This information will be used to develop the implementation		cate yes or no to the following questions. Where the answer is yes, pl the guidelines)	ease provide explanatory information
Will this recommendation result in changes in usual care	?		YES
			NO
Are there any resource implications associated with impl	ementing th	is recommendation?	YES
			NO
Will the implementation of this recommendation require	changes in	the way care is currently organised?	YES
			NO
Are the guideline development group aware of any barrie	ers to imple	mentation of this recommendation?	YES

Question 16b.

		ent - Streng	th of recom	mendation		• 1 0 • 11	improve
(Considered Judgem					. 1	improve
Question 16b: In infants hospitalised with bron clinically relevant end-points?	nchiolitis, does deej	p suctioning	in compari	son to supe	rficial suction	ing beneficially	mpiove
1. Outcome measures:		Quality of	evidence			nportance of out n making a deci	
	HIGH	MOD	LOW	V. LOW	Critical	Important	Not Important
O1 Length of Stay in hospital			x		х		
O2 Adverse events				х		х	
2. Is there is insufficient evidence to m	nake a recommenda	tion?	I		<u> </u>		J
Evidence statement: There is only one retrospective comparative study (3. What benefit will the proposed inter Evidence statement For the critical outcome of length of stay in hospir in comparison to superficial suctioning. Judging the benefits in context The evidence is applicable and generalisable to the	tal there is low level of	e?	deep suction	^ 	· ·		of evidence LOW
4. What harm might the proposed inter			ii settiigs.				
Evidence statement For the important outcome of adverse events there Judging the harms in context			ep suction in	creases adve	rse events.		of evidence AY LOW
The evidence is applicable and generalisable to the	New Zealand and Au	estualian healt					
		istranan nean	h settings.				
5. What is the likely balance between g		istranan nean	h settings.				
Evidence statement Harms probably outweigh benefits of deep suction Judging the balance of benefits and harms in c	good and harm? ing in comparison wi					quality	verall of evidence .OW
Evidence statement Harms probably outweigh benefits of deep suction Judging the balance of benefits and harms in c Benefits clearly don't outweigh harms.	good and harm? ing in comparison wi	th superficial				quality o L	of evidence
Evidence statement Harms probably outweigh benefits of deep suction: Judging the balance of benefits and harms in c Benefits clearly don't outweigh harms. Benefits clearly outweigh harms	good and harm? ing in comparison wi context Recommend	th superficial				quality of L	of evidence .OW
Evidence statement Harms probably outweigh benefits of deep suction: Judging the balance of benefits and harms in c Benefits clearly don't outweigh harms. Benefits clearly outweigh harms	good and harm? ing in comparison wi context Recommend Consider	th superficial	suctioning.			quality o L	of evidence .OW
Evidence statement Harms probably outweigh benefits of deep suction Judging the balance of benefits and harms in c Benefits clearly don't outweigh harms. Benefits clearly outweigh harms Benefits probably outweigh harms	good and harm? ing in comparison wi context Recommend	th superficial	suctioning.	(see 8 below)	quality of L	of evidence .OW
Evidence statement Harms probably outweigh benefits of deep suction Judging the balance of benefits and harms in c Benefits clearly don't outweigh harms. Benefits clearly outweigh harms Benefits probably outweigh harms Not known	zood and harm? ing in comparison wi context Recommend Consider Make a recor	th superficial	suctioning.	(see 8 below)	quality of L STRONG CONDITIO WEAK	OW OW
Evidence statement Harms probably outweigh benefits of deep suction Judging the balance of benefits and harms in c Benefits clearly don't outweigh harms. Benefits clearly outweigh harms Benefits probably outweigh harms Not known Benefits probably don't outweigh harms	good and harm? ing in comparison wi context Recommend Consider	th superficial	suctioning.	(see 8 below)	quality of L	OW OW
Evidence statement Harms probably outweigh benefits of deep suction Judging the balance of benefits and harms in c Benefits clearly don't outweigh harms Benefits clearly outweigh harms Benefits probably outweigh harms Not known Benefits probably don't outweigh harms Harms probably outweigh benefits	zood and harm? ing in comparison wi context Recommend Consider Make a recon Consider ag	th superficial	suctioning.	(see 8 below)	quality of L STRONG CONDITIO WEAK CONDITIO	OW OW
Evidence statement Harms probably outweigh benefits of deep suction Judging the balance of benefits and harms in c Benefits clearly don't outweigh harms Benefits clearly outweigh harms Benefits probably outweigh harms Not known Benefits probably don't outweigh harms Harms probably outweigh benefits Benefits clearly don't outweigh harms	zood and harm? ing in comparison wi context Recommend Consider Make a recor	th superficial	suctioning.	(see 8 below)	quality of L STRONG CONDITIO WEAK	OW OW
Evidence statement Harms probably outweigh benefits of deep suction Judging the balance of benefits and harms in c Benefits clearly don't outweigh harms. Benefits clearly outweigh harms Benefits probably outweigh harms Not known Benefits probably don't outweigh harms Harms probably outweigh benefits Benefits clearly don't outweigh harms Harms clearly outweigh benefits	good and harm? ing in comparison wi context Recommend Consider Make a recon Consider ag Recommend	th superficial mmendation gainst against	suctioning.	<u> </u>)	quality of L STRONG CONDITIO WEAK CONDITIO	OW OW
Evidence statement Harms probably outweigh benefits of deep suction Judging the balance of benefits and harms in c Benefits clearly don't outweigh harms Benefits clearly outweigh harms Benefits probably outweigh harms Not known Benefits probably don't outweigh harms Harms probably outweigh benefits Benefits clearly don't outweigh harms Harms clearly outweigh benefits 6. Is the intervention/action implement Summary statement The use of deep suctioning in bronchiolitis appears	zood and harm? ing in comparison wi context Recommend Consider Make a recor Consider ag Recommend Recommend ntable in the New Z	th superficial mmendation gainst against ealand and a stay in comp	suctioning. for research Australian c	context?		quality of L STRONG CONDITIO WEAK CONDITIO	OW OW
Evidence statement Harms probably outweigh benefits of deep suction Judging the balance of benefits and harms in c Benefits clearly don't outweigh harms Benefits probably outweigh harms Not known Benefits probably don't outweigh harms Harms probably outweigh benefits Benefits clearly don't outweigh harms Harms clearly don't outweigh harms Harms clearly outweigh benefits 6. Is the intervention/action implement The use of deep suctioning in bronchiolitis appears Yes	zood and harm? ing in comparison wi context Recommend Consider Make a recor Consider ag Recommend Recommend ntable in the New Z	th superficial mmendation gainst against ealand and a stay in comp Rec	suctioning. for research Australian c arison to sup	context? perficial sucti	oning.	quality of L STRONG CONDITIO WEAK CONDITIO	OW OW
Evidence statement Harms probably outweigh benefits of deep suction Judging the balance of benefits and harms in c Benefits clearly don't outweigh harms Benefits clearly outweigh harms Mot known Benefits probably outweigh harms Harms probably outweigh benefits Benefits clearly don't outweigh harms Harms clearly don't outweigh harms Harms clearly outweigh benefits 6. Is the intervention/action implement The use of deep suctioning in bronchiolitis appears Yes Not known	zood and harm? ing in comparison wi context Recommend Consider Make a recor Consider ag Recommend Recommend ntable in the New Z	th superficial mmendation gainst against ealand and a stay in comp Cor	suctioning. for research Australian c arison to sup commend/c	context? perficial sucti consider nic evaluatio	oning.	quality of L STRONG CONDITIO WEAK CONDITIO	OW OW
Evidence statement Harms probably outweigh benefits of deep suction Judging the balance of benefits and harms in c Benefits clearly don't outweigh harms Benefits probably outweigh harms Not known Benefits probably don't outweigh harms Harms probably outweigh benefits Benefits clearly don't outweigh harms Harms clearly outweigh benefits 6. Is the intervention/action implement The use of deep suctioning in bronchiolitis appears Yes Not known No	zood and harm? ing in comparison wi context Recommend Consider Make a recor Consider ag Recommend Recommend ntable in the New Z	th superficial mmendation gainst against ealand and a stay in comp Cor	suctioning. for research Australian c arison to sup	context? perficial sucti consider nic evaluatio	oning.	quality of L STRONG CONDITIO WEAK CONDITIO	OW OW
Evidence statement Harms probably outweigh benefits of deep suction Judging the balance of benefits and harms in c Benefits clearly don't outweigh harms Benefits clearly outweigh harms Benefits probably outweigh harms Not known Benefits probably don't outweigh harms Harms probably outweigh benefits Benefits clearly don't outweigh harms Harms clearly don't outweigh harms Harms clearly outweigh benefits 6. Is the intervention/action implement The use of deep suctioning in bronchiolitis appears Yes Not known No 7. Final recommendation	good and harm? ing in comparison wi context Recommend Consider Make a recommend Consider ag Recommend ntable in the New Z s to lengthen hospital	th superficial mmendation gainst against ealand and a stay in comp Rec Cor Rec	suctioning. for research Australian c arison to sup commend/c	context? perficial sucti consider nic evaluatio	oning.	quality of L STRONG CONDITIO WEAK CONDITIO	OW OW
Evidence statement Harms probably outweigh benefits of deep suctions Judging the balance of benefits and harms in c Benefits clearly don't outweigh harms. Benefits probably outweigh harms Not known Benefits probably don't outweigh harms Harms probably outweigh benefits Benefits clearly don't outweigh harms Harms clearly outweigh benefits 6. Is the intervention/action implement Summary statement The use of deep suctioning in bronchiolitis appears Yes Not known No	good and harm? ing in comparison wi context Recommend Consider Make a recommend Consider ag Recommend ntable in the New Z s to lengthen hospital	th superficial mmendation gainst against ealand and a stay in comp Rec Cor Rec	suctioning. for research Australian c arison to sup commend/c	context? perficial sucti consider nic evaluatio consider aga	oning. .n .inst	quality of L STRONG CONDITIO WEAK CONDITIO STRONG	OW OW
Evidence statement Harms probably outweigh benefits of deep suction Judging the balance of benefits and harms in c Benefits clearly don't outweigh harms. Benefits clearly outweigh harms Benefits probably outweigh harms Not known Benefits clearly don't outweigh harms Harms probably outweigh benefits Benefits clearly don't outweigh harms Harms probably outweigh benefits Benefits clearly don't outweigh harms Harms clearly don't outweigh harms Harms clearly outweigh benefits 6. Is the intervention/action implement The use of deep suctioning in bronchiolitis appears Yes Not known No 7. Final recommendation	good and harm? ing in comparison wi context Recommend Consider Make a recommend Consider ag Recommend ntable in the New Z s to lengthen hospital	th superficial mmendation gainst against ealand and a stay in comp Rec Cor Rec	suctioning. for research Australian c arison to sup commend/c	context? perficial sucti consider nic evaluatio consider aga	oning. in inst Strength of rea STRONG CONDITION	quality of L STRONG CONDITIO WEAK CONDITIO STRONG	OW OW

Question 16b. **NHMRC Evidence Summary** Question 16b: In infants hospitalised with bronchiolitis, does deep suctioning in comparison to Evidence table ref: Mussman 2013 (125). superficial suctioning beneficially improve clinically relevant end-points? 1. Evidence base (number of studies, level of evidence and risk of bias in the included studies) There is only one clinical trial - retrospective comparative trial of 740 patients One or more Level I studies with a low risk of bias, or several А Level II studies with a low risk of bias (125).One or two Level II studies with a low risk of bias, or SR/several в Level III studies with a low risk of bias One or two Level III studies with a low risk of bias or Level I or С II studies with moderate risk of bias Level IV studies or Level I to III studies/SRs with a high D risk of bias 2. Consistency (if only one study was available, rank this component as 'not applicable') All studies consistent А В Most studies consistent and inconsistency can be explained Some inconsistency, reflecting genuine uncertainty around С question D Evidence is not consistent NA Not applicable (one study only) 3. Clinical impact (indicate if the study results varied according to some unknown factor (not simply study quality or sample size) and thus the clinical impact of the intervention could not be determined) А Very large В Substantial С Moderate Slight/Restricted D 4. Generalisability (how well does the body of evidence match the population and clinical settings being targeted by the guideline?) Evidence directly generalisable to target population А Evidence directly generalisable to target population with В some caveats Evidence not directly generalisable to target population but could С be sensibly applied Evidence not directly generalisable to target population and hard D to judge whether sensible to apply 5. Applicability (is the body of evidence relevant to the Australian/New Zealand healthcare context in terms of health services / delivery of care and cultural factors?) Evidence directly applicable to Australian/New Zealand А healthcare context Evidence applicable to Australian/New Zealand healthcare В context with few caveats Evidence probably applicable to Australian/New Zealand С healthcare context with some caveats Evidence not applicable to Australian/New Zealand healthcare D context Other factors (indicate here any other factors that you took into account when assessing the evidence base (for example, issues that might cause the group to downgrade or upgrade the recommendation) EVIDENCE STATEMENT MATRIX (summarise the development group's synthesis of the evidence relating to the key question, taking all the above factors into account) Component Rating Description 1. Evidence base D Level IV studies or Level I to III studies/SRs with a high risk of bias 2. Consistency NA Not applicable (one study only) 3. Clinical Impact D Slight/Restricted 4. Generalisability B Evidence directly generalisable to target population with some caveats 5. Applicability С Evidence probably applicable to Australian/New Zealand healthcare context with some caveats Evidence statement: There is limited evidence that does not support the use of deep suctioning in comparison of superficial suctioning of the nose or naso-pharynx.

RECOMMENDATION (What recommendation(s) does		OVERALL GRADE OF RECOMMENDAT	ION			
the guideline development group draw from this evidence? Use	А	Body of evidence can be trusted to guide practice				
action statements where possible)	В	B Body of evidence can be trusted to guide practice in most situations				
Deep nasal suction for the management of	С	Body of evidence provides some support for recommendations(s) but care should be				
bronchiolitis is not recommended.	D	taken in its application	· · · · · · · · · · · · · · · · · · ·			
	PP	Body of evidence is weak and recommendation must b	be applied with caution			
		Practice Point				
UNRESOLVED ISSUES (If needed, keep a note of specific	issues that ari	ise when each recommendation is formulated and that require follow up)				
IMPLEMENTATION OF RECOMMENDATION	(Please indic	ate yes or no to the following questions. Where the answer is yes, please pr	rovide explanatory information			
about this. This information will be used to develop the implementation	tion plan for l	the guidelines)				
Will this recommendation result in changes in usual care)		YES			
			NO			
Are there any resource implications associated with imple	ementing th	is recommendation?	YES			
			NO			
Will the implementation of this recommendation require	changes in	the way care is currently organised?	YES			
			NO			
Are the guideline development group aware of any barrie	rs to impler	nentation of this recommendation?	YES			
			NO			

Question 17. GR	ADE Eviden	ce Summar	y			
C	Considered Judgen	ent - Strength of	frecomme	ndation		
Question 17: In infants hospitalised with bronc	hiolitis, does the u	se of nasal saline	e drops im	prove clinic:	ally relevant end-p	oints?
1. Outcome measures:	Qual	ity of evidence			Importance of in making a	
	HIGH M	DD LOW	V. LOW	Critical	Important	Not Important
O1 O2 saturations			x	x		
O ₂ Retractions			x	x		
O ₃ Dyspnoea			x		x	
2. Is there is insufficient evidence to ma	ake a recommenda	tion?				
There is no Cochrane review. Two RCTs use admin drops (126). A guideline (127) and a review article (1 3. What benefit will the proposed interv	128) recommend na	sal saline as a prac		use of chest I	physiotherapy (120)	or phenylephrine nasal
Evidence statement	chilon/ action hav				Qual	ity of oridon op
For the critical outcome of O_2 saturations there is v	ery low evidence of	effectiveness.			Qua	ity of evidence
					v	ERY LOW
For the critical outcome of retractions there is very	low evidence of imp	provement in work	s of breathi	ng.		
For the important outcome of dyspnoea there is ver	y low evidence of in	nprovement.				
Judging the benefits in context		. 1. 1. 1.1				
The evidence is applicable and generalisable to the N 4. What harm might the proposed inter			ttings.			
Evidence statement:		-			Oual	ity of evidence
Not assessed.					200	N/A
Judging the harms in context						
5. What is the likely balance between g	ood and harm?					
Evidence statement						Overall
The benefits are not known.					-	ity of evidence ERY LOW
Judging the balance of benefits and harms in co Benefits probably outweigh harms.	ontext					
Benefits clearly outweigh harms	Recommend				STRONG	
Benefits probably outweigh harms	Consider				CONDITION	JAL
Not known	Make a recomm (see 8 below)	endation for res	earch		WEAK	
Benefits probably don't outweigh harms	Consider against					
Harms probably outweigh benefits					CONDITION	JAL
1 , 0	Ĭ				CONDITION	JAL
Benefits clearly don't outweigh harms Harms clearly outweigh benefits	Recommend agai	nst			CONDITION	JAL .
Benefits clearly don't outweigh harms	Ť		ralian con	text?		JAL .
Benefits clearly don't outweigh harms Harms clearly outweigh benefits 6. Is the intervention/action implement Summary statement	table in the New Z		ralian con	.text?		JAL
Benefits clearly don't outweigh harms Harms clearly outweigh benefits 6. Is the intervention/action implement Summary statement Evidence applicable to Australia and New Zealand J	table in the New Z	cealand and Aust		text?		JAL
Benefits clearly don't outweigh harms Harms clearly outweigh benefits 6. Is the intervention/action implement Summary statement Evidence applicable to Australia and New Zealand p Yes	table in the New Z	Recommend/	consider			JAL
Benefits clearly don't outweigh harms Harms clearly outweigh benefits 6. Is the intervention/action implement Summary statement Evidence applicable to Australia and New Zealand J Yes Not known	table in the New Z	Recommend/	consider omic evalua	tion		JAL
Benefits clearly don't outweigh harms Harms clearly outweigh benefits 6. Is the intervention/action implement Summary statement Evidence applicable to Australia and New Zealand p Yes Not known No	table in the New Z	Recommend/	consider omic evalua	tion		JAL
Benefits clearly don't outweigh harms Harms clearly outweigh benefits 6. Is the intervention/action implement Summary statement Evidence applicable to Australia and New Zealand p Yes Not known No 7. Final recommendation	table in the New Z	Recommend/ Consider econo Recommend/c	consider omic evaluz onsider agz	ition	STRONG	JAL
Benefits clearly don't outweigh harms Harms clearly outweigh benefits 6. Is the intervention/action implement Summary statement Evidence applicable to Australia and New Zealand p Yes Not known No	table in the New Z	Recommend/ Consider econo Recommend/c	consider omic evalua onsider aga	ition	recommendation	JAL
Benefits clearly don't outweigh harms Harms clearly outweigh benefits 6. Is the intervention/action implement Summary statement Evidence applicable to Australia and New Zealand p Yes Not known No 7. Final recommendation Routine nasal saline drops are not recommended.	table in the New Z	Recommend/ Consider econo Recommend/c	consider omic evalua onsider aga	tion inst Strength of r STRONG CONDITIO	recommendation	JAL

Question 17.

Question 17: In infants ho	spitalised with br	conchiolitis, does the use of nasa	al saline d	lrops improve	Evidence table ref:		
clinically relevant end-poir	its?			• -	Gomes 2012, Soleimani 2014, Turner		
					2008, Verma 2013 (120, 126-128).		
4	. 1. 1. 1. C. 1.	1 • 1 - 61 • • • 1 • 1 1 1 • 1 •)				
1. Evidence base (number of .	studies, level of evident	ce and risk of bias in the included studie.	s)				
There are no Cochrane or sys	stematic reviews or	n the question. Two clinical trials	٨	One or more Level I	studies with a low risk of bias, or several		
		p for unrelated interventions:	А	Level II studies with a low risk of bias			
physiotherapy and phenyleph	rine drops (120, 12	26).	D	One or two Level II studies with a low risk of bias, or SR/several			
Nasal saline is recommended	in guidelines and	consensus statements as practice	В	Level III studies with a low risk of bias			
points.			С	One or two Level III	I studies with a low risk of bias or Level I or		
			C	II studies with mode	erate risk of bias		
			D		Level I to III studies/SRs with a high		
			-	risk of bias			
2. Consistency (if only one stu	dy was available, ran	k this component as 'not applicable')					
			А	All studies consistent	t		
			В	Most studies consiste	ent and inconsistency can be explained		
			С	Some inconsistency,	reflecting genuine uncertainty around		
			C	question			
			D	Evidence is not con	nsistent		
			NA	Not applicable (one	study only)		
			L . ,	7 7. 7			
	the study results varie	ed according to some unknown factor (no	t simply stu	dy quality or sample size) a	and thus the clinical impact of the intervention could		
not be determined) The intervention has not bee	n an anifi callu invas	tigated as the aliginal impost	r				
cannot be determined.	ii specifically lives	ugated so the chincal impact	А	Very large			
cannot be determined.			В	Substantial			
			C	N 1 .			
			С	Moderate			
			D	Slight/Restricted			
4. Generalisability (how well	does the body of evides	nce match the population and clinical setu	tinos heino ti	proeted by the ouideline?)			
. Generalisability (1000 with		the match inceptopmation and canted set			1. 11 1		
			А		neralisable to target population		
			В	caveats	neralisable to target population with some		
					y generalisable to target population but could		
			С	be sensibly applied	generalisable to target population but could		
					tly generalisable to target population and		
			D		her sensible to apply		
E Applicability (is the hade of	f anidan ao nalan ant to t	he Australian/New Zealand healthcare	anta din t				
5. Applicability (is the body of	evidence relevant to th	9e Australian i New Zealana heallhare		2	5 5 7		
			А		plicable to Australian/New Zealand		
				healthcare context			
			В	context with few cav	to Australian/New Zealand healthcare		
					applicable to Australian/New Zealand		
			С	healthcare context			
					able to Australian/New Zealand healthcare		
			D	context			
Other factors (indicate here an	iy other factors that yo	u took into account when assessing the en	vidence base		night cause the group to downgrade or upgrade the		
recommendation)	, , , , ,	0		y 1 .	0 01 0 10		
No specific studies to evaluat	te the intervention.						
EVIDENCE STATEMEN	JT MATRIX (sum	marise the development group's synthesis	of the evide	nce relating to the key quest	tion, taking all the above factors into account)		
Component	Rating	Description	5	0 51			
1. Evidence base	D	Level IV studies or Level I to I	II studies/	SRs with a high risk of	f bias		
2. Consistency	D	Evidence is not consistent	- 1	0			
3. Clinical Impact	D	Slight/Restricted					
4. Generalisability	D	_	able to tar	get population and hard	d to judge whether sensible to apply		
5. Applicability	С				hcare context with some caveats		
Evidence statement:							
There is no evidence to guide	e the use of nasal s	aline solution in the infant of bron	chiolitis.				

RECOMMENDATION (What recommendation(s) does		TION		
the guideline development group draw from this evidence? Use	A Body of evidence can be trusted to guide practice			
action statements where possible)	В	Body of evidence can be trusted to guide practice in most	t situations	
	С	Body of evidence provides some support for recommend	ations(s) but care should be	
Routine nasal saline drops are not recommended.	C	taken in its application		
Trial of intermittent saline drops may be		Body of evidence is weak and recommendation must be a	applied with caution	
considered at time of feeding.	PP	Practice Point		
UNRESOLVED ISSUES (If needed, keep a note of specific a	issues that ar	ise when each recommendation is formulated and that require follow up)		
about this. This information will be used to develop the implemental Will this recommendation result in changes in usual care?	1 5	the guidelines)	YES NO	
Are there any resource implications associated with imple	ementing th	is recommendation?	YES	
			NO	
Will the implementation of this recommendation require	changes in	the way care is currently organised?	YES	
			NO	
Are the guideline development group aware of any barrie	ers to impler	mentation of this recommendation?	YES	

Question 18.

Consi	dered Judgem	ent - Streng	gth of recom	mendatio	n			
Question 18: In infants hospitalised with bronchioli	tis, does the u	se of nasal/	bubble CPA	AP improv	e clinically relev	ant end-points?	1	
1. Outcome measures:		Quality of		1	In	Importance of outcome in making a decision		
	HIGH	MOD	LOW	V. LOW	Critical	Important	Not Important	
O1 Need for mechanical ventilation				х	X			
O2 Duration of ED stay				X		Х		
O3 Need for ICU admission				X		X		
O ₄ Adverse events				X		X		
2. Is there is insufficient evidence to make a	recommenda	tion?						
One Cochrane systematic review (129) analysed two RCT outcome such as intubation rates was addressed and a tree observational study (130) of low quality evaluated genera in the ICU setting only and was of very low quality. Two 3. What benefit will the proposed intervention	end towards rec l paediatric war systematic revi	luction in int d administra iews (116, 13	ubations sho tion of nCPA	wn with a AP. A retro	lack of high-level ospective study (1	significance. A re 31) compared HI	ecent prospective	
	,					Quality	of oridon on	
Evidence statement There is very low level evidence that nCPAP reduces the	need for mech	anical ventila	ation.			Quanty	of evidence	
There is no evidence that nCPAP affects the duration of There is very low level evidence that nCPAP affects the r	,	dmission				VEF	RY LOW	
Judging the benefits in context								
The evidence is applicable and generalisable to the New 2			th systems in	relation to	therapy outside	of the ICU settin	g.	
4. What harm might the proposed intervention	on/action do	?						
Evidence statement There is very low level evidence that nCPAP affects the n	rate of adverse	events					of evidence RY LOW	
Judging the harms in context	ate of adverse	events.						
The evidence is probably applicable and generalisable to		nd and Austi	alian health s	systems in	relation to therap	y outside of the I	CU setting.	
5. What is the likely balance between good a	and harm?							
Evidence statement Benefits probably outweigh harms.						quality	verall of evidence XY LOW	
Judging the balance of benefits and harms in contex	t							
Benefits clearly outweigh harms	Recommend	1				STRONG		
Benefits probably outweigh harms	Consider					CONDITI	ONAL	
Not known	Make a reco	mmendation	for research	(see 8 belo	ow)	WEAK		
Benefits probably don't outweigh harms	C 1	· .				CONDITI	ONIAL	
Harms probably outweigh benefits	- Consider ag	ainst				CONDITIO	JNAL	
Benefits clearly don't outweigh harms						offin on to		
Harms clearly outweigh benefits	Recommend	l against				STRONG		
6. Is the intervention/action implementable	in the New Z	ealand and	Australian o	context?				
Summary statement		h h a a a h i a li						
The use of nCPAP outside of the paediatric intensive car Yes	e iii iiitants wit		tis can be con					
Not known			nsider econo		tion			
No			commend/co					
7. Final recommendation		110						
Nasal CPAP therapy for infants with bronchiolitis may b	e considered fo	or the manag	ement of infa	ants	Strength of re STRONG CONDITION WEAK	commendation		
8. Recommendations for research								
Large RCT in paediatric wards and paediatric intensive ca	are is needed. I	Direct compa	rison of HFN	NC and CF	AP needs to be d	lone.		

Question 18: In infants hosp improve clinically relevant e	pitalised with bronchio end-points?	Evidence table ref: Metge 2014, Palanivel 2009, Oymar 2014, Kana 2015, Evans 2012, Sinha 2015 (116, 129-132, 166).		
1. Evidence base (number of sta	tudies, level of evidence and ra	isk of bias in the included s	tudies)	
In the non-PICU setting there	has been one low qualit	ty prospective study		One or more Level I studies with a low risk of bias, or severa
investigating nCPAP (130). A			А	Level II studies with a low risk of bias
studies of 50 patients on nCPA			В	One or two Level II studies with a low risk of bias, or
conclusions on the benefit. Or				SR/several Level III studies with a low risk of bias
compared HFNC to nCPAP a reviews (116, 132).	and there are two low qu	ality systematic	С	One or two Level III studies with a low risk of bias or Level I or II studies with moderate risk of bias
leviews (110, 152).				Level IV studies or Level I to III studies/SRs with a high risk
			D	of bias
2. Consistency (if only one study	ly was available, rank this co	omponent as 'not applicable)	
All studies are inconsistent as t	they evaluated different	populations (PICU vs		
ward) and interventions (HFN	NC, nCPAP).		А	All studies consistent
			В	Most studies consistent and inconsistency can be explained
			С	Some inconsistency, reflecting genuine uncertainty around
				question
			D	Evidence is not consistent
			NA	Not applicable (one study only)
3. Clinical impact (indicate if the not be determined)	the study results varied accord	ding to some unknown facto	or (not simply study	quality or sample size) and thus the clinical impact of the intervention could
			А	Very large
			D	
			В	Substantial
			B C	Substantial Moderate
				Moderate
4 Generalisability (how well de	lass the bady of evidence mate	th the population and clinic.	C D	Moderate Slight/Restricted
4. Generalisability (bow well do	loes the body of evidence matc	h the population and clinica	C D al settings being targ	Moderate Slight/Restricted geted by the guideline?)
4. Generalisability (how well do	loes the body of evidence matc	h the population and clinica	C D	Moderate Slight/Restricted geted by the guideline?) Evidence directly generalisable to target population
4. Generalisability (how well de	loes the body of evidence matc	h the population and clinica	C D al settings being targ	Moderate Slight/Restricted geted by the guideline?) Evidence directly generalisable to target population Evidence directly generalisable to target population with
4. Generalisability (how well de	loes the body of evidence matc	b the population and clinica	C D al settings being targ A B	Moderate Slight/Restricted geted by the guideline?) Evidence directly generalisable to target population Evidence directly generalisable to target population with some caveats
4. Generalisability (how well de	loes the body of evidence matc	h the population and clinica	C D al settings being targ	Moderate Slight/Restricted geted by the guideline?) Evidence directly generalisable to target population Evidence directly generalisable to target population with some caveats
4. Generalisability (bow well de	loes the body of evidence matc	h the population and clinica	C D Al settings being targ A B C	Moderate Slight/Restricted geted by the guideline?) Evidence directly generalisable to target population Evidence directly generalisable to target population with some caveats Evidence not directly generalisable to target population but could be sensibly applied Evidence not directly generalisable to target population and
4. Generalisability (how well do	loes the body of evidence matc	h the population and clinica	C D al settings being targ A B	Moderate Slight/Restricted geted by the guideline?) Evidence directly generalisable to target population Evidence directly generalisable to target population with some caveats Evidence not directly generalisable to target population but could be sensibly applied
			C D al settings being targ A B C D	Moderate Slight/Restricted geted by the guideline?) Evidence directly generalisable to target population Evidence directly generalisable to target population with some caveats Evidence not directly generalisable to target population but could be sensibly applied Evidence not directly generalisable to target population and
			C D al settings being targ A B C D hcare context in terr	Moderate Slight/Restricted geted by the guideline?) Evidence directly generalisable to target population Evidence directly generalisable to target population with some caveats Evidence not directly generalisable to target population but could be sensibly applied Evidence not directly generalisable to target population and hard to judge whether sensible to apply
			C D al settings being targ A B C D	Moderate Slight/Restricted geted by the guideline?) Evidence directly generalisable to target population Evidence directly generalisable to target population with some caveats Evidence not directly generalisable to target population but could be sensibly applied Evidence not directly generalisable to target population and hard to judge whether sensible to apply mms of health services / delivery of care and cultural factors?) Evidence directly applicable to Australian/New Zealand healthcare context
			C D al settings being targ A B C D hcare context in terr	Moderate Slight/Restricted geted by the guideline?) Evidence directly generalisable to target population Evidence directly generalisable to target population with some caveats Evidence not directly generalisable to target population but could be sensibly applied Evidence not directly generalisable to target population and hard to judge whether sensible to apply ms of health services / delivery of care and cultural factors?) Evidence directly applicable to Australian/New Zealand healthcare context Evidence applicable to Australian/New Zealand healthcare
			C D al settings being targ A B C D bcare context in terr A B	Moderate Slight/Restricted geted by the guideline?) Evidence directly generalisable to target population Evidence directly generalisable to target population with some caveats Evidence not directly generalisable to target population but could be sensibly applied Evidence not directly generalisable to target population and hard to judge whether sensible to apply ms of health services / delivery of care and cultural factors?) Evidence directly applicable to Australian/New Zealand healthcare context Evidence applicable to Australian/New Zealand healthcare context with few caveats
			C D al settings being targ A B C D hcare context in terr A	Moderate Slight/Restricted geted by the guideline?) Evidence directly generalisable to target population Evidence directly generalisable to target population with some caveats Evidence not directly generalisable to target population but could be sensibly applied Evidence not directly generalisable to target population and hard to judge whether sensible to apply ms of health services / delivery of care and cultural factors?) Evidence directly applicable to Australian/New Zealand healthcare context Evidence applicable to Australian/New Zealand healthcare
			C D al settings being targ A B C D bcare context in terr A B	Moderate Slight/Restricted geted by the guideline?) Evidence directly generalisable to target population Evidence directly generalisable to target population with some caveats Evidence not directly generalisable to target population but could be sensibly applied Evidence not directly generalisable to target population and hard to judge whether sensible to apply ms of health services / delivery of care and cultural factors?) Evidence directly applicable to Australian/New Zealand healthcare context Evidence applicable to Australian/New Zealand healthcare context with few caveats Evidence probably applicable to Australian/New
5. Applicability (is the body of e	evidence relevant to the Aust	ralian/New Zealand healt	C D A al settings being targ A B C D beare context in terr A B C D beare context in terr A D D D D	Moderate Slight/Restricted geted by the guideline?) Evidence directly generalisable to target population Evidence directly generalisable to target population with some caveats Evidence not directly generalisable to target population but could be sensibly applied Evidence not directly generalisable to target population and hard to judge whether sensible to apply ms of health services / delivery of care and cultural factors?) Evidence directly applicable to Australian/New Zealand healthcare context Evidence applicable to Australian/New Zealand healthcare context with few caveats Evidence not applicable to Australian/New Zealand healthcare context with some caveats Evidence not applicable to Australian/New Zealand healthcare context with some caveats
5. Applicability (is the body of e Other factors (indicate here any recommendation)	evidence relevant to the Aust other factors that you took i	ralian/New Zealand bealt into account when assessing	C D A al settings being targ A B C D beare context in terr A B C D the evidence base (fe	Moderate Slight/Restricted geted by the guideline?) Evidence directly generalisable to target population Evidence directly generalisable to target population with some caveats Evidence not directly generalisable to target population but could be sensibly applied Evidence not directly generalisable to target population and hard to judge whether sensible to apply ms of health services / delivery of care and cultural factors?) Evidence directly applicable to Australian/New Zealand healthcare context Evidence probably applicable to Australian/New Zealand healthcare context with few caveats Evidence not applicable to Australian/New Zealand healthcare context with some caveats Evidence not applicable to Australian/New Zealand healthcare context with some caveats Evidence not applicable to Australian/New Zealand healthcare context with some caveats Evidence not applicable to Australian/New Zealand healthcare context with some caveats Evidence not applicable to Australian/New Zealand healthcare context
5. Applicability (is the body of e Other factors (indicate here any recommendation) EVIDENCE STATEMENT	evidence relevant to the Aust o other factors that you took i T MATRIX (summarise t	ralian/New Zealand healt into account when assessing the development group's sym	C D A al settings being targ A B C D beare context in terr A B C D the evidence base (fe	Moderate Slight/Restricted geted by the guideline?) Evidence directly generalisable to target population Evidence directly generalisable to target population with some caveats Evidence not directly generalisable to target population but could be sensibly applied Evidence not directly generalisable to target population and hard to judge whether sensible to apply ms of health services / delivery of care and cultural factors?) Evidence directly applicable to Australian/New Zealand healthcare context Evidence applicable to Australian/New Zealand healthcare context with few caveats Evidence not applicable to Australian/New Zealand healthcare context with some caveats Evidence not applicable to Australian/New Zealand healthcare context with some caveats
5. Applicability (is the body of e Other factors (indicate here any recommendation) EVIDENCE STATEMENT Component	evidence relevant to the Aust o other factors that you took i T MATRIX (summarise t Rating D	ralian/New Zealand healt into account when assessing the development group's sym escription	C D dl settings being targ A B C D hcare context in terr A B C D the evidence base (fe	Moderate Slight/Restricted geted by the guideline?) Evidence directly generalisable to target population Evidence directly generalisable to target population with some caveats Evidence not directly generalisable to target population but could be sensibly applied Evidence not directly generalisable to target population and hard to judge whether sensible to apply ms of health services / delivery of care and cultural factors?) Evidence directly applicable to Australian/New Zealand healthcare context Evidence applicable to Australian/New Zealand healthcare context with few caveats Evidence not applicable to Australian/New Zealand healthcare context with some caveats Evidence not applicable to Australian/New Zealand healthcare context mith some caveats Evidence not applicable to Australian/New Zealand healthcare context mith some caveats Evidence not applicable to Australian/New Zealand healthcare context mith some caveats Evidence not applicable to Australian/New Zealand healthcare context Evidence not applicable to Australian/New Zealand healthcare context for example, issues that might cause the group to downgrade or upgrade the erelating to the key question, taking all the above factors into account)
5. Applicability (is the body of e Other factors (indicate here any recommendation) EVIDENCE STATEMENT Component 1. Evidence base	evidence relevant to the Aust other factors that you took i T MATRIX (summarise t Rating D C O	ralian/New Zealand healt into account when assessing the development group's sym escription ine or two Level III stud	C D al settings being targ A B C D hcare context in terr A B C D theare context in terr A B C D the evidence base (fit thesis of the evidence dies with a low response to the low response to	Moderate Slight/Restricted geted by the guideline?) Evidence directly generalisable to target population Evidence directly generalisable to target population with some caveats Evidence not directly generalisable to target population but could be sensibly applied Evidence not directly generalisable to target population and hard to judge whether sensible to apply ms of health services / delivery of care and cultural factors?) Evidence directly applicable to Australian/New Zealand healthcare context Evidence probably applicable to Australian/New Zealand healthcare context with few caveats Evidence not applicable to Australian/New Zealand healthcare context with some caveats Evidence not applicable to Australian/New Zealand healthcare context with some caveats Evidence not applicable to Australian/New Zealand healthcare context with some caveats Evidence not applicable to Australian/New Zealand healthcare context with some caveats Evidence not applicable to Australian/New Zealand healthcare context
5. Applicability (is the body of e Other factors (indicate bere any recommendation) EVIDENCE STATEMENT Component 1. Evidence base 2. Consistency	evidence relevant to the Aust o other factors that you took i T MATRIX (summarise t Rating D C O D Er	ralian/New Zealand bealt into account when assessing the development group's sym rescription ne or two Level III stua vidence is not consisten	C D al settings being targ A B C D hcare context in terr A B C D theare context in terr A B C D the evidence base (fit thesis of the evidence dies with a low response to the low response to	Moderate Slight/Restricted geted by the guideline?) Evidence directly generalisable to target population Evidence directly generalisable to target population with some caveats Evidence not directly generalisable to target population but could be sensibly applied Evidence not directly generalisable to target population and hard to judge whether sensible to apply ms of health services / delivery of care and cultural factors?) Evidence directly applicable to Australian/New Zealand healthcare context Evidence applicable to Australian/New Zealand healthcare context with few caveats Evidence not applicable to Australian/New Zealand healthcare context with some caveats Evidence not applicable to Australian/New Zealand healthcare context mith some caveats Evidence not applicable to Australian/New Zealand healthcare context mith some caveats Evidence not applicable to Australian/New Zealand healthcare context mith some caveats Evidence not applicable to Australian/New Zealand healthcare context Evidence not applicable to Australian/New Zealand healthcare context for example, issues that might cause the group to downgrade or upgrade the erelating to the key question, taking all the above factors into account)
5. Applicability (is the body of e Other factors (indicate here any recommendation) EVIDENCE STATEMENT Component 1. Evidence base 2. Consistency 3. Clinical Impact	evidence relevant to the Aust other factors that you took i T MATRIX (summarise t Rating D C O D Er C M	ralian/New Zealand bealt into account when assessing the development group's sym rescription ne or two Level III stua vidence is not consister foderate	C D al settings being targ A B C D hcare context in terr A B C D thear context in terr A B C D the evidence base (for the evidence base (for the sis of the evidence base (for the	Moderate Slight/Restricted geted by the guideline?) Evidence directly generalisable to target population Evidence directly generalisable to target population with some caveats Evidence not directly generalisable to target population but could be sensibly applied Evidence not directly generalisable to target population and hard to judge whether sensible to apply ms of bealth services / delivery of care and cultural factors?) Evidence directly applicable to Australian/New Zealand healthcare context Evidence applicable to Australian/New Zealand healthcare context with few caveats Evidence not applicable to Australian/New Zealand healthcare context with some caveats Evidence not applicable to Australian/New Zealand healthcare context mith some caveats Evidence not applicable to Australian/New Zealand healthcare context with few caveats Evidence not applicable to Australian/New Zealand healthcare context with some caveats Evidence not applicable to Australian/New Zealand healthcare context for example, issues that might cause the group to downgrade or upgrade the e relating to the key question, taking all the above factors into account) isk of bias or Level I or II studies with moderate risk of bias
5. Applicability (is the body of e Other factors (indicate here any recommendation) EVIDENCE STATEMENT Component 1. Evidence base 2. Consistency	evidence relevant to the Austr other factors that you took i T MATRIX (summarise t Rating D C O D Er C M C M	ralian/New Zealand bealt into account when assessing the development group's sym rescription ine or two Level III stua vidence is not consister foderate vidence not directly ger	C D al settings being targ A B C D hcare context in terr A B C D thear context in terr A B C D the evidence base (fit thesis of the evidence dies with a low rent nt	Moderate Slight/Restricted geted by the guideline?) Evidence directly generalisable to target population Evidence directly generalisable to target population with some caveats Evidence not directly generalisable to target population but could be sensibly applied Evidence not directly generalisable to target population and hard to judge whether sensible to apply ms of health services / delivery of care and cultural factors?) Evidence directly applicable to Australian/New Zealand healthcare context Evidence probably applicable to Australian/New Zealand healthcare context with few caveats Evidence not applicable to Australian/New Zealand healthcare context with some caveats Evidence not applicable to Australian/New Zealand healthcare context with some caveats Evidence not applicable to Australian/New Zealand healthcare context with some caveats Evidence not applicable to Australian/New Zealand healthcare context is proved to downgrade or upgrade the ior example, issues that might cause the group to downgrade or upgrade the

RECOMMENDATION (What	OVERALL GRADE OF RECOMMENDATION							
recommendation(s) does the guideline	А	A Body of evidence can be trusted to guide practice						
development group draw from this	В	B Body of evidence can be trusted to guide practice in most situations						
evidence? Use action statements where possible)	С	Body of evidence provides some support for recommendations(s) but care should be taken in application						
	D	Body of evid	ence is weak and recommendation must be applied with caution					
Nasal CPAP therapy for infants with bronchiolitis may be considered for the management of infants.	рр							
UNRESOLVED ISSUES (If needed,	keep a note of	specific issues that	t arise when each recommendation is formulated and that require follow up)					
IMPLEMENTATION OF RECO about this. This information will be used to a			indicate yes or no to the following questions. Where the answer is yes, please provide explanatory information for the guidelines)					
Will this recommendation result in cha	anges in usu	al care?	YES					
Increase in ward based respiratory sup	port.		NO					
Are there any resource implications as implementing this recommendation? Appropriate training and support for		h	YES NO					
Will the implementation of this recom	mendation	require	YES					
changes in the way care is currently or	ganised?		NO					
Are the guideline development group	aware of an	y barriers to	YES					
implementation of this recommendati	on?		NO					

Question 19.

	Considered Judgerr	ient - Streng	th of recom	mendation				
Question 19: In infants hospitalised with bron	nchiolitis, is provisio	n of home o	xygen a saf	e alternative	for managem	ent?		
1. Outcome measures:		Quality of evidence Imp						
	HIGH	MOD	LOW	V. LOW	Critical	n making a deci Important	Not Important	
O1 Length of stay in hospital				x	х			
D ₂ Readmission rate in seven days				x		Х		
D ₃ Length of oxygen therapy				x		Х		
D4 Adverse events				x		х		
D5 Cost savings				x		Х		
 There have been no systematic reviews on this qu (133) was stopped before the enrolment of the de numbers to compare the two groups in terms of e Additional evidence came from one prospective of (137-139). What benefit will the proposed interview. 	sired number of patien evaluating the cost save bservational study (13	nts in their sam ings and the p 55), one retros	mple-size ca patients were	lculation was recruited ov	achieved and T er a single Aust	fie et al (134) had ralian bronchiolit ee retrospective c	very low is season. hart reviews	
Evidence statement	- i - 1 i 1				- 6 - to		of evidence	
For the critical outcome of length of stay in hos reated with home oxygen therapy.	pital there is very low	quanty evide	nice of a rec	luced length	or stay in thos		YLOW	
For the critical outcome of total length of oxyge therapy in those treated with home oxygen therap For the important outcome of cost savings there	y.							
nome oxygen therapy. udging the benefits in context								
The evidence is applicable and can be generalised of supplying home oxygen in the New Zealand ar 4. What harm might the proposed int	d Australian health se	ttings.	litan health o	care facilities	caring for bron	chiolitic infants w	ith the intentio	
Evidence statement						Quality of ev	vidence	
For the critical outcome of readmission in seven or reated with home oxygen therapy.	lays there is very low	quality eviden	ce of a redu	ced readmissi	ion rate in thos		Y LOW	
For the important outcome of adverse events the reated with home oxygen therapy.	nere is very low qualit	y evidence o			events in thos			
udging the harms in context			f no increas	e in adverse				
Evidence to date indicates no increased risk of ha						observational wit	th risk of	
Evidence to date indicates no increased risk of har mprecision and inconsistency. The true effect on	harm has not been es					observational wit	th risk of	
Evidence to date indicates no increased risk of ha mprecision and inconsistency. The true effect on 5. What is the likely balance between	harm has not been es							
 Evidence to date indicates no increased risk of ha mprecision and inconsistency. The true effect on 5. What is the likely balance between Evidence statement The benefits are likely to outweigh the harms. 	harm has not been es good and harm?					O quality o	th risk of verall of evidence Y LOW	
Evidence to date indicates no increased risk of ha mprecision and inconsistency. The true effect on 5. What is the likely balance between Evidence statement The benefits are likely to outweigh the harms. udging the balance of benefits and harms in	harm has not been es good and harm?					O quality o	verall of evidence	
 Evidence to date indicates no increased risk of ha mprecision and inconsistency. The true effect on 5. What is the likely balance between Evidence statement The benefits are likely to outweigh the harms. Eudging the balance of benefits and harms in Benefits probably outweigh harms. 	harm has not been es good and harm?	tablished.				O quality o	verall of evidence	
Evidence to date indicates no increased risk of ha mprecision and inconsistency. The true effect on 5. What is the likely balance between Evidence statement The benefits are likely to outweigh the harms. udging the balance of benefits and harms in Benefits probably outweigh harms. Benefits clearly outweigh harms	harm has not been es good and harm? context	tablished.				Or quality of VER STRONG	verall of evidence Y LOW	
 Widence to date indicates no increased risk of ha mprecision and inconsistency. The true effect on 5. What is the likely balance between What is the likely balance between Widence statement The benefits are likely to outweigh the harms. Udging the balance of benefits and harms in Benefits probably outweigh harms. Benefits clearly outweigh harms Benefits probably outweigh harms 	harm has not been es good and harm? context Recommend Consider	tablished.	studies have	been underp	oowered or only	Quality o VER	verall of evidence Y LOW	
 Widence to date indicates no increased risk of hamprecision and inconsistency. The true effect on 5. What is the likely balance between Evidence statement The benefits are likely to outweigh the harms. udging the balance of benefits and harms in Benefits probably outweigh harms. Benefits clearly outweigh harms Benefits probably outweigh harms Not known 	harm has not been es good and harm? context Recommend Consider	tablished.	studies have	been underp	oowered or only	STRONG CONDITIO	verall of evidence Y LOW	
 Widence to date indicates no increased risk of ha mprecision and inconsistency. The true effect on 5. What is the likely balance between Evidence statement The benefits are likely to outweigh the harms. udging the balance of benefits and harms in Benefits probably outweigh harms. Benefits clearly outweigh harms Benefits probably outweigh harms Not known Benefits probably don't outweigh harms 	harm has not been es good and harm? context Recommend Consider	tablished.	studies have	been underp	oowered or only	STRONG CONDITIO	verall of evidence Y LOW ONAL	
Evidence to date indicates no increased risk of ha mprecision and inconsistency. The true effect on 5. What is the likely balance between Evidence statement The benefits are likely to outweigh the harms. udging the balance of benefits and harms in Benefits probably outweigh harms Benefits probably outweigh harms Benefits probably outweigh harms Not known Benefits probably don't outweigh harms Harms probably outweigh benefits	harm has not been es good and harm? context Recommend Consider Make a reco Consider ag	tablished.	studies have	been underp	oowered or only	STRONG CONDITION WEAK	verall of evidence Y LOW ONAL	
Evidence to date indicates no increased risk of ha mprecision and inconsistency. The true effect on 5. What is the likely balance between Evidence statement The benefits are likely to outweigh the harms. Udging the balance of benefits and harms in Benefits probably outweigh harms. Benefits clearly outweigh harms Not known Benefits probably don't outweigh harms Harms probably outweigh benefits Benefits clearly don't outweigh harms	harm has not been es good and harm? context Recommend Consider Make a reco	tablished.	studies have	been underp	oowered or only	STRONG CONDITION WEAK	verall of evidence Y LOW ONAL	
Evidence to date indicates no increased risk of ha mprecision and inconsistency. The true effect on 5. What is the likely balance between Evidence statement The benefits are likely to outweigh the harms. Iudging the balance of benefits and harms in Benefits probably outweigh harms. Benefits clearly outweigh harms Not known Benefits probably don't outweigh harms Harms probably outweigh benefits Benefits clearly don't outweigh harms Harms probably outweigh harms	harm has not been es good and harm? context Recommend Make a reco Consider ag Recommend	tablished.	studies have	been underp	oowered or only	STRONG CONDITIO	verall of evidence Y LOW ONAL	
Evidence to date indicates no increased risk of ha mprecision and inconsistency. The true effect on 5. What is the likely balance between Evidence statement The benefits are likely to outweigh the harms. Rudging the balance of benefits and harms in Benefits probably outweigh harms. Benefits probably outweigh harms Benefits probably outweigh harms Not known Benefits probably don't outweigh harms Harms probably outweigh benefits Benefits clearly outweigh benefits Benefits clearly outweigh benefits Benefits clearly outweigh benefits Banefits clearly outweigh benefits Banefits clearly outweigh benefits Banefits clearly outweigh benefits	harm has not been es good and harm? context Recommend Make a reco Consider ag Recommend	tablished.	studies have	been underp	oowered or only	STRONG CONDITIO	verall of evidence Y LOW ONAL	
Evidence to date indicates no increased risk of ha imprecision and inconsistency. The true effect on 5. What is the likely balance between Evidence statement The benefits are likely to outweigh the harms. Judging the balance of benefits and harms in Benefits probably outweigh harms. Benefits probably outweigh harms Benefits probably outweigh harms Not known Benefits probably don't outweigh harms Harms probably outweigh benefits Benefits clearly outweigh benefits Benefits clearly outweigh benefits Benefits clearly don't outweigh harms Harms clearly outweigh benefits 6. Is the intervention/action impleme Summary statement Home oxygen therapy has been implemented in a	harm has not been es good and harm? context Recommend Make a reco Make a reco Consider ag Recommend Recommend	tablished.	studies have	been underp (see 8 below context?	powered or only	STRONG CONDITIO STRONG CONDITIO STRONG	verall of evidence Y LOW ONAL	
Evidence to date indicates no increased risk of ha imprecision and inconsistency. The true effect on 5. What is the likely balance between Evidence statement The benefits are likely to outweigh the harms. Judging the balance of benefits and harms in Benefits probably outweigh harms. Benefits probably outweigh harms Benefits probably outweigh harms Not known Benefits probably don't outweigh harms Harms probably outweigh benefits Benefits clearly don't outweigh harms Harms clearly outweigh benefits 6. Is the intervention/action impleme Summary statement Home oxygen therapy has been implemented in a	harm has not been es good and harm? context Recommend Make a reco Make a reco Consider ag Recommend Recommend	tablished.	studies have	been underp (see 8 below context? te resourcing consider	powered or only	STRONG CONDITIO STRONG CONDITIO STRONG	verall of evidence Y LOW ONAL	
Evidence statement The benefits are likely to outweigh the harms. Judging the balance of benefits and harms in Benefits probably outweigh harms Benefits clearly outweigh harms Not known Benefits probably don't outweigh harms Harms probably outweigh benefits Benefits clearly don't outweigh harms Harms clearly outweigh benefits	harm has not been es good and harm? context Recommend Make a reco Make a reco Consider ag Recommend Recommend	tablished.	studies have	been underp (see 8 below context?	oowered or only	STRONG CONDITIO STRONG CONDITIO STRONG	verall of evidence Y LOW ONAL	

7. Final recommendation

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. STRONG CONDIT WEAK

Strength of recommendation STRONG CONDITIONAL

Recommendations for research

Large randomised controlled study with pre-defined outcomes and use of oxygen therapy is required to establish the position of this therapy in bronchiolitis.

Question 19.

8.

Question 19: In infants hospitalised with bronchiolitis, is provision of hom	e oxygen	a safe alternative	Evidence table ref:
for management?			Bajaj 2006, Flett 2014, Gauthier 2012,
			Halstead 2012, Sandweiss 2013, Tie 2009,
			Zappia 2013 (133-139).
1. Evidence base (number of studies, level of evidence and risk of bias in the included studie.	s)		
	/	1	
No systematic reviews.	А		I studies with a low risk of bias, or several
		Level II studies with	
Two RCTs involving 136 infants (Level III-1). Both studies are rated high for	В		studies with a low risk of bias, or SR/several
risk of bias.	Б	Level III studies with	h a low risk of bias
	С	One or two Level I	II studies with a low risk of bias or Level
There has been one additional prospective observational study of 112 infants	Ŭ	I or II studies with	moderate risk of bias
(Level IV) a retrospective historical control study of 692 infants and three		Level IV studies or l	Level I to III studies/SRs with a high risk of
retrospective chart reviews of 1060 children (Level III-3 - IV). All studies are	D	bias	
rated low for risk of bias.		0145	
2. Consistency (if only one study was available, rank this component as 'not applicable')			
Evidence is consistent that home oxygen therapy reduces length of stay in			
hospital. However, studies are variable in quality and reporting of all outcomes.	А	All studies consisten	t
	В	Most studies consist	ent and inconsistency can be explained
	_		
	_	Some inconsistence	y, reflecting genuine uncertainty around
	С	question	,
		-	
	D	Evidence is not cons	sistent
	NIA	Not applicable (one	aturdur a mlur)
	NA	Not applicable (one	study offiy)
3. Clinical impact (indicate if the study results varied according to some unknown factor (no	t simply stu	dy quality or sample size)	and thus the clinical impact of the intervention could
not be determined)			* *
Length of stay in hospital for the individual patient is reduced but no study has	А	Very large	
compared the total length of care for patients both in hospital and at home		, er j mige	
while receiving oxygen therapy. There is potential for cost savings and positive	В	Substantial	
patient satisfaction but only one study has looked at resource implications for	С	Moderate	
community practice. There appears to be no increase in adverse events or		01. 1 /D	
change in readmission rates following discharge.	D	Slight/Restricted	
4. Generalisability (how well does the body of evidence match the population and clinical set	tings being t	argeted by the guideline?)	
The majority of the studies were conducted in North America in an elevated	A		neralisable to target population
altitude where home oxygen therapy is used frequently. 2 studies were from	11		generalisable to target population with
Australia and hence generalizable to Australia and New Zealand.	В	some caveats	generalisable to target population with
			y generalisable to target population but could
	С	be sensibly applied	y generalisable to target population but could
		, , , ,	y generalisable to target population and hard
	D	to judge whether ser	
		, .	** *
5. Applicability (is the body of evidence relevant to the Australian/New Zealand healthcare	context in t	5	5 5 5 7
The results are directly applicable to the Australian/New Zealand healthcare	А	• •	plicable to Australian/New Zealand
context. The provision of home oxygen services would require some individual		healthcare context	
health services to provide appropriate equipment and follow up not currently	В		to Australian/New Zealand healthcare
available.		context with few cav	
	С		applicable to Australian/New Zealand
		healthcare context	
	D	Evidence not applic	cable to Australian/New Zealand healthcare
		context	
Other factors (indicate here any other factors that you took into account when assessing the end	vidence base	(for example, issues that n	night cause the group to downgrade or upgrade the
recommendation)			

Component	Rating	Description				
1. Evidence base	С	One or two Level III studies with a low risk of bias or Level I or II studies with moderate risk of bias				
2. Consistency	С	Some inconsistency, reflecting genuine uncertainty around question				
3. Clinical Impact	С	Moderate				
4. Generalisability	В	Eviden	ce directly	generalisable to target population with some caveats		
5. Applicability	С	Evidence probably applicable to Australian/New Zealand healthcare context with some cave				
Evidence statement:						
There is some evidence of I	benefits to infants with	n bronch	iolitis being	g considered for home oxygen therapy after a suitable period of observation in hospita		
The evidence is likely to be	generalizable to many	health s	ervices in A	Australia and New Zealand.		
RECOMMENDATION	(What recommendation(s) does		OVERALL GRADE OF RECOMMENDATION		
the guideline development group		Jse	А	Body of evidence can be trusted to guide practice		
action statements where possible))		В	Body of evidence can be trusted to guide practice in most situations		
		[С	Body of evidence provides some support for recommendations(s) but care		
After a period of observation, infants at low risk for		sk for	C	should be taken in its application		
severe bronchiolitis can be considered for discharge on home oxygen as part of an organised			D	Body of evidence is weak and recommendation must be applied with caution		
'Home Oxygen Program'	' which has clear 'Re	turn	PP	Practice Point		
to Hospital' advice.		C	.1			
				se when each recommendation is formulated and that require follow up)		
				tients were deemed suitable for discharge home on oxygen and after being sent home		
how the oxygen was weane				at any set of the fill wine and in the line of the set		
about this. This information wil				ate yes or no to the following questions. Where the answer is yes, please provide explanatory informations with the answer is yes.		
Will this recommendation r	A .		ion pian joi i	YES		
win and recommendation i	court in changes in ust	iai care!		NO		
		, · · ,				
Are there any resource impl			menting thi			
Easily accessible home oxyg	gen service is required			NO		
Will the implementation of this recommendation require changes in the way care is currently organised?			changes in t	the way care is currently organised? YES		
Will the implementation of						
Will the implementation of				NO		
- -		v barrier	s to implen	nentation of this recommendation? YES		

Question 20a.

Γ

GRADE Evidence Summary

Considered Judgment - Strength of recommendation

Consi	dered Judgmo	ent - Strengt	th of recomm	nendation			
Question 20a: In infants presenting to hospital or ho	spitalized wit	th bronchiol	itis, does th	e use of ant	ibiotic medica	ation improve cl	inically relevant
endpoints.							
1. Outcome measures:		Quality of	evidence			nportance of ou n making a dec	
	HIGH	MOD	LOW	V. LOW	Critical	Important	Not Important
O1 Length of hospital stay		х			X		
O2 Hospital readmission within 6 months		x				X	
O3 Adverse effects			x			Х	
O ₄ PICU admission			X				
O5 Persistent respiratory symptoms			x			X	
2. Is there is insufficient evidence to make a	recommenda	tion?	1	1			
The evidence is based on two Cochrane systematic review review (141) only a single study of 30 infants met inclusio 3. What benefit will the proposed interventio Evidence statement For the critical outcome of length of stay there is moderate	n criteria. Sub n/action have	osequently th	ere have bee	n a two furth	her RCTs of 40	(142) and 219 (14 Quality	
For the critical outcome of PICU admission there is low with one study (157) of 71 infants with only one admissio For the important outcome of persistent respiratory sy antibiotics. Judging the benefits in context	n to PICU.						
The evidence is applicable and generalizable to the New 2			ng.				
4. What harm might the proposed intervention	on/action do	2					
Evidence statement For the important outcome of adverse effects there	was no differe	ence found	in adverse o	rastro_intesti	nal effects wit		of evidence
antibiotic use in a study of 40 infants (167) and a study included studies.			c	·			DERATE
For the important outcome of hospital re-admission w compared to placebo.	vithin 6 month	hs there is r	noderate qua	ality evidenc	e of no benefi	it	
Judging the harms in context	1 1 1	с. <i>і</i> :	1.1.1.1	1 1 4 4		C	
Bronchiolitis is a viral infection and the low risk of second rash, diarrhoea, vomiting as well as increased hospital and				iced with the	e significant nar	ms of antibiotic t	ise, including
5. What is the likely balance between good a							
Evidence statement						0	verall
Harms probably outweigh the benefits.							of evidence DERATE
Judging the balance of benefits and harms in context	t						
Benefits clearly outweigh harms	Recommend	l				STRONG	
Benefits probably outweigh harms	Consider					CONDITI	ONAL
Not known	Make a recor	mmendation	for research	(see 8 below)	WEAK	
Benefits probably don't outweigh harms	<u> </u>	• ,				001017	
Harms probably outweigh benefits	Consider ag	gainst				CONDITI	UNAL
Benefits clearly don't outweigh harms	Recommend	l against				STRONG	
Harms clearly outweigh benefits		0					
6. Is the intervention/action implementable	in the New Z	ealand and	Australian c	context?			
Summary statement There is insufficient evidence to support the use of anti			onchiolitis.	Although ma	crolide antibio	tics have both ar	ntibiotic and anti-
inflammatory properties their use for treatment of viral by Yes	ronchiolitis is r	,	commend/c	oneidor			
Not known			nsider econor		2		
No		Re	commend/o	consider aga	unst		

7. Final recommendation	
Do not use antibiotics to treat infants with bronchiolitis.	Strength of recommendation
	STRONG
	CONDITIONAL
	WEAK

8. Recommendations for research

Studies on subgroups of high risk patients who may benefit from antibiotics, including those admitted to ICU with severe bronchiolitis are needed. The optimal treatment regime (single dose to 14 days) and timing (acute versus post-acute) is yet to be established.

Question 20a.

Question 20a: In infants presenting to hospital or hospitalised with brantibiotic medication improve clinically relevant end-points?	onchiolit	is, does the use of Evidence table ref: Beigleman 2014, Farley 2014, Kneyber 2008, Mazumder 2009, McCallum 2012, McCallum 2013, McCallum 2015, Pinto 2012, Tahan 2007 (140-143, 167-171)
1. Evidence base (number of studies, level of evidence and risk of bias in the included studies,	i)	
The evidence is based on two Cochrane systematic reviews and an RCT. The first review (140) contains seven RCTs involving 824 participants comparing	А	One or more Level I studies with a low risk of bias, or several Level II studies with a low risk of bias
antibiotics to placebo or other. In the second systematic review for persistent	в	One or two Level II studies with a low risk of bias, or
symptoms following acute bronchiolitis (141) only a single study of 30 infants	В	SR/several Level III studies with a low risk of bias
met inclusion criteria. Subsequently there have been a two further RCTs of 40 (142) and 219 (143) infants. Two studies with a high risk of bias showed	С	One or two Level III studies with a low risk of bias or Level I or II studies with moderate risk of bias
reduced hospital admission (167) or mixed results for effects on wheeze (169).	D	Level IV studies or Level I to III studies/SRs with a high risk of bias
2. Consistency (if only one study was available, rank this component as 'not applicable')		
For length of stay, data from three studies was combined (141, 157, 171) and showed no difference between azithromycin and placebo (pooled MD -0.58, 05% CL 118 to 0.02) with accessible excitation between azithromycin This provide the state of the state	А	All studies consistent
95% CI -1.18 to 0.02) with acceptable statistical heterogeneity. This result was further supported by a subsequent RCT of 219 infants (143).		Most studies consistent and inconsistency can be explained
Two studies providing data to compare hospital readmissions showed no significant difference but data was not pooled due to risk of heterogeneity (142).	С	Some inconsistency, reflecting genuine uncertainty around question
This result was further supported by a subsequent RCT of 219 infants (143).	D	Evidence is not consistent
	NA	Not applicable (one study only)
3. Clinical impact (indicate if the study results varied according to some unknown factor (not not be determined)	t simply stu	ly quality or sample size) and thus the clinical impact of the intervention could
There is no evidence of benefit of antibiotics and there are real concerns of potential harm caused by adverse effects such as gastrointestinal upset, rash and	А	Very large
impact on community and hospital antibiotic resistance.	В	Substantial
	С	Moderate
	D	Slight/Restricted
4. Generalisability (how well does the body of evidence match the population and clinical sett.	ings being t	argeted by the guideline?)
Two studies were conducted in Bangladesh, while three studies were conducted	Α	Evidence directly generalisable to target population
in high income countries (140). One study was conducted in indigenous infants	В	Evidence directly generalisable to target population with some
in Australia and New Zealand (143). All studies included participants who were hospitalised and only one recruited from an outpatients department.		caveats Evidence not directly generalisable to target population but could
	С	be sensibly applied
	D	Evidence not directly generalisable to target population and hard to judge whether sensible to apply
5. Applicability (is the body of evidence relevant to the Australian/New Zealand healthcare	context in t	erms of health services / delivery of care and cultural factors?)
Use of antibiotics for hospitalised febrile young infants is common but the evidence supports the low incidence of serious bacterial infection in infants with	Α	Evidence directly applicable to Australian/New Zealand healthcare context
a clinical diagnosis of bronchiolitis. One study was conducted in indigenous infants in Australia and New Zealand (143).	В	Evidence applicable to Australian/New Zealand healthcare context with few caveats
	С	Evidence probably applicable to Australian/New Zealand healthcare context with some caveats
	D	Evidence not applicable to Australian/New Zealand healthcare context
Other factors (indicate here any other factors that you took into account when assessing the ev	idence base	(for example, issues that might cause the group to downgrade or upgrade the
recommendation) Bronchiolitis is a clinical diagnosis, caused by viral infection with extremely low rate	e of coco	ndary bacterial infection, other than DICU population
Bronchiolitis is a clinical diagnosis, caused by viral infection with extremely low rate	es of seco	ndary bacterial infection, other than PICU population.

Component	Rating	Descr	Description					
1. Evidence base	В	One o	One or two Level II studies with a low risk of bias, or SR/several Level III studies with a low risk of bias					
2. Consistency	В	Most s	Most studies consistent and inconsistency can be explained					
3. Clinical Impact	В	Substa	Substantial					
4. Generalisability	А	Evider	Evidence directly generalisable to target population					
5. Applicability	А	Evider	Evidence directly applicable to Australian/New Zealand healthcare context					
Evidence statement	•	•						
There is evidence to supp	ort not using antibiotic	s for trea	ating infant	s with a clinical diagnosis of bronchiolitis.				
RECOMMENDATION	N (What recommendation((s) does		OVERALL GRADE OF RECOMMEND	DATION			
the guideline development grou		Use	А	Body of evidence can be trusted to guide practice				
action statements where possib	le)		В	Body of evidence can be trusted to guide practice in				
Do not use antibiotics to treat infants with bronchiolitis.		С	Body of evidence provides some support for recommendations(s) but care should taken in its application					
			D	Body of evidence is weak and recommendation must be applied with caution				
			PP	Practice Point				
UNRESOLVED ISSUE	ES (If needed, keep a note	of specific i	issues that an	ise when each recommendation is formulated and that require follow up	<i>p</i>)			
Sub-populations of high r								
IMPLEMENTATION	OF RECOMMEND	ATION	(Please indi	cate yes or no to the following questions. Where the answer is yes, plea	se provide explanatory information			
about this. This information w	*	1	1 2	the guidelines)				
Will this recommendation	result in changes in us	sual care?)		YES			
A number of infants with	bronchiolitis in Austra	lia and N	New Zealan	d receive antibiotics.	NO			
Are there any resource im	plications associated w	ith imple	ementing th	his recommendation?	YES			
	*	[^]			NO			
Will the implementation of	of this recommendation	1 require	changes in	the way care is currently organised?	YES			
					NO			
Are the guideline develop	ment group aware of a	ny barrie	rs to imple	mentation of this recommendation?	YES			
					NO			

Question 20b.

Question 20b: In Infants presenting to hospital or relevant end points?				nendation				
	or hospitalised wi	ith bronchio	litis, does th	e use of azi			-	
1. Outcome measures:		Quality of evidence				Importance of outcome in making a decision		
	HIGH	MOD	LOW	V. LOW	Critical	Important	Not Important	
O1 Length of stay		X			X			
O2 Hospital readmission		X				X		
O ₃ Duration of fever		X				X		
O4 Occurrence of recurrent wheeze			X			X		
O ₅ Adverse effects			X			X		
O ₆ PICU admission			X		X			
2. Is there is insufficient evidence to mal	ke a recommenda	tion?		1		L		
For the critical outcome of length of stay there is treated with azithromycin versus placebo. For the critical outcome of PICU admission there is with azithromycin versus placebo. For symptom resolution, including duration of fever, no benefit over placebo. For the occurrence of recurrent wheeze, there is low wheezing episode.	low quality eviden , there is moderate	ce of no diffe quality evide	erence in adr nce that trea	nission rate f	or those treate	d Is	DERATE	
Judging the benefits in context The evidence is applicable and generalizable to the A: 4. What harm might the proposed intervent Evidence statement For the important outcome of hospital readmission to those treated with azithromycin.	ention/action do	? uality evidenc	th settings.	ease in readm	ission rate in	Quality of e	vidence DERATE	
Judging the benefits in context The evidence is applicable and generalizable to the A: 4. What harm might the proposed interval Evidence statement For the important outcome of hospital readmission to those treated with azithromycin. For the important outcome of adverse effects there is effects in those treated with azithromycin. Judging the harms in context Evidence shows no increase in harms but the lack of and cost of treatment. 5. What is the likely balance between good	ention/action do here is moderate q s low quality evider beneficial effect m	? uality evidenc nce of no diff	th settings.	ease in readm	ission rate in intestinal side	Quality of e MOI	DERATE	
Judging the benefits in context The evidence is applicable and generalizable to the A: 4. What harm might the proposed interval Evidence statement For the important outcome of hospital readmission to those treated with azithromycin. For the important outcome of adverse effects there is effects in those treated with azithromycin. Judging the harms in context Evidence shows no increase in harms but the lack of and cost of treatment. 5. What is the likely balance between god Evidence statement The harms probably outweigh the benefits.	ention/action do here is moderate q s low quality evider beneficial effect m od and harm?	? uality evidenc nce of no diff	th settings.	ease in readm	ission rate in intestinal side	Quality of e MOI ets, increasing anti	DERATE	
Judging the benefits in context The evidence is applicable and generalizable to the A: 4. What harm might the proposed intervent Evidence statement For the important outcome of hospital readmission to those treated with azithromycin. For the important outcome of adverse effects there is effects in those treated with azithromycin. Judging the harms in context Evidence shows no increase in harms but the lack of and cost of treatment. 5. What is the likely balance between good Evidence statement The harms probably outweigh the benefits.	ention/action do here is moderate q s low quality evider beneficial effect m od and harm?	? uality evidenc nce of no diff	th settings.	ease in readm	ission rate in intestinal side	Quality of e MOI ets, increasing anti	DERATE ibiotic resistance verall of evidence	
Judging the benefits in context The evidence is applicable and generalizable to the A: 4. What harm might the proposed intervent Evidence statement For the important outcome of hospital readmission to those treated with azithromycin. For the important outcome of adverse effects there is effects in those treated with azithromycin. Judging the harms in context Evidence shows no increase in harms but the lack of and cost of treatment. 5. What is the likely balance between good Evidence statement The harms probably outweigh the benefits. Judging the balance of benefits and harms in context	ention/action do here is moderate q s low quality evider beneficial effect m od and harm?	? nce of no diff nust be weigh	th settings.	ease in readm	ission rate in intestinal side	Quality of e MOI etts, increasing anti Quality MOI STRONG	DERATE ibiotic resistance verall of evidence DERATE	
Judging the benefits in context The evidence is applicable and generalizable to the A 4. What harm might the proposed interval Evidence statement For the important outcome of hospital readmission to those treated with azithromycin. For the important outcome of adverse effects there is effects in those treated with azithromycin. Judging the harms in context Evidence shows no increase in harms but the lack of and cost of treatment. 5. What is the likely balance between good Evidence statement The harms probably outweigh the benefits. Judging the balance of benefits and harms in cordiant and harms in cord benefits clearly outweigh harms	ention/action do here is moderate q s low quality evider beneficial effect m od and harm?	? nce of no diff nust be weigh	th settings.	ease in readm	ission rate in intestinal side	Quality of e MOI ets, increasing anti quality MOI	DERATE ibiotic resistance verall of evidence DERATE	
Judging the benefits in context The evidence is applicable and generalizable to the A 4. What harm might the proposed interval Evidence statement For the important outcome of hospital readmission to those treated with azithromycin. For the important outcome of adverse effects there is effects in those treated with azithromycin. Judging the harms in context Evidence shows no increase in harms but the lack of and cost of treatment. 5. What is the likely balance between good Evidence statement The harms probably outweigh the benefits. Judging the balance of benefits and harms in cord Benefits clearly outweigh harms	ention/action do here is moderate q s low quality evider beneficial effect m od and harm? ntext Recommend Consider	? nce of no diff nust be weigh	th settings.	ease in readm	ission rate in intestinal side of adverse effec	Quality of e MOI etts, increasing anti Quality MOI STRONG	DERATE ibiotic resistance verall of evidence DERATE	
Judging the benefits in context The evidence is applicable and generalizable to the A 4. What harm might the proposed interval Evidence statement For the important outcome of hospital readmission to those treated with azithromycin. For the important outcome of adverse effects there is effects in those treated with azithromycin. Judging the harms in context Evidence statement. 5. What is the likely balance between good treatment. The harms probably outweigh the benefits. Judging the balance of benefits and harms in cord benefits clearly outweigh harms Benefits probably outweigh harms Not known	ention/action do here is moderate q s low quality evider beneficial effect m od and harm? ntext Recommend Consider Make a reco	Puality evidence Ince of no difference Ince weight Ince of no difference <p< td=""><td>th settings.</td><td>ease in readm</td><td>ission rate in intestinal side of adverse effec</td><td>Quality of e MOI Sts, increasing anti Quality MOI STRONG CONDITIO WEAK</td><td>DERATE ibiotic resistance verall of evidence DERATE</td></p<>	th settings.	ease in readm	ission rate in intestinal side of adverse effec	Quality of e MOI Sts, increasing anti Quality MOI STRONG CONDITIO WEAK	DERATE ibiotic resistance verall of evidence DERATE	
Judging the benefits in context The evidence is applicable and generalizable to the A: 4. What harm might the proposed intervent Evidence statement For the important outcome of hospital readmission to those treated with azithromycin. For the important outcome of adverse effects there is effects in those treated with azithromycin. Judging the harms in context Evidence shows no increase in harms but the lack of and cost of treatment. 5. What is the likely balance between good Evidence statement The harms probably outweigh the benefits. Judging the balance of benefits and harms in cord Benefits clearly outweigh harms Benefits probably outweigh harms	ention/action do here is moderate q s low quality evider beneficial effect m od and harm? ntext Recommend Consider	Puality evidence Ince of no difference Ince weight Ince of no difference <p< td=""><td>th settings.</td><td>ease in readm</td><td>ission rate in intestinal side of adverse effec</td><td>Quality of e MOI O quality of MOI STRONG CONDITIO</td><td>DERATE ibiotic resistance verall of evidence DERATE</td></p<>	th settings.	ease in readm	ission rate in intestinal side of adverse effec	Quality of e MOI O quality of MOI STRONG CONDITIO	DERATE ibiotic resistance verall of evidence DERATE	

6. Is the intervention/action implementable in the New Zealand	and Australian context?	
Summary statement		
Azithromycin is currently used for treatment of children with bronchiectasis an	d cystic fibrosis; however the	e anti-inflammatory effects have not been shown to
benefit infants with bronchiolitis.		
Yes	Recommend/consider	
Not known	Consider economic evalua	tion
No	Recommend/consider against	
7. Final recommendation		
Do not use azithromycin for treatment of infants admitted to hospital with bronchiolitis. Strength of recommendation of the second seco		Strength of recommendation
		STRONG
		CONDITIONAL
		WEAK
8. Recommendations for research		
Nil.		

Question 20b. NHMRC Evidence Summary

Question 20b: In Infants presenting to hospital or hospitalised with br	onchiolit	is, does the use of Evidence table ref:		
azithromycin medication improve clinically relevant end points?		Beigelman 2014, Farley 2014,		
		Macias 2015, McCallum 2015 (140, 142,		
		143, 172)		
1. Evidence base (number of studies, level of evidence and risk of bias in the included studies	り			
The evidence is based on one systematic review containing three RCTs that	А	One or more Level I studies with a low risk of bias, or several		
compared azithromycin to placebo, involving 353 hospitalised infants (140). All	Λ	Level II studies with a low risk of bias		
studies are rated are rated low or unclear risk of bias.	В	One or two Level II studies with a low risk of bias, or		
	Ь	SR/several Level III studies with a low risk of bias		
Subsequently there has been two RCTs, one of 40 infants (142), and one of 219 infants (143).	С	One or two Level III studies with a low risk of bias or Level I or II studies with moderate risk of bias		
	_	vel IV studies or Level I to III studies/SRs with a high risk of		
	D	bias		
2. Consistency (if only one study was available, rank this component as 'not applicable')				
Evidence is consistent that the use of azithromycin for treatment of bronchiolitis did not reduce length of stay, hospital readmission rates and PICU admission.	А	All studies consistent		
admission.	В	Most studies consistent and inconsistency can be explained		
	С	Some inconsistency, reflecting genuine uncertainty around question		
	D	Evidence is not consistent		
	NA	Not applicable (one study only)		
3. Clinical impact (indicate if the study results varied according to some unknown factor (not not be determined)	t simply stu	ly quality or sample size) and thus the clinical impact of the intervention could		
Rates of antibiotic use in bronchiolitis have been reported as high $(17 - 43\%)$ for inpatients in a multicentre observational study (172).	А	Very large		
The use of azithromycin in variable dosing regimens has no clinical benefit and	В	Substantial		
possible harms.	С	derate		
	D	Slight/Restricted		
4. Generalisability (how well does the body of evidence match the population and clinical sett	ings being t			
Three studies were conducted in high income countries and one study was	Α	Evidence directly generalisable to target population		
conducted in Brazil (140, 142). One study of 219 infants was conducted in indigenous infants in Australia and New Zealand (143). The patients are	В	Evidence directly generalisable to target population with some caveats		
directly generalisable to those seen in Australia and New Zealand.	С	Evidence not directly generalisable to target population but could be sensibly applied		
	D	Evidence not directly generalisable to target population and hard to judge whether sensible to apply		

The results are applicable to the Australian/ New Zealand healthcare context with a few caveats. One study of 219 infants was conducted in indigenous infants in Australia and New Zealand (143).			t A	Evidence directly applicable to Australian healthcare context	/New Zealand		
			В	Evidence applicable to Australian/New Zeala context with few caveats	lian/New Zealand healthcare		
			С	Evidence probably applicable to Australian/New Zealan healthcare context with some caveats			
			D	Evidence not applicable to Australian/New Zealand healthcar context			
Other factors (indicate here an recommendation)	ry other factors that you	took into	account when assessing	the evidence base	(for example, issues that might cause the group to downg	erade or upgrade the	
EVIDENCE STATEMEN	JT MATRIX (summ	arise the	development group's syn	thesis of the evide	nce relating to the key question, taking all the above fact	ors into account)	
Component	Rating		iption		~ ~ ~ ~ ~		
1. Evidence base	В	One o	r two Level II stud	es with a low r	isk of bias, or SR/several Level III studies with a	a low risk of bias	
2. Consistency	В	Most :	studies consistent a	nd inconsistent	y can be explained		
3. Clinical Impact	В	Substa	intial				
4. Generalisability	А		nce directly general				
5. Applicability	А	Evide	nce directly applical	ole to Australia	n/New Zealand healthcare context		
Currently there is no evidence RECOMMENDATION (What recommendation(s				LL GRADE OF RECOMMENDATION		
the guideline development group draw from this evidence? Use			A Body of evidence can be trusted to guide practice				
action statements where possible)				B Body of evidence can be trusted to guide practice in most situations			
Do not use azithromycin for treatment of infants admitted to hospital with bronchiolitis. C tal		C taker	Body of evidence provides some support for recommendations(s) but care should be taken in its application				
	<i>ac</i> 111			ctice Point			
UNRESOLVED ISSUES ((If needed, keep a note o	f specific .	issues that arise when e	ach recommendat	ion is formulated and that require follow up)		
					ng questions. Where the answer is yes, please provide exp	lanatory information	
about this. This information will be used to develop the implementation plan for the guidelines) Will this recommendation result in changes in usual care?					YES		
		54101				NO	
Ano there are recorded in all options are pieted with implementing this are served with a 2					YES		
Are there any resource implications associated with implementing this recommendation?							
			· · · · · ·	NO			
Will the implementation of this recommendation require changes in the way care is currently organised?			changes in the way	care 1s current	ly organised?	YES	
					NO		
						NO	
Are the guideline development	nt group aware of ar	ny barrie	rs to implementatio	n of this recon	nmendation?	YES	

Question 20c.

Consi	dered Judgm	ent - Streng	th of recom	nendation					
Question 20c: In infants presenting to hospital or ho of developing bronchiectasis, improve clinically relev	-		itis, does th	e use of an					
1. Outcome measures:		Quality of	evidence			nportance of out n making a deci			
	HIGH	MOD	LOW	V. LOW	Critical	Important	Not Important		
O1 Hospital readmission		х				Х			
O2 Recurrent symptoms				Х		Х			
O ₃ Prolonged symptoms		X	Х						
O ₄ Bronchiectasis X X									
2. Is there is insufficient evidence to make a	recommenda	tion?				1	1		
Evidence statement One RCT of azithromycin versus placebo, once a week for in length of hospital stay, symptoms at 21 days, adverse er 3. What benefit will the proposed interventio	vents or readm	ission rates a			Australia and N	lew Zealand foun	d no difference		
Evidence statement Quality of evidence One RCT of azithromycin versus placebo, once a week for three weeks, in 219 indigenous infants enrolled in Australia and LOW New Zealand found no difference in length of hospital stay, symptoms at 21 days, adverse events or readmission rates at six months (143). There are no reports on bronchiectasis as an outcome. Judging the benefits in context Version Version									
4. What harm might the proposed intervention	on/action do	?							
Evidence statement						Quality	of evidence		
There are concerns regarding development of macrolide n	esistance.					VEF	RY LOW		
Judging the harms in context Given the concerns of macrolide resistance, and a negativ	e RCT in thos	e at risk in A	ustralia and I	New Zealand	d, there is curren	ntly no evidence t	o support the		
use of azithromycin for the prevention of bronchiectasis					,	,	11		
5. What is the likely balance between good a	nd harm?								
Evidence statement There is one negative RCT (143), reporting surrogate e regarding the development of macrolide resistance.	nd-points for	the critical of	outcome of l	oronchiectas	is, and concerr	quality	verall of evidence .OW		
Judging the balance of benefits and harms in context	t					1			
Benefits clearly outweigh harms	Recommend	1				STRONG			
Benefits probably outweigh harms	Consider					CONDITIONAL			
Not known	Make a reco	mmendation	for research			WEAK	WEAK		
Benefits probably don't outweigh harms									
Harms probably outweigh benefits	Consider aş	gainst				CONDITI	ONAL		
Benefits clearly don't outweigh harms	Recommend	against				STRONG			
Harms clearly outweigh benefits		C				SIRONO			
6. Is the intervention/action implementable	in the New Z	ealand and	Australian o	context?					
Summary statement Evidence applicable.									
Yes		Re	commend/o	consider					
Not known									
No		Ree	commend/co	onsider agair	ist				
7. Final recommendation									
Do not use azithromycin for treatment of infants admitte of developing bronchiectasis.	d to hospital w	vith bronchic	litis who are	at risk	Strength of re STRONG CONDITION WEAK	commendation NAL			
8. Recommendations for research									
A RCT with longer follow-up for outcomes in at risk populations is required to determine benefit of antibiotics in infants at risk of bronchiectasis.									

Question 20c.	I	NHMRC Evidence Su	mmary	/			
antibiotic medication in relevant end-points?	infants who are	ospital or hospitalised with br at risk of developing broncl	hiectasis,		Evidence table ref: Nil studies.		
1. Evidence base (number of	studies, level of eviden	e and risk of bias in the included studie.	s)				
-	*	e a week for three weeks, in 219 w Zealand found no difference	А	One or more Level I Level II studies with	studies with a low risk of bias, or several a low risk of bias		
in length of hospital stay, symptoms at 21 days, adverse events or readmission rates at six months (143).				One or two Level II	studies with a low risk of bias, or I studies with a low risk of bias		
races at six months (145).	rates at six monuts (14.3).				studies with a low risk of bias or Level I or		
			D	II studies with moderate risk of bias Level IV studies or Level I to III studies/SRs with a high risk of			
2. Consistency (if only one stu	dy was available, ran	k this component as 'not applicable')		bias			
Only one study (143) has add			1				
Only one study (145) has ade	nesseu ine questio		А	All studies consistent			
			В	Most studies consiste	nt and inconsistency can be explained		
			С	Some inconsistency, a question	reflecting genuine uncertainty around		
			D	Evidence is not consi	istent		
			NA	Not applicable (one	e study only)		
3. Clinical impact (indicate if not be determined)	^c the study results varie	ed according to some unknown factor (no	t simply stu	dy quality or sample size) a	nd thus the clinical impact of the intervention could		
One RCT of azithromycin ve		a week for three weeks, in 219	А	Very large			
-		w Zealand found no difference adverse events or readmission	В	Substantial			
rates at six months (143).			С	Moderate			
				Slight/Restricted			
4. Generalisability (how well	does the body of evider	nce match the population and clinical set	tings being t	argeted by the guideline?)			
		ustralia and New Zealand (143).	A		eneralisable to target population		
			В		eralisable to target population with some		
			С		generalisable to target population but could		
			D	Evidence not directly generalisable to target population and hard to judge whether sensible to apply			
5. Applicability (is the body of	f evidence relevant to t	he Australian/New Zealand healthcare	context in t	, ,	** *		
		ustralia and New Zealand (143).	A	Evidence directly a	pplicable to Australian/New Zealand		
			В		o Australian/New Zealand healthcare		
			С	context with few cave Evidence probably ap	eats oplicable to Australian/New Zealand		
				healthcare context wi			
			D	context	ble to Australian/New Zealand healthcare		
Other factors (indicate here an recommendation)	ry other factors that yo	u took into account when assessing the en	vidence base	(for example, issues that mi	ight cause the group to downgrade or upgrade the		
					ion, taking all the above factors into account) regarding the development of macrolide		
Component	Rating	Description					
1. Evidence base	В		th a low ri	sk of bias, or SR/severa	l Level III studies with a low risk of bias		
2. Consistency	NA	Not applicable (one study only					
3. Clinical Impact	D	Slight/Restricted					
4. Generalisability	А	Evidence directly generalisable	to target f	oopulation			
5. Applicability	А	Evidence directly applicable to	Australiar	n/New Zealand healthc	are context		
Evidence statement							
There is no evidence to supp	ort the use of antil	piotics for treating bronchiolitis in	those at-ri	sk of bronchiectasis ou	tside of clinical research.		

RECOMMENDATION (What recommendation(s) does		OVERALL GRADE OF RECOMMENDATI	ON				
the guideline development group draw from this evidence? Use	A Body of evidence can be trusted to guide practice						
action statements where possible)	В	B Body of evidence can be trusted to guide practice in most situations					
Do not use azithromycin for treatment of infants		Body of evidence provides some support for recommen should be taken in its application	dations(s) but care				
admitted to hospital with bronchiolitis who are at	D	Body of evidence is weak and recommendation must be app	lied with caution				
risk of developing bronchiectasis.	PP	Practice Point					
UNRESOLVED ISSUES (If needed, keep a note of specific is	ssues that ar	ise when each recommendation is formulated and that require follow up)					
The critical outcome of bronchiectasis is not reported.							
IMPLEMENTATION OF RECOMMENDATION about this. This information will be used to develop the implementation		rate yes or no to the following questions. Where the answer is yes, please pro the guidelines)	vide explanatory information				
Will this recommendation result in changes in usual care?		YES					
			NO				
Are there any resource implications associated with imple	menting th	is recommendation?	YES				
			NO				
Will the implementation of this recommendation require	changes in	the way care is currently organised?	YES				
			NO				
Are the guideline development group aware of any barrier	rs to imple	nentation of this recommendation?	YES				

Question 21a.

Con	sidered Judgm	ent - Streng	th of recom	mendation				
Question 21a: In infants presenting to hospital or h end points?	nospitalised wi	th bronchio	itis, does th	e use of nor				
1. Outcome measures:		Quality of	evidence			portance of out n making a deci		
	HIGH	MOD	LOW	V. LOW	Critical	Important	Not Important	
O1 Length of stay								
O2 ICU admission								
2. Is there is insufficient evidence to make	a recommenda	ation?						
Evidence statement A retrospective cohort study of 102 infants (45) admitte was significantly different between subjects with hypons not available in this retrospective study. A prospective cohort study of 36 infants with moderate	atraemia and the	ose without.	Data of the t	ype of fluid,	amount of fluid	, and rate of adm	inistration were	
osmolality compared to admission despite improvemen bronchiolitis requiring ICU admission, with 4% sufferin								
There is insufficient evidence to make recommendation			ydration but	caution abo	ut the use of hyp	otonic IV fluids	exists.	
3. What benefit will the proposed intervent	ion/action hav	/e?						
Evidence statement There is insufficient evidence to make recommendation	about the use	of non-oral l	vidention				of evidence Y LOW	
Judging the benefits in context	is about the use	or non-oral i	iyuration.			VEP		
4. What harm might the proposed interven	tion/action do	?						
Evidence statement There are serious concerns with the administration of h of hyponatraemia and seizures.	nypotonic paren	teral fluids to	o infants with	h bronchiolit	is due to the r isl	Quality of e	vidence XY LOW	
Judging the harms in context								
5. What is the likely balance between good	and harm?							
Evidence statement Supplemental hydration is recommended to avoid renal principals). Evidence regarding the ideal volume of non regarding hyponatraemia. Judging the balance of benefits and harms in conte	-oral rehydration					quality	verall of evidence Y LOW	
Benefits clearly outweigh harms	Recommend	d				STRONG		
Benefits probably outweigh harms	Consider					CONDITIONAL		
Not known		ommendati	on for resea	rch (see & b	elow)	WEAK		
Benefits probably don't outweigh harms	intake a ree		on for resea			W LAIR		
Harms probably outweigh benefits	Consider ag	ainst				CONDITIO	DNAL	
Benefits clearly don't outweigh harms								
	Recommend	d against				STRONG		
Harms clearly outweigh benefits 6. Is the intervention/action implementabl	e in the New 7	ealand and	Australian	context?				
-			Australiali	context?				
Summary statement Non-oral hydration is routinely used in Australia and N	ew Zealand.							
Yes		Re	commend/	consider				
Not known Consider economic evaluation								
No		Re	commend/co	onsider agair	ist			
7. Final recommendation		I		-				
Supplemental hydration is recommended for infants wh	7. Final recommendation Supplemental hydration is recommended for infants who cannot maintain hydration orally. STRONG CONDITIONAL WEAK							
8. Recommendations for research								
The ideal volume (restricted versus 100% maintenance)	and type of nor	n-oral fluids (NG rehydrat	ion solution	s or milk, or typ	e of isotonic IV s	olution) to give	
to infants with bronchiolitis has not been studied.								

Question 21a.

NHMRC Evidence Summary

1. Evidence base (number of	studies, level of eviden	ce and risk of bias in the included st	udies)		
			,		
				One or more Level I	I studies with a low risk of bias, or several
			А	Level II studies with	
			В	One or two Level II	studies with a low risk of bias, or SR/severa
			D	Level III studies with	h a low risk of bias
			С	One or two Level II	I studies with a low risk of bias or Level I or
			C	II studies with mode	erate risk of bias
			D	Level IV studies or	Level I to III studies/SRs with a high
				risk of bias	
2. Consistency (if only one sta	ıdy was available, ran	k this component as 'not applicable')		
			А	All studies consisten	t
			В	Most studies consist	ent and inconsistency can be explained
			С	Some inconsistency, question	reflecting genuine uncertainty around
			D	Evidence is not cons	sistent
			NA	Not applicable (on	e study only)
3. Clinical impact (indicate is not be determined)	f the study results vari	ed according to some unknown factor	r (not simply stue	ly quality or sample size) a	and thus the clinical impact of the intervention could
			А	Very large	
			В	Substantial	
			С	Moderate	
			D	Slight/Restricted	
4. Generalisability (how well	does the body of evide	nce match the population and clinica	l settings being to	argeted by the guideline?)	
			А	Evidence directly get	neralisable to target population
			D		neralisable to target population with some
			В	caveats	0 1 1
			С	could be sensibly a	
			D	Evidence not directly to judge whether ser	y generalisable to target population and hard
5 A m 1 i m m m m m m m m m m	(L. A		, 0	
J. Applicability (15 The body of	evalence relevant to t	he Australian/New Zealand health	nare context in t		
			А	• • •	plicable to Australian/New Zealand
				healthcare context	
			В		to Australian/New Zealand healthcare
				context with few cav	
			С		applicable to Australian/New Zealand
				healthcare context Evidence not applic	with some caveats cable to Australian/New Zealand healthcare
			D	context	
Other factors (indicate here an	iy other factors that yo	u took into account when assessing i	the evidence base	(for example, issues that m	night cause the group to downgrade or upgrade the
recommendation)					
EVIDENCE STATEMEN	JT MATRIX (sun.	marise the development group's synt	hesis of the evider	nce relating to the key ques	tion, taking all the above factors into account)
Component	Rating	Description		4	
1. Evidence base	D	Level IV studies or Level I	to III studies/	SRs with a high risk o	f bias
2. Consistency	N/A	Not applicable (one study of		~ ~	
3. Clinical Impact	С	Moderate			
4. Generalisability	С	Evidence not directly gener	ralisable to tar	get population but cou	ld be sensibly applied
2	С	•		0 X X	hcare context with some caveats
5. Applicability	C	Evidence probably applicat	sie to mustiana		
5. Applicability Evidence statement	C	Evidence probably applicat	sie to riustian		

RECOMMENDATION (What recommendation(s) does	OVERALL GRADE OF RECOMMENDATION						
the guideline development group draw from this evidence? Use	А	A Body of evidence can be trusted to guide practice					
action statements where possible)	В	B Body of evidence can be trusted to guide practice in most situations					
Supplemental hydration is recommended for		Body of evidence provides some support for recommentation	dations(s) but care should be				
infants who cannot maintain hydration orally.	D	Body of evidence is weak and recommendation must be applied with caution					
		Practice Point					
UNRESOLVED ISSUES (If needed, keep a note of specific	issues that ar	ise when each recommendation is formulated and that require follow up	b)				
The ideal volume and type of non-oral fluids to give to	nfants with	bronchiolitis has not been studied.					
IMPLEMENTATION OF RECOMMENDATION	Ŋ (Please indi	cate yes or no to the following questions. Where the answer is yes, pleas	se provide explanatory information				
about this. This information will be used to develop the implement	ation plan for	the guidelines)					
Will this recommendation result in changes in usual care	-2		YES				
			NO				
Are there any resource implications associated with imp	lementing th	is recommendation?	YES				
			NO				
Will the implementation of this recommendation require	e changes in	the way care is currently organised?	YES				
			NO				
Are the guideline development group aware of any barri	ers to imple	mentation of this recommendation?	YES				

Question 21b.

	(Considered Judgem	ent - Streng	th of recom	mendation			
Question points?	n 21b: In infants presenting to hospital	or hospitalised wit	th bronchiol	litis, what fo	rms of non-	oral hydration	n improve clinica	ally relevant end
1.	Outcome measures:		Quality of	evidence			nportance of ou in making a dec	
		HIGH	MOD	LOW	V. LOW	Critical	Important	Not Important
O1 Leng	th of stay		Х			X		
O ₂ Adve	erse effects		Х				Х	
O3 Hosp	pital Readmission			X			Х	
O ₄ Succ	ess of insertion		Х					
2.	Is there is insufficient evidence to m	ake a recommenda	tion?		1			
The evide a small ra systemati	e statement ence is based on one large randomized cor andomised prospective pilot study (174) of ic reviews on the question.	51 infants with high	dropout rate				-	
3.	What benefit will the proposed interv	vention/action hav	e?					
For the c for non-c 82.2 hour	er statement critical outcome of length of stay there is n oral hydration with no statistical difference rs (SD 58.8) for NG feeds (145). the benefits in context					*	15	of evidence DERATE
4.	What harm might the proposed inter	rvention/action do	?					
IV attem For the rehydrati Other ad treatmen For the i between	NG rehydration had one insertion attempt pts recorded having three or more attempt important outcome of adverse effects th on. The most common complications were liverse effects including IV line site bruising t (9% for NG versus 14% for IV). There we important outcome of hospital readmission IV and NG rehydration due to the low nut the harms in context	ts. ere is moderate qua re NG tube pulled o g, nasal trauma occur vere no events of clir on for bronchiolitis t	llity evidence ut (131 infar rred in 11% o nical aspiration there is low	e of no diffe hts) or IV flu of those who on recorded in quality evide	erence betwe id extravasat received rar n either stud	een IV and NG ion (80 infants idomly allocate y (145, 174).	MODEF G). d	RATE
	l hydration is essential when an infant with		ole to maintai	in oral feedin	g due to sev	erity of illness.		
5.	What is the likely balance between g	ood and harm?						
NG and	e statement IV hydration appear to be similar, although	*	es more atter	npts.			quality	verall of evidence DERATE
Judging	the balance of benefits and harms in co							
Benefits	clearly outweigh harms	Recommen	ıd				STRONG	
Benefits	probably outweigh harms	Consider					CONDITI	ONAL
Not know	Wn	Make a reco	mmendation	for research	(see 8 below	r)	WEAK	
Benefits	probably don't outweigh harms	Consider an	ainst				CONDITI	ONAI
Harms p	robably outweigh benefits	Consider aga	amist				CONDITI	UIN/IL
Benefits	clearly don't outweigh harms	Description	laminat				CTRONC	
Harms cl	learly outweigh benefits	Recommend	i against				STRONG	
6.	Is the intervention/action implement	table in the New Z	ealand and	Australian o	context?			
Summar	ry statement							
	and NG means of hydration are standard t	treatment for infants				ll in Australia a	nd New Zealand.	
Yes				commend/o				
Not know	wn			nsider econo				
No Recommend/consider against								

7. Final recommendation	
Both NG and IV routes are acceptable means for non-oral hydration in infants admitted to hospital with	Strength of recommendation
bronchiolitis.	STRONG
	CONDITIONAL
	WEAK
8. Recommendations for research	

The use of non-oral hydration in infants less than two months has not been studied as they were excluded from published studies.

Question 21b.

NHMRC Evidence Summary

Question 21b: In infants presenting to hospital or hospitalised with brond oral hydration improve clinically relevant end points?	chiolitis,	what forms of non- Babl 2008, Kugelman 2013, Oakley 2013 (145, 174, 175).			
1. Evidence base (number of studies, level of evidence and risk of bias in the included studies	5)				
The evidence is based on one large randomised control trail (145) comparing NG and IV rehydration in 759 infants admitted to hospital with bronchiolitis	А	One or more Level I studies with a low risk of bias, or several Level II studies with a low risk of bias			
and small randomised prospective pilot study (174) of 51 infants with high dropout rate.	В	One or two Level II studies with a low risk of bias, or SR/several Level III studies with a low risk of bias			
	С	One or two Level III studies with a low risk of bias or Level I or II studies with moderate risk of bias			
	D	Level IV studies or Level I to III studies/SRs with a high risk of bias			
2. Consistency (if only one study was available, rank this component as 'not applicable')					
Both studies (145, 174) showed no difference in the primary outcome of hospital length of stay between IV hydration and NG hydration.	A	All studies consistent			
	В	Most studies consistent and inconsistency can be explained			
	С	Some inconsistency, reflecting genuine uncertainty around question			
	D	Evidence is not consistent			
	NA	Not applicable (one study only)			
3. Clinical impact (<i>indicate if the study results varied according to some unknown factor (not not be determined)</i>	t simply stu	dy quality or sample size) and thus the clinical impact of the intervention could			
Both means of non-oral hydration are appropriate to hydrate infants however higher success rate with fewer insertion attempts using NG tube feeding favours	А	Very large			
this method and may support change in practice.	В	Substantial			
	С	Moderate			
	D	Slight/Restricted			
4. Generalisability (how well does the body of evidence match the population and clinical sett	tings being t	argeted by the guideline?)			
The large multicentre RCT (Oakley 2013) enrolled infants aged 2 months to 12	Α	Evidence directly generalisable to target population			
months, who presented to EDs in seven hospitals in Australia and New Zealand across three bronchiolitis seasons.	В	Evidence directly generalisable to target population with some caveats			
	С	Evidence not directly generalisable to target population but could be sensibly applied			
	D	Evidence not directly generalisable to target population and hard to judge whether sensible to apply			
5. Applicability (is the body of evidence relevant to the Australian/New Zealand healthcare	context in 1	terms of health services / delivery of care and cultural factors?)			
Both IV and NG means of hydration are standard treatment for infants with bronchiolitis admitted to hospital in Australia and New Zealand	A	Evidence directly applicable to Australian/New Zealand healthcare context			
	В	Evidence applicable to Australian/New Zealand healthcare context with few caveats			
	С	Evidence probably applicable to Australian/New Zealand healthcare context with some caveats			
	D	Evidence not applicable to Australian/New Zealand healthcare context			
Other factors (indicate here any other factors that you took into account when assessing the et	vidence base	(for example, issues that might cause the group to downgrade or upgrade the			
recommendation)					

Component	Rating	Description					
1. Evidence base	В	One or two Level II studies with a low risk of bias, or SR/several Level III studies with a low risk of bias					
2. Consistency	А	All studies	s consis	tent			
3. Clinical Impact	С	Moderate					
4. Generalisability	А	Evidence directly generalisable to target population					
5. Applicability	А	Evidence directly applicable to Australian/New Zealand healthcare context					
Evidence statement							
NG and IV hydration app		·	tion rec				
RECOMMENDATION	(()			OVERALL GRADE OF RECOMMENDATION			
the guideline development group		se	A	Body of evidence can be trusted to guide practice			
action statements where possible	le)		В	Body of evidence can be trusted to guide practice in most situation	tuations		
Both NG and IV routes are acceptable means for			С	Body of evidence provides some support for recommendations(s) but care should be taken in its application			
non-oral hydration in infants admitted to hospital D Body of evidence is weak and recommendation must be applied				lied with caution			
with bronchiolitis. PP Practice Point							
UNRESOLVED ISSUE	ΞS (If needed, keep a note of	specific issues	s that ari	ise when each recommendation is formulated and that require follow up)			
	-						
IMPLEMENTATION	OF RECOMMENDA	TION (Ple	ease india	cate yes or no to the following questions. Where the answer is yes, please provide e	xplanatory information		
about this. This information n	vill be used to develop the imp	lementation			xplanatory information		
IMPLEMENTATION <i>about this. This information n</i> Will this recommendation	vill be used to develop the imp	lementation			xplanatory information YES		
about this. This information n Will this recommendation A survey of Australian and	will be used to develop the imp n result in changes in usu d New Zealand emergen	olementation] al care?	plan for				
about this. This information in Will this recommendation A survey of Australian and bronchiolitis requiring non-	will be used to develop the important of the second	olementation j al care? cy physicia	<i>plan for</i>	the guidelines) orted 48% used NG and 52% used IV hydration in infants with	YES NO		
about this. This information in Will this recommendation A survey of Australian and bronchiolitis requiring non-	will be used to develop the important of the second	olementation j al care? cy physicia	<i>plan for</i>	the guidelines) orted 48% used NG and 52% used IV hydration in infants with	YES		
about this. This information n Will this recommendation A survey of Australian and bronchiolitis requiring non-	will be used to develop the important of the second	olementation j al care? cy physicia	<i>plan for</i>	the guidelines) orted 48% used NG and 52% used IV hydration in infants with	YES NO		
about this. This information u Will this recommendation A survey of Australian and bronchiolitis requiring non Are there any resource im	will be used to develop the imp n result in changes in usu d New Zealand emergen n-oral hydration (175). aplications associated with	al care? cy physicia: h implemen	<i>plan for</i> and repo	the guidelines) orted 48% used NG and 52% used IV hydration in infants with	YES NO YES		
about this. This information u Will this recommendation A survey of Australian and bronchiolitis requiring non Are there any resource im	will be used to develop the imp n result in changes in usu d New Zealand emergen n-oral hydration (175). aplications associated with	al care? cy physicia: h implemen	<i>plan for</i> and repo	the guidelines) orted 48% used NG and 52% used IV hydration in infants with his recommendation?	YES NO YES NO		
about this. This information n Will this recommendation A survey of Australian and bronchiolitis requiring non Are there any resource im Will the implementation of	will be used to develop the imp n result in changes in usu d New Zealand emergen on-oral hydration (175). applications associated with of this recommendation a	al care? cy physicia: h implemen	<i>plan for</i> ins repo nting th nges in	the guidelines) orted 48% used NG and 52% used IV hydration in infants with his recommendation?	YES NO YES NO YES YES		

Question 21c.

GRADE Evidence Summary

Con	sidered Judgem	nent - Str	ength of recom	mendation	1			
Question 21c: In Infants presenting to hospital or	hospitalized wi	th bronc	hiolitis, does lii	niting the	volume of non-o	ral hydration i	mpact on	
clinically relevant end-points?								
1. Outcome measures:		Quality	y of evidence		-	portance of out making a deci		
	HIGH	MO	D LOW	V. LOW	Critical	Important	Not Important	
O1 Length of stay								
O2 Hyponatremia			Х					
2. Is there is insufficient evidence to make	a recommenda	tion?		I			I	
Evidence statement								
There is insufficient evidence to make a recommendati A prospective cohort study of 36 infants with moderate osmolality compared to admission despite improvement	e bronchiolitis wl		*	renteral hyp	ootonic solution sh	lowed drop in se	erum sodium and	
An earlier study (173) of hyponatraemia in 91 infants w three of the four had received hypotonic fluids.	with severe bronch	hiolitis re	equiring ICU adm	nission, wit	n 4% suffering hyp	oonatraemic seiz	ures showed that	
There is insufficient evidence to make recommendation A systematic review (144) of benefit versus harm from to identify any evidence from RCTs in the primary care	advice to increas or outpatient se	se fluid in etting.	•		• •		dren was unable	
3. What benefit will the proposed interven	tion/action hav	re?						
Evidence statement There is insufficient evidence to make recommendation hypotonic fluids.	ns about the use o	of non-or	ral hydration but	evidence c	autions the use of		of evidence N/A	
Judging the benefits in context								
4. What harm might the proposed interver	ntion/action do	?						
Evidence statement						Quality	of evidence	
There is insufficient evidence to make recommendation hypotonic fluids.	ns about the use	of non-or	ral hydration but	evidence c	autions the use of	1	N/A	
Judging the harms in context								
5. What is the likely balance between good	l and harm?							
Evidence statement						0	verall	
There is insufficient evidence to make a recommendati ICU setting. The previous use of hypotonic IV fluids n hyponatraemia.							of evidence N/A	
Judging the balance of benefits and harms in conte	ext							
Benefits clearly outweigh harms	Recommend	ł				STRONG		
Benefits probably outweigh harms	Consider					CONDITIO	DNAL	
Not known	Make a rec	ommenc	lation for resea	rch (see 8	below)	WEAK		
Benefits probably don't outweigh harms	0 1	•				CONDITIO		
Harms probably outweigh benefits	Consider aga	ainst				CONDITIO	JNAL	
Benefits clearly don't outweigh harms								
Harms clearly outweigh benefits	Recommend	d against				STRONG		
6. Is the intervention/action implementab	le in the New Z	Lealand a	and Australian o	context?				
Summary statement								
Yes			Recommend/	consider				
Not known			Consider econo	mic evaluat	ion			
No			Recommend/co	onsider agai	nst			
7. Final recommendation				~				
There is insufficient evidence to recommend a specific of fluid overload and judicious and vigilant use of hydr recommended.					Strength of rec STRONG CONDITIONA WEAK			
8. Recommendations for research								
The use of restricted versus maintenance volumes of n	on-oral hydratior	n fluids ac	dministered to in	fants with l	pronchiolitis needs	to be studied in	an RCT in the	
current era of isotonic fluid use.								

Question 21c.	1	NHMRC Evidence Sur	nmary	,	
		spital or hospitalized with bro nically relevant end-points?	nchiolitis	, does limiting the	Evidence table ref: Guppy 2011, Hanna 2003, Rodrigues 2014 (144, 146, 173)
1. Evidence base (number of	studies, level of evident	e and risk of bias in the included studies	.)		
There is insufficient evidence	e to make a recomm	nendation	А	One or more Level I Level II studies with	studies with a low risk of bias, or several a low risk of bias
			В	One or two Level II Level III studies with	studies with a low risk of bias, or SR/several
			С	One or two Level III	studies with a low risk of bias or Level I or
			D	II studies with mode Level IV studies or	Level I to III studies/SRs with a high
			D	risk of bias	
2. Consistency (if only one sta	udy was available, ran	k this component as 'not applicable')	r	Γ	
			А	All studies consistent	t
			В	Most studies consiste	ent and inconsistency can be explained
			С	Some inconsistency, question	reflecting genuine uncertainty around
			D	Evidence is not cons	istent
			NA	Not applicable (on	e study only)
	f the study results varie	ed according to some unknown factor (not	t simply stud	ly quality or sample size) a	nd thus the clinical impact of the intervention could
not be determined)			А	Very large	
			В	Substantial	
			С	Moderate	
			D	Slight/Restricted	
4. Generalisability (how well	does the body of evider	ace match the population and clinical sett.	ings being to	urgeted by the guideline?)	
			А	Evidence directly gen	neralisable to target population
			В	Evidence directly ger caveats	neralisable to target population with some
			С		generalisable to target population but could
			D	• • •	tly generalisable to target population and
			D		her sensible to apply
5. Applicability (is the body of	f evidence relevant to th	he Australian/New Zealand healthcare	context in t	erms of health services / de	livery of care and cultural factors?)
			А	Evidence directly app healthcare context	plicable to Australian/New Zealand
			В	Evidence applicable context with few cav	to Australian/New Zealand healthcare eats
			С		applicable to Australian/New Zealand
			D	Evidence not application context	able to Australian/New Zealand healthcare
Other factors (indicate here an recommendation)	ny other factors that yo	u took into account when assessing the en	idence base		ight cause the group to downgrade or upgrade the
			of the evider	ice relating to the key quesi	tion, taking all the above factors into account)
Component	Rating	Description		(op 11 11 11 11 11	c1 ·
1. Evidence base	D	Level IV studies or Level I to I		SKs with a high risk of	t bias
2. Consistency	N/A	Not applicable (one study only)			
3. Clinical Impact	C	Moderate	h1. 6 ·		
4. Generalisability	D				d to judge whether sensible to apply
5. Applicability	С	Evidence probably applicable to) Australia	ui/ New Zealand health	ncare context with some caveats
Evidence statement There is insufficient evidence	e to males a resource	nendation			
increas insumicient evidence	e to make a recomf	nendau011.			

RECOMMENDATION (What recommendation(s) does	OVERALL GRADE OF RECOMMENDATION				
the guideline development group draw from this evidence? Use	А	A Body of evidence can be trusted to guide practice			
action statements where possible)	В	Body of evidence can be trusted to guide practice in most situations			
There is insufficient evidence to recommend a	C Body of evidence provides some support for recommendations(s) but care should				
specific proportion of maintenance fluid.	C	taken in its application			
	D	D Body of evidence is weak and recommendation must be applied with caution			
There is a risk of fluid overload and judicious and					
vigilant use of hydration fluid is recommended.	PP	Practice Point			
Isotonic fluid is recommended.					
UNRESOLVED ISSUES (If needed, keep a note of specific issues that arise when each recommendation is formulated and that require follow up)					
IMPLEMENTATION OF RECOMMENDATION (Please indicate yes or no to the following questions. Where the answer is yes, please provide explanatory information					
about this. This information will be used to develop the implementation plan for the guidelines)					
Will this recommendation result in changes in usual care?		YES			
		NO			
Are there any resource implications associated with imple	is recommendation?	YES			
	NO				
Will the implementation of this recommendation require changes in the way care is currently organised?			YES		
	NO				
Are the guideline development group aware of any barrier	nentation of this recommendation?	YES			
	NO				

Question 22.

Consi	Considered Judgment - Strength of recommendation							
Question 22: In infants presenting to hospital or hos	spitalised wit	h bronchio	litis, does inf	ection con	trol practices in	nprove clinically	y relevant end	
points??								
1. Outcome measures:	Quality of evidence					Importance of outcome in making a decision		
	HIGH	MOD	LOW	V. LOW	Critical	Important	Not Important	
O1 Nosocomial infection			X		X			
O2 Adverse Events				Х		Х		
O ₃ Cost effectiveness				X		X		
2. Is there is insufficient evidence to make a	recommenda	tion?						
Evidence statement The current evidence is derived from five observational studies (147-150). No RCT on containing common viral infections such as RSV by different infection control practices in ED or general paediatric ward setting is available. The Cochrane review (151) focuses on different pandemic viral infections affecting a range of population in a variety of settings. This evidence could be extrapolated as indirect evidence for infants with bronchiolitis secondary to common respiratory viral infections. 3. What benefit will the proposed intervention/action have? Quality of evidence For the critical outcome of nosocomial infection there is low quality evidence of a reduced rate of nosocomial infection in RSV positive infants managed with infection control procedures.								
Judging the benefits in context								
The evidence is applicable and generalizable to the			alian health s	ettings.				
4. What harm might the proposed interventi	on/action do	?						
Evidence statement Quality of evidence There has been no significant adverse effect of the infection control practices reported. VERY LOW For the important outcome of cost effectiveness of these practices, there is very little evidence in literature to support or refute these practices. VERY LOW								
Evidence to date is still lacking on the cost effectiveness known whether the costs associated with isolation or coh- infections. 5. What is the likely balance between good a	orting the RSV						-	
Evidence statement						0	verall	
The benefits are likely to outweigh the harms.							quality of evidence LOW	
Judging the balance of benefits and harms in contex	t							
Benefits clearly outweigh harms	Recommend	d				STRONG		
Benefits probably outweigh harms	Consider				CONDITI	CONDITIONAL		
Not known	Make a recommendation for research (see 8 below)			WEAK				
Benefits probably don't outweigh harms								
Harms probably outweigh benefits	Consider against				CONDITIO	ONAL		
Benefits clearly don't outweigh harms	Recommend against			STRONG				
Harms clearly outweigh benefits 6. Is the intervention/action implementable	ble in the New Zealand and Australian context?							
	In the INew Z		u Australiali (context?				
Summary statement Infection control practices are widely adopted in Australi	a and New Zea				ne cost effectiven	ess is not yet avai	lable.	
Yes Recommend/consider								
ot known Consider economic evaluation								
No Recommend/consider against								
7. Final recommendation								
recommended. It has not been specifically looked at in patients with Bronchiolitis. There is inadequate STRONG					STRONG CONDITION	commendation AL		
8. Recommendations for research								
Whilst studies to date examined different regimes of infe- cost effectiveness of these procedures to prevent nosoco specifically looked at the practice of cohorting on the bas	mial viral infec	tions such a	as comparing o	cohorting to				

Question 22. NHMRC Evidence Summary							
Question 22: In infants presenting to hospital or hospitalised with bronchiolitis, does infection Evidence table ref:							
control practices improve clinically relevant end points?					Jefferson 2011, Mills 2011, Simon 2006, Simon		
					2008, Thorburn 2012 (147-151).		
1. Evidence base (number of studies, level of evidence and risk of bias in the included studies)							
The current evidence is derived from five observational studies with historical				One or more Level I studies with a low risk of bias, or sev			
controls. No RCT on containing common viral infection such as RSV by different infection control practices in ED or general paediatric ward setting is available. The Cochrane review (151) focus on different pandemic viral			А		with a low risk of bias		
			В	One or two Level II studies with a low risk of bias, or SR/several			
			Б		s with a low risk of bias		
		riety of settings. This evidence	с		vel III studies with a low risk of bias or Level		
could be extrapolated as indirect evidence for infants with bronchiolitis secondary to common respiratory viral infections.					with moderate risk of bias		
			D	Level IV studies bias	s or Level I to III studies/SRs with a high risk of		
				DIAS			
	-	this component as 'not applicable')	1	1			
Most of the evidence from observation studies showed consistent reduction of nosocomial RSV infections.			А	All studies cons	istent		
			В	Most studies consistent and inconsistency can be explained			
			С	Some inconsistency, reflecting genuine uncertainty around question			
			D	Evidence is not consistent			
			NA	Not applicable (one study only)			
	the study results varie	d according to some unknown factor (no	t simply stu	dy quality or sample .	size) and thus the clinical impact of the intervention could		
not be determined) Risk of nosocomial infection	is significantly red	aced by infection control					
	· ·	0.40). No increase of significant	А	Very large			
adverse events has been repo			В	Substantial			
			С	Moderate			
			D	Slight/Restricte	d		
				Ű			
		ce match the population and clinical set	tings being t				
Many studies were conducted			Α		ctly generalisable to target population		
directly generalisable to patie	nts with bronchioli	tis seen in Australia and New	В		ly generalisable to target population with some		
Zealand.				caveats	rectly generalisable to target population but could		
			С	be sensibly appl			
			~		irectly generalisable to target population and hard		
			D	to judge whether sensible to apply			
5. Applicability (is the body of	f evidence relevant to th	e Australian/New Zealand healthcare	context in 1	erms of health service	s / delivery of care and cultural factors?)		
The results are applicable to	the Australian/Nev	v Zealand healthcare context.		Evidence direct	ly applicable to Australian/New Zealand		
Infection control practices in	many forms are in	general universal in Australia	А	healthcare conte	ext		
and New Zealand, very much more so in paediatric intensive care settings.			В		icable to Australian/New Zealand healthcare		
			context with fe				
		С	-	bly applicable to Australian/New Zealand ext with some caveats			
				pplicable to Australian/New Zealand healthcare			
			D	context	ppreadle to rustianan, rew Zeanand neartheare		
	iy other factors that yoi	i took into account when assessing the ei	vidence base	(for example, issues i	that might cause the group to downgrade or upgrade the		
recommendation)	- 1 -6						
Cost effectiveness is yet to be determined due to lack of evidence in this area. EVIDENCE STATEMENT MATRIX (summarise the development group's synthesis of the evidence relating to the key question, taking all the above factors into account)							
	1	1 0 1 5	of the evide:	nce relating to the key	question, taking all the above factors into account)		
Component 1. Evidence base	Rating C	Description One or two Level III studies with a low risk of bias or Level I or II studies with moderate risk of bias					
2. Consistency	B	Most studies consistent and inconsistency can be explained					
3. Clinical Impact	В	Substantial					
4. Generalisability	А	Evidence directly generalisable to target population					
5. Applicability	В	Evidence applicable to Australian/New Zealand healthcare context with few caveats					
Evidence statement							
There is low level of evidence for infection control practices to infants with bronchiolitis. These practices are widely adopted in many health care settings and no adverse events have been reported. The evidence is generalizable to Australia and New Zealand.							
	r · · · · · · · · · · · · · · · · · ·	- o					

RECOMMENDATION (What recommendation(s) does	OVERALL GRADE OF RECOMMENDATION					
the guideline development group draw from this evidence? Use	А	A Body of evidence can be trusted to guide practice				
action statements where possible)	В	Body of evidence can be trusted to guide practice in most situations				
Hand hygiene is the most effective intervention to	С	Body of evidence provides some support for recommendations(s) but care should be taken in its application				
reduce hospital acquired infections and is	D	Body of evidence is weak and recommendation must be applied with caution				
recommended. It has not been specifically looked at in patients with Bronchiolitis. There is inadequate evidence for the benefits of cohorting bronchiolitic patients.	рр	Practice Point				
1	sues that ari	se when each recommendation is formulated and that require follow up)				
		st analysis of each regime and the optimal regime is still to be determine	ned.			
IMPLEMENTATION OF RECOMMENDATION	(Please indic	ate yes or no to the following questions. Where the answer is yes, please provide ex	blanatory information			
about this. This information will be used to develop the implementat						
Will this recommendation result in changes in usual care?			YES			
			NO			
Are there any resource implications associated with implementing this recommendation?			YES			
			NO			
Will the implementation of this recommendation require changes in the way care is currently organised?			YES			
			NO			
Are the guideline development group aware of any barriers to implementation of this recommendation?			YES			
			NO			

RESEARCH RECOMMENDATIONS

- Research defining the positive and negative predictive values of clinical criteria for diagnosing bronchiolitis is needed, especially that which gives strength to the ability to refute the diagnosis of bronchiolitis when other conditions are present (e.g. cardiac failure, immunodeficiency).
- 2. Large cohort studies are needed to define the relative risk of particular factors and to define subpopulations with increased risk.
- 3. Research on infants with more severe bronchiolitis is needed to define the role of CXR.
- 4. Research on subpopulations at high risk for UTI when the infant is diagnosed with bronchiolitis is needed.
- 5. Research to determine if patient cohorting based on virological results reduces in-hospital transmission more than appropriate contact precautions is warranted.
- 6. Further research is needed to derive and validate a bronchiolitis scoring system for infants diagnosed with bronchiolitis that is generalizable for different populations, and that has significance for patient centred outcomes.
- 7. Research on outcomes of infants with differing levels of oxygen saturations and duration of adequate feeding at the time of discharge.
- 8. Previous studies should be reviewed to clarify rates of readmission in infants administered beta 2 agonists and discharged home.
- Research on the use of beta 2 agonists in infants presenting to hospital or hospitalised with bronchiolitis with a personal or family history of atopy is needed.
- 10. Previous studies should be reviewed to clarify the effects of beta 2 agonists in infants aged between 6 and 12 months of age.

- 11. Studies to date have used different regimens of nebulised hypertonic saline, and the optimal regime is still to be determined. Further large multicentre trials are required to confirm the overall benefits of nebulised hypertonic saline in both inpatient and the ED settings.
- 12. Research on the long-term effects in infants with bronchiolitis who have received systemic or local glucocorticoids (nebulisation, oral, IM or IV) is required.
- 13. Research on the use of glucocorticoids in infants presenting to hospital or hospitalised with bronchiolitis and with a positive response to beta 2 agonists is needed.
- Research on the use of a combination of glucocorticoids and adrenaline/epinephrine in infants presenting to hospital or hospitalised with bronchiolitis is needed.
- 15. RCTs with pre-defined indications and protocols for supplemental oxygen are required to determine the effect on hospital admission, length of stay, oxygen saturation targets and effect on feeding difficulties.
- 16. Further RCTs are needed to confirm the level of oxygen saturations to establish oxygen therapy.
- Research on the effect of prolonged hypoxia (saturations less than 92%) on long term development is required.
- Further research is needed in determining an appropriate oxygen saturation level at which to consider discharge of an infant from hospital (inpatient ward or ED) with bronchiolitis.
- 19. RCTs are needed to establish use of continuous oximetry in the setting of hypoxic infants with bronchiolitis.

- 20. Further research is needed to determine what effect continuous oximetry monitoring has on time to discharge for inpatients or ED patients.
- 21. RCTs comparing HFNC with standard oxygen therapy, including sub-groups of infants with hypoxia and respiratory distress without hypoxia, outside of the PICU setting are required.
- 22. Further research into techniques of chest physiotherapy to determine any benefit in specific patient cohorts with bronchiolitis is required.
- 23. RCTs using pre-set protocols are needed for use of nasal suction in infants with bronchiolitis.
- 24. RCTs with pre-set protocols are required to establish the benefit or harm of nasal saline drops.
- 25. RCTs in paediatric wards and PICUs are needed to directly compare HFNC and nasal CPAP.
- 26. RCTs with pre-defined indications for oxygen therapy and patient outcomes are required to establish home oxygen programmes for infants with bronchiolitis.
- 27. Research on subgroups of high risk patients who may benefit from antibiotics, including those admitted to PICU with severe bronchiolitis, is needed. The optimal treatment regime (single dose to 14 days) and timing (acute versus post-acute) is yet to be established.
- 28. A RCT with longer follow up for outcomes in at risk population is required to determine benefit of antibiotics in infants at risk of bronchiectasis

- 29. In infants with bronchiolitis, research on the ideal volume (restricted vs. 100% maintenance) and type of non-oral fluids (NG rehydration solutions or milk, or type of isotonic IV solution) and the effect on infants less than two months of age is needed. The use of non-oral hydration in infants less than two months has not been studied as they were excluded from published studies.
- 30. Research on the cost effectiveness of procedures to prevent nosocomial infections such as cohorting or hand hygiene measures is required.

REFERENCES

- Oakley E, Borland M, Neutze J, Acworth J, Krieser D, Dalziel S, et al. Nasogastric hydration versus intravenous hydration for infants with bronchiolitis: a randomised trial. Lancet Respir Med. 2013;1(2):113–20.
- Guyatt G, Oxman A, Akl E, Kunz R, Vist G, Brozek J, et al. GRADE guidelines: 1. Introduction-GRADE evidence profiles and summary of findings tables. J Clin Epidemiol. 2011;64(4):383-94.
- National Health and Medical Research Council. NHMRC additional levels of evidence and grades for recommendations for developers of guidelines [Internet]. National Health and Medical Research Council; 2009 [cited 2015 21 Aug]. Available from: https://www.nhmrc. gov.au/_files_nhmrc/file/guidelines/developers/nhmrc_ levels_grades_evidence_120423.pdf.
- Infants and children: acute management of bronchiolitis [Internet]. North Sydney, N.S.W.: NSW Ministry of Health; 2012 [cited 2015 10 Mar]. Available from: http://www0. health.nsw.gov.au/policies/pd/2012/pdf/PD2012_004.pdf.
- Bronchiolitis in children [Internet]. North Adelaide, S.A.: SA Child Health Clinical Network; 2012 [cited 2015 10 Mar]. Available from: https://www.sahealth.sa.gov.au /wps/wcm connect/0a3fd50040d03f4d96fbbe40b897efc8/ Bronchiolitis+in+Children_Aug2013
- Bronchiolitis Management (Paediatric) RDH Guideline. Darwin, NT: Northern Territory Government Department of Health; 2013.
- Paediatric acute care guideline: bronchiolitis [Internet]. Perth, W.A.: Child and Adolescent Health Service; 2013 [cited 2015 3 Aug]. Available from: http://kidshealthwa. com/guidelines/bronchiolitis/.
- National Health and Medical Research Council. How NHMRC develops its guidelines [Internet]. 2015. Available from: https://www.nhmrc.gov.au/guidelines-publications/ how-nhmrc-develops-its-guidelines.
- Guyatt GH, Oxman AD, Vist GE, Kunz R, Falck-Ytter Y, Alonso-Coello P, et al. GRADE: An emerging consensus on rating quality of evidence and strength of recommendations. BMJ. 2008;336(7650):924-6.
- Ricci V, Delgado Nunes V, Murphy MS, Cunningham S. Bronchiolitis in children: summary of NICE guidance. BMJ. 2015;350:h2305.
- Durani Y, Friedman MJ, Attia MW. Clinical predictors of respiratory syncytial virus infection in children. Pediatr Int. 2008;50(3):352-5.

signs in infants presenting to A&E with bronchiolitis. Eur J Emerg Med. 2014;21(6):436-41.

- Ralston SL, Lieberthal AS, Meissner HC, Alverson BK, Baley JE, Gadomski AM, et al. Clinical practice guideline: the diagnosis, management, and prevention of bronchiolitis. Pediatrics. 2014;134(5):e1474-e502.
- 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(4):299-304.
- Alvarez AE, De Lima Marson FA, Bertuzzo CS, Arns CW, Ribeiro JD. Epidemiological and genetic characteristics associated with the severity of acute viral bronchiolitis by respiratory syncytial virus. Jornal de Pediatria. 2013;89(6):531-43.
- Bailey EJ, Maclennan C, Morris PS, Kruske SG, Brown N, Chang AB. Risks of severity and readmission of Indigenous and non-Indigenous children hospitalised for bronchiolitis. J Paediatr Child Health. 2009;45(10):593-7.
- Bradley JP, Bacharier LB, Bonfiglio J, Schechtman KB, Strunk R, Storch G, et al. Severity of respiratory syncytial virus bronchiolitis is affected by cigarette smoke exposure and atopy. Pediatrics. 2005;115(1):e7-14.
- Brand HK, de Groot R, Galama JM, Brouwer ML, Teuwen K, Hermans PW, et al. Infection with multiple viruses is not associated with increased disease severity in children with bronchiolitis. Pediatr Pulmonol. 2012;47(4):393-400.
- Chan PW, Lok FY, Khatijah SB. Risk factors for hypoxemia and respiratory failure in respiratory syncytial virus bronchiolitis. Southeast Asian J Trop Med Public Health. 2002;33(4):806-10.
- Chatzimichael A, Tsalkidis A, Cassimos D, Gardikis S, Tripsianis G, Deftereos S, et al. The role of breastfeeding and passive smoking on the development of severe bronchiolitis in infants. Minerva Pediatr. 2007;59(3):199-206.
- Corneli HM, Zorc JJ, Holubkov R, Bregstein JS, Brown KM, Mahajan P, et al. Bronchiolitis: clinical characteristics associated with hospitalization and length of stay. Pediatr Emerg Care. 2012;28(2):99-103.
- Craig E, Anderson P, Jackson C. The health status of children and young people in Auckland DHB [Internet]. Auckland, NZ: New Zealand Child and Youth Epidemiology Service; 2008. Available from: http://www.otago.ac.nz/ nzcyes/otago085999.pdf.
- 12. McLellan KE, Schwarze J, Beattie T. Chest auscultatory

- Damore D, Mansbach JM, Clark S, Ramundo M, Camargo CA. Prospective multicenter bronchiolitis study: predicting intensive care unit admissions. Acad Emerg Med. 2008;15(10):887-94.
- 24. DiFranza JR, Masaquel A, Barrett AM, Colosia AD, Mahadevia PJ. Systematic literature review assessing tobacco smoke exposure as a risk factor for serious respiratory syncytial virus disease among infants and young children. BMC Pediatr [Internet]. 2012 [cited 2015 5 Jun]; 12:[1-16 pp.]. Available from: http://www. biomedcentral.com/1471-2431/12/81.
- 25. Figueras-Aloy J, Carbonell-Estrany X, Quero J, IRIS Study Group. Case-control study of the risk factors linked to respiratory syncytial virus infection requiring hospitalization in premature infants born at a gestational age of 33-35 weeks in Spain. Pediatr Infect Dis J. 2004;23(9):815-20.
- Garcia CG, Bhore R, Soriano-Fallas A, Trost M, Chason R, Ramilo O, et al. Risk factors in children hospitalized with RSV bronchiolitis versus non-RSV bronchiolitis. Pediatrics. 2010;126(6):e1453-60.
- Gouyon JB, Roze JC, Guillermet-Fromentin C, Glorieux I, Adamon L, DI Maio M, et al. Hospitalizations for respiratory syncytial virus bronchiolitis in preterm infants at <33 weeks gestation without bronchopulmonary dysplasia: the CASTOR study. Epidemiol Infect. 2013;141(4):816-26.
- Hasegawa K, Stevenson MD, Mansbach JM, Schroeder AR, Sullivan AF, Espinola JA, et al. Association between hyponatremia and higher bronchiolitis severity among children in the ICU with bronchiolitis. Hosp Pediatr. 2015;5(7):385-9.
- 29. Helfrich AM, Nylund CM, Eberly MD, Eide MB, Stagliano DR. Healthy late-preterm infants born 33-36+6 weeks gestational age have higher risk for respiratory syncytial virus hospitalization. Early Hum Dev. 2015;91(9):541-6.
- Holman RC, Shay DK, Curns AT, Lingappa JR, Anderson LJ. Risk factors for bronchiolitis-associated deaths among infants in the United States. Pediatr Infect Dis J. 2003;22(6):483-90.
- Marlais M, Evans J, Abrahamson E. Clinical predictors of admission in infants with acute bronchiolitis. Arch Dis Child. 2011;96(7):648-52.
- 32. Papoff P, Moretti C, Cangiano G, Bonci E, Roggini M, Pierangeli A, et al. Incidence and predisposing factors for severe disease in previously healthy term infants experiencing their first episode of bronchiolitis. Acta Paediatr. 2011;100(7):e17-23.
- Sala KA, Moore A, Desai S, Welch K, Bhandari S, Carroll CL. Factors associated with disease severity in children with bronchiolitis. J Asthma. 2015;52(3):268-72.

- 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(7):621-7.
- 35. Stagliano DR, Nylund CM, Eide MB, Eberly MD. Children with Down syndrome are high-risk for severe respiratory syncytial virus disease. J Pediatr. 2015;166(3):703-9.e2.
- Trefny P, Stricker T, Baerlocher C, Sennhauser FH. Family history of atopy and clinical course of RSV infection in ambulatory and hospitalized infants. Pediatr Pulmonol. 2000;30(4):302-6.
- Voets S, van Berlaer G, Hachimi-Idrissi S. Clinical predictors of the severity of bronchiolitis. Eur J Emerg Med. 2006;13(3):134-8.
- Bordley WC, Viswanathan M, King VJ, Sutton SF, Jackman AM, Sterling L, et al. Diagnosis and testing in bronchiolitis: a systematic review. Arch Pediatr Adolesc Med. 2004;158(2):119-26.
- Williams C, Bartram T. Towards evidence based emergency medicine: best BETs from the Manchester Royal Infirmary. BET 4: Chest x-rays in bronchiolitis. Emerg Med J. 2012;29(6):514-5.
- Quintero DR, Gershan WM. Diagnosis and treatment of infants with bronchiolitis. J Clin Outcomes Manag. 2007;14(4):205-10.
- Schuh S, Lalani A, Allen U, Manson D, Babyn P, Stephens D, et al. Evaluation of the utility of radiography in acute bronchiolitis. J Pediatr. 2007;150(4):429-33.
- Yong JH, Schuh S, Rashidi R, Vanderby S, Lau R, Laporte A, et al. A cost effectiveness analysis of omitting radiography in diagnosis of acute bronchiolitis. Pediatr Pulmonol. 2009;44(2):122-7.
- 43. 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(3):152-6.
- 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(1):11-5.
- 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(6):1652-6.e1.
- 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(10):951-6.

- 47. 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 (10):1093.
- Dayan PS, Roskind CG, Levine DA, Kuppermann N. Controversies in the management of children with bronchiolitis. Clin Pediatr Emerg Med. 2004;5(1):41-53.
- Bamberger E, Srugo I, Abu Raya B, Segal E, Chaim B, Kassis I, et al. What is the clinical relevance of respiratory syncytial virus bronchiolitis?: findings from a multi-center, prospective study. Eur J Clin Microbiol Infect Dis. 2012;31(12):3323-30.
- 50. Friedman MJ, Attia MW. Influenza a in young children with suspected respiratory syncytial virus infection. Acad Emerg Med. 2003;10(12):1400-3.
- Garcia-Garcia ML, Calvo C, Martin F, Perez-Brena P, Acosta B, Casas I. Human metapneumovirus infections in hospitalised infants in Spain. Arch Dis Child. 2006;91(4):290-5.
- 52. Mackie PL, Joannidis PA, Beattie J. Evaluation of an acute point-of-care system screening for respiratory syncytial virus infection. J Hosp Infect. 2001;48(1):66-71.
- Mansbach JM, Piedra PA, Teach SJ, Sullivan AF, Forgey T, Clark S, et al. Prospective multicenter study of viral etiology and hospital length of stay in children with severe bronchiolitis. Arch Pediatr Adolesc Med. 2012;166(8):700-6.
- 54. Nascimento MS, Souza AV, Ferreira AV, Rodrigues JC, Abramovici S, Silva Filho LV. High rate of viral identification and coinfections in infants with acute bronchiolitis. Clinics. 2010;65(11):1133-7.
- Ricart S, Marcos MA, Sarda M, Anton A, Munoz-Almagro C, Pumarola T, et al. Clinical risk factors are more relevant than respiratory viruses in predicting bronchiolitis severity. Pediatr Pulmonol. 2013;48(5):456-63.
- Wishaupt JO, Russcher A, Smeets LC, Versteegh FG, Hartwig NG. Clinical impact of RT-PCR for pediatric acute respiratory infections: a controlled clinical trial. Pediatrics. 2011;128(5):e1113-20.
- Yu D, Jiehua C, Hua B, Lijia W, Wei L, Xiqiang Y, et al. The severity of bronchiolitis is not dependent on the coinfection of RSV with other respiratory viruses. J Pediatr Infect Dis. 2010;5(3):255-61.
- Chin HJ, Seng QB. Reliability and validity of the respiratory score in the assessment of acute bronchiolitis. Malays J Med Sci. 2004;11(2):34-40.
- Destino L, Weisgerber MC, Soung P, Bakalarski D, Yan K, Rehborg R, et al. Validity of respiratory scores in bronchiolitis. Hosp Pediatr. 2012;2(4):202-9.
- 60. Duarte-Dorado DM, Madero-Orostegui DS, Rodriguez-Martinez CE, Nino G. Validation of a scale to assess the severity of bronchiolitis in a population of hospitalized infants. J Asthma. 2013;50(10):1056-61.

- Liu LL, Gallaher MM, Davis RL, Rutter CM, Lewis TC, Marcuse EK. Use of a respiratory clinical score among different providers. Pediatr Pulmonol. 2004;37(3):243-8.
- McCallum GB, Morris PS, Wilson CC, Versteegh LA, Ward LM, Chatfield MD, et al. Severity scoring systems: are they internally valid, reliable and predictive of oxygen use in children with acute bronchiolitis? Pediatr Pulmonol. 2013;48(8):797-803.
- Shete S, Nagori G, Nagori P, Hamid M. Relation between pulse oximetry and clinical score in infants with acute bronchiolitis. Natl J Physiol Pharm Pharmacol. 2014;4(2):124-7.
- 64. Walsh P, Gonzales A, Satar A, Rothenberg SJ. The interrater reliability of a validated bronchiolitis severity assessment tool. Pediatr Emerg Care. 2006;22(5):316-20.
- Baraldi E, Lanari M, Manzoni P, Rossi GA, Vandini S, Rimini A, et al. Inter-society consensus document on treatment and prevention of bronchiolitis in newborns and infants. Ital J Pediatr. 2014;40:65.
- 66. Baumer JH. SIGN guideline on bronchiolitis in infants. Arch Dis Child Educ Prac Ed. 2007;92(5):ep149-51.
- Mansbach JM, Clark S, Christopher NC, LoVecchio F, Kunz S, Acholonu U, et al. Prospective multicenter study of bronchiolitis: predicting safe discharges from the emergency department. Pediatrics. 2008;121(4):680-8.
- Mansbach JM, Clark S, Piedra PA, Macias CG, Schroeder AR, Pate BM, et al. Hospital course and discharge criteria for children hospitalized with bronchiolitis. J Hosp Med. 2015;10(4):205-11.
- Gadomski AM, Scribani MB. Bronchodilators for bronchiolitis. Cochrane Database Syst Rev [Internet]. 2014 [cited 2015 24 Mar]; 2015. Available from: http:// onlinelibrary.wiley.com/doi/10.1002/14651858.CD001266. pub4/full.
- Kose M, Ozturk MA, Poyrazoglu H, Elmas T, Ekinci D, Tubas F, et al. The efficacy of nebulized salbutamol, magnesium sulfate, and salbutamol/magnesium sulfate combination in moderate bronchiolitis. Eur J Pediatr. 2014;173(9):1157-60.
- Chavasse R, Seddon P, Bara A, McKean MC. Short acting beta2-agonists for recurrent wheeze in children under two years of age. Cochrane Database Syst Rev [Internet].
 2002 [cited 2015 8 Jun]. Available from: http:// onlinelibrary.wiley.com/doi/10.1002/14651858.CD002873/ abstract.
- Hartling L, Bialy LM, Vandermeer B, Tjosvold L, Johnson DW, Plint AC, et al. Epinephrine for bronchiolitis. Cochrane Database Syst Rev [Internet]. 2011 [cited 2015 24 Mar]. Available from: http://onlinelibrary.wiley.com/ doi/10.1002/14651858.CD003123.pub3/full.

- 73. Livni G, Rachmel A, Marom D, Yaari A, Tirosh N, Ashkenazi S. A randomized, double-blind study examining the comparative efficacies and safety of inhaled epinephrine and nasal decongestant in hospitalized infants with acute bronchiolitis. Pediatr Infect Dis J. 2010;29(1):71-3.
- 74. Modaressi MR, Asadian A, Faghihinia J, Arashpour M, Mousavinasab F. Comparison of epinephrine to salbutamol in acute bronchiolitis. Iran J Pediatr. 2012;22(2):241-4.
- Simsek-Kiper PO, Kiper N, Hascelik G, Dolgun A, Yalcin E, Dogru-Ersoz D, et al. Emergency room management of acute bronchiolitis: a randomized trial of nebulized epinephrine. Turk J Pediatr. 2011;53(6):651-60.
- Sarrell EM, Meyerovitch J. Epinephrine and bromhexine in the ambulatory treatment of bronchiolitis. J Pediatr Infect Dis. 2010;5(4):377-84.
- Skjerven HO, Hunderi JO, Brugmann-Pieper SK, Brun AC, Engen H, Eskedal L, et al. Racemic adrenaline and inhalation strategies in acute bronchiolitis. N Engl J Med. 2013;368(24):2286-93.
- Zhang L, Mendoza-Sassi RA, Wainwright C, Klassen TP. Nebulised hypertonic saline solution for acute bronchiolitis in infants. Cochrane Database Syst Rev [Internet]. 2013 [cited 2015 24 Mar]. Available from: http://onlinelibrary. wiley.com/doi/10.1002/14651858.CD006458.pub3/full.
- Everard ML, Hind D, Ugonna K, Freeman J, Bradburn M, Cooper CL, et al. SABRE: a multicentre randomised control trial of nebulised hypertonic saline in infants hospitalised with acute bronchiolitis. Thorax. 2014;69(12):1105-12.
- 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(7):664-70.
- Jacobs JD, Foster M, Wan J, Pershad J. 7% Hypertonic saline in acute bronchiolitis: a randomized controlled trial. Pediatrics. 2014;133(1):e8-13.
- 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(1).
- 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(26):39-43.
- 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(8):743-7.
- Silver AH, Esteban-Cruciani N, Azzarone G, Douglas LC, Lee DS, Liewehr S, et al. 3% Hypertonic saline versus normal saline in inpatient bronchiolitis: a randomized controlled trial. Pediatrics. 2015;136(6):1036-43.

- Teunissen J, Hochs AH, Vaessen-Verberne A, Boehmer AL, Smeets CC, Brackel H, et al. The effect of 3% and 6% hypertonic saline in viral bronchiolitis: a randomised controlled trial. Eur Respir J. 2014;44(4):913-21.
- Wu S, Baker C, Lang ME, Schrager SM, Liley FF, Papa C, et al. Nebulized hypertonic saline for bronchiolitis: a randomized clinical trial. JAMA Pediatr. 2014;168(7):657-63.
- 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(6):431-8.
- Maguire C, Cantrill H, Hind D, Bradburn M, Everard ML. Hypertonic saline (HS) for acute bronchiolitis: systematic review and meta-analysis. BMC Pulm Med [Internet]. 2015 [cited 2016 23 Feb]; 15:[1-17 pp.]. Available from: http:// bmcpulmmed.biomedcentral.com/articles/10.1186/ s12890-015-0140-x.
- Mitchell MD, Schast AP, Umscheid CA. Nebulized hypertonic saline treatment for infants with bronchiolitis (Structured abstract). Health Technology Assessment Database [Internet]. 2013 [cited 2015 5 Jun]. Available from: http://onlinelibrary.wiley.com/o/cochrane/clhta/ articles/HTA-32013000424/frame.html.
- Zhang L, Mendoza-Sassi RA, Klassen TP, Wainwright C. Nebulized hypertonic saline for acute bronchiolitis: a systematic review. Pediatrics. 2015;136(4):687-701.
- 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(8):788-9.
- Fernandes RM, Bialy LM, Vandermeer B, Tjosvold L, Plint AC, Patel H, et al. Glucocorticoids for acute viral bronchiolitis in infants and young children. Cochrane Database Syst Rev [Internet]. 2013 [cited 2015 24 Mar]. Available from: http://onlinelibrary.wiley.com/ doi/10.1002/14651858.CD004878.pub4/full.
- 94. Alansari K, Sakran M, Davidson BL, Ibrahim K, Alrefai M, Zakaria I. Oral dexamethasone for bronchiolitis: a randomized trial. Pediatrics. 2013;132(4):e810-6.
- 95. Jartti T, Nieminen R, Vuorinen T, Lehtinen P, Vahlberg T, Gern J, et al. Short- and long-term efficacy of prednisolone for first acute rhinovirus-induced wheezing episode. J Allergy Clin Immunol. 2015;135(3):691-8.e9.
- 96. Flores-Gonzalez JC, Matamala-Morillo MA, Rodriguez-Campoy P, Perez-Guerrero JJ, Serrano-Moyano B, Comino-Vazquez P, et al. Epinephrine improves the efficacy of nebulized hypertonic saline in moderate bronchiolitis: a randomised clinical trial. PloS One [Internet]. 2015 [cited 2016 23 Feb]; 10(11):[1-11 pp.]. Available from: http://www.ncbi.nlm.nih.gov/pmc/articles/ PMC4648584/pdf/pone.0142847.pdf.

- 97. John BM, Singh D. Comparision of nebulised salbutamol and L-epinephrine in first time wheezy children. Med J Armed Forces India. 2010;66(1):9-13.
- Plint AC, Johnson DW, Patel H, Wiebe N, Correll R, Brant R, et al. Epinephrine and dexamethasone in children with bronchiolitis. N Engl J Med. 2009;360(20):2079-89.
- 99. Mitchell MD, Schast AP, Umscheid CA. Oxygen saturation discharge thresholds for infants admitted with bronchiolitis (Structured abstract). Health Technology Assessment Database [Internet]. 2013 [cited 2015 5 Jun]. Available from: http://onlinelibrary.wiley.com/o/cochrane/clhta/ articles/HTA-32013000425/frame.html.
- Cunningham S, McMurray A. Observational study of two oxygen saturation targets for discharge in bronchiolitis. Arch Dis Child. 2012;97(4):361-3.
- Unger S, Cunningham S. Effect of oxygen supplementation on length of stay for infants hospitalized with acute viral bronchiolitis. Pediatrics. 2008;121(3):470-5.
- Hendaus MA, Jomha FA, Alhammadi AH. Pulse oximetry in bronchiolitis: is it needed? Ther Clin Risk Manag. 2015;11:1573-8.
- 103. Cunningham S, Rodriguez A, Adams T, Boyd KA, Butcher I, Enderby B, et al. Oxygen saturation targets in infants with bronchiolitis (BIDS): a double-blind, randomised, equivalence trial. Lancet. 2015;386(9998):1041-8.
- 104. Schuh S, Freedman S, Coates A, Allen U, Parkin PC, Stephens D, et al. Effect of oximetry on hospitalization in bronchiolitis: a randomized clinical trial. JAMA. 2014;312(7):712-8.
- 105. Choi J, Claudius I. Decrease in emergency department length of stay as a result of triage pulse oximetry. Pediatr Emerg Care. 2006;22(6):412-4.
- 106. 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(6):527-30.
- 107. McCulloh R, Koster M, Ralston S, Johnson M, Hill V, Koehn K, et al. Use of intermittent vs continuous pulse oximetry for nonhypoxemic infants and young children hospitalized for bronchiolitis: a randomized clinical trial. JAMA Pediatr. 2015;169(10):898-904.
- 108. 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(3):e106-e11.
- 109. Beggs S, Wong ZH, Kaul S, Ogden KJ, Walters JA. High-flow nasal cannula therapy for infants with bronchiolitis. Cochrane Database Syst Rev [Internet]. 2014 [cited 2015 8 Jun]. Available from: http://onlinelibrary.wiley. com/doi/10.1002/14651858.CD009609.pub2/full.

- Bueno Campana M, Olivares Ortiz J, Notario Munoz C, Ruperez Lucas M, Fernandez Rincon A, Patino Hernandez O, et al. High flow therapy versus hypertonic saline in bronchiolitis: randomised controlled trial. Arch Dis Child. 2014;99(6):511-5.
- 111. Bressan S, Balzani M, Krauss B, Pettenazzo A, Zanconato S, Baraldi E. High-flow nasal cannula oxygen for bronchiolitis in a pediatric ward: a pilot study. Eur J Pediatr. 2013;172(12):1649-56.
- 112. Mayfield S, Bogossian F, O'Malley L, Schibler A. High-flow nasal cannula oxygen therapy for infants with bronchiolitis: pilot study. J Paediatr Child Health. 2014;50(5):373-8.
- Da Dalt L, Bressan S, Martinolli F, Perilongo G, Baraldi E. Treatment of bronchiolitis: state of the art. Early Hum Dev. 2013;89 Suppl 1:S31-6.
- Haq I, Gopalakaje S, Fenton AC, McKean MC, O'Brien CJ, Brodlie M. The evidence for high flow nasal cannula devices in infants. Paediatr Respir Rev. 2014;15(2):124-34.
- 115. Lee JH, Rehder KJ, Williford L, Cheifetz IM, Turner DA. Use of high flow nasal cannula in critically ill infants, children, and adults: a critical review of the literature. Intensive Care Med. 2013;39(2):247-57.
- Sinha IP, McBride AKS, Smith R, Fernandes RM. CPAP and high-flow nasal cannula oxygen in bronchiolitis. Chest. 2015;148(3):810-23.
- 117. Kelly GS, Simon HK, Sturm JJ. High-flow nasal cannula use in children with respiratory distress in the emergency department: predicting the need for subsequent intubation. Pediatr Emerg Care. 2013;29(8):888-92.
- 118. Pham TM, O'Malley L, Mayfield S, Martin S, Schibler A. The effect of high flow nasal cannula therapy on the work of breathing in infants with bronchiolitis. Pediatr Pulmonol. 2015;50(7):713-20.
- 119. Roque i Figuls M, Gine-Garriga M, Granados Rugeles C, Perrotta C. Chest physiotherapy for acute bronchiolitis in paediatric patients between 0 and 24 months old. Cochrane Database Syst Rev [Internet]. 2012 [cited 2015 8 Jun]. Available from: http://onlinelibrary.wiley.com/ doi/10.1002/14651858.CD004873.pub4/abstract.
- 120. Gomes EL, Postiaux G, Medeiros DR, Monteiro KK, Sampaio LM, Costa D. Chest physical therapy is effective in reducing the clinical score in bronchiolitis: randomized controlled trial. Braz J Phys Ther. 2012;16(3):241-7.
- 121. Pupin MK, Riccetto AG, Ribeiro JD, Baracat EC. Comparison of the effects that two different respiratory physical therapy techniques have on cardiorespiratory parameters in infants with acute viral bronchiolitis. J Bras Pneumol. 2009;35(9):860-7.

- 122. Remondini R, dos Santos AZ, de Castro G, do Prado C, da Silva Filho LV. Comparative analysis of the effects of two chest physical therapy interventions in patients with bronchiolitis during hospitalization period. Einstein (Sao Paulo) [Internet]. 2014 Oct-Dec [cited 2015 7 Jun]; 12(4):[452-8 pp.]. Available from: https://www.ncbi.nlm. nih.gov/pmc/articles/PMC4879911/pdf/1679-4508eins-12-4-0452.pdf.
- 123. Goncalves R, Feitosa S, De Castro Selestrin C, Valenti VE, De Sousa FH, Siqueira AA, et al. Evaluation of physiological parameters before and after respiratory physiotherapy in newborns with acute viral bronchiolitis. Int Arch Med. 2014;7(1).
- 124. Jacinto CP, Gastaldi AC, Aguiar DY, Maida KD, Souza HC. Physical therapy for airway clearance improves cardiac autonomic modulation in children with acute bronchiolitis. Braz J Phys Ther. 2013;17(6):533-40.
- 125. Mussman GM, Parker MW, Statile A, Sucharew H, Brady PW. Suctioning and length of stay in infants hospitalized with bronchiolitis. JAMA Pediatr. 2013;167(5):414-21.
- 126. Soleimani G, Akbarpour M, Mohammadi M. Safety and efficacy of phenylephrine nasal drops in bronchiolitis. Iran J Pediatr. 2014;24(5):593-7.
- 127. Turner T, Wilkinson F, Harris C, Mazza D, Health for Kids Guideline Development Group. Evidence based guideline for the management of bronchiolitis. Aust Fam Physician. 2008;37(6 Spec No):6-13.
- Verma N, Lodha R, Kabra SK. Recent advances in management of bronchiolitis. Indian Pediatr. 2013;50(10):939-49.
- 129. Kana RJ, Mathew JL. Continuous positive airway pressure (CPAP) for acute bronchiolitis in children. Cochrane Database Syst Rev [Internet]. 2015 [cited 2015 8 Jun]. Available from: http://onlinelibrary.wiley.com/ doi/10.1002/14651858.CD010473.pub2/full.
- Oymar K, Bardsen K. Continuous positive airway pressure for bronchiolitis in a general paediatric ward: a feasibility study. BMC Pediatr [Internet]. 2014 [cited 2015 5 Jun]; 14:[1-6 pp.]. Available from: https://www.ncbi.nlm.nih.gov/ pmc/articles/PMC4020573/pdf/1471-2431-14-122.pdf.
- 131. Metge P, Grimaldi C, Hassid S, Thomachot L, Loundou A, Martin C, et al. Comparison of a high-flow humidified nasal cannula to nasal continuous positive airway pressure in children with acute bronchiolitis: experience in a pediatric intensive care unit. Eur J Pediatr. 2014;173(7):953-8.
- Palanivel V, Anjay MA. Question 3. Is continuous positive airway pressure effective in bronchiolitis? Arch Dis Child. 2009;94(4):324-6.
- 133. Bajaj L, Turner CG, Bothner J. A randomized trial of home oxygen therapy from the emergency department for acute bronchiolitis. Pediatrics. 2006;117(3):633-40.

- 134. Tie SW, Hall GL, Peter S, Vine J, Verheggen M, Pascoe EM, et al. Home oxygen for children with acute bronchiolitis. Arch Dis Child. 2009;94(8):641-3.
- 135. Zappia T, Peter S, Hall G, Vine J, Martin A, Munns A, et al. Home oxygen therapy for infants and young children with acute bronchiolitis and other lower respiratory tract infections: the HiTHOx program. Issues Compr Pediatr Nurs. 2013;36(4):309-18.
- 136. Sandweiss DR, Mundorff MB, Hill T, Wolfe D, Greene T, Andrews S, et al. Decreasing hospital length of stay for bronchiolitis by using an observation unit and home oxygen therapy. JAMA Pediatr. 2013;167(5):422-8.
- Flett KB, Breslin K, Braun PA, Hambidge SJ. Outpatient course and complications associated with home oxygen therapy for mild bronchiolitis. Pediatrics. 2014;133(5):769-75.
- 138. Gauthier M, Vincent M, Morneau S, Chevalier I. Impact of home oxygen therapy on hospital stay for infants with acute bronchiolitis. Eur J Pediatr. 2012;171(12):1839-44.
- 139. Halstead S, Roosevelt G, Deakyne S, Bajaj L. Discharged on supplemental oxygen from an emergency department in patients with bronchiolitis. Pediatrics. 2012;129(3):e605-10.
- 140. Farley R, Spurling GK, Eriksson L, Del Mar CB. Antibiotics for bronchiolitis in children under two years of age.
 Cochrane Database Syst Rev [Internet]. 2014 [cited 2016 8 Jun]. Available from: http://onlinelibrary.wiley.com/ doi/10.1002/14651858.CD005189.pub4/full.
- 141. McCallum GB, Morris PS, Chang AB. Antibiotics for persistent cough or wheeze following acute bronchiolitis in children. Cochrane Database Syst Rev [Internet]. 2012 [cited 2016 8 Jun]. Available from: http://onlinelibrary.wiley. com/doi/10.1002/14651858.CD009834.pub2/full.
- 142. 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 [Internet]. 2014 [cited 2015 12 Jun]. Available from: http:// onlinelibrary.wiley.com/o/cochrane/clcentral/articles/228/ CN-01043228/frame.html.
- 143. McCallum GB, Morris PS, Grimwood K, Maclennan C, White AV, Chatfield MD, et al. Three-weekly doses of azithromycin for Indigenous infants hospitalized with bronchiolitis: a multicentre, randomized, placebocontrolled trial. Frontiers in Pediatrics. 2015;3.
- 144. Guppy M, Mickan SM, Del Mar CB, Thorning S, Rack A. Advising patients to increase fluid intake for treating acute respiratory infections. Cochrane Database Syst Rev [Internet]. 2011 [cited 2016 8 Jun]. Available from: http:// onlinelibrary.wiley.com/doi/10.1002/14651858.CD004419. pub3/full.

- 145. Oakley E, Borland M, Neutze J, Acworth J, Krieser D, Dalziel S, et al. Nasogastric hydration versus intravenous hydration for infants with bronchiolitis: a randomised trial. Lancet Respir Med. 2013;1(2):113-20.
- 146. Rodrigues RM, Schvartsman BG, Farhat SC, Schvartsman C. Hypotonic solution decreases serum sodium in infants with moderate bronchiolitis. Acta Paediatr. 2014;103(3):e111-5.
- 147. Mills JM, Harper J, Broomfield D, Templeton KE. Rapid testing for respiratory syncytial virus in a paediatric emergency department: benefits for infection control and bed management. J Hosp Infect. 2011;77(3):248-51.
- 148. Simon A, Khurana K, Wilkesmann A, Muller A, Engelhart S, Exner M, et al. Nosocomial respiratory syncytial virus infection: impact of prospective surveillance and targeted infection control. Int J Hyg Environ Health. 2006;209(4):317-24.
- 149. Simon A, Muller A, Khurana K, Engelhart S, Exner M, Schildgen O, et al. Nosocomial infection: a risk factor for a complicated course in children with respiratory syncytial virus infection--results from a prospective multicenter German surveillance study. Int J Hyg Environ Health. 2008;211(3-4):241-50.
- 150. Thorburn K, Eisenhut M, Riordan A. Mortality and morbidity of nosocomial respiratory syncytial virus (RSV) infection in ventilated children--a ten year perspective. Minerva Anestesiol. 2012;78(7):782.
- 151. Jefferson T, Del Mar CB, Dooley L, Ferroni E, Al-Ansary LA, Bawazeer GA, et al. Physical interventions to interrupt or reduce the spread of respiratory viruses. Cochrane Database Syst Rev [Internet]. 2011 [cited 2016 8 Jun]. Available from: http://onlinelibrary.wiley.com/ doi/10.1002/14651858.CD006207.pub4/full.
- 152. Amat F, Henquell C, Verdan M, Roszyk L, Mulliez A, Labbe A. Predicting the severity of acute bronchiolitis in infants: should we use a clinical score or a biomarker? J Med Virol. 2014;86(11):1944-52.
- 153. Drolia A, Dewan P, Gupta P. Predicting the severity of bronchiolitis in a resource-poor setting. Internet J Pediatr Neonatol. 2010;11(1).
- 154. Caiulo VA, Gargani L, Caiulo S, Fisicaro A, Moramarco F, Latini G, et al. Lung ultrasound in bronchiolitis: comparison with chest X-ray. Eur J Pediatr. 2011;170(11):1427-33.
- 155. Farah MM, Padgett LB, McLario DJ, Sullivan KM, Simon HK. First-time wheezing in infants during respiratory syncytial virus season: chest radiograph findings. Pediatr Emerg Care. 2002;18(5):333-6.
- 156. Kern S, Uhl M, Berner R, Schwoerer T, Langer M. Respiratory syncytial virus infection of the lower respiratory tract: radiological findings in 108 children. Eur Radiol. 2001;11(12):2581-4.

- 157. Kneyber MC, Moons KG, de Groot R, Moll HA. Predictors of a normal chest x-ray in respiratory syncytial virus infection. Pediatr Pulmonol. 2001;31(4):277-83.
- 158. Offer I, Ashkenazi S, Livni G, Shalit I. The diagnostic and therapeutic approach to acute bronchiolitis in hospitalized children in Israel: a nationwide survey. Isr Med Assoc J. 2000;2(2):108-10.
- 159. Titus MO, Wright SW. Prevalence of serious bacterial infections in febrile infants with respiratory syncytial virus infection. Pediatrics. 2003;112(2):282-4.
- Huijskens EG, Biesmans RC, Buiting AG, Obihara CC, Rossen JW. Diagnostic value of respiratory virus detection in symptomatic children using real-time PCR. Virol J. 2012;9(276).
- Fernandes RM, Plint AC, Terwee CB, Sampaio C, Klassen TP, Offringa M, et al. Validity of bronchiolitis outcome measures. Pediatrics. 2015;135(6):e1399-408.
- 162. Gajdos V, Katsahian S, Beydon N, Abadie V, de Pontual L, Larrar S, et al. Effectiveness of chest physiotherapy in infants hospitalized with acute bronchiolitis: a multicenter, randomized, controlled trial. PLoS Med [Internet]. 2010 Sep [cited 2015 7 Jun]; 7(9):[e1000345 p.]. Available from: https://www.ncbi.nlm.nih.gov/pmc/articles/PMC2946956/ pdf/pmed.1000345.pdf.
- 163. Mosalli R, Abdul Moez AM, Janish M, Paes B. Value of a risk scoring tool to predict respiratory syncytial virus disease severity and need for hospitalization in term infants. J Med Virol. 2015;87(8):1285-91.
- 164. Hartling L, Fernandes RM, Bialy L, Milne A, Johnson D, Plint A, et al. Steroids and bronchodilators for acute bronchiolitis in the first two years of life: systematic review and meta-analysis. BMJ. 2011;342:d1714.
- 165. Hanlon D. High flow nasal cannula oxygen therapy for infants and young children with bronchiolitis. Aust Nurs Midwifery J. 2014;22(3):28-31.
- 166. Evans J, Marlais M, Abrahamson E. Clinical predictors of nasal continuous positive airway pressure requirement in acute bronchiolitis. Pediatr Pulmonol. 2012;47(4):381-5.
- 167. Tahan F, Ozcan A, Koc N. Clarithromycin in the treatment of RSV bronchiolitis: a double-blind, randomised, placebocontrolled trial. Eur Respir J. 2007;29(1):91-7.
- 168. Kneyber MC, van Woensel JB, Uijtendaal E, Uiterwaal CS, Kimpen JL, Dutch Antibiotics in RSVTRG. Azithromycin does not improve disease course in hospitalized infants with respiratory syncytial virus (RSV) lower respiratory tract disease: a randomized equivalence trial. Pediatric Pulmonology. 2008;43(2):142-9.
- Mazumder MJU, Hossain MM, Kabir ARML. Management of bronchiolitis with or without antibiotics: A randomized controlled trial. J Bangladesh Coll Phys Surg. 2009;27(2):63-9.

- 170. McCallum GB, Morris PS, Chatfield MD, Maclennan C, White AV, Sloots TP, et al. A single dose of azithromycin does not improve clinical outcomes of children hospitalised with bronchiolitis: a randomised, placebocontrolled trial. PLoS ONE [Electronic Resource]. 2013;8(9):e74316.
- 171. Pinto LA, Pitrez PM, Luisi F, de Mello PP, Gerhardt M, Ferlini R, et al. Azithromycin therapy in hospitalized infants with acute bronchiolitis is not associated with better clinical outcomes: a randomized, double-blinded, and placebo-controlled clinical trial. J Pediatr. 2012;161(6):1104-8.
- 172. Macias CG, Mansbach JM, Fisher ES, Riederer M, Piedra PA, Sullivan AF, et al. Variability in inpatient management of children hospitalized with bronchiolitis. Acad Pediatr. 2015;15(1):69-76.

- 173. Hanna S, Tibby SM, Durward A, Murdoch IA. Incidence of hyponatraemia and hyponatraemic seizures in severe respiratory syncytial virus bronchiolitis. Acta Paediatr. 2003;92(4):430-4.
- 174. Kugelman A, Raibin K, Dabbah H, Chistyakov I, Srugo I, Even L, et al. Intravenous fluids versus gastric-tube feeding in hospitalized infants with viral bronchiolitis: a randomized, prospective pilot study. J Pediatr. 2013;162(3):640-2.e1.
- 175. 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(10):656-8.

DISCLAIMER

The information set out in this publication is current at the date of first publication and is intended for use as a guide only and may or may not be relevant to patients or circumstances. This Guideline was developed for use within the inpatient wards and emergency departments of hospitals in Australia and New Zealand. The Guideline details the initial assessment and management of infants presenting with Bronchiolitis and is designed to acquaint the reader rapidly with the clinical problem and provide practical advice regarding assessment and management.

These Clinical Practice Guidelines were produced by the PREDICT research network and do not reflect the views of the NHMRC. Where possible we have achieved consensus between practicing clinicians. The recommendations contained in these guidelines do not indicate an exclusive course of action, or serve as a standard of medical care. Variations, taking individual circumstances into account, may be appropriate.

The authors of these guidelines have made considerable efforts to ensure the information upon which they are based is accurate and up to date. The authors accept no responsibility for any inaccuracies, information perceived as misleading, or the success of any treatment regimen detailed in the guidelines.

If you wish to contact the authors please email: predict@mcri.edu.au