Bilaga 1 Systematiska översikter med hög och medelhög kvalitet som ligger till grund för resultaten
Appendix 1 Main characteristics of systematic reviews with low or moderate risk of bias

First author Year Reference	Objectives Age	Number of included studies (participants)	Main results and the estimated level of evidence according to authors	Risk of bias assessed by SBU
Common colds and acute upper respiratory tract infection				
De Sutter AI 2012 [19]	To assess the effectiveness of antihistamine-decongestant-analgesic combinations in reducing the duration and alleviating the symptoms of the common cold in adults and children Children and adults Any age	27 RCT (5117) antihistamines combined with decongestants adults 8 RCT Children only 2 RCT (113) including older children 4 RCT (214) antihistamines with analgesics 3RCT in adults 0 RCT children	Current evidence suggests that antihistamine-analgesic-decongestant combinations have some general benefit in adults and older children (over 6 years). These benefits must be weighed against the risk of adverse effects.	Low

First author Year Reference	Objectives Age	Number of included studies (participants)	Main results and the estimated level of evidence according to authors	Risk of bias assessed by SBU
		analgesics with decongestants 5 RCT adults 1 RCT in children antihistamines with decongestants and analgesics 4 RCT in adults 1 RCT in children		
Hayward G 2009 [21]	To evaluate whether systemic corticosteroids improve symptoms of sore throat in adults and children. Children and adults Any age	8 RCT (743) 2 RCT Children only (309)	We did not find significant changes in mean time to onset of pain relief in trials with children only.	Low
Hayward G 2015 [22]	To compare corticosteroids versus usual care for the common cold on measures of symptom resolution and improvement in children and adults. Children and adults Any age	3 RCT (353) Children only: 1 RCT (100)	**Low level of evidence:** The trial comparing steroid spray to no spray in children did find some evidence of benefit but we rated the quality of the evidence from this trial as very poor and the results were unclear.	Low

First author Year Reference	Objectives Age	Number of included studies (participants)	Main results and the estimated level of evidence according to authors	Risk of bias assessed by SBU
Hemilä H 2013 [23]	To find out whether vitamin C reduces the incidence, the duration or severity of the common cold when used either as a continuous regular supplementation every day or as a therapy at the onset of cold symptoms. Children and adults Any age	The effect on cold duration 31 RCT (9745) Children 14 RCT (2530) Therapeutic effect 7 RCT (3249), none in children	In children, 1 to 2 g/day vitamin C shortened colds by 18%. The severity of colds was also reduced by regular vitamin C administration. Only a few therapeutic trials on the effect of vitamin C on cold symptoms have been carried out and none have examined children.	Low
Kenealy T 2013 [20]	a) To determine the efficacy of antibiotics compared with placebo for reducing general and specific nasopharyngeal symptoms of acute upper respiratory tract infections (URTIs) (common colds). b)To determine if antibiotics have any influence on the outcomes for acute purulent rhinitis and acute clear rhinitis lasting less than 10 days before the intervention. c)To determine whether there are significant adverse outcomes associated with	11 RCT Children only 5 RCT	a) and b) When we analysed results for children and adults separately, there was no significant finding for lack of cure or persistence of symptoms in either group. There is no evidence of benefit from antibiotics for the common cold or for persisting acute purulent rhinitis in children or adults. c) There was no greater risk for adverse events in children (RR 0.91, 95% CI 0.51 to 1.63).	Low

First author Year Reference	Objectives Age	Number of included studies (participants)	Main results and the estimated level of evidence according to authors	Risk of bias assessed by SBU
	antibiotic therapy for participants with a clinical diagnosis of acute URTI or acute purulent rhinitis Children and adults Any age			
Science M 2012 [18]	To evaluate the efficacy and safety of zinc for the treatment of the common cold Children and adults Any age	RCT 17 (2121) Children only 3 RCT (934)	No significant effect off Zinc sulfate on the duration of cold symptoms was seen among children.	Low
Sinusitis				
Cronin MJ 2013 [24]	To assess the effectiveness of antibiotics compared with placebo in the treatment of acute rhinosinusitis in children Children 1-18 years	4 RCT (435)	**Low level of evidence:** This review of four RCTs comparing antibiotic and placebo in the management of acute rhinosinusitis would suggest to us that there is same but nevertheless insufficient evidence to support the routine use of antibiotics.	Moderate
Falagas ME 2008 [25]	To assess the therapeutic role of antibiotics for acute	17 RCT (3291) Only children 3 RCT (326)	**High level of evidence:** In conclusion, use of antibiotics for acute sinusitis confers a small therapeutic benefit over placebo with a	Moderate

First author Year Reference	Objectives Age	Number of included studies (participants)	Main results and the estimated level of evidence according to authors	Risk of bias assessed by SBU
	sinusitis compared with placebo. Children and adults Any age		corresponding rise in the risk for adverse events. However, in the subgroup analysis limited to children, only a small number of patients were included.	
Shaikh N 2014 [26]	To determine the efficacy of decongestants, antihistamines or nasal irrigation in improving symptoms of acute sinusitis in children Children 0-18	0 RCT	There is no evidence to determine whether the use of antihistamines, decongestants or nasal irrigation is efficacious in children with acute sinusitis.	Low
Tonsillitis				
Altamimi S 2012 [27]	To summarize the evidence regarding the efficacy of two to six day s of newer oral antibiotics (short duration) compared to 10 days of oral penicillin (standard duration) in treating children with acute group A beta hemolytic streptococcus pharyngitis. Children: 1 to 18 years	20 RCT (13,102)	Three to six days of oral antibiotics had comparable efficacy compared to the standard duration 10-day course of oral penicillin in treating children with acute GABHS pharyngitis. In areas where the prevalence of rheumatic heart disease is still high, our results must be interpreted with caution.	Moderate

First author Year Reference	Objectives Age	Number of included studies (participants)	Main results and the estimated level of evidence according to authors	Risk of bias assessed by SBU
Casey JR 2004 [29]	To conduct a meta-analysis of randomized, controlled trials of cephalosporin versus penicillin treatment of group A β-hemolytic streptococcal (GABHS) tonsillopharyngitis in children. Children 0-18 years	35 RCT (7125)	Our findings clearly show that the likelihood of a bacteriologic and clinical cure of GABHS tonsillopharyngitis in children is significantly higher after 10 days of oral cephalosporin therapy with cephalexin, cefadroxil, cefuroxime, cefpodoxiine, cefprozil, cefixime, ceftibuten, or cefdinir than after 10 days of oral penicillin.	Moderate
Falagas ME 2008 [28]	To evaluate the effectiveness and safety of short- course antibiotic treatment of group A hemolytic streptococcal (GAS) tonsillopharyngitis. Children and adultsAny age	11 RCT 6 RCT children only (1258)	In trials involving mainly children or adolescents (aged <18 years), microbiological eradication rates were significantly lower for short-course than for long-course treatment.	Low
van Driel ML 2013 [30]	To assess the comparative efficacy of different antibiotics in patients with positive throat swabs for group A beta-aemolytic streptococci. To assess the comparative incidence of adverse effects and the risk-	17 RCT (5352)	Evidence is insufficient to show clinically meaningful differences between antibiotics for GABHS tonsillopharyngitis. Limited evidence in children suggests carbacephem is more effective for symptom resolution. Children experienced more adverse events with macrolides.	Low

First author Year Reference	Objectives Age	Number of included studies (participants)	Main results and the estimated level of evidence according to authors	Risk of bias assessed by SBU
	benefit of antibiotic treatment for streptococcal pharyngitis. Adults and Children Any Age			
Peritonsillar abscess				
No systematic reviews with low or moderate risk of bias found				
Infectious mononucleosis				
Rezk 2015 [31]	The objectives of the review were to determine the efficacy and safety of steroid therapy versus placebo, usual care or different drug therapies for symptom control in infectious mononucleosis. Children and adults Any age	7 RCT (362)	There is insufficient evidence to the efficacy of steroids for symptom control in infectious mononucleosis.	Low

First author Year Reference	Objectives Age	Number of included studies (participants)	Main results and the estimated level of evidence according to authors	Risk of bias assessed by SBU
Otitis media				
Coker TR 2010 [32]	To perform a systematic review on Acute otitis media (AOM) diagnosis, treatment, and the association of heptavalent pneumococcal conjugate vaccine (PENICILLIN V7) use with AOM microbiology. Children 4 weeks -18 years	Antibiotic treatment: 125	Antibiotics are modestly more effective than no treatment but cause adverse effects in 4% to 10% of children. Most antibiotics have comparable clinical success.	Moderate
Coleman C 2011 [38]	To determine the efficacy of decongestant and antihistamine therapy in children with AOM on outcomes of AOM resolution, symptom resolution, medication side effects, and complications of AOM. Children 0-18 years	15 RCT (2695)	This review found that for the medication subgroup of combined decongestant and antihistamines a very small statistical benefit in healing rates at two weeks was noted. Otherwise this review of trials found no other evidence to support the use of decongestants or antihistamines for AOM. Both medications have side effects including drowsiness and hyperactivity although only a small proportion of studies evaluated this	Moderate
Courter JD 2010 [33]	To assess the effectiveness of amoxicillin or amoxicillin/ calvulanate to that of macrolide antibiotics in the	10 RCT (2766)	**Moderate level of evidence:** Children treated with macrolides for AOM may be more likely to have clinical faliures.	Moderate

First author Year Reference	Objectives Age	Number of included studies (participants)	Main results and the estimated level of evidence according to authors	Risk of bias assessed by SBU
	treatment of children with AOM Children 6 months-15 years			
Foxlee R 2006 [39]	To assess the effectiveness of topical analgesia for AOM in adults and children. Children 3-18 years	5 RCT or quasi RCT (391)	**Limited evidence:** Evidence from five RCTs, only two of which addressed the most relevant question of primary effectiveness, provides limited evidence that ear drops are effective 30 minutes after administration in older children with AOM. Uncertainty exists as to the magnitude of this effect and more high-quality studies are needed.	Low
Kozyrskyj A 2010 [34]	To determine the effectiveness of a short course of antibiotics (less than seven days) in comparison to a long course of antibiotics (seven days or greater) for the treatment of AOM in children. Children 1 months-18 years	49 RCT (12045)	Treating children with a short course (less than seven days) of antibiotics, compared to treatment with a long course (seven days or greater) of antibiotics, increases the likelihood of treatment failure in the short term. No differences are seen one month later. The amount of gastrointestinal adverse events decreased with a shorter course of antibiotics.	Low
Shekelle PG 2010 [35]	Updates the findings on diagnosis and treatment of uncomplicated AOM, assesses the evidence for treatment of recurrent AOM, and assesses the impact of	72 primary studies both RCT and observational	Data were insufficient to draw conclusions about comparative effectiveness of different treatment strategies in subgroups of children with uncomplicated AOM. Adverse events were generally more frequent for amoxicillin-clavulanate than for cefdinir, ceftriaxone, or azithromycin.	Low

First author Year Reference	Objectives Age	Number of included studies (participants)	Main results and the estimated level of evidence according to authors	Risk of bias assessed by SBU
	the heptavalent pneumococcal conjugate (PENICILLIN V7) vaccine on the microbiology of AOM. Children			
Thanaviratananich S 2013 [37]	To compare the effectiveness of one or two daily doses with three or four daily doses of amoxicillin, with or without clavulanate, for the treatment of AOM in children; and to compare complication rates and adverse reactions. Children 0-12 years	5 RCT (1601)	The results showed that treating acute middle ear infection with either once/twice daily or three times daily amoxicillin, with or without clavulanate, has the same results using our outcome measures, including adverse events such as diarrhoea and skin reactions.	Low
Venekamp R 2015 [36]	To assess the effects of antibiotics for children with AOM. Children 1 month-15 years	13 RCT (3401) Comparing antibiotics against placebo 5 RCT (1149) comparing immediate antibiotics against expectant observation	**High quality of evidence:** We found that antibiotics were not very useful for most children with AOM; antibiotics did not decrease the number of children with pain at 24 hours (when 60% of children were better anyway), only slightly reduced the number of children with pain in the days following and did not reduce the number of children with late AOM recurrences and hearing loss (that can last several weeks) at three months compared with placebo.	Moderate

First author Year Reference	Objectives Age	Number of included studies (participants)	Main results and the estimated level of evidence according to authors	Risk of bias assessed by SBU
			However, antibiotics did slightly reduce the number of children with perforations of the eardrum and AOM episodes in the initially unaffected ear compared with placebo. **Moderate quality of evidence:** We found no difference between immediate antibiotics and expectant observational approaches in the number of children with pain three to seven days and 11 to 14 days after assessment. Furthermore, no differences in the number of children with hearing loss at four weeks, perforations of the eardrum and late AOM recurrences were observed between groups.	
Mastoiditis				
No systematic reviews with low or moderate risk of bias found				
Epiglottitis, laryngitis or tracheitis				
No systematic reviews with low or moderate risk of bias found				

First author Year Reference	Objectives Age	Number of included studies (participants)	Main results and the estimated level of evidence according to authors	Risk of bias assessed by SBU
Croup				
Bjornsson 2013 [40]	To assess the efficacy (measured by croup scores, rate of intubation and health care utilization such as rate of hospitalization) and safety (frequency and severity of side effects) of nebulized epinephrine versus placebo in children with croup, evaluated in an emergency department (ED) or hospital setting Children 0-18 years	8 RCT or quasi RCT (225 participants)	Compared to no medication, inhaled epinephrine improved croup symptoms in children at 30 minutes following treatment (three studies, 94children). This treatment effect disappeared two hours after treatment (one study, 20children). However, children's symptoms did not become worse than prior to treatment. Evidence does not favor racemic epinephrine or L-epinephrine, or IPPB over simple nebulization.	Low
Moraa 2013 [42]	To examine the effect of heliox on relieving symptoms and signs of croup, as determined by a croup score To examine the effect of croup on rates of admission or intubation (or both), through comparisons of heliox with placebo or any	3 RCT (91)	There is some evidence to suggest a short-term benefit of heliox inhalation in children with moderate to severe croup who have been administered oral or intramuscular dexamethasone.	Low

First author Year Reference	Objectives Age	Number of included studies (participants)	Main results and the estimated level of evidence according to authors	Risk of bias assessed by SBU
	active intervention(s) in children with croup. Children 0-18 years			
Russell 2011 [41]	To determine the effect of glucocorticoids for children with croup. Children 0-18 years	38 RCT (4299)	Glucocorticoids can reduce the swelling and make it easier for the child to breathe. We found that glucocorticoids can start improving croup in children within six hours (14 studies, 1031 children). The effect lasts at 12 h but not at 24 h (eight studies, 532 children), lessens the need for other drugs, and shortens hospital stays by 12 hours (eight studies, 795 children). There were no adverse events associated with glucocorticoids.	Low
Bronchiolitis				
Beggs 2014 [48]	To assess the effects of HFNC therapy compared with conventional respiratory support in the treatment of infants with bronchiolitis. Children 0-24 months	1 RCT (19)	There is insufficient evidence to determine the effectiveness of HFNC therapy for treating infants with bronchiolitis	Low
Brodlie 2015 [88]	To evaluate the evidence for the efficacy and safety of maintenance and intermittent leukotriene	5 RCT (3741)	**Moderate level of evidence:** In pre-school children with EVW, there is no evidence of benefit associated with maintenance or intermittent LTRA treatment, compared to placebo, for reducing the	Low

First author Year Reference	Objectives Age	Number of included studies (participants)	Main results and the estimated level of evidence according to authors	Risk of bias assessed by SBU
	receptor antagonists (LTRAs) in the management of Episodic viral wheeze (EVW) in children aged one to six years. Children 1-6 years		number of children with one or more viral-induced episodes requiring rescue oral corticosteroids, and little evidence of significant clinical benefit for other secondary outcomes.	
Chang 2015 [66]	In children with chronic (>4-weeks) wet/productive cough not related to bronchiectasis: (KQI) how effective are antibiotics in improving the resolution of cough? Children 0-14 years	3 systematic reviews 3 RCT 5 prospective studies 4 retrospective studies	There is high quality evidence that in children aged ≤ 14-years with chronic (>4- weeks duration) wet or productive cough, the use of appropriate antibiotics improves cough resolution. Combining data from RCTs (KQI), the number needed to treat for benefit was 3 (95%CI 2.0-4.3) in achieving cough resolution.	Moderate
Chen 2014 [50]	Assess the effectiveness and safety of the nebulized hypertonic saline treatment for acute bronchiolitis in infants. Children 6 weeks to 24 months	11 RCT (1070)	In conclusion, our meta-analysis demonstrates that nebulized HS therapy not only reduces the duration of hospitalization for acute bronchiolitis in infants, but also is beneficial in decreasing the rate of admission.	Moderate
Enriquez 2012 [47]	To determine the effect of nebulised rhDNase on the severity and duration of viral bronchiolitis in children	3 RCT (333)	The results based on the three included studies in this review did not support the use of nebulised rhDNase in children under 24 months of age hospitalised with acute bronchiolitis. In these patients, treatment did not shorten	Low

First author Year Reference	Objectives Age	Number of included studies (participants)	Main results and the estimated level of evidence according to authors	Risk of bias assessed by SBU
	younger than 24 months of age in the hospital setting. Children 0-24 month		the length of hospitalisation or improve clinical outcomes.	
Everard 2015 [51]	To assess the effectivness of nebulised hypertonic saline for infants hospitalised with primary acute bronchiolitis. Includes a health economic evaluation Children 0-2 years	18 RCT (2225)	Overall, the defining feature of this systematic review is its heterogeneity, which limits any attempt to synthesise the evidence.	Low
Farley 2014 [49]	To evaluate the effectiveness of antibiotics for bronchiolitis in children under two years of age compared to placebo or other interventions. Children 0-2 years	7 RCT (824)	This review did not find sufficient evidence to support the use of antibiotics for bronchiolitis, although research may be justified to identify a subgroup of patients who may benefit from antibiotics.	Low
Fernandes 2013 [45]	To review the efficacy and safety of systemic and inhaled glucocorticoids in children with acute viral bronchiolitis. Children 0-24months	17 RCT (2596)	**High or moderate level of evidence depending on outcome:** Current evidence does not support a clinically relevant effect of systemic or inhaled glucocorticoids on admissions or length of hospitalization. Combined dexamethasone and epinephrine may reduce outpatient	Low

First author Year Reference	Objectives Age	Number of included studies (participants)	Main results and the estimated level of evidence according to authors	Risk of bias assessed by SBU
			admissions, but results are exploratory and safety data limited.	
Gadomski 2014 [44]	To assess the effects of bronchodilators on clinical outcomes in infants with acute bronchiolitis. 0 to 12 months	30 RCT ,35 data sets (1992)	Bronchodilators such as albuterol or salbutamol do not improve oxygen saturation, do not reduce hospital admission after outpatient treatment, do not shorten the duration of hospitalization and do not reduce the time to resolution of illness at home. Given the adverse side effects and the expense associated with these treatments, bronchodilators are not effective in the routine management of bronchiolitis.	Low
Hartling 2011 [43]	To examine the efficacy and safety of epinephrine in children less than two with acute viral bronchiolitis. Children 0-2 years	19 studies (2256)	This review demonstrates the superiority of epinephrine compared to placebo for short-term outcomes for outpatients, particularly in the first 24 hours of care. Exploratory evidence from a single study suggests benefits of epinephrine and steroid combined for later time points. There is insufficient evidence to support the use of epinephrine for the treatment of bronchiolitis among children admitted to the hospital. There is no evidence of effectiveness for repeated dose and prolonged use of epinephrine and epinephrine and dexamethasone combined among inpatients.	Low
Jat 2012 [46]	Evaluate the efficacy of exogenous surfactant administration compared to placebo, no intervention or standard care in reducing mortality and the duration of ventilation in infants and	3 RCT (79)	Evidence is insufficient to establish the effectiveness of surfactant therapy for bronchiolitis in critically ill infants who require mechanical ventilation	Moderate

First author Year Reference	Objectives Age	Number of included studies (participants)	Main results and the estimated level of evidence according to authors	Risk of bias assessed by SBU
	children with bronchiolitis, requiring mechanical ventilation. Children 0-60 months			
Liet 2015 [90]	To assess heliox inhalation therapy in addition to standard medical care for acute bronchiolitis in infants with respiratory distress, as measured by clinical endpoints (in particular the rate of endotracheal intubation, the rate of emergency department discharge, the length of treatment for respiratory distress) and pulmonary function testing (mainly clinical respiratory scores). Children 0-2 years	7 RCT or quasi RCT (447)	**Both Low, moderate and high level of evidence:** Current evidence suggests that the addition of heliox therapy may significantly reduce a clinical score evaluating respiratory distress in the first hour after starting treatment in infants with acute RSV bronchiolitis. We noticed this beneficial effect regardless of which heliox inhalation protocol was used. Nevertheless, there was no reduction in the rate of intubation, in the rate of emergency department discharge, or in the length of treatment for respiratory distress.	Low
Maguire 2015 [53]	To access the effect of nebulised hypertonic	15 RCT (1922)	There is disparity between the overall combined effect on LoS as compared with the negative results from the largest and most precise trials. Together with high levels of heterogeneity, this means that neither	Moderate

First author Year Reference	Objectives Age	Number of included studies (participants)	Main results and the estimated level of evidence according to authors	Risk of bias assessed by SBU
	saline (HS) for infants hospitalised with primary acute bronchiolitis Children 0-2 Years		individual trials nor pooled estimates provide a firm evidence-base for routine use of HS in inpatient acute bronchiolitis.	
Umoren 2011 [87]	Evaluate the effect of steam inhalation or humidified oxygen to relieve respiratory distress and to evaluate adverse events. Children 0-3 years	1 RCT (156)	There is insufficient evidence to inform practice regarding using steam inhalation or mist therapy for acute bronchiolitis in children up to three years old.	Low
Zhang 2015 [52]	To assess the effects of nebulised hypertonic saline solution in infants with acute bronchiolitis. Children 0-24 months	24 trials (3209)	Nebulised hypertonic saline solution is a safe and potentially effective treatment in infants with acute bronchiolitis.	Low
Whooping cough				
Altunaiji 2007 [54]	To study the risks and benefits of antibiotic treatment of, and contact prophylaxis against, whooping cough.	Treatment 10 RCT and 1 quasi RCT Prophylaxis 2 RCT	We found that several antibiotic treatments were equally effective in eliminating the bacteria infecting patients, but they did not alter the clinical outcome. There was insufficient evidence to decide whether there is benefit for treating healthy contacts. Side effects were reported	Moderate

First author Year Reference	Objectives Age	Number of included studies (participants)	Main results and the estimated level of evidence according to authors	Risk of bias assessed by SBU
	Children and adults Any age		with antibiotics and they varied from one antibiotic to another.	
Wang 2014 [55]	Assess the effectiveness and safety of interventions to reduce the severity of paroxysmal cough in whooping cough in children and adults. Children and adults Any age	12 RCT or quasi RCT (578) Children: 10 RCT or quasi RCT (448)	Based on these results, antihistamines (one study, 49 participants), pertussis immunoglobulin (one study, 24 participants) and salbutamol (two studies, 42 participants) did not reduce the number of coughing bouts in patients with whooping cough. Neither pertussis immunoglobulin (one study, 46 participants) nor steroids (one study, 11 participants) decreased the length of time participants spent in hospital. There is insufficient evidence to draw conclusions about the effectiveness of interventions for the cough in whooping cough.	Low
Influenza				
Alves Galvao 2014 [83]	To assess the effectiveness and safety of amantadine and imantadine in preventing, treating and shortening the duration of influenza A in children and the elderly. Children and elderly	Amantadine and rimantadine 12 RCT or quasi RCT (2494) children (1586) Paracetamol Children 1 RCT or quasi RCT (69) Zanamivir	The effectiveness of both antivirals was limited to a benefit from rimantadine in the reduction of fever by day three of treatment in children. The quality of the evidence was moderate. The quality of the evidence combined with a lack of knowledge about the safety of amantadine and the limited benefits of rimantadine, do not indicate that amantadine and rimantadine compared to control (placebo or paracetamol) could be useful in preventing, treating and shortening the duration of influenza A in children and the elderly.	Low

First author Year Reference	Objectives Age	Number of included studies (participants)	Main results and the estimated level of evidence according to authors	Risk of bias assessed by SBU
		Children 0 RCT or quasi RCT		
Burch 2009 [56]	The objective of this review is to evaluate the clinical effectiveness (including adverse events) and cost-effectiveness of antivirals for the treatment of naturally acquired influenza. Children and adults Any age	29 RCT Zanamivir Children 1 RCT Oseltamivir Children 1 RCT	The results for the otherwise healthy children were more varied across the separate analyses due to more limited data being available.	Moderate
Jefferson 2014 [57]	To describe the potential benefits and harms of NIs for influenza in all age groups by reviewing all clinical study reports of published and unpublished randomised, placebo-controlled trials and regulatory comments Adults and children Any age	20 RCT oseltamivir (9623) 26 RCT zanamivir (14628)	We did not find any credible evidence that either oseltamivir or zanamivir reduce the risk of complications of influenza, particularly pneumonia, nor reduce risk of hospitalisation or death. Moreover, even in individuals at higher risk of complications, such as children with asthma or the elderly, we found no evidence of a beneficial effect for reducing risks of complications. The use of oseltamivir increases the risk of adverse effects, such as nausea, vomiting, psychiatric effects and renal events in adults and vomiting in children.	Low

First author Year Reference	Objectives Age	Number of included studies (participants)	Main results and the estimated level of evidence according to authors	Risk of bias assessed by SBU
Wang 2012 [58]	To assess the efficacy, safety and tolerability of neuraminidase inhibitors in the treatment and prevention of influenza in children. Children 0-12 years	6 RCT (2356, 1255 had laboratory-confirmed influenza)	Oseltamivir and zanamivir appear to have modest benefit in reducing duration of illness in children with influenza. Treatment with oseltamivir or zanamivir shortened the duration of illness in healthy children by about one day. Oseltamivir reduces the incidence of acute otitis media in children aged one to five years but is associated with a significantly increased risk of vomiting.	Low
Non specific lower respiratory tract infection or cough or bronchitis				
Anderson-James 2013 [63]	To evaluate the efficacy of inhaled corticosteroids (ICS) in reducing the severity of cough in children with subacute cough. Children 0-18 years	2 RCT (98)	There is currently no evidence to support the use of ICS for treatment of subacute cough in children.	Moderate
Becker 2015 [68]	To determine whether beta2-agonists improve acute bronchitis symptoms in people with no underlying pulmonary disease (such as asthma, COPD or pulmonary fibrosis).	7 RCT (552) Children only 2RCT (134)	**Moderate level of evidence:** There is no evidence to support the use of beta2-agonists in children with acute cough who do not have evidence of airflow restriction.	Low

First author Year Reference	Objectives Age	Number of included studies (participants)	Main results and the estimated level of evidence according to authors	Risk of bias assessed by SBU
	Adults and children over 2 years			
Brodlie 2015 [88]	To evaluate the evidence for the efficacy and safety of maintenance and intermittent leukotriene receptor antagonists (LTRAs) in the management of Episodic viral wheeze (EVW) in children aged one to six years. Children 1-6 years	5 RCT (3741)	**Moderate level of evidence:** In pre-school children with EVW, there is no evidence of benefit associated with maintenance or intermittent LTRA treatment, compared to placebo, for reducing the number of children with one or more viral-induced episodes requiring rescue oral corticosteroids, and little evidence of significant clinical benefit for other secondary outcomes.	Low
Chalumeau 2013 [65]	The objective was to assess the efficacy and safety and to establish a benefit-risk ratio of acetylcysteine and carbocysteine as symptomatic treatments for acute upper and lower RTIs in paediatric patients without chronic broncho-pulmonary disease. Children 0-18 years	Six RCTs on children (497)	The results of this review suggest actual but limited efficacy of acetylcysteine and carbocysteine (e.g. reduction of cough at day seven) and good overall safety (except for rare mild gastrointestinal side effects) among children older than two years of age	Low

First author Year Reference	Objectives Age	Number of included studies (participants)	Main results and the estimated level of evidence according to authors	Risk of bias assessed by SBU
Chang 2014 [59]	To evaluate the efficacy of over-the-counter (OTC) cough medications as an adjunct to antibiotics in children and adults with pneumonia. Children and adults Any age	4 RCT (224) Children only 1 RCT (120) (ambroxol or placebo)	There is insufficient evidence to decide whether OTC medications for cough associated with acute pneumonia are beneficial. This leaves only theoretical recommendations that OTC medications containing codeine and antihistamines should not be used in young children.	Low
Chang 2004 [69]	To detetermine the efficacy of inhaled cromoncs in the management of prolonged non-specific cough in children. Children 0-18 years	0 RCT	There is currently an absence of evidence to support the routine use of inhaled cromones for symptomatic control of non-specific cough in children.	Low
Everard 2005 [70]	To assess the effects of anti-cholinergic therapy in the treatment of wheezing infants. Children 0 – 2 years	6 RCT (311)	There is not enough evidence to support the uncritical use of anti-cholinergic therapy for wheezing infants, although parents using it at home were able to identify benefits.	Moderate
Mulholland 2009 [60]	To evaluate the efficacy of honey and lozenges in the management of children with chronic non-specific cough.	No studies fulfilled inclusion criteria.	This review was unable to provide any justifiable recommendation for or against honey and/or lozenges due to the lack of evidence.	Moderate

First author Year Reference	Objectives Age	Number of included studies (participants)	Main results and the estimated level of evidence according to authors	Risk of bias assessed by SBU
	Children >4 weeks			
Oduwole 2014 [62]	To evaluate the effectiveness of honey for acute cough in children in ambulatory settings. Children 1-18 years	3 RCT (568)	Moderate quality evidence showed that honey may be better than 'no treatment' in reducing the frequency of cough. High quality evidence also suggests that honey may be better than placebo for reduction of cough frequency. Moderate quality evidence suggests that honey does not differ significantly from dextromethorphan in reducing cough frequency. Low quality evidence suggests that honey may be slightly better than diphenhydramine in reducing cough frequency	Moderate
Rojas-Reyes 2014 [86]	To determine the effectiveness and safety of oxygen therapy and oxygen delivery methods in the treatment of lower respiratory tract infections and to define the indications for oxygen therapy in children. Children 3 months to 15 years	4 RCTs (479)	It appears that oxygen therapy given early in the course of pneumonia via nasal prongs at a flow rate of 1 to 2 L/min does not prevent children with severe pneumonia from developing hypoxaemia. However, the applicability of this evidence is limited as it comes from a small pilot trial. Nasal prongs and nasopharyngeal catheter are similar in effectiveness when used for children with acute LRTI. Nasal prongs are associated with less nasal obstruction. The use of a face mask and head box has been poorly studied and appears not to be superior to nasopharyngeal catheter in terms of effectiveness or safety when used in children with acute LRTI.	Low

First author Year Reference	Objectives Age	Number of included studies (participants)	Main results and the estimated level of evidence according to authors	Risk of bias assessed by SBU
Smith 2014 [61]	To assess the effects of oral OTC cough preparations for acute cough in children and adults in community settings. Children and adults Any age	29 RCTs(4835) 10 RCT in children only (1036)	Due to the small numbers of trials in each category, the limited quantitative data available and the marked differences between trials in terms of participants, interventions and outcome measurement, we felt that pooling of the results was inappropriate. There is no good evidence for or against the effectiveness of OTC medicines in acute cough. This should be taken into account when considering prescribing antihistamines and centrally active antitussive agents in children; drugs that are known to have the potential to cause serious harm.	Low
Tomerak 2005 [67]	To determine the effectiveness of inhaled Beta-2 agonists in non-specific chronic cough in children. Children 6-17 years	1 RCT (43)	Salbutamol was no different from placebo in reducing the frequency of cough measured objectively or scored subjectively.	Low
Tomerak 2005 [64]	To determine the efficacy of inhaled corticosteroids in non-specific cough in children. Children 0-16 years	2 RCT (123)	The review found that there is currently no good evidence to suggest that treatment with standard doses of inhaled corticosteroids will be beneficial.	Low

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Pneumonia				
Biondi 2014 [78]	Evaluate the effect of treating M. pneumoniae in children with community-acquired lower respiratory tract infection Children 0-18 years	17 RCT Included in meta-analysis 5 RCT (472)	Our systematic review provides insufficient evidence to support conclusions about the efficacy of macrolide treatment of CA-LRTI due to M. pneumoniae in children.	Moderate
Das 2012 [84]	To find the therapeutic role of zinc in children <5 years of age hospitalized for severe acute lower respiratory tract infection (ALRTI). Children 2 months to 5 years	7 RCT (1066)	To conclude, present data do not support therapeutic zinc supplementation in the management of children 2 months to < 5 years of age hospitalized for severe ALRTI.	Moderate
Das 2013 [72]	To assess the evidence regarding efficacy of oral amoxicillin compared to standard treatment for WHO-defined severe community acquired pneumonia in under-five children in developing country.	5 RCT (12364)	**Low quality of evidence:** Though oral amoxicillin is effective in treatment of severe CAP in under-five children in developing country, the evidence generated is of low-quality.	Low

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	Children 2 months to 5 years			
Gardiner 2015 [79]	To determine whether antibiotics are effective in the treatment of childhood LRTI secondary to *M. pneumoniae* infections acquired in the community. Children 0-18 years	7 RCT (1912)	**Low quality of evidence:** There is insufficient evidence to draw any specific conclusions about the efficacy of antibiotics for this condition in children.	Low
Haider 2011 [76]	To evaluate zinc supplementation, as an adjunct to antibiotics, in the treatment (clinical recovery) of pneumonia in children aged two to 59 months. Children 2-59 months	4 RCT (3267)	Evidence provided in this review is insufficient to recommend the use of zinc as an adjunct to standard antibiotic therapy for pneumonia in children aged two to 35 months.	Moderate
Haider 2008 [74]	To evaluate the efficacy of short-course versus long-course therapy with the same antibiotic for non-severe community-acquired pneumonia (CAP) in children aged 2 to 59 months.	4 RCT (6177)	This review of four studies involving 6177 children found that a short course (three days) of antibiotic therapy is equally as effective as a longer treatment (five days) for non-severe pneumonia. We also found that different durations of either amoxicillin or cotrimoxazole give similar results in terms of clinical cure, failure of the treatment and rate of relapse.	Moderate

First author Year Reference	Objectives Age	Number of included studies (participants)	Main results and the estimated level of evidence according to authors	Risk of bias assessed by SBU
	Children 2-59 months			
Ioannidou 2014 [80]	To evaluate the efficacy and safety of linezolid in children with infections caused by Gram-positive pathogens. Children	2 RCT (815)	The use of linezolid cannot be steadily supported from the results of the current meta-analysis. It appears to be slightly more effective than control antibiotic agents, but the difference was not significant, and the serious limitations present in this study restrict its use.	Low
Lassi 2015 [89]	To evaluate the efficacy of short-course (two to three days) versus long-course (five days) intravenous therapy with the same antibiotic for severe community-acquired pneumonia (CAP) in children aged two months to 59 months. Children two months- 59 months	0 RCT	We did not identify any RCTs comparing a short course (two to three days) of intravenous antibiotics compared to a long course (five days) for severe pneumonia in children aged two to 59 months.	Low
Lassi 2014 [75]	To evaluate the efficacy of antibiotic therapy versus no antibiotic therapy for children aged two to 59 months with WHO-defined nonsevere pneumonia and wheeze.	No RCT found	We do not currently have evidence to support or challenge the continued use of antibiotics for the treatment of non-severe pneumonia, as suggested by WHO guidelines.	Moderate

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	2-59 month			
Lassi 2014 [73]	To determine the most suitable antibiotic therapy (the choice of drug, duration, route and combination of antibiotics) for treating pneumonia in children specifically between 2 and 59 months of age in low and middle income-countries Children 2-59 months	22 RCT or quasi RCT (20 593)	Evidence from these trials showed a combination of penicillin/ampicillin and gentamicin to be effective for managing very severe pneumonia in children between 2 and 59 months of age, and oral amoxicillin to be equally efficacious, as other parenteral antibiotics for managing severe pneumonia in children of this particular age group. Oral amoxicillin was also found to be effective in nonsevere pneumonia as well. The review further found a short 3 day course of antibiotics to be equally beneficial as 5 day course for managing non-severe pneumonia	Moderate
Lodha 2010 [71]	To identify effective antibiotic drug therapies for community-acquired pneumonia (CAP) of varying severity in children by comparing various antibiotics. Children 0-18 years	29 RCT (14,188)	We found that for outpatient treatment of pneumonia, amoxycillin is an alternative treatment to co-trimoxazole (trimetoprin-sulfametoxazol). Oral amoxycillin in children with severe pneumonia without hypoxia (i.e. a decreased level of oxygen), and who are feeding well, may be effective. For very severe pneumonia, a combination of penicillin or ampicillin and gentamycin is more effective than chloramphenicol alone. Reports of adverse events were not available in many studies. Wherever information on adverse events was available, it did not differ between two drugs compared except that gastrointestinal side effects were more commonly reported with erythromycin compared to azithromycin.	Low

First author Year Reference	Objectives Age	Number of included studies (participants)	Main results and the estimated level of evidence according to authors	Risk of bias assessed by SBU
Punpanich 2012 [85]	To identify effective antimicrobial and/or adjunctive systemic therapy for pneumonia in HIV-infected and HIV-exposed, uninfected children. 3- to 59-month-old children	A sub-analysis of an RCT (163)	Insufficient evidence exists to identify effective antimicrobial treatment regimens for HIV-associated pneumonia in pediatric populations or confirm the beneficial effect of corticosteroid treatment for HIV-infected children with PCP.	Moderate
Wu 2005 [77]	To determine whether adjunctive vitamin A is effective in children diagnosed with non-measles pneumonia. Children 0-15 years	6 RCT (1740)	There was no significant reduction in mortality associated with pneumonia in children treated with vitamin A. The evidence does not suggest a significant reduction in mortality, nor an effect on the clinical course of pneumonia with vitamin A adjunctive treatment in children with non-measles pneumonia.	Low
Emphyema or Lung abscess				
Krenke 2010 [81]	Evaluate data from randomized controlled trials (RCTs) on the efficacy of using intrapleural fibrinolytic agents in the treatment of complicated parapneumonic effusions or empyema in children.	Four RCT (194)	There is little evidence that intrapleural fibrinolysis is more effective than normal saline in the local treatment of complicated parapneumonic effusions or empyema in children. There is no evidence that video-assisted thoracoscopic surgery is more effective than fibrinolytic treatment.	Moderate

First author Year Reference	Objectives Age	Number of included studies (participants)	Main results and the estimated level of evidence according to authors	Risk of bias assessed by SBU
	Children 1 month to 18 years			