Antibiotics for community-acquired pneumonia in children (Review)

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[Intervention Review]

Antibiotics for community-acquired pneumonia in children

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ABSTRACT

Background

Pneumonia caused by bacterial pathogens is the leading cause of mortality in children in low-income countries. Early administration of antibiotics improves outcomes.

Objectives

To identify effective antibiotic drug therapies for community-acquired pneumonia (CAP) of varying severity in children by comparing various antibiotics.

Search methods

We searched CENTRAL 2012, Issue 10; MEDLINE (1966 to October week 4, 2012); EMBASE (1990 to November 2012); CINAHL (2009 to November 2012); Web of Science (2009 to November 2012) and LILACS (2009 to November 2012).

Selection criteria

Randomised controlled trials (RCTs) in children of either sex, comparing at least two antibiotics for CAP within hospital or ambulatory (outpatient) settings.

Data collection and analysis

Two review authors independently extracted data from the full articles of selected studies.

Main results

We included 29 trials, which enrolled 14,188 children, comparing multiple antibiotics. None compared antibiotics with placebo.

Assessment of quality of study revealed that 5 out of 29 studies were double-blind and allocation concealment was adequate. Another 12 studies were unblinded but had adequate allocation concealment, classifying them as good quality studies. There was more than one study comparing co-trimoxazole with amoxycillin, oral amoxycillin with injectable penicillin/ampicillin and chloramphenicol with ampicillin/penicillin and studies were of good quality, suggesting the evidence for these comparisons was of high quality compared to other comparisons.

In ambulatory settings, for treatment of World Health Organization (WHO) defined non-severe CAP, amoxycillin compared with co-trimoxazole had similar failure rates (odds ratio (OR) 1.18, 95% confidence interval (CI) 0.91 to 1.51) and cure rates (OR 1.03, 95% CI 0.56 to 1.89). Three studies involved 3952 children.

In children with severe pneumonia without hypoxaemia, oral antibiotics (amoxycillin/co-trimoxazole) compared with injectable penicillin had similar failure rates (OR 0.84, 95% CI 0.56 to 1.24), hospitalisation rates (OR 1.13, 95% CI 0.38 to 3.34) and relapse rates (OR 1.28, 95% CI 0.34 to 4.82). Six studies involved 4331 children below 18 years of age.

In very severe CAP, death rates were higher in children receiving chloramphenicol compared to those receiving penicillin/ampicillin plus gentamicin (OR 1.25, 95% CI 0.76 to 2.07). One study involved 1116 children.

Authors' conclusions

For treatment of patients with CAP in ambulatory settings, amoxycillin is an alternative to co-trimoxazole. With limited data on other antibiotics, co-amoxyclavulanic acid and cefpodoxime may be alternative second-line drugs. Children with severe pneumonia without hypoxaemia can be treated with oral amoxycillin in an ambulatory setting. For children hospitalised with severe and very severe CAP, penicillin/ampicillin plus gentamycin is superior to chloramphenicol. The other alternative drugs for such patients are co-amoxyclavulanic acid and cefuroxime. Until more studies are available, these can be used as second-line therapies.

There is a need for more studies with radiographically confirmed pneumonia in larger patient populations and similar methodologies to compare newer antibiotics. Recommendations in this review are applicable to countries with high case fatalities due to pneumonia in children without underlying morbidities and where point of care tests for identification of aetiological agents for pneumonia are not available.

PLAIN LANGUAGE SUMMARY

Different antibiotics for community-acquired pneumonia in otherwise healthy children younger than 18 years of age in hospital and outpatient settings

Pneumonia is the leading cause of mortality in children under five years of age. Most cases of community-acquired pneumonia (CAP) in low-income countries are caused by bacteria. This systematic review identified 29 randomised controlled trials from many different countries enrolling 14,188 children and comparing antibiotics for treatment of CAP in children. Most were single studies only.

We found that for outpatient treatment of pneumonia, amoxycillin is an alternative treatment to co-trimoxazole. 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.

Limitations of this review are that only five studies met all the quality assessment criteria and for most comparisons of the efficacy of antibiotics only one or two studies were available.

BACKGROUND

Pneumonia is the leading single cause of mortality in children aged less than five years, with an estimated incidence of 0.29 and 0.05 episodes per child-year in low-income and high-income countries, respectively. It is estimated that a total of around 156 million new episodes occur each year and most of these occur in India (43 million), China (21 million), Pakistan (10 million) and Bangladesh, Indonesia and Nigeria (six million each) (Rudan 2008). In 2010, out of 7.6 million deaths in children below five years of age, 1.4 million (18.3%) deaths were due to pneumonia (Liu 2012). Reducing mortality due to pneumonia may help in reducing childhood and under five-year old mortality rates (Liu

2012). The commonest bacterial pathogens isolated in children under five years with pneumonia are *Streptococcus pneumoniae* (*S. pneumoniae*) (30% to 50%) and *Haemophilus influenzae* (*H. influenzae*) (10% to 30%) (Falade 2011), and 50% of deaths due to pneumonia in this age group are attributed to these two organisms (Shann 1995). To reduce the infant and under five-year child mortality rate, it is important to reduce mortality due to pneumonia by appropriate intervention in the form of antibiotics. Selection of first-line antibiotics for empirical treatment of pneumonia is crucial for office practice as well as public health.

Description of the condition

Pneumonia is defined as an infection of the lung parenchyma (alveoli) by microbial agents. It is difficult to identify the causative organism in most cases of pneumonia. The methods used for identification of the aetiologic agents include blood culture, lung puncture, nasopharyngeal aspiration and immune assays of blood and urine tests. Lung puncture is an invasive procedure associated with significant morbidity and hence cannot be performed routinely in most cases. The yield from blood cultures is too low (5% to 15% for bacterial pathogens) to be relied upon (MacCracken 2000). There are few studies that document the aetiology of pneumonia in children below five years of age from low-income countries. Most studies carried out blood cultures for bacterial aetiology of pneumonia. Some studies carried out nasopharyngeal aspirates and identification of virus and atypical organisms. A review of 14 studies involving 1096 lung aspirates taken from hospitalised children prior to administration of antibiotics reported bacterial pathogens in 62% of cases (Berman 1990). In 27% of patients, the common bacterial pathogens identified were *Streptococcus pneumoniae* (*S. pneumoniae*) and *Haemophilus influenzae* (*H. influenzae*) (Berman 1990). Studies using nasopharyngeal aspirates for identification of viral agents suggest that about 40% of pneumonia in children below five years of age is caused by viral agents, with the commonest viral pathogen being respiratory syncytial virus (Maitreyi 2000). In infants under three months of age, common pathogens include *S. pneumoniae*,*H. influenzae*, gram-negative bacilli and *Staphylococcus* (WHOYISG 1999). The causative organisms are different in high-income countries and include more viral and atypical organisms (Gendrel 1997; Ishiwada 1993; Numazaki 2004; Wubbel 1999). Therefore, treatment regimens may be different in high-income and low-income countries. The reference standard for diagnosis of pneumonia is X-ray film of the chest. However, it does not have the necessary sensitivity and specificity to identify aetiological agents (i e. bacterial or viral). Obtaining an X-ray film in all suspected pneumonia cases may not be cost-effective as it does not affect the outcome. Therefore, diagnosis of pneumonia is based on clinical criteria. Treatment of pneumonia includes administration of antibiotics, either in hospital or in an ambulatory setting. Administration of antibiotics for all clinically diagnosed pneumonia may lead to antibiotic prescription even for those cases caused by viral infection. Since clinical or radiological findings cannot differentiate viral or bacterial pneumonia and due to the absence of point of care tests for routine use, empirical treatment with antibiotics in countries with high case fatalities due to pneumonia is recommended by the World health Organization (WHO).

Description of the intervention

Administration of appropriate antibiotics at an early stage of pneumonia improves the outcome of the illness, particularly when the causative agent is bacterial. The WHO has provided guidelines for early diagnosis and assessment of the severity of pneumonia on the basis of clinical features (WHOYISG 1999) and suggests administration of co-trimoxazole as a first-line drug. The commonly used antibiotics for community-acquired pneumonia (CAP) include co-trimoxazole, amoxycillin, oral cephalosporins and macrolide drugs. Despite evidence of rising bacterial resistance to co-trimoxazole (IBIS 1999; Timothy 1993), studies conducted in the same time period showed good clinical efficacy of oral co-trimoxazole for non-severe pneumonia (Awasthi 2008; Rasmussen 1997; Straus 1998). However, one study reported a doubling of clinical failure rates with co-trimoxazole treatment when compared to treatment with amoxycillin in severe and radiologically confirmed pneumonia (Straus 1998). A meta-analysis of all the trials on pneumonia based on the case-management approach proposed by the WHO (identification of pneumonia on clinical symptoms/signs and administration of empirical antimicrobial agents) has found a reduction in overall mortality as well as pneumonia-related mortality (Sazawal 2003). Various antibiotics have been used for varying severities of pneumonia. Antibiotics are administered in hospital or in ambulatory settings.

How the intervention might work

Pneumonia is the leading cause of mortality in children below five years of age. It is not easy to identify aetiological agents in children with pneumonia. To meet the public health goal of reducing child mortality due to pneumonia, empirical antibiotic administration is relied upon in most instances. This is necessary in view of the inability of most commonly available laboratory tests to identify causative pathogens.

Why it is important to do this review

Empirical antibiotic administration is the mainstay of treatment of pneumonia in children. Administration of the most appropriate antibiotic as the first-line treatment may improve the outcome of pneumonia. Many antibiotics are prescribed to treat pneumonia. Therefore, it is important to know which works best for pneumonia in children. The last review of all available randomised controlled trials (RCTs) on antibiotics used for pneumonia in children

was published in 2010 (Kabra 2010). Since then, five new trials (Ambroggio 2012; Bari 2011; Nogeova 1997; Ribeiro 2011; Soofi 2012) have been published. Additional information on the epidemiology of pneumonia in children has been published. Therefore, we have updated this review and included new data and also carried out a meta-analysis on the treatment of severe pneumonia with oral antibiotics.

OBJECTIVES

To identify effective antibiotic drug therapies for community-acquired pneumonia (CAP) of varying severity in children by comparing various antibiotics.

METHODS

Criteria for considering studies for this review

Types of studies

Randomised controlled trials (RCTs) comparing antibiotics for CAP in children. We considered only those studies using the case definition of pneumonia (as given by the WHO) or radiologically confirmed pneumonia in this review.

Types of participants

We included children under 18 years of age with CAP treated in a hospital or community setting. We excluded studies describing pneumonia post-hospitalisation in immunocompromised patients (for example, following surgical procedures) or patients with underlying illnesses like congenital heart disease or those in an immune deficient state.

Types of interventions

We compared any intervention with antibiotics (administered by intravenous route, intramuscular route or orally) with another antibiotic for the treatment of CAP.

Types of outcome measures

Primary outcomes

1. Clinical cure. The definition of clinical cure is symptomatic and involves clinical recovery by the end of treatment.

2. Treatment failure rates. The definition of treatment failure is the presence of any of the following: development of chest indrawing, convulsions, drowsiness or inability to drink at any time, respiratory rate above the age-specific cut-off point on completion of treatment, or oxygen saturation of less than 90% (measured by pulse oximetry) after completion of the treatment. Loss to follow-up or withdrawal from the study at any time after recruitment indicated failure in the analysis.

Secondary outcomes

The clinically relevant outcome measures were as follows.

1. Relapse rate: defined as children declared 'cured', but developing recurrence of disease at follow-up in a defined period.
2. Hospitalisation rate (in outpatient studies only): defined as the need for hospitalisation in children who were getting treatment or in an ambulatory (outpatient) setting.
3. Length of hospital stay: duration of total hospital stay (from day of admission to discharge) in days.
4. Need for change in antibiotics: children required change in antibiotics from the primary regimen.
5. Additional interventions used: any additional intervention in the form of mechanical ventilation, steroids, vaso-pressure agents, etc.
6. Mortality rate.

Search methods for identification of studies

We retrieved studies through a search strategy which included cross-referencing. We checked the cross-references of all the studies manually.

Electronic searches

For this update we searched the Cochrane Central Register of Controlled Trials (CENTRAL) 2012, Issue 10, part of *The Cochrane Library,* www.thecochranelibrary.com (accessed 7 November 2012); MEDLINE (September 2009 to October week 4, 2012); EMBASE (September 2009 to November 2012); CINAHL (2009 to November 2012); Web of Science (2009 to November 2012) and LILACS (2009 to November 2012). Details of the previous search are in Appendix 1.

To search CENTRAL and MEDLINE we combined the following search strategy with the validated search strategy for identifying child studies developed by Boluyt (Boluyt 2008). We used the Cochrane Highly Sensitive Search Strategy to identify randomised trials in MEDLINE: sensitivity- and precision-maximising version (2008 revision); Ovid format (Lefebvre 2011). We adapted the search strategy to search EMBASE (Appendix 2), CINAHL (Appendix 3), Web of Science (Appendix 4) and LILACS (Appendix 5).

MEDLINE (Ovid)

1 exp Pneumonia/
2 pneumon*.tw.
3 bronchopneumon*.tw.
4 pleuropneumon*.tw.
5 cap.tw.
6 or/1-5
7 exp Anti-Bacterial Agents/
8 antibiotic*.tw.
9 (amoxycillin* or amoxycillin* or ampicillin* or azithromycin* or augmentin* or benzylpenicillin* or b-lactam* or beta-lactam* or clarithromycin* or ceftriaxone* or cefuroxime* or cotrimoxazole* or co-trimoxazole* or co-amoxyclavulanic acid or cefotaxime* or ceftriaxone* or ceftrioxone* or cefditoren* or chloramphenicol* or cefpodioxime* or cephradine* or cephalexin* or cefaclor* or cefetamet* or cephalosporin* or erythromycin* or gentamicin* or gentamycin* or levofloxacin* or macrolide* or minocyclin* or moxifloxacin* or penicillin* or quinolone* or roxithromycin* or sulphamethoxazole* or sulfamethoxazole* or tetracyclin* or trimethoprim*).tw,nm. (248104)
10 or/7-9
11 6 and 10

Searching other resources

We also searched bibliographies of selected articles to identify any additional trials not recovered by the electronic searches.

Data collection and analysis

Selection of studies

Two review authors (SKK, RL) independently selected potentially relevant studies based on their title and abstract. We retrieved the complete texts of these studies electronically or by contacting the trial authors. Two review authors (SKK, RL) independently reviewed the results for inclusion.

Data extraction and management

A person who was not involved in the review gave all relevant studies a serial number to mask the authors' names and institutions, the location of the study, reference lists and any other potential identifiers. Two review authors (SKK, RL) independently reviewed the results for inclusion in the analysis. We resolved differences about study quality through discussion. We recorded data on a pre-structured data extraction form. We assessed publication bias using The Cochrane Collaboration's 'Risk of bias' tool (Higgins 2011). We included data from cluster-RCTs after adjustment for the design effect. We calculated the design effect by 1+(M-1) ICC; where M is the average cluster size and ICC is the intracluster correlation coefficient (Higgins 2011).

Before combining the studies for each of the outcome variables, we carried out an assessment of heterogeneity using Review Manager (RevMan 2012) software. We performed a sensitivity analysis to check the importance of each study in order to see the effect of inclusion and exclusion criteria. We computed both the effect size and summary measures with 95% confidence intervals (CIs) using RevMan 2012. We used a random-effects model to combine the study results for all the outcome variables.

We collected data on the primary outcome (cure rate/failure rate) and secondary outcomes (relapse rate, rate of hospitalisation and complications, need for change in antibiotics, need for additional interventions and mortality). When available, we also recorded additional data on potential confounders such as prior antibiotic therapy and nutritional status.

We did multiple analyses, firstly on studies comparing the same antibiotics. We also attempted to perform indirect comparisons of various drugs when studies with direct comparisons were not available. For example, we compared antibiotics A and C when a comparison of antibiotics A and B was available and likewise a separate comparison between antibiotics B and C. We only did this type of comparison if the inclusion and exclusion criteria of these studies, the dose and duration of the common intervention (antibiotic B), baseline characteristics and the outcomes assessed were similar (Bucher 1997).

Assessment of risk of bias in included studies

We assessed risk of bias in all included studies using The Cochrane Collaboration's 'Risk of bias' tool (Higgins 2011).

1. Sequence generation: assessed as yes, no or unclear
Yes: when the study described the method used to generate the allocation sequence in sufficient detail.
No: sequence not generated.
Unclear: when it was not described or incompletely described.

2. Allocation concealment: assessed as yes, no or unclear
Yes: when the study described the method used to conceal the allocation sequence in sufficient detail.
No: described details where allocation concealment was not done.
Unclear: when it was not described or incompletely described.

3. Blinding of participants, personnel and outcome assessors: assessed as yes, no or unclear
Yes: when it was a double-blind study.
No: when it was an unblinded study.
Unclear: not clearly described.

4. *Incomplete outcome data: assessed as yes, unclear*
Yes: describe the completeness of outcome data for each main outcome, including attrition and exclusions from the analysis.
Unclear: either not described or incompletely described.

5. Free of selective outcome reporting: assessed as yes, no or unclear

Yes: results of study free of selective reporting. Details of all the participants enrolled in the study are included in the paper.
No: details of all the enrolled participants not given in the paper.
Unclear: details of all the enrolled participants incompletely described.

6. Other sources of bias

Among the other sources of potential bias considered was funding agencies and their role in the study. We recorded funding agencies as governmental agencies, universities and research organisations or pharmaceutical companies. We considered studies supported by pharmaceutical companies to be unclear unless the study defined the role of the pharmaceutical companies. We also considered studies not mentioning the source of funding as unclear under this heading.

Measures of treatment effect

The main outcome variables were failure rates or cure rates. Treatment effect in the form of failure rates was calculated by making 2 x 2 tables and calculating odds ratios (ORs) for each comparison. We expressed the results as ORs with 95% confidence intervals (CIs).

Unit of analysis issues

All except one study were RCTs. One was a cluster-RCT (Awasthi 2008). We included data from cluster-RCTs after adjustment for the design effect. We calculated the design effect by 1+(M-1) ICC; where M is the average cluster size and ICC is the intracluster correlation coefficient (Higgins 2011).

Dealing with missing data

We contacted trial authors for missing data. However, we could not retrieve any missing data from any of the studies. We excluded two new studies in this update (Bari 2011; Soofi 2012).

Assessment of heterogeneity

For each of the outcome variables, we carried out an assessment of heterogeneity with Breslow's test of homogeneity in accordance with the *Cochrane Handbook for Systematic Reviews of Interventions* (Higgins 2011).

Assessment of reporting biases

Before combining the study results, we checked for publication bias using a funnel plot. For each of the outcome variables (cure rate, failure rate, relapse rate, rate of hospitalisation, the complications needed for change in antibiotics and mortality rate) we used a 2 x 2 table for each study and performed Breslow's test of homogeneity to determine variation in study results.

Data synthesis

For each comparison, we prepared 2 x 2 tables. We calculated ORs and 95% CIs. We used a random-effects model for all the comparisons.

Subgroup analysis and investigation of heterogeneity

In this review we included RCTs that compared two antibiotics in children with pneumonia. We performed a subgroup analysis of children with radiologically confirmed pneumonia. For each of the outcome variables, we carried out an assessment of heterogeneity with Breslow's test of homogeneity using RevMan 2012 (see Data collection and analysis).

Sensitivity analysis

Most comparisons were for two to three trials. If there was significant heterogeneity, we conducted a sensitivity analysis. We conducted multiple analyses after excluding one study data at a time.

RESULTS

Description of studies

Results of the search

Two review authors (SKK, RL) screened the article titles. We shortlisted 49 trials as potential RCTs to be included and we attempted to collect the full-text articles. We obtained the full text for 48 trials. A third person who was not involved in the review masked the papers for identifiers. Two review authors (SKK, RL) independently extracted data by using a pre-designed data extraction form; the extracted data matched completely.

Included studies

We identified 29 studies for inclusion, with the following comparisons.

- Azithromycin with erythromycin: four studies (Harris 1998; Kogan 2003; Roord 1996; Wubbel 1999), involving 457 children aged two months to 16 years.
- Clarithromycin with erythromycin: one study (Block 1995), involving 357 children below 15 years of age with clinical or radiographically confirmed pneumonia treated in an ambulatory setting.
- Co-trimoxazole with amoxycillin: three studies (Awasthi 2008; CATCHUP 2002; Straus 1998), involving 2347 children aged two months to 59 months. Total numbers of events and

effective sample size in one cluster-randomised controlled trial (Awasthi 2008) were calculated after adjusting for the design effect.

- Co-trimoxazole with procaine penicillin: two studies (Keeley 1990; Sidal 1994), involving 723 children aged three months to 12 years.
- Chloramphenicol with penicillin and gentamycin together: one study (Duke 2002), involving 1116 children aged one month to five years.
- Single-dose benzathine penicillin with procaine penicillin: two studies (Camargos 1997; Sidal 1994), involving 176 children between two and 12 years of age in one study (Sidal 1994) and 105 children aged between three months to 14 years in the other similar study (Camargos 1997).
- Amoxycillin with procaine penicillin: one study (Tsarouhas 1998), involving 170 children aged six months to 18 years.
- Ampicillin with chloramphenicol plus penicillin: one study (Deivanayagam 1996), involving 115 children aged five months to four years.
- Co-trimoxazole with single-dose procaine penicillin followed by oral ampicillin: one study (Campbell 1988), involving 134 children aged below five years.
- Penicillin with amoxycillin: two studies (Addo-Yobo 2004; Atkinson 2007), involving 1905 children aged three months to 59 months.
- Co-trimoxazole with chloramphenicol: one study (Mulholland 1995), involving 111 children aged under five years.
- Cefpodoxime with co-amoxyclavulanic acid: one study (Klein 1995), involving 348 children aged three months to 11.5 years.
- Azithromycin with amoxycillin: one study (Kogan 2003), involving 47 children aged one month to 14 years.
- Amoxycillin with co-amoxyclavulanic acid: one study (Jibril 1989), involving 100 children aged two months to 12 years.
- Chloramphenicol in addition to penicillin with ceftriaxone: one study (Cetinkaya 2004), involving 97 children aged between two to 24 months admitted to hospital with severe pneumonia.
- Levofloxacin and comparator (co-amoxyclavulanic acid or ceftriaxone): one study (Bradley 2007) involving 709 children aged 0.5 to 16 years of age with CAP treated in hospital or in an ambulatory setting.
- Parenteral ampicillin followed by oral amoxycillin with home-based oral amoxycillin: one study (Hazir 2008) involving 2037 children between three months to 59 months of age with WHO-defined severe pneumonia.
- Chloramphenicol with ampicillin and gentamicin: one study (Asghar 2008), involving 958 children between two to 59 months with very severe pneumonia.
- Penicillin and gentamicin with co-amoxyclavulanic acid (Bansal 2006), involving 71 children with severe and very severe pneumonia between two months to 59 months of age.
- Co-amoxyclavulanic acid with cefuroxime or clarithromycin: one study (Aurangzeb 2003), involving 126 children between two to 72 months of age.
- Ceftibuten with cefuroxime axetil: one study involving 140 children between one to 12 years of age with CAP that was radiographically confirmed (Nogeova 1997).
- Oxacillin/ceftriaxone with co-amoxyclavulanic acid: one study involving 104 children between age two months to five years with very severe pneumonia (Ribeiro 2011).

Excluded studies

We excluded 20 trials.

- Four studies were carried out in adult participants (Bonvehi 2003; Fogarty 2002; Higuera 1996; van Zyl 2002).
- Three studies included children with severe infections or sepsis (Haffejee 1984; Mouallem 1976; Vuori-Holopaine 2000).
- One study did not provide separate data for children (Sanchez 1998).
- Two cluster-RCTs (Bari 2011; Soofi 2012) compared oral amoxycillin or standard treatment for severe pneumonia in children below five years of age. Patients on conventional treatment received either intravenous antibiotics in hospital or oral medications at home or no treatment. Results were available as oral treatment with amoxycillin in comparison with standard treatment (referral and antibiotics). Separate data on patients who received intravenous antibiotics were not available and data could not be obtained from the trial authors.
- Three studies were not RCTs (Agostoni 1988; Ambroggio 2012; Paupe 1992).
- Three studies only compared the duration of antibiotic use (Hasali 2005; Peltola 2001; Ruhrmann 1982); of these, one study (Hasali 2005) also did not report the outcome in the form of cure or failure rates.
- One studied only sequential antibiotic use (Al-Eiden 1999).
- One compared azithromycin with symptomatic treatment for recurrent respiratory tract infection only (Esposito 2005).
- The full-text article could not be obtained for one study (Lu 2006).
- One study (Lee 2008) was excluded because the outcome was not in the form of cure or failure rates.

Risk of bias in included studies

The overall risk of bias is presented graphically and summarised (Figure 1; Figure 2)

Figure 1. 'Risk of bias' summary: review authors' judgements about each risk of bias item for each included study.

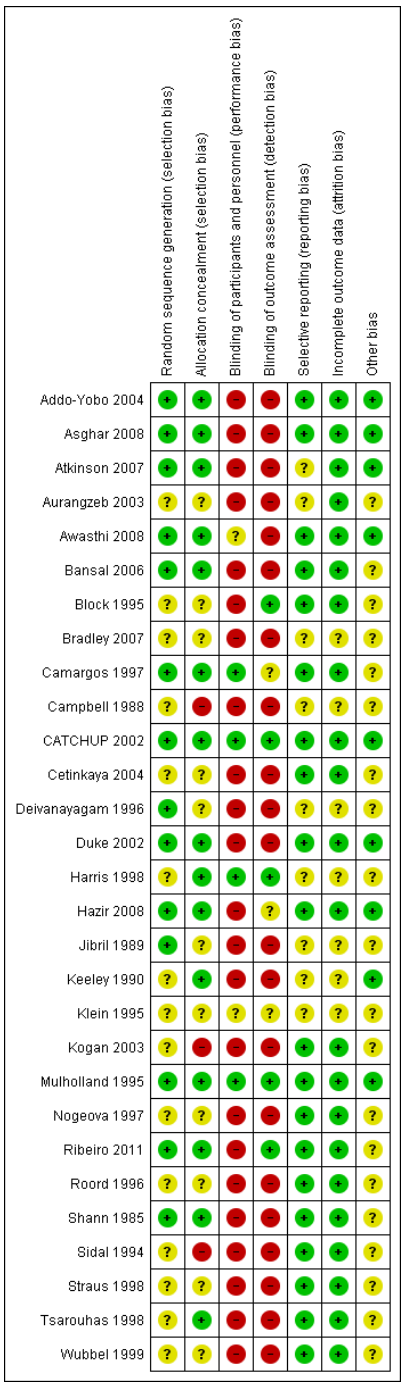
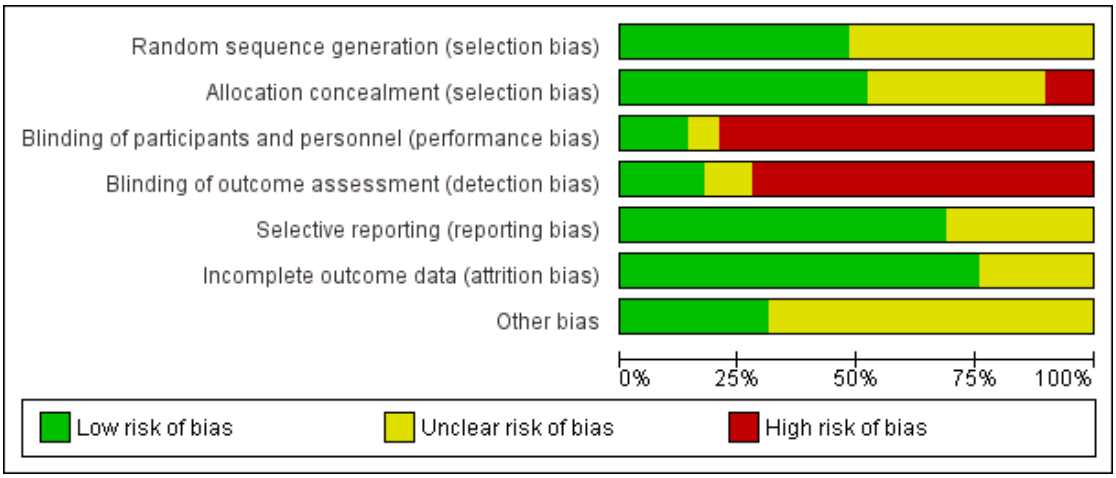


Figure 2. 'Risk of bias' graph: review authors' judgements about each risk of bias item presented as percentages across all included studies.



Details of sequence generation were described in 17 studies (Addo-Yobo 2004; Asghar 2008; Atkinson 2007; Awasthi 2008; Bansal 2006; Camargos 1997; CATCHUP 2002; Cetinkaya 2004; Deivanayagam 1996; Duke 2002; Hazir 2008; Jibril 1989; Keeley 1990; Mulholland 1995; Ribeiro 2011; Roord 1996; Shann 1985), were not clear in 10 studies (Aurangzeb 2003; Block 1995; Bradley 2007; Campbell 1988; Harris 1998; Klein 1995; Nogeova 1997; Straus 1998; Tsarouhas 1998; Wubbel 1999) and sequence was not generated in two studies (Kogan 2003; Sidal 1994).

Allocation

Allocation concealment was adequate in 17 studies (Addo-Yobo 2004; Asghar 2008; Atkinson 2007; Awasthi 2008; Bansal 2006; Camargos 1997; CATCHUP 2002; Cetinkaya 2004; Deivanayagam 1996; Duke 2002; Harris 1998; Hazir 2008; Keeley 1990; Mulholland 1995; Ribeiro 2011; Shann 1985; Tsarouhas 1998), it was unclear in nine studies (Aurangzeb 2003; Block 1995; Bradley 2007; Campbell 1988; Jibril 1989; Klein 1995; Nogeova 1997; Straus 1998; Wubbel 1999) and no concealment was done in three studies (Kogan 2003; Roord 1996; Sidal 1994).

Blinding

Only five studies (CATCHUP 2002; Cetinkaya 2004; Harris 1998; Mulholland 1995; Straus 1998) were double-blinded. The rest of the studies were unblinded.

Incomplete outcome data

Data were fully detailed in 20 studies (Addo-Yobo 2004; Asghar 2008; Atkinson 2007; Aurangzeb 2003; Awasthi 2008; Bansal 2006; Block 1995; Camargos 1997; CATCHUP 2002; Cetinkaya 2004; Duke 2002; Hazir 2008; Kogan 2003; Mulholland 1995; Nogeova 1997; Ribeiro 2011; Roord 1996; Straus 1998; Tsarouhas 1998; Wubbel 1999) and in the remaining studies details of attrition and exclusions from the analysis were unavailable.

Selective reporting

Selective reporting of data was unclear in 12 studies (Atkinson 2007; Aurangzeb 2003; Bradley 2007; Campbell 1988; Deivanayagam 1996; Harris 1998; Jibril 1989; Keeley 1990; Klein 1995; Shann 1985; Sidal 1994; Wubbel 1999). The rest of the studies were free from selective reporting.

Other potential sources of bias

The source of funding was not mentioned in 15 studies (Aurangzeb 2003; Bansal 2006; Camargos 1997; Campbell 1988; Cetinkaya 2004; Deivanayagam 1996; Jibril 1989; Klein 1995; Kogan 2003; Nogeova 1997; Ribeiro 2011; Shann 1985; Sidal 1994; Straus 1998; Tsarouhas 1998). Five studies were funded by pharmaceutical companies (Block 1995; Bradley 2007; Harris 1998; Roord 1996; Wubbel 1999). Eight studies were supported by the WHO,

Medical Research Council or universities (Addo-Yobo 2004; Asghar 2008; Atkinson 2007; Awasthi 2008; Duke 2002; Hazir 2008; Keeley 1990; Mulholland 1995). One study (CATCHUP 2002) was supported by the WHO in addition to pharmaceutical companies. Information on clearance by Ethics Committees or Institutional Review Boards was available for all except four studies (Aurangzeb 2003; Jibril 1989; Keeley 1990; Sidal 1994).

Effects of interventions

Studies comparing ambulatory setting treatment of non-severe pneumonia

Azithromycin versus erythromycin (Analysis 1)

Four studies (Harris 1998; Kogan 2003; Roord 1996; Wubbel 1999) compared erythromycin with azithromycin and enrolled 623 children. One study (Harris 1998) was double-blinded with adequate allocation concealment and three studies (Kogan 2003; Roord 1996; Wubbel 1999) were unblinded and did not have adequate allocation concealment. Information on the presence of wheezing was available in two studies (Harris 1998; Kogan 2003): 104 out of 318 (33%) children experienced wheezing in the azithromycin group, while 62 out of 161 (39%) in the erythromycin group experienced wheezing. The failure rates in the azithromycin and erythromycin groups were six out of 236 (2.5%) and six out of 156 (3.8%), respectively (OR 0.73, 95% CI 0.18 to 2.89) (Analysis 1.5) There were no significant side effects in either group. Three studies reported data on aetiologic organisms separately for each of the two treatment groups (Harris 1998; Kogan 2003; Roord 1996); there were 234 organisms identified in the azithromycin group and 135 in the erythromycin group (Roord 1996). The distribution of different organisms was similar in the two groups. There were 24 organisms identified in the fourth study (Wubbel 1999) in 59 participants tested.

Clarithromycin versus erythromycin (Analysis 2)

One study (Block 1995) compared erythromycin and clarithromycin; 234 children below 15 years of age with clinical or radiographically confirmed pneumonia were treated in an ambulatory setting. The trial was single-blinded and allocation concealment was unclear. The following outcomes were similar between the two groups: cure rate (OR 1.61, 95% CI 0.84 to 3.08) (Analysis 2.2), clinical success rate (OR 1.92, 95% CI 0.45 to 8.23) (Analysis 2.3), failure rate (OR 0.52, 95% CI 0.12 to 2.23) (Analysis 2.4) , relapse rate (OR 0.17, 95% CI 0.02 to 1.45) (Analysis 2.5) and adverse events (OR 1.07, 95% CI 0.6 to 1.90) (Analysis 2.9). Resolution of pneumonia (diagnosed radiologically) was more frequent in the clarithromycin group as compared to the erythromycin group (OR 2.51, 95% CI 1.02 to 6.16) (Analysis 2.6). However, there were no differences in the radiologic improvement rates (OR 3.55, 95% CI 0.7 to 18.04) (Analysis 2.7) or radiologic failure rates (OR 0.34, 95% CI 0.06 to 1.80) (,Analysis 2.8) both of which were established with radiological evidence.

Azithromycin versus co-amoxyclavulanic acid (Analysis 3)

Two studies (Harris 1998; Wubbel 1999) compared these two drugs in 283 children below five years of age. One study (Harris 1998) was double-blinded and allocation concealment was adequate while the other study (Wubbel 1999) was unblinded with inadequate allocation concealment. The cure rates (available for one study) (OR 1.02, 95% CI 0.54 to 1.95) (Analysis 3.1), failure rates (available for both studies) (OR 1.21, 95% CI 0.42 to 3.53) (Analysis 3.2) and improvement rates (OR 0.85, 95% CI 0.43 to 1.71) (Analysis 3.3) were similar in the two groups. There were fewer side effects reported in the azithromycin group (OR 0.15, 95% CI 0.04 to 0.61) (Analysis 3.4). The organisms isolated were *S. pneumoniae* in 28 children, *H. influenzae* in one, *Mycoplasma pneumoniae* (*M. pneumoniae*) in 36 and *Chlamydia pneumoniae* (*C. pneumoniae*) in 20. The separate data for isolation of organisms in the two groups were available in one study only (Harris 1998). The organisms isolated in this study (Harris 1998) were *S. pneumoniae* and *H. influenza*e in one patient each in the azithromycin group. Investigations for mycoplasma were positive in 21 out of the 129 children (16%) tested in the azithromycin group and nine out of the 66 children (14%) tested in the co-amoxyclavulanic acid group. Investigations for *C. pneumoniae* were positive in 13 out of the 129 children (10%) tested in the azithromycin group and four out of the 66 children (6%) tested in the co-amoxyclavulanic acid group.

Azithromycin versus amoxycillin (Analysis 4)

One study involving 47 children aged between one month and 14 years with classical pneumonia compared these two drugs (Kogan 2003). Children treated with azithromycin were older than those treated with amoxycillin (OR 58.1, 95% CI 35.59, 80.61). The study was unblinded and allocation concealment was also inadequate. All children recovered at the end of treatment in both the groups. There were 19 organisms identified in the 47 children tested (10 in the azithromycin group and nine in the amoxycillin group). The identification rates were similar in the two groups. Organisms included *M. pneumoniae* (in five and three children for the azithromycin and amoxycillin groups, respectively), *S. pneumoniae* (in four and three, respectively) and others (in one and three, respectively).

Amoxycillin versus procaine penicillin (Analysis 5)

One study involving 170 children aged six months to 18 years was identified (Tsarouhas 1998). The study was unblinded but allocation concealment was adequate. The age distribution in the

two groups was comparable. The failure rates were similar in the two groups (OR 0.75, 95% CI 0.17 to 3.25) (Analysis 5.2).

Co-amoxyclavulanic acid versus amoxycillin (Analysis 6)

One study involved 100 children between two and 12 years of age. It was an open-label study on children suffering from clinically diagnosed bacterial pneumonia (Jibril 1989). The study was unblinded and allocation concealment was also inadequate. Age and sex distribution, presence of wheeze and mean weight in the two groups were comparable. Cure rate was better with co-amoxyclavulanic acid (OR 10.44, 95% CI 2.85 to 38.21) (Analysis 6.2).

Co-trimoxazole versus amoxycillin (Analysis 7)

Three multicentre studies (Awasthi 2008; CATCHUP 2002; Straus 1998) involving 2346 children (1270 in the co-trimoxazole group and 1077 in the amoxycillin group) between two months and 59 months of age have compared co-trimoxazole and amoxycillin. The diagnosis of pneumonia was based on clinical criteria. Two studies (CATCHUP 2002; Straus 1998) were double-blinded and allocation concealment was adequate. A third study (Awasthi 2008) was open-label and cluster-randomisation was done (the randomisation unit was Primary Health Centre) and in this study assessment of the primary outcome of treatment failure was done on day four for the amoxycillin group and day six for the co-trimoxazole group; total numbers of events and effective sample size in this study (Awasthi 2008) were calculated after adjusting for the design effect. All studies included children with non-severe pneumonia; one study (Straus 1998) also included 301 children with severe pneumonia. In pooled data the failure rate in non-severe pneumonia was similar in the two groups (OR 1.18, 95% CI 0.91 to 1.51) (Analysis 7.7). The cure rate could be extracted in two studies (Awasthi 2008; CATCHUP 2002) and it was not different in either treatment group (OR 1.03, 95% CI 0.56 to 1.89) (Analysis 7.14) Loss to follow-up was comparable in the two groups (OR 0.96, 95% CI 0.59 to 1.57) (Analysis 7.12). There were only two deaths in both the groups. The organisms isolated from blood cultures were *H. influenzae* in 79 children (52 in the co-trimoxazole group and 27 in the amoxycillin group) and *S. pneumoniae* in 49 children (36 in the co-trimoxazole group and 13 in the amoxycillin group); the distribution was similar in the two groups. In view of the difference in the time of assessment for the primary outcome in one study (Awasthi 2008), we performed analysis for failure rates in non-severe pneumonia after excluding this study. The results did not alter significantly; failure rates in the two groups were similar (OR 1.19, 95% CI 0.92 to 1.53) (.Analysis 7.16) Failure rate in severe pneumonia available in one study was similar in the two groups (OR 1.71, 95% CI 0.94 to 3.11) (Analysis 7.8)).

Co-trimoxazole versus procaine penicillin (Analysis 8)

Two studies (Keeley 1990; Sidal 1994) enrolled 723 children between three months and 12 years of age. Both studies were unblinded and allocation concealment was adequate in one study (Keeley 1990). The cure rate was similar in the two groups (OR 1.58, 95% CI 0.26 to 9.69) (.Analysis 8.6) Rate of hospitalisation was available in only one study and was similar in the two groups (OR 2.52, 95% CI 0.88 to 7.25) (.Analysis 8.7) There was only one death.

Co-trimoxazole versus single-dose procaine penicillin followed by oral ampicillin for five days (Analysis 9)

One study was included that had enrolled 134 children below five years of age with severe pneumonia as defined by WHO criteria (Campbell 1988). The study was unblinded and allocation concealment was not clearly stated. The cure rates (OR 1.15, 95% CI 0.36 to 3.61) (Analysis 9.4), hospitalisation rates (OR 1.57, 95% CI 0.25 to 9.72) (Analysis 9.5) and death rates (OR 0.20, 95% CI 0.01 to 4.25) (Analysis 9.6) were similar for the two groups.

Cefpodoxime versus co-amoxyclavulanic acid (Analysis 10)

One multicentre study (Klein 1995) enrolled 348 children between three months and 11.5 years of age. The study was unblinded and allocation concealment was inadequate. The age distribution in the two groups was comparable. The response rate at the end of 10 days of treatment was comparable in the two groups (OR 0.69, 95% CI 0.18 to 2.60) (Analysis 10.1). Organisms were isolated in 59 cases. These organisms were *H. influenzae* in 28 participants (47.5%), *S. pneumoniae* in 14 (23%), *M. catarrhalis* in seven (11.9%) and *H. parainfluenzae* in four (6.8). There was no significant difference in the bacteriologic efficacy of either group (100% versus 96.4%).

Studies comparing treatment of hospitalised children with severe/very severe pneumonia

Chloramphenicol versus penicillin plus gentamycin (Analysis 11)

One multicentre study including 1116 children aged between one month and five years compared chloramphenicol with penicillin and gentamycin. This was an open-label RCT in children with severe pneumonia that was carried out in Papua New Guinea (Duke 2002). Allocation concealment was adequate. There was no significant difference between the two groups in positive cultures, children who had received antibiotics earlier and loss to follow-up. Need for change in antibiotics (OR 0.80, 95% CI 0.54 to 1.18) (Analysis 11.3), death rates (OR 1.25, 95% CI 0.76 to 2.07) (Analysis 11.2) and adverse events (OR 1.26, 95% CI 0.96 to

1.66) (Analysis 11.1) were similar in the two groups. However, re-admission rates before 30 days favoured the penicillin-gentamycin combination over chloramphenicol (OR 1.61, 95% CI 1.02 to 2.55) (Analysis 11.4). Bacterial pathogens were identified in 144 children (67 in children receiving chloramphenicol and 77 in the other group). Isolation rates or sensitivity of the organism and failure rates did not differ between the two groups.

Chloramphenicol with ampicillin and gentamycin (Analysis 12)

One multicentre study was identified; this study enrolled 958 children who were hospitalised with WHO-defined very severe pneumonia (Asghar 2008). The study was unblinded and allocation concealment was adequate. Mean age, proportion of boys and number of children who had received antibiotics before enrolment were comparable in the two groups. Failure rates on day five (OR 1.51, 95% CI 1.04 to 2.19) (Analysis 12.4), day 10 (OR 1.46, 95% CI 1.04 to 2.06) (Analysis 12.5) and day 21 (OR 1.43, 95% CI 1.03 to 1.98) (Analysis 12.6) were significantly higher in those receiving chloramphenicol as compared to ampicillin and gentamycin. Death rates were higher in those receiving chloramphenicol (OR 1.65, 95% CI 0.99 to 2.77) (Analysis 12.10).

Chloramphenicol plus penicillin versus ceftriaxone (Analysis 13)

One double-blind study fulfilled the inclusion criteria; the study enrolled 97 children between 2 and 24 months of age diagnosed with severe CAP with probable bacterial aetiology (Cetinkaya 2004). Allocation concealment was adequate. Ages in the two groups were comparable (details not available). Cure rates in the two groups were similar (OR 1.36, 95% CI 0.47 to 3.93) (Analysis 13.1).

Chloramphenicol alone versus chloramphenicol plus penicillin (Analysis 14)

One study (Shann 1985) from Papua New Guinea involved 748 hospitalised children (age not clear) with severe pneumonia. The study was unblinded but allocation concealment was adequate. Need for change in antibiotics (OR 0.49, 95% CI 0.12 to 1.97) (Analysis 14.1), loss to follow-up (OR 1.11, 95% CI 0.80 to 1.53) (Analysis 14.3) and deaths rates (OR 0.73, 95% CI 0.48 to 1.09) (Analysis 14.2) were comparable in the two groups.

Ampicillin alone versus penicillin with chloramphenicol (Analysis 15)

One trial involving 115 children between five months and four years of age was identified (Deivanayagam 1996). The study was unblinded and allocation concealment was adequate. Age and sex distribution and proportion of children with severe malnutrition were comparable in the two groups. The cure rates (OR 0.48, 95% CI 0.15 to 1.51) (Analysis 15.1) and duration of hospitalisation were similar in the two groups (mean difference (MD) 0.1, 95% CI -1.13 to 0.93) (Analysis 15.4).

Benzathine penicillin versus procaine penicillin (Analysis 16)

Two studies fulfilled the inclusion criteria; one which included 176 children between two and 12 years of age with chest X-ray films showing lobar consolidation or infiltration (presumed streptococcal infection) (Camargos 1997) and another study of 105 children between three months and 14 years of age (Sidal 1994). Both studies were unblinded and allocation concealment was adequate in one (Camargos 1997). Cure rates were not significantly different in the two groups (OR 0.53, 95% CI 0.27 to 1.01) (Analysis 16.1). Failure rates were also similar between the groups (OR 3.17, 95% CI 0.9 to 11.11) (Analysis 16.2). Bacterial pathogens were identified in only one study. The isolation rate for *S. pneumoniae* was six out of 90 blood cultures performed (four participants in the benzathine group and two in the procaine penicillin group). The clinical outcome did not differ in relation to the organism identified.

Amoxycillin versus penicillin (Analysis 17)

Two multicentre non-blinded studies were identified; these enrolled 1702 children between three months and 59 months of age, suffering from severe pneumonia (diagnosed on the basis of WHO criteria) (Addo-Yobo 2004) and 203 children with radiographically confirmed pneumonia (Atkinson 2007). The studies were unblinded and allocation concealment was adequate. The second study (Atkinson 2007) measured outcome as time from randomisation until the temperature was < 38 degrees celsius for 24 hours and oxygen requirement had ceased. However, it provided data on need for change of antibiotics due to worsening of respiratory/radiological findings. For the purposes of this analysis we considered them as failure on day five. Age, sex, severe malnutrition, breast feeding and the number of children who had received antibiotics in the last week were similar in both the groups. The failure rates measured at 48 hours (OR 1.03, 95% CI 0.81 to 1.31) (Analysis 17.7), five days (OR 1.15, 95% CI 0.58 to 2.30) (Analysis 17.8) and 14 days (OR 1.04, 95% CI 0.84 to 1.29) (Analysis 17.9) were similar in both groups. There were seven deaths in the group receiving penicillin in one study (Addo-Yobo 2004) while no deaths were observed in the other study (Atkinson 2007).

Amoxycillin with intravenous (IV) ampicillin (Analysis 18)

One non-blinded study involving 237 children between two and 59 months of age with severe pneumonia was identified (Hazir 2008). Allocation concealment was adequate. Number of infants in each group, sex distribution and presence of wheeze were comparable in the two groups. Failure rates (OR 0.86, 95% CI 0.63

to 1.19) (Analysis 18.5), relapse rates (OR 0.78, 95% CI 0.46 to 1.33) (Analysis 18.6) and death rates (OR 0.25, 95% CI 0.03 to 2.21) (Analysis 18.7) were similar in the two groups.

Amoxycillin with cefuroxime (Analysis 19)

One randomised, non-blinded controlled study was identified; this included 83 children with non-severe and severe pneumonia (Aurangzeb 2003). Allocation concealment was unclear. Baseline data in the form of mean age and proportion of boys were similar in the two groups. Cure rates (OR 2.05, 95% CI 0.18 to 23.51) (Analysis 19.3) and failure rates (OR 0.49, 95% CI 0.04 to 5.59) (Analysis 19.4) were similar in the two groups.

Amoxycillin with clarithromycin (Analysis 20)

One randomised, non-blinded controlled study compared these two drugs; 85 children with non-severe and severe pneumonia were enrolled (Aurangzeb 2003). The sequence generation and allocation concealment in the study is not clear. Baseline data in the form of mean age and proportion of boys were similar in the two groups. Cure rates (OR 1.05, 95% CI 0.06 to 17.40) (Analysis 20.3) and failure rates (OR 0.95, 95% CI 0.06 to 15.74) (Analysis 20.4) were similar in the two groups.

Penicillin and gentamycin with co-amoxyclavulanic acid (Analysis 21)

One study involving 71 children between two months and 59 months of age with very severe pneumonia fulfilled the inclusion criteria (Bansal 2006). The study was non-blinded and allocation concealment was adequate. Baseline characteristics, including number of infants and sex distribution, were comparable. Failure rates in the two groups were similar (OR 0.86, 95% CI 0.05 to 14.39) (Analysis 21.3).

Levofloxacin with comparator group (Analysis 22)

One non-blinded study, involving 709 children below 16 years of age, compared oral levofloxacin with either ceftriaxone or co-amoxyclavulanic acid (Bradley 2007). Sequence generation and allocation concealment is not clear from the study. The mean age, sex and number who received antibiotics before enrolment were comparable in the two groups. Cure rates were similar in the two groups (OR 1.05, 95% CI 0.46 to 2.42) (Analysis 22.4).

Cefuroxime with clarithromycin (Analysis 23)

One randomised, non-blinded, controlled study involving 85 children with non-severe and severe pneumonia was identified (Aurangzeb 2003). Allocation concealment was unclear. Baseline data in the form of mean age and proportion of boys were similar in the two groups. Cure rates (OR 0.51, 95% CI 0.04 to 5.89) (Analysis 23.3) and failure rates (OR 2.05, 95% CI 0.18 to 23.51) (Analysis 23.4) were similar in the two groups.

Co-trimoxazole versus chloramphenicol (Analysis 24)

One double-blind study involving 111 malnourished children under five years of age fulfilled the inclusion criteria for this review (Mulholland 1995). Allocation concealment was adequate. The age and sex distribution, nutritional status, children with wheezing and numbers excluded were similar in the two groups. Cure rates (OR 1.06, 95% CI 0.47 to 2.40) (Analysis 24.5), failure rates (OR 1.03, 95% CI 0.45 to 2.33) (Analysis 24.6), number of participants requiring a change in antibiotics (OR 1.42, 95% CI 0.46 to 4.40) (Analysis 24.9), relapse rates (OR 1.02, 95% CI 0.24 to 4.30) (Analysis 24.8) and death rates (OR 2.21, 95% CI 0.63 to 7.83) (Analysis 24.10) were similar in the two groups.

Ceftibuten with cefuroxime axetil (Analysis 25)

One study involving 140 children between one and 12 years of age with radiographically confirmed CAP compared ceftibuten with cefuroxime axetil (Nogeova 1997). The study was unblinded. Sequence generation and allocation concealment were not clear from the paper. Age and sex distribution were similar in the two groups. Cure rate (OR 0.32 95% CI 0.11 to 0.94) (Analysis 25.4) was significantly higher and failure rate (OR 6.81, 95% CI 1.46 to 31.70) (Analysis 25.5) was significantly lower in children receiving cefuroxime. Organisms were isolated in 83 participants (53 in the ceftibuten group and 30 in the cefuroxime group). Identification of organisms was significantly higher in children who received ceftibuten (OR 3.83, 95% CI 1.87 to 7.83) (Analysis 25.2). Organisms identified in children who received ceftibuten were *S. pneumoniae* (17), *H. influenzae* (13), *Staphylococcus aureus* (*S. aureus)* (eight), group A beta haemolytic streptococcus (seven), *Moraxella catarrhalis* (*M. catarrhalis*) (four), respiratory syncytial virus (onr) and *Mycoplasma pneumoniae* (*M. pneumoniae*) (one). The organisms identified in children receiving cefuroxime axetil were: *S. pneumoniae* (seven), *H. influenzae* (eight), *S. aureus* (three), group A beta haemolytic streptococcus (four), *Moraxella catarrhalis* (seven), respiratory syncytial virus (three) and *M. pneumoniae* (three).

Oxacillin/ceftriaxone with co-amoxyclavulanic acid (Analysis 26)

One study involving 104 children aged between two months to five years with very severe pneumonia was included (Ribeiro 2011). The study was unblinded; random sequence generation, allocation concealment and reporting of data were adequate. Age and sex distribution, days before admission in hospital, receipt of antibiotics before enrolment and failure rates (OR 0.98, 95% CI 0.33 to 2.92) (Analysis 26.5) were similar in the two groups of participants. Mean time for improvement (MD -1.00 day, 95% CI -1.89

to -0.11) (Analysis 26.6) and total hospital stay (MD -3.40 days, 95% CI -5.46 to -1.34) (Analysis 26.7) were significantly better in children receiving co-amoxyclavulanic acid.

Antibiotics in radiographically confirmed pneumonia

Out of 29 studies, 12 (Atkinson 2007; Bansal 2006; Block 1995; Bradley 2007; Camargos 1997; Deivanayagam 1996; Klein 1995; Kogan 2003; Mulholland 1995; Nogeova 1997; Wubbel 1999; Tsarouhas 1998) enrolled children with radiographically confirmed pneumonia. Ten studies (Addo-Yobo 2004; Asghar 2008; Awasthi 2008; Campbell 1988; CATCHUP 2002; Cetinkaya 2004; Duke 2002; Hazir 2008; Shann 1985; Straus 1998) used clinical criteria to diagnose pneumonia. Three studies (Harris 1998; Ribeiro 2011; Roord 1996) used clinical criteria or radiography for diagnosis of pneumonia. In four studies (Aurangzeb 2003; Jibril 1989; Keeley 1990; Sidal 1994) the role of radiography in the diagnosis of pneumonia was not clear from the description. The following comparisons were carried out in radiographically confirmed pneumonia.

Azithromycin versus erythromycin (Analysis 1)

Out of four studies (Harris 1998; Kogan 2003; Roord 1996; Wubbel 1999), radiographs were performed for diagnosis of pneumonia in only two studies (Kogan 2003; Wubbel 1999). A total of 147 children were enrolled in these two studies. Failure rates (OR 0.62, 95% CI 0.23 to 1.63) (Analysis 1.9) and cure rates (OR 1.72, 95% CI 0.65 to 4.56) (Analysis 1.8) were not different in the two groups.

Clarithromycin versus erythromycin (Analysis 2)

One study (Block 1995) compared erythromycin and clarithromycin; 234 children below 15 years of age with radiographically confirmed pneumonia were treated on in an ambulatory setting. Resolution of pneumonia (diagnosed radiologically) was more frequent in the clarithromycin group compared to the erythromycin group (OR 2.51, 95% CI 1.02 to 6.16) (Analysis 2.6). However, there were no differences in radiologic cure rates (OR 3.55, 95% CI 0.7 to 18.04) (Analysis 2.7) or radiologic failure rates (OR 0.34, 95% CI 0.06 to 1.80) (Analysis 2.8).

Erythromycin versus co-amoxyclavulanic acid (Analysis 3)

Out of two studies (Harris 1998; Wubbel 1999), one study (Wubbel 1999) involving 88 children enrolled participants with radiographically confirmed pneumonia. Failure rates were similar in the two groups (OR 0.62, 95% CI 0.05 to 7.08) (Analysis 3.7)

Azithromycin versus amoxycillin (Analysis 4)

One study involving 47 children aged between one month and 14 years with radiographically confirmed pneumonia compared azithromycin and amoxycillin (Kogan 2003). Children treated with azithromycin were older than those treated with amoxycillin (OR 58.1, 95% CI 35.59 to 80.61) (Analysis 4.1). Cure rates were not significantly different in the two groups (OR 2.85, 95% CI 0.73 to 11.09) (Analysis 4.5).

Amoxycillin versus procaine penicillin (Analysis 5)

One study involving 170 children with radiographically confirmed pneumonia, aged six months to 18 years, was identified (Tsarouhas 1998). The failure rates were similar in the two groups (OR 0.75, 95% CI 0.17 to 3.25) (Analysis 5.2).

Cefpodoxime versus co-amoxyclavulanic acid (Analysis 10)

One multicentre study (Klein 1995) enrolled 348 children with radiographically confirmed pneumonia aged three months to 11.5 years of age. Cure rates in the two groups were similar (OR 0.69, 95% CI 0.18 to 2.60) (Analysis 10.1).

Studies comparing treatment of hospitalised children with severe/very severe pneumonia

Ampicillin alone versus penicillin with chloramphenicol (Analysis 15)

One trial involving 115 children with radiographically confirmed pneumonia, between five months and four years of age, was identified (Deivanayagam 1996). The study was unblinded and allocation concealment was adequate. The cure rates (OR 0.48, 95% CI 0.15 to 1.51) (Analysis 15.1) and duration of hospitalisation were similar in the two groups (MD 0.1, 95% CI -1.13 to 0.93) (Analysis 15.4).

Benzathine penicillin versus procaine penicillin (Analysis 16)

Out of two studies, radiographically confirmed pneumonia was only assessed in one study which included 176 children between two and 12 years of age with chest X-ray films showing lobar consolidation or infiltration (presumed streptococcal infection) (Camargos 1997). Failure rates were similar between the groups (OR 1.61, 95% CI 0.45 to 5.70) (Analysis 16.7).

Amoxycillin versus penicillin (Analysis 17)

Out of two studies, children with radiographically confirmed pneumonia were enrolled in one study involving 203 children (Atkinson 2007). The failure rate on day five was similar in the two groups (OR 2.36, 95% CI 0.59 to 9.39) (Analysis 17.15).

Penicillin and gentamycin with co-amoxyclavulanic acid (Analysis 21)

One study involving 71 children between two months and 59 months of age with very severe, radiographically confirmed pneumonia fulfilled the inclusion criteria (Bansal 2006). Failure rates in the two groups were similar (OR 0.86, 95% CI 0.05 to 14.39) (Analysis 21.3).

Levofloxacin with comparator group (Analysis 22)

One non-blinded study, involving 709 children below 16 years of age, compared oral levofloxacin with either ceftriaxone or co-amoxyclavulanic acid (Bradley 2007). The sequence generation and allocation concealment were not clear from the study. The mean age, sex and number who received antibiotics before enrolment were comparable in the two groups. Cure rates were similar in the two groups (OR 1.05, 95% CI 0.46 to 2.42) (Analysis 22.4).

Co-trimoxazole versus chloramphenicol (Analysis 24)

One double-blind study involving 111 malnourished children with radiographically confirmed pneumonia under five years of age fulfilled the inclusion criteria for this review (Mulholland 1995). Cure rates (OR 1.06, 95% CI 0.47 to 2.40) (Analysis 24.5), failure rates (OR 1.03, 95% CI 0.45 to 2.33) (Analysis 24.6), number of participants requiring a change in antibiotics (OR 1.42, 95% CI 0.46 to 4.40) (Analysis 24.9), relapse rates (OR 1.02, 95% CI 0.24 to 4.30) (Analysis 24.8) and death rates (OR 2.21, 95% CI 0.63 to 7.83) (Analysis 24.10) were similar in the two groups.

Ceftibuten with cefuroxime axetil (Analysis 25)

One study (Nogeova 1997) involved 140 children between one and 12 years of age with radiographically confirmed CAP. Cure rate (OR 0.32, 95% CI 0.11 to 0.94) (Analysis 25.4) and failure rate (OR 6.81, 95% CI 1.46 to 31.70) (Analysis 25.5) were significantly better in the children receiving cefuroxime.

Oral treatment of severe pneumonia with parenteral treatment (Analysis 27)

There were six studies (Addo-Yobo 2004; Atkinson 2007; Campbell 1988; Hazir 2008; Sidal 1994; Tsarouhas 1998) that included children with severe pneumonia and compared oral antimicrobial agents with initial intravenous or intramuscular medications. Four studies compared oral amoxycillin with intravenous penicillin/ampicillin (Addo-Yobo 2004; Atkinson 2007; Hazir 2008; Tsarouhas 1998). Two studies compared oral cotrimoxazole with intramuscular penicillin (Campbell 1988; Sidal 1994). In four studies (Campbell 1988; Hazir 2008; Sidal 1994; Tsarouhas 1998) children were treated in an ambulatory setting with injections as well as oral medications. A total of 4331 children below 18 years of age were enrolled; 2174 received oral antibiotics (cotrimoxazole or amoxycillin) and 2157 received intravenous or intramuscular antibiotics (penicillin or ampicillin). The baseline characteristics (age and sex distribution) in the two groups and proportion of children who had received antibiotics before enrolment were comparable in the two groups. Failure rates were similar in the two groups (OR 0.84, 95% CI 0.56 to 1.24) (Analysis 27.7). Separate data for children below five years of age were not available. We re-analysed data after removing studies that also enrolled children above five years of age (Atkinson 2007; Sidal 1994; Tsarouhas 1998). Failure rates were similar in the two groups (OR 0.91, 95% CI 0.76 to 1.09) (Analysis 27.8). Failure rates did not show significant differences when children receiving amoxycillin (OR 0.92, 95% CI 0.77 to 1.10) (Analysis 27.9) or cotrimoxazole (OR 0.31, 95% CI 0.03 to 3.29) (Analysis 27.10) were analysed separately.

Analysis of studies that treated both the groups in an ambulatory setting (after removing studies that gave both the treatments in hospital) showed that failure rates in the two groups were not different (OR 0.92, 95% CI 0.77 to 1.10) (Analysis 27.9). Cure rates were available in two studies (Atkinson 2007; Sidal 1994) and were significantly better in children receiving oral antibiotics (OR 5.05, 95% CI 1.19 to 21.33).

Hospitalisation rate in children receiving treatment in an ambulatory setting was available in three studies (Campbell 1988; Sidal 1994; Tsarouhas 1998). The need for hospitalisation was similar in the two groups (OR 1.13, 95% CI 0.38, 3.34) (Analysis 27.13). Relapse rates were available in two studies (Atkinson 2007; Hazir 2008) and there was no significant difference in the two groups (OR 1.28, 95% CI 0.34 to 4.82) (Analysis 27.14). Death rate was available in three studies (Addo-Yobo 2004; Atkinson 2007; Hazir 2008) and was significantly higher in those who received injectable treatments (OR 0.15, 95% CI 0.03 to 0.87) (Analysis 27.15). There were no deaths in one study (Atkinson 2007) and seven deaths in another study (but only in those receiving intravenous penicillin (Addo-Yobo 2004)) and five deaths in the third study (one in the oral group and four in the intravenous ampicillin group) (Hazir 2008). Re-analysis after removing one study with seven deaths in only one group (Addo-Yobo 2004) suggests no significant difference between the two groups (OR 0.25, 95% CI 0.03, 2.21) (Analysis 27.19). Data on loss to follow-up were available in one study (Hazir 2008) and were similar in the two groups (OR 0.45, 95% CI 0.17 to 1.20) (Analysis 27.16).

Only two studies (Atkinson 2007; Tsarouhas 1998) enrolled children with radiographically confirmed pneumonia. A total of 373 children were enrolled. The failure rates were similar in the two groups (OR 1.33, 95% CI 0.41 to 4.29) (Analysis 27.18).

Identification of aetiological agents

Out of 29 studies reviewed, attempts were made to isolate or demonstrate the aetiological organisms in 14 studies. The methods used in these studies for identification of bacteria were a blood culture, sputum examination or urinary antigen detection. For this review, results of a throat swab for bacterial isolation were ignored. Bacterial pathogens could be identified in blood cultures or serology/sputum in 591 (12%) out of 4882 participants tested. Out of the bacterial pathogens identified, 236 (40%) participants had *S. pneumoniae*, 150 (25%) had *H. influenzae*, 69 (12%) had *S. aureus* and 136 (23%) had other pathogens including the gram-negative bacilli *M. catarrhalis* and *Staphylococcus albus* (*S. albus*) and Group A beta haemolytic streptococcus (Table 1).

Information regarding the sensitivity pattern of bacterial isolates was available in four studies (Asghar 2008; Bansal 2006; Mulholland 1995; Roord 1996). This information was only available for the antibiotics studied and sensitivity was not tested in all the isolates. In the study by Asghar 2008, out of a total of 22 *S. pneumoniae* isolates, 13/14 were sensitive to chloramphenicol, 12/17 to gentamycin, 15/16 to ampicillin and 12/12 to third-generation cephalosporins.

Out of a total of eight isolates of *H. influenzae*, 6/7 were sensitive to chloramphenicol, 12/17 to gentamicin, 15/16 to ampicillin and 6/6 to third-generation cephalosporins.

Out of a total of 47 isolates of *S. aureus*, 19/37 were sensitive to chloramphenicol, 29/45 to gentamycin, 15/16 to ampicillin and 6/6 to third-generation cephalosporins.

In the study by Bansal 2006, all the three isolates of *S. pneumoniae* were sensitive to penicillin, amoxycillin, erythromycin and gentamycin. However, out of two isolates of *H. influenzae*, one was sensitive and the other isolate was resistant to penicillin, amoxycillin, erythromycin and gentamycin. The one that was resistant was sensitive to ciprofloxacin, cefotaxime and chloramphenicol. In the study by Mulholland 1995, all 10 isolates of *S. pneumoniae* were susceptible to co-trimoxazole and nine of these were also susceptible to chloramphenicol. All three *Salmonella spp.* isolates were susceptible to co-trimoxazole and chloramphenicol. A single isolate of *H. influenzae* was resistant to co-trimoxazole. In the study by Roord (Roord 1996), all 20 isolates were sensitive to azithromycin while three organisms were resistant to erythromycin.

Respiratory syncytial virus (RSV) was tested in five studies. Nasopharyngeal aspirates were tested for RSV in four studies (Atkinson 2007; Addo-Yobo 2004; Mulholland 1995; Wubbel 1999) involving 1916 children and RSV was identified by positive serology in one study (Nogeova 1997) involving 140 children. RSV was identified in 407 children (20%).

Identification of atypical organisms was attempted in six studies (Block 1995; Bradley 2007; Harris 1998; Kogan 2003; Nogeova 1997; Wubbel 1999). Out of the 1734 participants tested for *M. pneumoniae*, 385 (22%) tested positive. In participants aged under five years 141 out of 659 (21%) tested positive for mycoplasma. Tests for *Chlamydia spp*. were positive in 158 out of 1534 (10%) participants. In children under five years, there were positive test results for *Chlamydia spp*. in 45 out of 658 (7%) participants.

Indirect comparisons

We attempted to compare various antibiotics (A and C) when comparisons of antibiotics A and B were available and B and C were available. We utilised this process to compare co-trimoxazole with co-amoxyclavulanic acid (Analysis 28), amoxycillin with cefpodoxime (Analysis 29) and amoxycillin with chloramphenicol (Analysis 30). Baseline data for age and sex were not comparable in the first two comparisons and therefore no valid comparison could be carried out. In the comparison of amoxycillin with chloramphenicol (CATCHUP 2002; Mulholland 1995; Straus 1998) sex distribution was not comparable although age distribution was. Cure rates were better in the amoxycillin group compared to the chloramphenicol group (OR 4.26, 95% CI 2.57 to 7.08) (Analysis 30.3) and failure rates were lower in the amoxycillin group (OR 0.64, 95% CI 0.41 to 1.00) (Analysis 30.4).

DISCUSSION

The aim of this review was to establish the most effective antibiotics for first-line empirical treatment community-acquired pneumonia (CAP) of different severity. A limited number of randomised controlled trials (RCTs) fulfilled the inclusion criteria. Most of the antibiotic comparisons were available in single studies only.

Summary of main results

Studies comparing treatment of pneumonia in an ambulatory setting suggest that the failure rate with co-trimoxazole was comparable to amoxycillin; co-amoxyclavulanic acid was better than amoxycillin. Resolution of radiographically confirmed pneumonia was better with clarithromycin as compared to erythromycin and side effects were fewer with azithromycin as compared to co-amoxyclavulanic acid. For children with severe pneumonia, treatment with oral antibiotics was similar to treatment with injectable ampicillin or penicillin. Death rates were higher in children getting chloramphenicol as compared to those getting penicillin/ampicillin plus gentamycin.

For severe/very severe pneumonia, penicillin/ampicillin plus gentamycin was associated with lower re-admission rates as compared to chloramphenicol.

For very severe pneumonia, failure rates were significantly higher in those receiving chloramphenicol as compared to ampicillin and gentamycin.

The rest of the comparisons for treatment in ambulatory settings involved azithromycin with erythromycin, clarithromycin, clarithromycin with erythromycin, amoxycillin with procaine penicillin, co-trimoxazole with single-dose procaine penicillin followed

by oral ampicillin and cefpodoxime with co-amoxyclavulanic acid and there were no statistically significant differences in these comparisons.

Comparisons for severe and very severe pneumonia involved chloramphenicol plus ampicillin with penicillin, amoxycillin with cefuroxime, amoxycillin with clarithromycin, penicillin and gentamycin with co-amoxyclavulanic acid, levofloxacin with ceftriaxone or co-amoxyclavulanic acid, cefuroxime with clarithromycin and chloramphenicol with co-trimoxazole and were comparable. Co-amoxyclavulanic acid was better than oxacillin/ceftriaxone and cefuroxime was better than ceftibuten.

Overall completeness and applicability of evidence

Treatment of pneumonia depends on the age of the child, the severity of illness, the likely aetiological agents and their resistance pattern. The aetiological agents vary with age and possibly geographic location. Most of the studies included in this review were from underdeveloped countries with age groups below five years, and identification of aetiological agents was limited to a few studies. The burden of pneumonia is significant in infants from developing countries. Attempts to isolate aetiological agents may not be cost-effective and therefore empirical treatment of pneumonia is justified. The results of this review may therefore be more applicable to the management of pneumonia in developing countries. However, data comparing two different antibiotics may also be useful in guiding antibiotic therapy in industrialised countries.

The World Health Organization (WHO) recommends treatment of non-severe pneumonia with co-trimoxazole as a first-line empirical antimicrobial treatment in countries with an infant mortality rate higher than 40 per 1000 live births (WHO 1991). Concerns about increasing resistance of common pathogens (*S. pneumoniae* and *H. influenzae*) to co-trimoxazole have been raised (Krishnan 2011) and amoxycillin has been suggested as an alternative. This review suggests that amoxycillin and co-trimoxazole are associated with similar failure rates. Reports of in vitro resistance of common organisms of pneumonia to cotrimoxazole and relatively more sensitivity to amoxycillin have not resulted in more failure rates in the co-trimoxazole group. All clinical trials included in this review included children with pneumonia diagnosed by the WHO clinical definition of pneumonia. None had chest X-rays. It can be concluded that there are insufficient data to show superiority of amoxycillin to co-trimoxazole. It should be noted that amoxycillin is more expensive than co-trimoxazole for five days of treatment for a child weighing between 5 kg and 10 kg (in India US USD 0.6 versus USD 0.3). Two recent studies (Agarwal 2004; MASCOT Group 2002) reported similar cure rates with amoxycillin given for three or five days. The cost of amoxycillin would be reduced to some extent if the treatment duration of amoxycillin was lowered to three days. Most studies comparing co-trimoxazole and amoxycillin used clinical case definition of pneumonia (rapid respiration). Respiratory symptoms and rapid respiratory rates in children may be due to bacterial pneumonia, viral infection associated wheeze, asthma etc. In a study from Pakistan chest radiographs were normal in 82% of children diagnosed with non-severe pneumonia using the WHO case definition (Hazir 2006). The majority of such children, except those with bacterial pneumonia, may not require antimicrobial agents and are likely to recover over three to seven days with supportive care. Giving them co-trimoxazole or amoxycillin or any other antibiotics may not alter their outcome. Another study from Pakistan observed that children with non-severe pneumonia treated with amoxycillin or placebo had similar failure rates, suggesting that the specificity of the WHO criteria for diagnosis of true bacterial pneumonia is low. Therefore, it is important to have well-designed clinical trials in children with true pneumonia (radiologically confirmed/direct or indirect evidence of bacterial pneumonia).

Alternative antibiotics for CAP include macrolides, co-amoxyclavulanic acid, oral cephalosporins (cefpodoxime, ceftibuten, cefuroxime), procaine penicillin and benzathine penicillin. Comparisons of various macrolides shows similar efficacy, with the exception of more radiological clearance with clarithromycin without any clinical implications. Macrolides may acquire resistance very quickly if used indiscriminately (Inoue 2006). Therefore macrolides should not be used as a first line drug in pneumonia. Amoxycillin was comparable with macrolides (azithromycin and clarithromycin), procaine penicillin and cefuroxime. Amoxycillin may therefore be preferable over these drugs. Co-amoxyclavulanic acid has been shown to give better results than amoxycillin and oxacillin plus ceftriaxone combination. The results are based on single studies for each drug. In children with severe and very severe pneumonia, co-amoxyclavulanic acid may be used as an alternative to penicillin. Cefpodoxime was comparable to co-amoxyclavulanic acid in a single study and may be an alternative where co-amoxyclavulanic acid cannot be administered. Injectable penicillins (procaine penicillin or benzathine penicillin) are associated with injection-site problems and therefore have a limited role in non-severe pneumonia.

The WHO recommends admission to hospital and treatment with penicillin for severe pneumonia and chloramphenicol for very severe pneumonia (WHO 1999). In this review it clearly emerged that children with severe pneumonia without hypoxia, who are feeding well, can be treated with oral amoxycillin. The mortality rates were higher in children receiving injectable antibiotics. Quality assessment of these trials comparing oral with injectable medications reveals adequate allocation concealment but all were unblinded. There is no explanation for the increased death rates in those who received injectable antibiotics, as they were treated with either ampicillin/penicillin or amoxycillin. After excluding one study that reported seven deaths in children receiving injections (Addo-Yobo 2004), the difference in death rate becomes non-significant. In view of the similar antimicrobial spectrum of all these drugs (ampicillin/amoxycillin/cotrimoxazole/penicillin) and the

possible benefit of better bioavailability with parenteral administration of antibiotics, a better outcome could be expected with use of injectable antibiotics for the treatment of children with severe pneumonia. More recently two cluster-RCTs (Bari 2011; Soofi 2012) in children with WHO-defined severe pneumonia without hypoxaemia compared oral amoxycillin with standard care (referral to healthcare services with injectable antibiotics). Results of these studies reveal that the outcome of patients with oral amoxycillin is the same or better than with standard treatment. Many patients on standard treatment did not take injectable medications or follow the instructions. Based on the results of these studies and the observations in the present review, it may be concluded that children with severe pneumonia without hypoxia may be treated with oral amoxycillin. There is a need to re-define severe pneumonia with or without hypoxia to identify children who may be treated with oral amoxycillin.

In children with severe or very severe pneumonia, it was evident that chloramphenicol was inferior to the combination of penicillin/ampicillin plus gentamycin. Therefore, there is a need to change the WHO guidelines. Alternative antibiotics for hospitalised children with severe and very severe pneumonia include ceftriaxone, levofloxacin, co-amoxyclavulanic acid and cefuroxime. However, comparisons were based on single studies and these drugs are relatively more expensive. Another study showed that co-amoxyclavulanic acid is better than an oxacillin-ceftriaxone combination suggesting that co-amoxyclavulanic acid may be an alternative to penicillin/ampicillin.

Cure and failure rates of CAP depend not only on the choice of antibiotics but also on the aetiology of the pneumonia, the age of the patient, the sensitivity pattern of the bacterial pathogen, the severity of disease and any antibiotic usage in the recent past. While information on resistance patterns was not included in the studies evaluated in the review, this is likely to be of major importance in the future, in terms of both clinical practice and research.

In the management of CAP, isolation of bacterial pathogens in order to make a decision about the choice of antibiotics is not feasible in most circumstances. Even if bacterial pathogens are isolated, the child will need to be treated with empirical antibiotics until the result of the culture is available. In this review identification of bacterial pathogens was attempted in 14 studies (Asghar 2008; Bansal 2006; Block 1995; Bradley 2007; Camargos 1997; Duke 2002; Harris 1998; Klein 1995; Kogan 2003; Mulholland 1995; Nogeova 1997; Roord 1996; Straus 1998; Wubbel 1999). Bacterial pathogens could be isolated in only 12% of the study participants. *S. pneumoniae* and *H. influenzae* constituted 65% of all the bacterial isolates. Therefore, empirical antibiotic therapy for CAP should be effective against these two pathogens.

Respiratory syncytial virus (RSV) could be isolated in 20% of patients, suggesting that a sizeable proportion of patients may have a viral aetiology of CAP. These patients may not need antibiotics. A child with viral pneumonia can be identified from rapid diagnostic tests such as nasopharyngeal aspirates (Maitreyi 2000) and can avoid administration of antibiotics. However, the possibility of mixed infection (bacterial agents with viruses) has been observed in 10% to 40% of cases (Kabra 2003). At present, it is policy to treat all children with pneumonia with antibiotics due to a lack of point of care tests that can reliably rule out bacterial pneumonia.

Another important issue is the aetiological role of atypical organisms (*Chlamydia* and *Mycoplasma spp*.) in CAP (Chaudhary 1998; Normann 1998; Pandey 2005). Six studies included in this review identified atypical organisms (Block 1995; Bradley 2007; Harris 1998; Kogan 2003; Nogeova 1997; Wubbel 1999). Out of 1734 children tested for*M. pneumoniae*, 385 (22%) tested positive. The positivity for *Mycoplasma* in children under five years age was 21% (141/659). Tests for *Chlamydia spp*. were positive in 158 out of the 1534 children (10%). In children under five years of age, positive tests for *Chlamydia spp*. occurred in 45 out of 658 (7%). The most effective antibiotics against atypical organisms are tetracycline and macrolides. In this review, the studies that attempted to identify atypical organisms showed equal cure rates between erythromycin and azithromycin. Two studies (Harris 1998; Wubbel 1999) comparing azithromycin with co-amoxyclavulanic acid in children under five years of age also showed equal cure and failure rates. In these studies the incidence of atypical organisms in children under five years of age was 15% and 11% for *Mycoplasma spp*. and *Chlamydia*, respectively. The cure rates in children receiving co-amoxyclavulanic acid were comparable to those receiving azithromycin. From this observation it can be inferred that either the diagnostic tests used for atypical organisms in these studies may not indicate invasive infections, or that the study was not adequately powered to detect small differences. A recent retrospective cohort study (Ambroggio 2012) compared the effectiveness of beta-lactam monotherapy and beta-lactam and macrolide combination therapy on the outcomes of children hospitalised with CAP. The results of this study suggest that mean hospital stay was 20% less in school-going children who received macrolide in addition to beta-lactamase therapy. The study did not observe a difference in re-admission rates or a difference in length of stay in children below six years of age. More studies are required to recommend the addition of macrolides to beta-lactamase antibiotics.

Exposure to antibiotics in the recent past may adversely affect the outcome of bacterial pneumonia as the chances of infection with a resistant organism increases (Chenoweth 2000). In this review, information on past antibiotic use was available in eight studies (Addo-Yobo 2004; Asghar 2008; Atkinson 2007; Bradley 2007; Duke 2002; Hazir 2008; Ribeiro 2011; Straus 1998). The distribution of patients who had received antibiotics in the recent past was similar in the two treatment groups in all the studies. However, subgroup analysis was not available in these studies. In one study (Hazir 2008) antibiotic use in the last week was associated with increased failure rates on univariate analysis. In a study comparing co-trimoxazole and amoxycillin the number of patients who had received antibiotics in the recent past was higher in the amoxycillin group (34% compared with 25.6% in the co-trimoxazole group)

(Straus 1998). In this study separate data regarding failure rates in those received antibiotics and those did not receive antibiotics are not available. However, failure rates in children with severe pneumonia who received cotrimoxazole was 56/203 (27.5%), is higher than those who received amoxycillin (18/99) (18%). Failure rates in those with non severe pneumonia in the same study were 12.8% and 12.5% in those receiving co-trimoxazole or amoxycillin respectively (Straus 1998). These results suggest that children suffering from severe pneumonia who have received antibiotics in the recent past may benefit from treatment with amoxycillin. However, these results are based on a single study and care should be taken when drawing any definite conclusions.

Malnutrition may affect the treatment outcome of pneumonia. There was only one study in malnourished children (Mulholland 1995) which compared co-trimoxazole and chloramphenicol. The study did not show any significant difference in cure rates, failure rates or need for change in antibiotics.

The aetiology of pneumonia depends on the age of the patient. In this review, the majority of enrolled participants were below five years of age and separate data according to age were not available for primary and secondary outcomes in the studies that also enrolled older children. We tried to see the effect on outcomes after removing studies that included children older than five years for severe pneumonia and observed that the age of participants did not change the outcome. Therefore, we feel that the recommendation may be applicable to all age groups. However, more studies are required for children older than five years of age.

There are limitations in reviewing antibiotic usage in CAP. Comparisons are often performed among groups of children for whom identification of aetiological agents is lacking. This means that if the distribution of viral cases is not uniform, the conclusions regarding the efficacy of antibiotics can be debatable. Several individual factors, such as malnutrition, can deeply modify the evolution of CAP and the response to antibiotic therapy. In the present review, only one study addressed this problem; it is highly probable that this issue can influence the correct evaluation of the data. No data regarding antibiotic resistance were reported in the majority of the studies. It is well known that in some cases the level of resistance to commonly used antibiotics can have a great influence on the response to therapy. The role of atypical bacteria in the determination of CAP in children living in low-income countries is not established, probably because the methods for identifying these pathogens are too complicated or too expensive, or both. These data are needed to more accurately define the best antibiotic therapy. The results may be more applicable for developing countries as most studies were done in these countries.

Quality of the evidence

Five out of 29 studies were double-blind and allocation concealment was adequate. Another 12 studies were unblinded but had adequate allocation concealment, classifying them as good-quality studies. Data were fully detailed in 20 studies, selective reporting of data was unclear in 12 studies and 13 studies were funded by WHO or universities. There was more than one study comparing co-trimoxazole with amoxycillin, oral amoxycillin with injectable penicillin/ampicillin and chloramphenicol with ampicillin/penicillin and studies were of good quality, suggesting the evidence for these comparisons is of high quality compared to other comparisons.

Potential biases in the review process

In this review we included one study (Awasthi 2008) of which one of the authors of the present review (Kabra) was a co-author.

Agreements and disagreements with other studies or reviews

The important changes in this updated review in comparison to the previous version (Kabra 2010) include the following.

1. Outcomes of children with radiographically confirmed or clinically diagnosed pneumonia are not different.
2. WHO-defined severe pneumonia without hypoxaemia can be managed with oral antibiotics in an ambulatory setting. There is a need to divide WHO-defined severe pneumonia into those with hypoxia and those without hypoxia to identify children who can be treated with oral antibiotics in an ambulatory setting.
3. For very severe pneumonia, co-amoxyclavulanic acid may be an alternative to ceftriaxone or penicillin/ampicillin, gentamycin combination.

A review comparing oral and intravenous antibiotics in pneumonia suggested no difference in cure and failure rates in children getting oral or intravenous antibiotics for the treatment of pneumonia (Rojas-Reyes 2006). In the present review we also found that oral and intravenous antibiotics (amoxycillin versus penicillin/ampicillin and co-trimoxazole versus procaine penicillin) for pneumonia are equally effective.

A recent retrospective cohort study (Ambroggio 2012) suggests that the addition of macrolide to beta-lactam antibiotics in children above six years of age may improve outcomes in the form of reduced hospital stay. In the present review, we did not find any study that compared beta-lactam antibiotics with and without macrolide for treatment of CAP. Studies comparing macrolides with other antibiotics (amoxycillin, co-amoxyclavulanic acid) gave similar failure rates suggesting no advantage of macrolides. We conclude that there is a need for RCTs to document the advantages of the addition of macrolide antibiotics to conventional beta-lactam antibiotics.

AUTHORS' CONCLUSIONS

Implications for practice

In children presenting with community-acquired pneumonia without underlying illness, and where point of care tests for identification of aetiological agents for pneumonia are not available, empirical antibiotics may be used as follows. For the treatment of WHO-defined non-severe community-acquired pneumonia (CAP) in children below five years of age amoxycillin is an alternative to co-trimoxazole. There are no apparent differences between azithromycin and erythromycin, azithromycin and co-amoxyclavulanic acid, or cefpodoxime and co-amoxyclavulanic acid. There are limited data on other antibiotics: co-amoxyclavulanic acid and cefpodoxime may be alternative second-line drugs.

Severe pneumonia in children below five years of age, without hypoxia and accepting oral feeds, can be managed with oral amoxycillin on an ambulatory basis.

For children below five years of age, hospitalised with severe and very severe CAP, penicillin/ampicillin plus gentamycin is superior to chloramphenicol. Other alternatives may be co-amoxyclavulanic acid, ceftriaxone, levofloxacin and cefuroxime. Until more studies are available these can be used as second-line therapies.

More studies are required to assess the role of the addition of macrolide antibiotics to beta-lactam antibiotics in children above five years of age.

More randomised controlled trials are required for a review of these antibiotics in order to make more accurate recommendations for their prescription.

There is need for surveillance studies to document antibiotic resistance in different geographic regions for developing empiric antibiotic treatment for pneumonia.

Implications for research

There is a need to compare various antibiotics for the treatment of pneumonia of varying severity. Studies should include radiographically confirmed pneumonia in place of clinically diagnosed pneumonia. Studies should try to identify the aetiological agents and their susceptibilities to various antibiotics and the risk factors that lead to failure of treatment. The results of such studies will help in the formation of guidelines to identify children at risk of failure who can be managed with second-line antimicrobials early.

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* *Indicates the major publication for the study*

CHARACTERISTICS OF STUDIES

Characteristics of included studies *[ordered by study ID]*

Addo-Yobo 2004

Methods	RCT comparing amoxycillin and penicillin
Participants	Children 3 to 59 months with severe pneumonia
Interventions	Daily IM penicillin 200,000 IU/kg or PO amoxycillin 45 mg/kg/day
Outcomes	Failure rate at 48 hours, 5 days and 14 days and death rate
Notes	Exclusion criteria: asthma, audible wheeze, non-severe pneumonia, very severe disease, clinical HIV, persistent vomiting, penicillin allergy

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Low risk	Random sequence generated by World Health Organization (WHO)
Allocation concealment (selection bias)	Low risk	Randomisation codes were sealed in opaque envelopes in accordance with allocation sequence, stratified by site and prepared in advance by the WHO
Blinding of participants and personnel (performance bias) All outcomes	High risk	Open-label study
Blinding of outcome assessment (detection bias) All outcomes	High risk	Open-label study
Selective reporting (reporting bias)	Low risk	No selective reporting
Incomplete outcome data (attrition bias) All outcomes	Low risk	Incomplete data adequately addressed
Other bias	Low risk	Funded by World Heath Organization and Applied Research Child Health Project, Boston University

Asghar 2008

Methods	Randomised, non-blinded, multi-site efficacy study
Participants	Children between 2 to 59 months of age with very severe pneumonia
Interventions	Ampicillin plus gentamicin (ampicillin 200 mg/kg/d in 4 doses every 6 hours, and gentamicin 7.5 mg/kg/d as in a single daily dose) or chloramphenicol (75 mg/kg/d given in 3 doses) every 8 hours for minimum of 5 days. After that first group received oral amoxycillin (45 mg/kg/day in 3 divided doses) and the other group received oral chloramphenicol 75 mg/kg/day to complete 10 days
Outcomes	**Primary outcome** 1. Treatment failure by 5 days after admission, defined as new development or persistence of at least 2 of the following: inability to drink; tachypnoea (≥ 50 breaths/minute in children aged 2 to 11 months and ≥ 40 breaths/minute in children aged 12 to 59 months) and abnormally sleepy or difficult to wake 2. Development or diagnosis of any of the following: bacterial meningitis, empyema, septic shock, renal failure or newly diagnosed co-morbid conditions. Serious adverse drug reaction 3. Modification of antibiotic treatment 4. Voluntary withdrawal or absconding 5. Death **Secondary outcomes** Treatment failure as defined above at 48 to 60 hours Treatment failure as defined above plus relapse (hypoxaemic pneumonia at 10 to 12 days and 21 to 30 days, with oxygen saturations ≤ 90%, or ≤ 88% in the 2 high altitude sites in Mexico and Yemen) Death by 30 days after enrolment Bacterial pathogens isolated from blood or other sterile sites Antimicrobial susceptibility of the isolated pathogens
Notes	Exclusion criteria: wheezing, with a history of 3 or more attacks, or known asthma, known heart disease, duration of present illness more than 10 days, history of serious adverse reaction to any of the study drugs, previous enrolment in the study Admission to hospital for more than 24 hours within past 7 days Documented evidence of injectable antibiotic treatment for more than 24 hours before enrolment, stridor, known renal failure or not passed urine during past 6 hours, evidence of cerebral malaria Evidence of bacterial meningitis, clinical jaundice, residence of patient in an area where follow-up was not possible, empyema or presence of pneumatoceles on chest radiograph

Risk of bias

Bias	**Authors' judgement**	**Support for judgement**
Random sequence generation (selection bias)	Low risk	Sequence generated by World Health Organization by using variable size blocks

Asghar 2008 (*Continued*)

Allocation concealment (selection bias)	Low risk	Separate randomisation lists were prepared for each site examination, and individual patient assignments were placed in opaque, sealed envelopes. Before opening each envelope the doctor in charge signed and dated the opening flap of the envelope
Blinding of participants and personnel (performance bias) All outcomes	High risk	Open-label randomised controlled trial
Blinding of outcome assessment (detection bias) All outcomes	High risk	Open-label randomised controlled trial
Selective reporting (reporting bias)	Low risk	No selective reporting
Incomplete outcome data (attrition bias) All outcomes	Low risk	Incomplete data adequately addressed
Other bias	Low risk	Funded by World Health Organization and Center of International Health and Development, Boston University and Johns Hopkins Bloomberg School of Public Health, Baltimore

Atkinson 2007

Methods	Multicentre randomised controlled trial
Participants	Children admitted with pneumonia in 8 hospitals. At least 3 inclusion criteria for diagnosis of pneumonia. Respiratory symptoms or signs, fever > 37.5 °C, radiographically confirmed pneumonia (defined as confluent area of consolidation agreed subsequently by 2 independent radiologists)
Interventions	Oral amoxycillin (doses for 6 months to 12 years of age 8 mg/kg/dose 3 times a day above 12 years of age 500 mg 3 times a day) or IV benzyl penicillin (doses 25 mg/kg/dose 4 times a day)
Outcomes	The primary outcome measure was time from randomisation until the temperature was 38 °C for 24 continuous hours and oxygen requirement had ceased (the latter only applicable to those children who required oxygen during the admission) Secondary outcomes included time in hospital, complications (empyema, re-admission, further courses of antibiotics), duration of oxygen requirement and time to resolution of illness
Notes	Exclusion criteria were wheeze, oxygen saturations, 85% in air, shock requiring 20 ml/kg fluid resuscitation, immunodeficiency, pleural effusion at presentation requiring

Atkinson 2007 (*Continued*)

	drainage, chronic lung condition (excluding asthma), penicillin allergy and age 6 months Treatment with oral antibiotics in the 5 days prior to admission, including amoxycillin, was not an exclusion criterion

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Low risk	Block randomisation list generated
Allocation concealment (selection bias)	Low risk	A block randomisation sequence stratified by centre was produced using a random number generator. The sequence was accessed via the Internet, therefore allowing concealment of allocation
Blinding of participants and personnel (performance bias) All outcomes	High risk	Open-label study
Blinding of outcome assessment (detection bias) All outcomes	High risk	Open-label study
Selective reporting (reporting bias)	Unclear risk	While the authors mention the primary outcome as "the time from randomisation until the temperature was less than 38 degree celsius for 24 continuous hours and oxygen requirement had ceased", they calculated the sample size based on the proportion meeting the primary outcome measure at any time. The authors have not reported on these proportions in the results
Incomplete outcome data (attrition bias) All outcomes	Low risk	None
Other bias	Low risk	Funded by the British Lung Foundation

Aurangzeb 2003

Methods	Randomised, non-blinded controlled clinical trial
Participants	Children between 3 to 72 months of age, admitted in the hospital with community-acquired pneumonia

Aurangzeb 2003 (*Continued*)

Interventions	The patients were randomly allotted to 1 of the 3 groups Group 1 was given amoxycillin 75 mg/kg/d IV in 3 divided doses, Group 2 was given cefuroxime 75 mg/kg/d IV in 3 divided doses and Group 3 was given clarithromycin 15 mg/kg/d IV divided into 2 divided doses
Outcomes	1. Improvement defined as slower respiratory rate (either back to normal for the age of the child), or more than 5 as compared to the previous day evaluation without retractions. The same defined as still breathing fast as before as or higher than that with no chest in drawing or danger signs 2. Worse was defined as development of severe pneumonia or very severe disease 3. Cure was defined as return of respiratory rate to age specific normal range
Notes	-

Risk of bias

Bias	**Authors' judgement**	**Support for judgement**
Random sequence generation (selection bias)	Unclear risk	No information provided
Allocation concealment (selection bias)	Unclear risk	No information provided
Blinding of participants and personnel (performance bias) All outcomes	High risk	Open-label study
Blinding of outcome assessment (detection bias) All outcomes	High risk	Open-label study
Selective reporting (reporting bias)	Unclear risk	There are discrepancies in the number of patients in different study arms
Incomplete outcome data (attrition bias) All outcomes	Low risk	None
Other bias	Unclear risk	Source of funding not mentioned

Awasthi 2008

Methods	Cluster-randomised, open-label trial
Participants	Children of either sex, between 2 months to 59 months with WHO-defined non-severe pneumonia

Interventions	Eligible children were randomised to receive oral dispersible scored amoxycillin (125 mg per tablet) given thrice a day (tds) for 3 days or co-trimoxazole (20 mg trimethoprim per tablet) given twice a day (bd) for 5 days. Doses of amoxycillin were between 31 to 51 mg/kg/day and trimethoprim 7 to 11 mg/kg/day
Outcomes	Primary outcome measure was clinical failure defined as presence of at least 1 of the following: (i) development of signs of WHO-defined severe pneumonia or very severe disease (ii) respiratory rate above age specific cut-off, (iii) documented axillary temperature > 38.3 °C on the day of outcome assessment, that is day 4 for amoxycillin and day 6 for co-trimoxazole arm, (iv) death within the follow-up period of 14 days, (v) lost to follow-up on day 4 or day 6 in the amoxycillin and co-trimoxazole arms, respectively, or (vi) withdrawal at any time (requirement of intention-to-treat (ITT) analysis) The secondary outcome measure was clinical relapse on day 13 to 15, defined as development of signs of WHO-defined pneumonia among the clinically cured in either arm
Notes	-

Risk of bias

Bias	**Authors' judgement**	**Support for judgement**
Random sequence generation (selection bias)	Low risk	Patients were randomly allocated
Allocation concealment (selection bias)	Low risk	This was an open-label study and the unit of randomisation was primary health centre
Blinding of participants and personnel (performance bias) All outcomes	Unclear risk	Open-label randomised controlled trial
Blinding of outcome assessment (detection bias) All outcomes	High risk	Open-label randomised controlled trial
Selective reporting (reporting bias)	Low risk	No selective reporting
Incomplete outcome data (attrition bias) All outcomes	Low risk	Incomplete data adequately addressed
Other bias	Low risk	Funded by Indian Council of Medical Research

Bansal 2006

Methods	Open-label randomised controlled trial
Participants	Children aged 2 to 59 months with WHO-defined severe or very severe pneumonia with hypoxaemia ($Sp0_2$ < 90%) were included in the study
Interventions	Patients in Group A received crystalline penicillin (benzyl penicillin) - 50,000 IV/kg IV, q6h and gentamycin 2.5 mg/kg, IV, q8h for at least 3 days. After that, oral amoxycillin 15 mg/kg 8-hourly was substituted for crystalline penicillin. Group B patients were given amoxycillin-clavulanate 30 mg/kg IV q12h for at least 3 days and were changed to oral amoxycillin-clavulanic acid when able to feed
Outcomes	Treatment failure was defined as any change, modification or discontinuation of allocated antibiotic therapy because of deterioration in patient's condition, development of serious intercurrent illness or complications such as refractory septic shock, acute renal failure, meningitis etc., persistence of danger signs such as inability to drink after 48 hours of treatment or relapse of the hypoxaemic pneumonia during the following 2 weeks
Notes	Patients with fever > 10 days, bacterial meningitis, prior antibiotic therapy > 24 hours, stridor, heart disease and allergy to any of the study drugs were excluded

Risk of bias

Bias	**Authors' judgement**	**Support for judgement**
Random sequence generation (selection bias)	Low risk	Patients were randomly allocated
Allocation concealment (selection bias)	Low risk	Randomisation list was prepared before starting the study and random treatment assignment was placed in serially labelled sealed envelopes. The assignment was opened when the patient had met all the inclusion and exclusion criteria and written consent was available
Blinding of participants and personnel (performance bias) All outcomes	High risk	Open-label randomised controlled trial
Blinding of outcome assessment (detection bias) All outcomes	High risk	Open-label randomised controlled trial
Selective reporting (reporting bias)	Low risk	No selective reporting
Incomplete outcome data (attrition bias) All outcomes	Low risk	Incomplete data adequately addressed
Other bias	Unclear risk	Source of funding not mentioned

Block 1995

Methods	RCT comparing clarithromycin with erythromycin in children with pneumonia
Participants	Children between 3 to 16 years of age with radiographically confirmed pneumonia
Interventions	PO clarithromycin (15 mg/kg/day) for 10 days or erythromycin 40 mg/kg/day for 10 days
Outcomes	Cure rates, resolution of signs and symptoms, improvement, improved but non-resolution of signs and symptoms, failure or worsening
Notes	Exclusion: hypersensitivity to macrolides, severe renal or hepatic diseases, active tuberculosis, severe infections requiring intravenous antibiotics

Risk of bias

Bias	**Authors' judgement**	**Support for judgement**
Random sequence generation (selection bias)	Unclear risk	Patients were randomly allocated
Allocation concealment (selection bias)	Unclear risk	Not mentioned clearly. Open-label study. Study drugs were dispensed and compliance was monitored by third party
Blinding of participants and personnel (performance bias) All outcomes	High risk	Unblinded study
Blinding of outcome assessment (detection bias) All outcomes	Low risk	Investigator-blinded study
Selective reporting (reporting bias)	Low risk	No selective reporting
Incomplete outcome data (attrition bias) All outcomes	Low risk	Incomplete data adequately addressed
Other bias	Unclear risk	Funded by Abbott Laboratories and role of funding agency not clear

Bradley 2007

Methods	This was a randomised (3:1, levofloxacin:comparator), open-label, active-comparator, non-inferiority, multicentre study
Participants	Children between 0.5 to 16 years old with a diagnosis of community-acquired pneumonia (CAP). A diagnosis of CAP was defined as radiographic evidence of pulmonary infiltrate consistent with acute infection requiring antibiotic therapy, and the presence of 2 or more

	of the indications of pneumonia: fever (rectal or oral temperature 38 °C for children 2 years, or 38.3 °C for children 0.5 to 2 years), shortness of breath, cough, chest pain, abnormal white blood cell count (15,000/L or 5000/L), or physical signs of pneumonia on examination (e.g. rales on auscultation, dullness to percussion, egophony)
Interventions	Levofloxacin or a comparator antibiotic for 10 days. Levofloxacin and comparators were given either orally or by intravenous (IV) administration. The patients were randomised in a 3:1 levofloxacin:comparator ratio within 14 strata in the study (1 for the 2 age groups within each country). For Group I (6 months to 5 years), levofloxacin was administered (a) 10 mg/kg/dose as oral suspension bd (up to 500 mg/d) or (b) 10 mg/kg/dose IV q12 hours (up to 500 mg/d). The comparator administration was (a) amoxycillin and clavulanic acid (7:1) oral suspension bd, with dose determined by calculating amoxycillin 22.5 mg/kg/dose (up to 875 mg/d), or (b) ceftriaxone 25 mg/kg/dose IV q12 hours (up to 4 G/d) For Group II (5 to 16 years), levofloxacin was administered (a) as 10 mg/kg/dose as oral suspension qd (up to 500 mg/d), (b) as 1 250 mg tablet qd (for children weighing 22.5 to 27.5 kg) or 2 250 mg tablets qd (for children weighing 45.5 kg), or (c) 10 mg/kg/dose IV q24 hours (up to 500 mg/d). The comparator administration was (a) clarithromycin 7.5 mg/kg/dose as oral suspension (or as a 250 mg tablet) bd (up to 250 mg bd), clarithromycin 250 mg oral tablet bd, or (b) ceftriaxone 25 mg/kg/dose IV q12 hours (up to 4 G/d), with either erythromycin lactobionate 10 mg/kg/dose IV q6 hours (up to 4 G/24 hours) or clarithromycin 7.5 mg/kg/dose as oral suspension (or as a 250 mg tablet) bd (up to 250 mg bd)
Outcomes	Clinical response was categorised as cured, improved, clinical failure, relapse at test of cure visit (TOCV) 10 to 17 days after the last dose of study drug: (1) cured: resolution of signs and symptoms associated with active infection along with an improvement or lack of progression of abnormal findings of chest roentgenogram; (2) improved: continued incomplete resolution of signs and symptoms with no deterioration or relapse after post-therapy visit (PTV) and no requirement for additional antimicrobial therapy; (3) clinical relapse: resolution or improvement of signs and symptoms at PTV evaluation with reappearance or deterioration of signs and symptoms of infection at test of cure visit (TOCV); (4) failure: patient was considered a clinical failure at PTV, response was carried forward to TOCV; and (5) unable to evaluate: unable to determine response because patient was not evaluated after PTV
Notes	Exclusion criteria: received systemic antibiotics for more than 24 hours immediately before enrolment, required a systemic antibiotic other than the study drugs, or had a suspected infection with micro-organisms known to be resistant to the study drugs. Other exclusion criteria included hospitalisation or residence in a long-term care facility for 14 or more days before the onset of symptoms; infection acquired in a hospital (48 hours after hospital admission and 7 days after hospital discharge); signs and symptoms of a bacterial infection of the central nervous system; history or presence of arthropathy or periarticular disease or any other musculoskeletal signs or symptoms that in the opinion of the investigator may have confounded a future safety evaluation of musculoskeletal complaints qd: once a day bd: twice a day

Bradley 2007 (*Continued*)

Risk of bias		
Bias	**Authors' judgement**	**Support for judgement**
Random sequence generation (selection bias)	Unclear risk	Sequence generation not mentioned
Allocation concealment (selection bias)	Unclear risk	Not mentioned clearly in the paper
Blinding of participants and personnel (performance bias) All outcomes	High risk	Open-label randomised controlled trial
Blinding of outcome assessment (detection bias) All outcomes	High risk	Open-label randomised controlled trial
Selective reporting (reporting bias)	Unclear risk	Information not clear
Incomplete outcome data (attrition bias) All outcomes	Unclear risk	Information not provided clearly
Other bias	Unclear risk	Funded by Johnson & Johnson Pharmaceutical Research and Development; details of role of funding agency not mentioned

Camargos 1997

Methods	RCT comparing benzathine penicillin and procaine penicillin
Participants	Children 2 years to 12 years with non-severe pneumonia
Interventions	Single dose of benzathine penicillin (600,000 U for patients below 20 kg weight and 1, 200,000 U for those above 20 kg), procaine penicillin 300,000 IU/kg/day IM for 7 days
Outcomes	Cure rate, failure rate, lost to follow-up
Notes	Exclusion criteria: severe disease, atelectasis, post-measles pneumonia, sickle cell cardiomyopathy, immunodeficiency, allergic to penicillin, hospitalisation in previous 2 weeks

Risk of bias		
Bias	**Authors' judgement**	**Support for judgement**
Random sequence generation (selection bias)	Low risk	Patients assigned randomly

Camargos 1997 (*Continued*)

Allocation concealment (selection bias)	Low risk	Randomisation done by trained staff member blinded to control or treatment using 4 identifying letters randomly selected for benzathine (W and Z) and procaine (X Y) enclosed in sealed envelope
Blinding of participants and personnel (performance bias) All outcomes	Low risk	Randomisation done by trained staff member blinded to control or treatment
Blinding of outcome assessment (detection bias) All outcomes	Unclear risk	Information not provided
Selective reporting (reporting bias)	Low risk	No selective reporting
Incomplete outcome data (attrition bias) All outcomes	Low risk	Incomplete data adequately addressed
Other bias	Unclear risk	Source of funding not mentioned

Campbell 1988

Methods	RCT comparing co-trimoxazole for 5 days and procaine penicillin single dose with ampicillin for 5 days
Participants	Children 1 month to 4 years of age with non-severe pneumonia
Interventions	Daily co-trimoxazole PO for 5 days or single-dose procaine penicillin with daily PO ampicillin
Outcomes	Cure rate, hospitalisation rate and death rate
Notes	Exclusion criteria: very severe disease, refusal of consent, unable to take tablets

Risk of bias

Bias	**Authors' judgement**	**Support for judgement**
Random sequence generation (selection bias)	Unclear risk	Sequence generation and randomisation not clear
Allocation concealment (selection bias)	High risk	Eligible children were allocated sequentially to 2 treatment groups by study physician

Campbell 1988 (*Continued*)

Blinding of participants and personnel (performance bias) All outcomes	High risk	Open-label study
Blinding of outcome assessment (detection bias) All outcomes	High risk	Open-label study
Selective reporting (reporting bias)	Unclear risk	Data not recorded clearly
Incomplete outcome data (attrition bias) All outcomes	Unclear risk	Data not recorded clearly
Other bias	Unclear risk	Source of funding not mentioned

CATCHUP 2002

Methods	RCT comparing amoxycillin and co-trimoxazole in non-severe pneumonia
Participants	Children 2 to 59 months with non-severe pneumonia
Interventions	PO amoxycillin 25 mg/kg/day for 5 days or co-trimoxazole 20/4 mg/kg/day for 5 days
Outcomes	Cure rate, failure rate, change of antibiotics
Notes	Blinded, exclusion criteria: severe pneumonia, very severe disease, chronic illness, past history of 2 or more episodes of wheeze, acute bronchial asthma, antibiotics in past 48 hours

Risk of bias

Bias	**Authors' judgement**	**Support for judgement**
Random sequence generation (selection bias)	Low risk	Random numbers generated using a computer program
Allocation concealment (selection bias)	Low risk	The drug assignment was concealed from patients parents and study personnel
Blinding of participants and personnel (performance bias) All outcomes	Low risk	Double-blind randomised controlled trial
Blinding of outcome assessment (detection bias) All outcomes	Low risk	Double-blind randomised controlled trial
Selective reporting (reporting bias)	Low risk	No selective reporting

CATCHUP 2002 (*Continued*)

Incomplete outcome data (attrition bias) All outcomes	Low risk	Incomplete data adequately addressed
Other bias	Low risk	Funded by World Health Organization

Cetinkaya 2004

Methods	RCT comparing chloramphenicol in combination with penicillin with ceftriaxone
Participants	Children aged 6 months to 16 years with clinical or graphically confirmed pneumonia
Interventions	IV chloramphenicol 15 mg/kg every 6 hours plus penicillin 25,000 IU/kg every 4 hours for 10 days and ceftriaxone 50 mg/kg every 12 hours
Outcomes	Clinical recovery
Notes	Blinded, children clinically diagnosed with bacterial pneumonia were enrolled

Risk of bias

Bias	**Authors' judgement**	**Support for judgement**
Random sequence generation (selection bias)	Unclear risk	Generation of random list/numbers not mentioned
Allocation concealment (selection bias)	Unclear risk	Allocation concealment not mentioned
Blinding of participants and personnel (performance bias) All outcomes	High risk	Open-label study
Blinding of outcome assessment (detection bias) All outcomes	High risk	Open-label study
Selective reporting (reporting bias)	Low risk	No selective reporting
Incomplete outcome data (attrition bias) All outcomes	Low risk	Incomplete data adequately addressed
Other bias	Unclear risk	Source of funding not mentioned

Deivanayagam 1996

Methods	RCT comparing ampicillin in combination with penicillin with chloramphenicol for pneumonia diagnosed by clinical/radiological evidence
Participants	Children 5 months to 4 years with pneumonia admitted to hospital
Interventions	IM/IV ampicillin (100 mg/kg/day) for 48 hours than PO, IV penicillin (100,000 IU/kg/day) plus chloramphenicol (100 mg/kg/day)
Outcomes	Cure rate, failure rate
Notes	Not blinded. Exclusion criteria: acute bronchiolitis, allergy to penicillin, antibiotics in past 2 days, other drugs by treating physician receiving anti-tuberculosis drugs

Risk of bias

Bias	**Authors' judgement**	**Support for judgement**
Random sequence generation (selection bias)	Low risk	Computer-generated random listen
Allocation concealment (selection bias)	Unclear risk	Information not provided
Blinding of participants and personnel (performance bias) All outcomes	High risk	Open-label study
Blinding of outcome assessment (detection bias) All outcomes	High risk	Open-label study
Selective reporting (reporting bias)	Unclear risk	Data not completely described
Incomplete outcome data (attrition bias) All outcomes	Unclear risk	No intention-to-treat analysis and details of excluded patients not clear
Other bias	Unclear risk	Source of funding not mentioned

Duke 2002

Methods	RCT comparing chloramphenicol with combination of penicillin and gentamicin in children with severe pneumonia
Participants	Children aged 1 to 59 months age, with severe pneumonia
Interventions	IM chloramphenicol (25 mg/kg 6-hourly for at least 5 days) versus penicillin (50 mg/kg 6-hourly) and gentamycin (7.5 mg/kg/d single dose) for at least 5 days

Duke 2002 (*Continued*)

Outcomes	Adverse outcome (death, change in antibiotics, absconded, readmission within 30 days) , rate of hospitalisation, duration of hospital stay
Notes	Not blinded Exclusion criteria: wheezing, bronchiolitis, meningitis, tuberculosis, CHD, renal failure, jaundice, received study antibiotics for more than 48 hours in last 1 week

Risk of bias

Bias	**Authors' judgement**	**Support for judgement**
Random sequence generation (selection bias)	Low risk	Computer-generated
Allocation concealment (selection bias)	Low risk	Sealed envelopes
Blinding of participants and personnel (performance bias) All outcomes	High risk	Open-label study
Blinding of outcome assessment (detection bias) All outcomes	High risk	Open-label study
Selective reporting (reporting bias)	Low risk	No selective reporting
Incomplete outcome data (attrition bias) All outcomes	Low risk	Incomplete data adequately addressed
Other bias	Low risk	Funded by the World Health Organization and the Papua New Guinea Health Department

Harris 1998

Methods	RCT comparing azithromycin, co-amoxyclavulanic acid and erythromycin in pneumonia
Participants	Children aged 6 months to 16 years with clinical or radiological evidence of pneumonia
Interventions	PO azithromycin (10 mg/kg/day 1 followed by 5 mg/kg/day for 4 days) or amoxycillin clavulanic acid (40 mg/kg/day) for 10 days or erythromycin (40 mg/kg/day) for 10 days
Outcomes	Cure rate (day 15 to 19), improvement rate, failure rate
Notes	Exclusion criteria: known hypersensitivity, intolerance to drugs, pregnancy, lactation, need for parental antibiotics, severe pneumonia, antibiotics in past 72 hours, chronic steroid therapy, on carbamazepine, ergotamine, terfenadine, loratadine

Harris 1998 (*Continued*)

Risk of bias		
Bias	**Authors' judgement**	**Support for judgement**
Random sequence generation (selection bias)	Unclear risk	Sequence generation not mentioned
Allocation concealment (selection bias)	Low risk	Double-blind
Blinding of participants and personnel (performance bias) All outcomes	Low risk	Double-blind
Blinding of outcome assessment (detection bias) All outcomes	Low risk	Double-blind
Selective reporting (reporting bias)	Unclear risk	No details
Incomplete outcome data (attrition bias) All outcomes	Unclear risk	Intention-to-treat analysis not performed and no details of excluded patients
Other bias	Unclear risk	Funded by Pfizer Inc., New York

Hazir 2008

Methods	Randomised, open-label equivalency trial
Participants	Children aged 3 to 59 months with WHO-defined severe pneumonia
Interventions	Oral amoxycillin syrup (80 to 90 mg/kg per day in 2 doses) and sent home (ambulatory group), or to receive intravenous ampicillin (100 mg/kg per day in 4 doses) for 48 hours as an inpatient (hospitalised group)
Outcomes	**Primary outcome** (treatment failure up to or on day 6). Any of the following: clinical deterioration; inability to take oral medication due to persistent vomiting; development of a comorbid condition requiring an antibiotic; persistence of fever > 38 ºC with lower chest in-drawing (LCI) from day 3 to day 6; either fever or lower chest in-drawing alone at day 6; hospitalisation related to pneumonia; serious adverse event; left against medical advice or lost to follow-up; voluntary withdrawal of consent; death **Secondary outcome** (treatment failure between day 6 and day 14; relapse). Any of the following: clinical deterioration; development of a comorbid condition requiring an antibiotic; development of lower chest in-drawing or fast breathing non-responsive to 3 trials in children with wheeze
Notes	Exclusion criteria: known asthma, those with a history of 3 or more episodes of wheezing in 1 year, or those in whom lower chest in-drawing resolved after 3 doses of a bronchodilator over 30 minutes were excluded. Children showing signs of WHO-defined

	very severe pneumonia (panel 1) were also excluded; such individuals were admitted to hospital for treatment with intravenous antibiotics. Children who were known to have anaphylactic reactions to penicillin or amoxycillin, those with persistent vomiting, those who had been hospitalised within the previous 2 weeks, and those with other infectious diseases that needed antibiotic treatment, were also excluded

Risk of bias

Bias	**Authors' judgement**	**Support for judgement**
Random sequence generation (selection bias)	Low risk	Randomisation list generated by uneven block size
Allocation concealment (selection bias)	Low risk	The randomisation scheme was generated by a computer program in uneven blocks of 4, 6 and 8 by an individual not involved in study. Randomisation codes were sealed in opaque envelopes in accordance with the allocation sequence and stratified by site. After being deemed eligible for enrolment, participants were assigned the next envelope in the sequence to determine treatment assignment. The randomisation code was held at the co-ordinating centre and was broken at the time of data analysis
Blinding of participants and personnel (performance bias) All outcomes	High risk	Open-label study
Blinding of outcome assessment (detection bias) All outcomes	Unclear risk	Open-label study
Selective reporting (reporting bias)	Low risk	No selective reporting
Incomplete outcome data (attrition bias) All outcomes	Low risk	Incomplete data adequately addressed
Other bias	Low risk	Funded by the World Health Organization and Family Applied Research Project, Boston University

Jibril 1989

Methods	RCT comparing amoxycillin and co-amoxyclavulanic acid with amoxycillin alone in bacterial pneumonia (non-severe)
Participants	Children aged 2 years to 12 years age, with non-severe pneumonia
Interventions	Amoxycillin and co-amoxyclavulanic acid (250 mg + 62.5 mg or 500 + 125 mg tds) with amoxycillin (250 mg or 500 mg tds) for 10 days
Outcomes	Poor or no response; cure rate
Notes	Exclusion criteria: renal/hepatic impairment; hypersensitivity to penicillin/cephalosporin

Risk of bias

Bias	**Authors' judgement**	**Support for judgement**
Random sequence generation (selection bias)	Low risk	Serial number selected on random basis
Allocation concealment (selection bias)	Unclear risk	Not mentioned
Blinding of participants and personnel (performance bias) All outcomes	High risk	Unblinded study
Blinding of outcome assessment (detection bias) All outcomes	High risk	Unblinded study
Selective reporting (reporting bias)	Unclear risk	No selective reporting
Incomplete outcome data (attrition bias) All outcomes	Unclear risk	Incomplete data adequately addressed
Other bias	Unclear risk	Source of funding not mentioned

Keeley 1990

Methods	RCT comparing co-trimoxazole and procaine penicillin
Participants	Children aged 3 months to 12 years with non-severe pneumonia
Interventions	Co-trimoxazole per oral for 5 days. Procaine penicillin IM daily for 5 days
Outcomes	Cure rate, treatment failure, hospitalisation, well at final follow-up and death rate
Notes	Exclusion criteria: children with chest in-drawing, unable to feed and requiring immediate referral

Keeley 1990 (*Continued*)

Risk of bias		
Bias	**Authors' judgement**	**Support for judgement**
Random sequence generation (selection bias)	Unclear risk	Information not provided in the paper
Allocation concealment (selection bias)	Low risk	Used sealed envelopes
Blinding of participants and personnel (performance bias) All outcomes	High risk	Open-label
Blinding of outcome assessment (detection bias) All outcomes	High risk	Open-label
Selective reporting (reporting bias)	Unclear risk	No selective reporting
Incomplete outcome data (attrition bias) All outcomes	Unclear risk	Incomplete data adequately addressed
Other bias	Low risk	Funded by University of Zimbabwe, Harare

Klein 1995

Methods	RCT comparing cefpodoxime and co-amoxyclavulanic acid in LRTI
Participants	Children aged 3 months to 11.5 years
Interventions	Cefpodoxime 5 to 12 mg/kg/day PO for 10 days or co-amoxyclavulanic acid 6 to 13 mg/kg/day for 10 days
Outcomes	Response rate
Notes	Exclusion criteria: nosocomial infection, antibiotics in past 48 hours, allergy to beta-lactam antibiotics, suspected/confirmed TB, congenital anomalies

Risk of bias		
Bias	**Authors' judgement**	**Support for judgement**
Random sequence generation (selection bias)	Unclear risk	Information not provided

Klein 1995 (*Continued*)

Allocation concealment (selection bias)	Unclear risk	No mention about details of allocation concealment
Blinding of participants and personnel (performance bias) All outcomes	Unclear risk	Information not provided
Blinding of outcome assessment (detection bias) All outcomes	Unclear risk	Information not provided
Selective reporting (reporting bias)	Unclear risk	No intention-to-treat analysis. No details of children excluded from the analysis
Incomplete outcome data (attrition bias) All outcomes	Unclear risk	No intention-to-treat analysis. No details of children excluded from the analysis
Other bias	Unclear risk	Source of funding not mentioned

Kogan 2003

Methods	RCT comparing azithromycin and amoxycillin
Participants	Children aged 1 month to 14 years with non-severe pneumonia
Interventions	Azithromycin (10 mg/kg/day) PO for 3 days or amoxycillin PO 75 mg/kg/day for 7 days
Outcomes	Clinical and radiological cure rates, fever on day 3 and day 7, chest X-ray on day 14
Notes	Exclusion criteria: chronic pathology, preterm, received antibiotics in past 5 days

Risk of bias

Bias	**Authors' judgement**	**Support for judgement**
Random sequence generation (selection bias)	Unclear risk	Information on sequence generation not mentioned
Allocation concealment (selection bias)	High risk	Allocated by investigators
Blinding of participants and personnel (performance bias) All outcomes	High risk	Open-label study
Blinding of outcome assessment (detection bias) All outcomes	High risk	Open-label study

Kogan 2003 (*Continued*)

Selective reporting (reporting bias)	Low risk	No selective reporting
Incomplete outcome data (attrition bias) All outcomes	Low risk	Incomplete data adequately addressed
Other bias	Unclear risk	Source of funding not mentioned

Mulholland 1995

Methods	RCT comparing chloramphenicol and co-trimoxazole in malnourished children with clinical or radiological pneumonia
Participants	Children below 5 years of age with malnutrition and clinical or radiological evidence of pneumonia
Interventions	Enrolled subjects received either chloramphenicol with TMP/SMX placebo or TMP/SMX with chloramphenicol placebo
Outcomes	Cure rate, relapse rate, failure rate and exclusion, death rate
Notes	Blinded Exclusion criteria: already receiving antibiotics, clinical or radiological signs of TB, severe pneumonia TMP/SMX: trimethoprim/ sulphamethoxazole (co-trimoxazole)

Risk of bias

Bias	**Authors' judgement**	**Support for judgement**
Random sequence generation (selection bias)	Low risk	Random list generated in advance
Allocation concealment (selection bias)	Low risk	Double-blind study. Randomisation codes were kept with senior nurse and pharmacist
Blinding of participants and personnel (performance bias) All outcomes	Low risk	Double-blind study
Blinding of outcome assessment (detection bias) All outcomes	Low risk	Double-blind study
Selective reporting (reporting bias)	Low risk	No selective reporting
Incomplete outcome data (attrition bias) All outcomes	Low risk	Incomplete data adequately addressed

Mulholland 1995 (*Continued*)

Other bias	Low risk	Funded by the World Health Organization

Nogeova 1997

Methods	Randomised, controlled, multicentre trial on children between 1 to 12 years of age with radiologically documented pneumonia to compare efficacy of ceftibuten with cefuroxime axetil. Sputum and blood were tested for aetiological agents
Participants	Children 1 to 12 years of age with radiographically confirmed pneumonia
Interventions	Ceftibuten or cefuroxime axetil in 2 divided doses
Outcomes	Cure or failure rates
Notes	Duration of treatment not clear

Risk of bias

Bias	**Authors' judgement**	**Support for judgement**
Random sequence generation (selection bias)	Unclear risk	Details of randomisation including sequence generation not mentioned
Allocation concealment (selection bias)	Unclear risk	Details of allocation concealment not mentioned
Blinding of participants and personnel (performance bias) All outcomes	High risk	Open-label study. Details not included in the text
Blinding of outcome assessment (detection bias) All outcomes	High risk	Open-label study. Details not included in the text
Selective reporting (reporting bias)	Low risk	No selective reporting
Incomplete outcome data (attrition bias) All outcomes	Low risk	Incomplete data adequately addressed
Other bias	Unclear risk	No mention about ethical clearance and source of funding

Ribeiro 2011

Methods	Randomised controlled trial comparing oxacillin + ceftriaxone with co-amoxyclavulanic acid for treatment of very severe pneumonia that was radiologically diagnosed
Participants	Children between 2 months to 5 years of age, hospitalised with very severe pneumonia
Interventions	Patients received either intravenous (IV) oxacillin 200 mg/kg/day every 6 hours for 10 days and ceftriaxone 100 mg/kg/day every 12 hours for 10 days or co-amoxyclavulanic acid 100 mg/kg/day every 8 hours (amoxycillin base). Children receiving oxacillin + ceftriaxone continued to get IV antibiotics for 10 days while those receiving co-amoxyclavulanic acid were switched over to oral medications after improvement at 48 hours
Outcomes	Cure rate, failure rate, time for response in tachypnoea, total hospital stay
Notes	Unblinded study. Source of funding not mentioned. 5 bacterial isolates from blood culture. In oxacillin + ceftriaxone group: *Enterobacter* and *S. aureus* (1 each); in co-amoxyclavulanic acid group: coagulase-negative staphylococci (2 patients), *Pseudomonas aeruginosa* (1 patient)

Risk of bias

Bias	**Authors' judgement**	**Support for judgement**
Random sequence generation (selection bias)	Low risk	Computer-generated randomisation list
Allocation concealment (selection bias)	Low risk	Kept in opaque envelope
Blinding of participants and personnel (performance bias) All outcomes	High risk	Open-label
Blinding of outcome assessment (detection bias) All outcomes	Low risk	Physicians were blinded
Selective reporting (reporting bias)	Low risk	No selective reporting
Incomplete outcome data (attrition bias) All outcomes	Low risk	Incomplete data adequately addressed
Other bias	Unclear risk	Source of funding not mentioned

Roord 1996

Methods	RCT comparing azithromycin and erythromycin in non-severe pneumonia (acute LRTI)
Participants	Children aged 2 months to 16 years with non-severe pneumonia (acute LRTI)
Interventions	Azithromycin 10 mg/kg/day for 3 days or erythromycin 40 mg/kg/day for 10 days
Outcomes	Cure rate, failure rate at day 10 to 14, improvement at day 10 and between days 25 to 30
Notes	Exclusion criteria: not able to take oral medications, known hypersensitivity to azithromycin or erythromycin, cystic fibrosis, immunodeficiency, need for oxygen, nosocomial pneumonia, leucocyte count less than 300,000 per litre, bacteraemia, receiving alternative treatment

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Unclear risk	Information not provided
Allocation concealment (selection bias)	Unclear risk	Open-label randomised controlled trial. Block randomisation. No mention about allocation concealment
Blinding of participants and personnel (performance bias) All outcomes	High risk	Open-label study
Blinding of outcome assessment (detection bias) All outcomes	High risk	Open-label study
Selective reporting (reporting bias)	Low risk	No selective reporting
Incomplete outcome data (attrition bias) All outcomes	Low risk	Incomplete data adequately addressed
Other bias	Unclear risk	Funded by Pfizer - BV

Shann 1985

Methods	RCT comparing chloramphenicol and chloramphenicol in combination with penicillin in severe pneumonia
Participants	Children
Interventions	IM chloramphenicol daily until switched over to oral, or IM chloramphenicol with benzyl penicillin until switched over to oral

Shann 1985 (*Continued*)

Outcomes	Discharge from hospital and good improvement of symptoms	
Notes	Not blinded	
Risk of bias		
Bias	**Authors' judgement**	**Support for judgement**
Random sequence generation (selection bias)	Low risk	Random table was prepared
Allocation concealment (selection bias)	Low risk	Sealed numbered envelopes used
Blinding of participants and personnel (performance bias) All outcomes	High risk	Open-label study
Blinding of outcome assessment (detection bias) All outcomes	High risk	Open-label study
Selective reporting (reporting bias)	Low risk	No selective reporting
Incomplete outcome data (attrition bias) All outcomes	Low risk	Incomplete data adequately addressed
Other bias	Unclear risk	Source of funding not mentioned

Sidal 1994

Methods	RCT comparing co-trimoxazole and penicillin in non-severe pneumonia (including moderate pneumonia)	
Participants	Children aged 3 months to 14 years with non-severe pneumonia (including moderate pneumonia)	
Interventions	PO co-trimoxazole (40 mg/kg/day) for 10 days or IM procaine penicillin (50,000 IU/kg/day) for 10 days	
Outcomes	Cure rate at day 5 and day 10, evident improvement at day 5 and day 10, failure rate	
Notes	Exclusion criteria: severe chest in-drawing, inability to eat or drink, moderate to severe malnutrition, antibiotics in last 2 weeks, wheezing	
Risk of bias		
Bias	**Authors' judgement**	**Support for judgement**

Sidal 1994 (*Continued*)

Random sequence generation (selection bias)	Unclear risk	Information not provided
Allocation concealment (selection bias)	High risk	No details of randomisation or allocation concealment
Blinding of participants and personnel (performance bias) All outcomes	High risk	Open-label study
Blinding of outcome assessment (detection bias) All outcomes	High risk	Open-label study
Selective reporting (reporting bias)	Low risk	No selective reporting
Incomplete outcome data (attrition bias) All outcomes	Low risk	Incomplete data adequately addressed
Other bias	Unclear risk	Source of funding not mentioned

Straus 1998

Methods	RCT comparing co-trimoxazole and amoxycillin in non-severe pneumonia
Participants	Children aged 2 months to 59 months with non-severe pneumonia
Interventions	PO co-trimoxazole 20 mg/kg/day for 5 days or amoxycillin 45 mg/kg/day for 5 days
Outcomes	Failure rate, determined by clinical and radiological evidence
Notes	Blinded. Exclusion criteria: very severe pneumonia, antibiotics in past 48 hours, hospitalisation in past 7 days, hypoxaemia

Risk of bias

Bias	**Authors' judgement**	**Support for judgement**
Random sequence generation (selection bias)	Unclear risk	Sequence generation not mentioned
Allocation concealment (selection bias)	Unclear risk	Drug allotment was concealed from participants. Details not clear
Blinding of participants and personnel (performance bias) All outcomes	High risk	Open-label study. Details not included

Straus 1998 (*Continued*)

Blinding of outcome assessment (detection bias) All outcomes	High risk	Open-label study. Details not included
Selective reporting (reporting bias)	Low risk	No selective reporting
Incomplete outcome data (attrition bias) All outcomes	Low risk	Incomplete data adequately addressed
Other bias	Unclear risk	Source of funding not mentioned

Tsarouhas 1998

Methods	RCT comparing procaine penicillin and amoxycillin for radiographically confirmed pneumonia
Participants	Children aged 6 months to 18 years with pneumonia
Interventions	PO amoxycillin (50 mg/kg/day) or procaine penicillin IM (50,000 IU/kg/day)
Outcomes	Hospitalisation rate, failure rate, temperature more than 38.5 °C, ill appearance, increased respiratory rate
Notes	Unblinded Exclusion criteria: chronic illness, asthma, sickle cell disease, cystic fibrosis, allergy to amoxycillin, or penicillin, antibiotics in past 1 week, wheezing, concurrent febrile illness

Risk of bias

Bias	**Authors' judgement**	**Support for judgement**
Random sequence generation (selection bias)	Unclear risk	Sequence generation not mentioned
Allocation concealment (selection bias)	Low risk	Sealed envelope opened by Emergency Department nurse
Blinding of participants and personnel (performance bias) All outcomes	High risk	Open-label study
Blinding of outcome assessment (detection bias) All outcomes	High risk	Open-label study
Selective reporting (reporting bias)	Low risk	No selective reporting

Tsarouhas 1998 (*Continued*)

Incomplete outcome data (attrition bias) All outcomes	Low risk	Incomplete data adequately addressed
Other bias	Unclear risk	Source of funding not mentioned

Wubbel 1999

Methods	RCT comparing azithromycin and erythromycin in children over 5 years of age with pneumonia; and comparing azithromycin with co-amoxyclavulanic acid in children under 5 years of age
Participants	Children aged between 6 months a 16 years with pneumonia
Interventions	PO azithromycin (10 mg/kg on day 1 followed by 5 mg/kg/day for next 4 days) or co-amoxyclavulanic acid 40 mg/kg/day for 10 days in children under 5 years of age; and erythromycin 40 mg/kg/day for 10 days in children over 5 years
Outcomes	Clinically diagnosed cure rates, failure rates and improvement
Notes	Non-blinded. Exclusion criteria: hypersensitivity to study drugs, nosocomial pneumonia, hospitalisation, antibiotics in last 7 days

Risk of bias

Bias	**Authors' judgement**	**Support for judgement**
Random sequence generation (selection bias)	Unclear risk	Details not mentioned
Allocation concealment (selection bias)	Unclear risk	Allocation concealment not clearly described
Blinding of participants and personnel (performance bias) All outcomes	High risk	Unblinded study
Blinding of outcome assessment (detection bias) All outcomes	High risk	Unblinded study
Selective reporting (reporting bias)	Low risk	No selective reporting
Incomplete outcome data (attrition bias) All outcomes	Low risk	Incomplete data adequately addressed
Other bias	Unclear risk	Funded by Pfizer Inc.

bd: twice a day
CHD: congenital heart disease
CPZ: carbamazepine
IM: intramuscular
IV: intravenous
LRTI: lower respiratory tract infection
PO: orally
PTV: post-therapy visit
q6h: every 6 hours
q8h: every 8 hours
q12h: every 12 hours
RCT: randomised controlled trial
$Sp0_2$: oxygen saturation
TB: tuberculosis
tds: three times a day
TOCV: test of cure visit
WHO: World Health Organization

Characteristics of excluded studies *[ordered by study ID]*

Study	Reason for exclusion
Agostoni 1988	Compares minocycline and amoxycillin in 23 children between 3 to 11.5 years with pneumonia. Not a RCT
Al-Eiden 1999	Describes results of sequential antibiotic therapy (SAT) in 89 patients with severe lower respiratory tract infection. The sequential antibiotic use was the reason for exclusion
Ambroggio 2012	A retrospective cohort study, analysed 20,743 patients hospitalised with community-acquired pneumonia. Of these, 24% received beta-lactam and macrolide combination therapy on admission. Compared outcome in form of hospital stay and relapse rates between children who received beta-lactam monotherapy or children who received beta-lactam plus macrolide combination therapy Excluded because it was not randomised controlled trial
Bari 2011	A cluster-randomised controlled trial on children below 5 years of age with severe pneumonia compared oral amoxicillin with standard treatment (referral and parenteral/oral antibiotics). The study compared 2 modalities of treatment (oral amoxicillin with standard treatment); did not compare 2 antibiotics
Bonvehi 2003	Compared clarithromycin and co-amoxyclavulanic acid in adult patients with CAP due to penicillin-resistant and/or macrolide-resistant *S. pneumoniae*. The study was excluded because of its adult study population
Esposito 2005	Compared azithromycin in addition to symptomatic treatment with symptomatic treatment alone in children with recurrent respiratory tract infections. The study did not compare 2 or more antibiotics for pneumonia
Fogarty 2002	Compared cefditoren with co-amoxyclavulanic acid in the management of community-acquired pneumonia in adult patients. The study had an adult population

(*Continued*)

Haffejee 1984	A single-blind therapeutic trial using cefotaxime or a benzyl-penicillin-gentamycin combination in 68 hospitalised paediatric patients with 72 episodes of severe infection (septicaemia, pneumonia, neonatal meningitis and others). No separate data were available for pneumonia
Hasali 2005	A randomised comparative study of clarithromycin and erythromycin in the treatment of community-acquired pneumonia in children. Outcome in form of cure or failure available only for children with mycoplasma or chlamydia pneumonia
Higuera 1996	Compared oral cefuroxime axetil and oral co-amoxyclavulanic acid in the treatment of community-acquired pneumonia in adult patients. The study was in adult patients
Lee 2008	A randomised controlled trial comparing ampicillin versus ampicillin + gentamycin in children with community-acquired pneumonia. Outcome variables were total hospital stay and time taken for improvement in clinical symptoms. No clear data on cure or failure rates
Lu 2006	Full paper could not be obtained
Mouallem 1976	Compared cephradine and cephalexin for the treatment of bacterial infections in 162 children between 4 months and 11 years of age. There were no separate data for pneumonia
Paupe 1992	Compares cefetamet (2 doses) with cefaclor. The doses of antibiotics were inconsistent
Peltola 2001	Describes results of treatment with a short (4-day) duration of antibiotics
Ruhrmann 1982	Randomised controlled study. Compared erythromycin with amoxycillin in the treatment of 120 children with community-acquired pneumonia. Measured outcomes were duration of clinical symptoms, aetiology of pneumonia and side effects of antibiotics. The study does not provide cure rates, failure rates, death rates or relapse rates
Sanchez 1998	Randomised controlled trial involving 409 patients admitted to internal medicine department. Compared ceftriaxone, cefuroxime and amoxycillin-clavulanic acid. Study does not provide separate data for children
Soofi 2012	A cluster-randomised controlled trial on children below 5 years of age with severe pneumonia compared oral amoxycillin with standard treatment (referral and parenteral/oral antibiotics). The study compared 2 modalities of treatment (oral amoxicillin with standard treatment); did not compare 2 antibiotics
van Zyl 2002	Randomised controlled trial compared cefditoren with cefpodoxime in community-acquired pneumonia in adult patients. The study had an adult study population
Vuori-Holopaine 2000	Compared procaine penicillin and cefuroxime in children between 3 months and 15 years of age with suspected sepsis. There were no separate data for pneumonia available

CAP: community-acquired pneumonia
RCT: randomised controlled trial

DATA AND ANALYSES

Comparison 1. Azithromycin versus erythromycin

Outcome or subgroup title	No. of studies	No. of participants	Statistical method	Effect size
1 Mean age (months)	3	369	Mean Difference (IV, Random, 95% CI)	-4.48 [-18.54, 9.57]
2 Male sex	3	564	Odds Ratio (M-H, Random, 95% CI)	0.83 [0.58, 1.18]
3 Wheezing present	2	479	Odds Ratio (M-H, Random, 95% CI)	1.23 [0.31, 4.87]
4 Cure rate	3	363	Odds Ratio (M-H, Random, 95% CI)	1.22 [0.50, 2.94]
5 Failure rate	3	392	Odds Ratio (M-H, Random, 95% CI)	0.73 [0.18, 2.89]
6 Side effects	2	153	Odds Ratio (M-H, Random, 95% CI)	0.92 [0.18, 4.73]
7 Organisms identified by serology or nasopharyngeal cultures	3	368	Odds Ratio (M-H, Random, 95% CI)	0.75 [0.30, 1.87]
8 Cure rate in radiographically confirmed pneumonia	2	147	Odds Ratio (M-H, Random, 95% CI)	1.72 [0.65, 4.56]
9 Failure rate in radiographically confirmed pneumonia	2	147	Odds Ratio (M-H, Random, 95% CI)	0.62 [0.23, 1.63]

Comparison 2. Clarithromycin versus erythromycin

Outcome or subgroup title	No. of studies	No. of participants	Statistical method	Effect size
1 Age below 5 years	1	260	Odds Ratio (M-H, Random, 95% CI)	0.93 [0.56, 1.55]
2 Cure rates	1	234	Odds Ratio (M-H, Random, 95% CI)	1.61 [0.84, 3.08]
3 Clinical success rate	1	234	Odds Ratio (M-H, Random, 95% CI)	1.92 [0.45, 8.23]
4 Failure rate	1	234	Odds Ratio (M-H, Random, 95% CI)	0.52 [0.12, 2.23]
5 Relapse rate	1	226	Odds Ratio (M-H, Random, 95% CI)	0.17 [0.02, 1.45]
6 Radiologic resolution	1	209	Odds Ratio (M-H, Random, 95% CI)	2.51 [1.02, 6.16]
7 Radiologic success	1	209	Odds Ratio (M-H, Random, 95% CI)	3.55 [0.70, 18.04]
8 Radiologic failure	1	209	Odds Ratio (M-H, Random, 95% CI)	0.34 [0.06, 1.80]
9 Adverse events	1	260	Odds Ratio (M-H, Random, 95% CI)	1.07 [0.60, 1.90]
10 Bacteriologic response	1	45	Odds Ratio (M-H, Random, 95% CI)	1.0 [0.15, 6.67]

Comparison 3. Azithromycin versus co-amoxyclavulanic acid

Outcome or subgroup title	No. of studies	No. of participants	Statistical method	Effect size
1 Cure rate	1	188	Odds Ratio (M-H, Random, 95% CI)	1.02 [0.54, 1.95]
2 Failure rate	2	276	Odds Ratio (M-H, Random, 95% CI)	1.21 [0.42, 3.53]
3 Improved	1	188	Odds Ratio (M-H, Random, 95% CI)	0.85 [0.43, 1.71]
4 Side effects	2	276	Odds Ratio (M-H, Random, 95% CI)	0.15 [0.04, 0.61]
5 Organisms isolated	1	188	Odds Ratio (M-H, Random, 95% CI)	1.27 [0.24, 6.74]
6 Mycoplasma serology positive	1	192	Odds Ratio (M-H, Random, 95% CI)	1.19 [0.64, 2.22]
7 Failure rates in radiographically confirmed pneumonia	1	88	Odds Ratio (M-H, Random, 95% CI)	0.62 [0.05, 7.08]

Comparison 4. Azithromycin versus amoxycillin

Outcome or subgroup title	No. of studies	No. of participants	Statistical method	Effect size
1 Age in months	1	76	Mean Difference (IV, Random, 95% CI)	58.10 [35.59, 80.61]
2 Duration of illness	1	47	Mean Difference (IV, Random, 95% CI)	-0.10 [-1.50, 1.30]
3 Wheezing present	1	47	Odds Ratio (M-H, Random, 95% CI)	2.02 [0.59, 6.96]
4 Cure rate clinical	1	47	Odds Ratio (M-H, Random, 95% CI)	0.0 [0.0, 0.0]
5 Cure rate radiological	1	47	Odds Ratio (M-H, Random, 95% CI)	2.85 [0.73, 11.09]
6 Fever day 7	1	47	Odds Ratio (M-H, Random, 95% CI)	1.37 [0.41, 4.61]

Comparison 5. Amoxycillin versus procaine penicillin

Outcome or subgroup title	No. of studies	No. of participants	Statistical method	Effect size
1 Median age	1	170	Mean Difference (IV, Random, 95% CI)	0.30 [-0.52, 1.12]
2 Failure rate	1	154	Odds Ratio (M-H, Random, 95% CI)	0.75 [0.17, 3.25]

Comparison 6. Co-amoxyclavulanic acid versus amoxycillin

Outcome or subgroup title	No. of studies	No. of participants	Statistical method	Effect size
1 Poor or no response	1	100	Odds Ratio (M-H, Random, 95% CI)	0.08 [0.01, 0.67]
2 Cure rate	1	100	Odds Ratio (M-H, Random, 95% CI)	10.44 [2.85, 38.21]
3 Complications	1	100	Odds Ratio (M-H, Random, 95% CI)	5.21 [0.24, 111.24]
4 Age (months)	1	100	Mean Difference (IV, Random, 95% CI)	4.80 [-8.09, 17.69]
5 Weight	1	100	Mean Difference (IV, Random, 95% CI)	1.10 [-1.06, 3.26]
6 Male sex	1	100	Odds Ratio (M-H, Random, 95% CI)	1.31 [0.57, 3.03]
7 Wheeze present	1	100	Odds Ratio (M-H, Random, 95% CI)	0.58 [0.18, 1.92]
8 Side effects	1	100	Odds Ratio (M-H, Random, 95% CI)	5.21 [0.24, 111.24]

Comparison 7. Co-trimoxazole versus amoxycillin

Outcome or subgroup title	No. of studies	No. of participants	Statistical method	Effect size
1 Age less than 1 year	3	2347	Odds Ratio (M-H, Random, 95% CI)	0.97 [0.74, 1.29]
2 Male sex	3	2318	Odds Ratio (M-H, Random, 95% CI)	0.70 [0.59, 0.83]
3 Mean Z score for weight	2	2066	Mean Difference (IV, Random, 95% CI)	-0.06 [-0.27, 0.15]
4 Non-severe pneumonia	1	595	Odds Ratio (M-H, Random, 95% CI)	0.97 [0.69, 1.37]
5 Received antibiotics in previous week	1	595	Odds Ratio (M-H, Random, 95% CI)	0.67 [0.46, 0.97]
6 Severe pneumonia	1	595	Odds Ratio (M-H, Random, 95% CI)	1.03 [0.73, 1.45]
7 Failure rate in non-severe pneumonia	3	1787	Odds Ratio (M-H, Random, 95% CI)	1.18 [0.91, 1.51]
8 Failure rate severe pneumonia clinical diagnosis	1	302	Odds Ratio (M-H, Random, 95% CI)	1.71 [0.94, 3.11]
9 Failure rate radiological positive pneumonia	1	153	Odds Ratio (M-H, Random, 95% CI)	2.14 [0.96, 4.78]
10 Failure rate radiological negative pneumonia	1	424	Odds Ratio (M-H, Random, 95% CI)	1.72 [0.96, 3.09]
11 Death rate	2	2050	Odds Ratio (M-H, Random, 95% CI)	2.08 [0.22, 20.06]
12 Lost to follow-up	3	2325	Odds Ratio (M-H, Random, 95% CI)	0.96 [0.59, 1.57]
13 Wheeze positive	1	1471	Odds Ratio (M-H, Random, 95% CI)	0.76 [0.49, 1.19]
14 Cure rate	2	1732	Odds Ratio (M-H, Random, 95% CI)	1.03 [0.56, 1.89]
15 Change of antibiotics	1	1459	Odds Ratio (M-H, Random, 95% CI)	1.26 [0.95, 1.69]
16 Failure rates after excluding study by Awasthi 2008	2	1750	Odds Ratio (M-H, Random, 95% CI)	1.19 [0.92, 1.53]

Comparison 8. Co-trimoxazole versus procaine penicillin

Outcome or subgroup title	No. of studies	No. of participants	Statistical method	Effect size
1 Age less than 1 year	2	723	Odds Ratio (M-H, Random, 95% CI)	1.30 [0.96, 1.75]
2 Age 1 to 5 years	1	614	Odds Ratio (M-H, Random, 95% CI)	0.84 [0.61, 1.16]
3 Age 5 to 12 years	2	723	Odds Ratio (M-H, Random, 95% CI)	0.79 [0.45, 1.39]
4 Duration of illness in days	2	723	Mean Difference (IV, Fixed, 95% CI)	-0.15 [-0.49, 0.20]
5 Male sex	1	614	Odds Ratio (M-H, Random, 95% CI)	0.93 [0.67, 1.27]
6 Cure rate	2	723	Odds Ratio (M-H, Random, 95% CI)	1.58 [0.26, 9.69]
7 Hospitalisation rate	1	614	Odds Ratio (M-H, Random, 95% CI)	2.52 [0.88, 7.25]
8 Well at end of follow-up	1	614	Odds Ratio (M-H, Random, 95% CI)	0.90 [0.51, 1.57]
9 Death	1	614	Odds Ratio (M-H, Random, 95% CI)	3.09 [0.13, 76.13]
10 Treatment failure	1	614	Odds Ratio (M-H, Random, 95% CI)	1.72 [0.41, 7.27]

Comparison 9. Co-trimoxazole versus procaine penicillin and ampicillin

Outcome or subgroup title	No. of studies	No. of participants	Statistical method	Effect size
1 Mean age in months	1	134	Mean Difference (IV, Random, 95% CI)	0.0 [0.0, 0.0]
2 Age less than 1 year	1	134	Odds Ratio (M-H, Random, 95% CI)	0.80 [0.39, 1.64]
3 Male sex	1	134	Odds Ratio (M-H, Random, 95% CI)	1.29 [0.65, 2.58]
4 Cure rate	1	134	Odds Ratio (M-H, Random, 95% CI)	1.15 [0.36, 3.61]
5 Hospitalisation rate	1	134	Odds Ratio (M-H, Random, 95% CI)	1.57 [0.25, 9.72]
6 Death rate	1	134	Odds Ratio (M-H, Random, 95% CI)	0.20 [0.01, 4.25]

Comparison 10. Cefpodoxime versus co-amoxyclavulanic acid

Outcome or subgroup title	No. of studies	No. of participants	Statistical method	Effect size
1 Cure rate (response rate) at end of treatment	1	278	Odds Ratio (M-H, Random, 95% CI)	0.69 [0.18, 2.60]
2 Mean age (months)	1	348	Mean Difference (IV, Random, 95% CI)	0.0 [0.0, 0.0]
3 Adverse effects	1	278	Odds Ratio (M-H, Random, 95% CI)	0.46 [0.16, 1.35]
4 Age in years	1	348	Mean Difference (IV, Random, 95% CI)	0.0 [0.0, 0.0]
5 Follow-up	1	278	Odds Ratio (M-H, Random, 95% CI)	0.37 [0.11, 1.31]

Comparison 11. Chloramphenicol versus penicillin plus gentamicin

Outcome or subgroup title	No. of studies	No. of participants	Statistical method	Effect size
1 Adverse events	1	1116	Odds Ratio (M-H, Random, 95% CI)	1.26 [0.96, 1.66]
2 Death	1	1116	Odds Ratio (M-H, Random, 95% CI)	1.25 [0.76, 2.07]
3 Change of antibiotics	1	1116	Odds Ratio (M-H, Random, 95% CI)	0.80 [0.54, 1.18]
4 Readmission before 30 days	1	1116	Odds Ratio (M-H, Random, 95% CI)	1.61 [1.02, 2.55]
5 Absconded	1	1116	Odds Ratio (M-H, Random, 95% CI)	1.31 [0.83, 2.09]
6 Age (months)	1	1116	Mean Difference (IV, Random, 95% CI)	0.0 [0.0, 0.0]
7 Culture positive	1	1116	Odds Ratio (M-H, Random, 95% CI)	0.85 [0.60, 1.21]
8 Male sex	1	1116	Odds Ratio (M-H, Random, 95% CI)	0.88 [0.69, 1.12]
9 Received antibiotics in previous 1 week	1	1116	Odds Ratio (M-H, Random, 95% CI)	0.96 [0.75, 1.22]
10 Lost to follow-up	1	1116	Odds Ratio (M-H, Random, 95% CI)	1.31 [0.83, 2.09]

Comparison 12. Chloramphenicol with ampicillin and gentamicin

Outcome or subgroup title	No. of studies	No. of participants	Statistical method	Effect size
1 Mean age	1	958	Mean Difference (IV, Random, 95% CI)	-0.10 [-1.12, 0.92]
2 Male sex	1	958	Odds Ratio (M-H, Random, 95% CI)	0.85 [0.66, 1.11]
3 Number received antibiotics in past 7 days	1	950	Odds Ratio (M-H, Random, 95% CI)	0.87 [0.67, 1.14]
4 Failure rates on day 5	1	958	Odds Ratio (M-H, Random, 95% CI)	1.51 [1.04, 2.19]
5 Failure rates on day 10	1	958	Odds Ratio (M-H, Random, 95% CI)	1.46 [1.04, 2.06]
6 Failure rates on day 21	1	958	Odds Ratio (M-H, Random, 95% CI)	1.43 [1.03, 1.98]
7 Need for change in antibiotics (day 5)	1	958	Odds Ratio (M-H, Random, 95% CI)	1.81 [1.10, 2.98]
8 Need for change in antibiotics (day 10)	1	958	Odds Ratio (M-H, Random, 95% CI)	1.71 [1.10, 2.66]
9 Need for change in antibiotics (day 21)	1	958	Odds Ratio (M-H, Random, 95% CI)	1.65 [1.09, 2.49]
10 Death rates	1	958	Odds Ratio (M-H, Random, 95% CI)	1.65 [0.99, 2.77]

Comparison 13. Chloramphenicol plus penicillin versus ceftriaxone

Outcome or subgroup title	No. of studies	No. of participants	Statistical method	Effect size
1 Cure rates	1	97	Odds Ratio (M-H, Random, 95% CI)	1.36 [0.47, 3.93]

Comparison 14. Chloramphenicol versus chloramphenicol plus penicillin

Outcome or subgroup title	No. of studies	No. of participants	Statistical method	Effect size
1 Need for change of antibiotics	1	748	Odds Ratio (M-H, Random, 95% CI)	0.49 [0.12, 1.97]
2 Death rates	1	748	Odds Ratio (M-H, Random, 95% CI)	0.73 [0.48, 1.09]
3 Lost to follow-up	1	748	Odds Ratio (M-H, Random, 95% CI)	1.11 [0.80, 1.53]

Comparison 15. Ampicillin alone versus penicillin with chloramphenicol

Outcome or subgroup title	No. of studies	No. of participants	Statistical method	Effect size
1 Cure rates	1	101	Odds Ratio (M-H, Random, 95% CI)	0.48 [0.15, 1.51]
2 Age (months)	1	101	Mean Difference (IV, Random, 95% CI)	-1.69 [-5.54, 2.16]
3 Male sex	1	101	Odds Ratio (M-H, Random, 95% CI)	0.88 [0.41, 1.93]
4 Duration of hospital stay	1	101	Mean Difference (IV, Random, 95% CI)	-0.10 [-1.13, 0.93]
5 Grade 2 to 4 malnutrition	1	101	Odds Ratio (M-H, Random, 95% CI)	0.88 [0.41, 1.93]

Comparison 16. Benzathine penicillin versus procaine penicillin

Outcome or subgroup title	No. of studies	No. of participants	Statistical method	Effect size
1 Cure rate	2	281	Odds Ratio (M-H, Random, 95% CI)	0.53 [0.27, 1.01]
2 Failure rate	2	281	Odds Ratio (M-H, Random, 95% CI)	3.17 [0.90, 11.11]
3 Male sex	2	281	Odds Ratio (M-H, Random, 95% CI)	1.09 [0.67, 1.76]
4 Age between 2 to 6 years	2	301	Odds Ratio (M-H, Random, 95% CI)	1.08 [0.47, 2.48]
5 Age between 7 to 12 years	2	301	Odds Ratio (M-H, Random, 95% CI)	0.52 [0.31, 0.88]
6 Lost to follow-up	1	176	Odds Ratio (M-H, Random, 95% CI)	1.80 [0.16, 20.25]
7 Failure rates in radiographically confirmed pneumonia	1	176	Odds Ratio (M-H, Random, 95% CI)	1.61 [0.45, 5.70]

Comparison 17. Amoxycillin versus penicillin

Outcome or subgroup title	No. of studies	No. of participants	Statistical method	Effect size
1 Nasopharyngeal aspirates for *S. pneumoniae*	1	1486	Odds Ratio (M-H, Random, 95% CI)	0.90 [0.72, 1.13]
2 Age less than 1 year	1	1702	Odds Ratio (M-H, Random, 95% CI)	1.06 [0.87, 1.29]
3 Male sex	2	1905	Odds Ratio (M-H, Random, 95% CI)	1.04 [0.87, 1.25]
4 Weight below 2 Z score (indicating severe malnutrition)	1	1686	Odds Ratio (M-H, Random, 95% CI)	0.92 [0.70, 1.19]
5 Breast fed	1	1702	Odds Ratio (M-H, Random, 95% CI)	1.12 [0.92, 1.37]
6 Received antibiotics in last 7 days	2	1905	Odds Ratio (M-H, Random, 95% CI)	0.97 [0.69, 1.38]
7 Failure rate at 48 hours	1	1702	Odds Ratio (M-H, Random, 95% CI)	1.03 [0.81, 1.31]
8 Failure rate on day 5	2	1905	Odds Ratio (M-H, Random, 95% CI)	1.15 [0.58, 2.30]
9 Failure rate on day 14	1	1702	Odds Ratio (M-H, Random, 95% CI)	1.04 [0.84, 1.29]
10 Death rates	2	1905	Odds Ratio (M-H, Random, 95% CI)	0.07 [0.00, 1.18]
11 Nasopharyngeal *H. influenzae*	1	1482	Odds Ratio (M-H, Fixed, 95% CI)	1.00 [0.78, 1.29]
12 Respiratory syncytial virus (RSV) in nasopharyngeal swabs	2	1731	Odds Ratio (M-H, Random, 95% CI)	1.04 [0.83, 1.31]
13 Mean age	1	203	Mean Difference (IV, Random, 95% CI)	0.0 [0.0, 0.0]
14 Blood culture positive for *S. pneumoniae*	1	203	Odds Ratio (M-H, Random, 95% CI)	0.34 [0.03, 3.29]
15 Failure rate on day 5 in radiographically confirmed pneumonia	1	203	Odds Ratio (M-H, Random, 95% CI)	2.36 [0.59, 9.39]

Comparison 18. Amoxycillin with IV ampicillin

Outcome or subgroup title	No. of studies	No. of participants	Statistical method	Effect size
1 Age below one year	1	2037	Odds Ratio (M-H, Random, 95% CI)	0.94 [0.79, 1.13]
2 Male sex	1	2037	Odds Ratio (M-H, Random, 95% CI)	1.09 [0.91, 1.30]
3 Wheezing in infants	1	1311	Odds Ratio (M-H, Random, 95% CI)	1.03 [0.78, 1.37]
4 Wheezing in age group one to five years	1	726	Odds Ratio (M-H, Random, 95% CI)	0.77 [0.56, 1.04]
5 Failure rates	1	2037	Odds Ratio (M-H, Random, 95% CI)	0.86 [0.63, 1.19]
6 Relapse rates	1	1873	Odds Ratio (M-H, Random, 95% CI)	0.78 [0.46, 1.33]
7 Death rates	1	2037	Odds Ratio (M-H, Random, 95% CI)	0.25 [0.03, 2.21]
8 Lost to follow-up	1	2037	Odds Ratio (M-H, Random, 95% CI)	0.45 [0.17, 1.20]
9 Protocol violation	1	2037	Odds Ratio (M-H, Random, 95% CI)	0.92 [0.43, 1.96]

Comparison 19. Amoxycillin with cefuroxime

Outcome or subgroup title	No. of studies	No. of participants	Statistical method	Effect size
1 Mean age in months	1	84	Mean Difference (IV, Random, 95% CI)	4.47 [-1.45, 10.39]
2 Male sex	1	85	Odds Ratio (M-H, Random, 95% CI)	0.11 [0.01, 0.90]
3 Cure rates	1	84	Odds Ratio (M-H, Random, 95% CI)	2.05 [0.18, 23.51]
4 Failure rates	1	84	Odds Ratio (M-H, Random, 95% CI)	0.49 [0.04, 5.59]

Comparison 20. Amoxycillin with clarithromycin

Outcome or subgroup title	No. of studies	No. of participants	Statistical method	Effect size
1 Mean age	1	85	Mean Difference (IV, Random, 95% CI)	-3.16 [-10.30, 3.98]
2 Male sex	1	85	Odds Ratio (M-H, Random, 95% CI)	1.55 [0.55, 4.35]
3 Cure rates	1	82	Odds Ratio (M-H, Random, 95% CI)	1.05 [0.06, 17.40]
4 Failure rates	1	82	Odds Ratio (M-H, Random, 95% CI)	0.95 [0.06, 15.74]

Comparison 21. Penicillin and gentamycin with co-amoxyclavulanic acid

Outcome or subgroup title	No. of studies	No. of participants	Statistical method	Effect size
1 Number of children less than 1 year age	1	71	Odds Ratio (M-H, Random, 95% CI)	0.54 [0.20, 1.43]
2 Male sex	1	63	Odds Ratio (M-H, Random, 95% CI)	1.35 [0.42, 4.32]
3 Failure rates	1	71	Odds Ratio (M-H, Random, 95% CI)	0.86 [0.05, 14.39]

Comparison 22. Levofloxacin with comparator (co-amoxyclavulanic acid/ceftriaxone)

Outcome or subgroup title	No. of studies	No. of participants	Statistical method	Effect size
1 Mean age	1	709	Mean Difference (IV, Random, 95% CI)	0.05 [-0.64, 0.74]
2 Male sex	1	709	Odds Ratio (M-H, Random, 95% CI)	0.97 [0.69, 1.36]
3 Numbers received antibiotics in past 1 week	1	709	Odds Ratio (M-H, Random, 95% CI)	0.93 [0.64, 1.35]
4 Cure rates	1	539	Odds Ratio (M-H, Random, 95% CI)	1.05 [0.46, 2.42]

Comparison 23. Cefuroxime with clarithromycin

Outcome or subgroup title	No. of studies	No. of participants	Statistical method	Effect size
1 Mean age	1	83	Mean Difference (IV, Random, 95% CI)	-7.03 [-13.16, -0.90]
2 Male sex	1	84	Odds Ratio (M-H, Random, 95% CI)	14.55 [1.78, 118.76]
3 Cure rates	1	82	Odds Ratio (M-H, Random, 95% CI)	0.51 [0.04, 5.89]
4 Failure rates	1	84	Odds Ratio (M-H, Random, 95% CI)	2.05 [0.18, 23.51]

Comparison 24. Co-trimoxazole versus chloramphenicol

Outcome or subgroup title	No. of studies	No. of participants	Statistical method	Effect size
1 Age in months	1	111	Mean Difference (IV, Random, 95% CI)	1.90 [-0.64, 4.44]
2 Male sex	1	111	Odds Ratio (M-H, Random, 95% CI)	0.89 [0.42, 1.89]
3 Weight for age	1	111	Mean Difference (IV, Random, 95% CI)	0.0 [-3.11, 3.11]
4 Wheezing positive	1	111	Odds Ratio (M-H, Random, 95% CI)	0.67 [0.11, 4.15]
5 Cure rate	1	111	Odds Ratio (M-H, Random, 95% CI)	1.06 [0.47, 2.40]
6 Failure rate	1	111	Odds Ratio (M-H, Random, 95% CI)	1.03 [0.45, 2.33]
7 Excluded	1	111	Odds Ratio (M-H, Random, 95% CI)	0.94 [0.42, 2.12]
8 Relapse rate	1	111	Odds Ratio (M-H, Random, 95% CI)	1.02 [0.24, 4.30]
9 Need for change in antibiotics	1	111	Odds Ratio (M-H, Random, 95% CI)	1.42 [0.46, 4.40]
10 Death rate	1	111	Odds Ratio (M-H, Random, 95% CI)	2.21 [0.63, 7.83]
11 Organisms isolated on blood culture or lung puncture	1	111	Odds Ratio (M-H, Random, 95% CI)	1.25 [0.47, 3.30]

Comparison 25. Ceftibuten versus cefuroxime

Outcome or subgroup title	No. of studies	No. of participants	Statistical method	Effect size
1 Male sex	1	140	Odds Ratio (M-H, Random, 95% CI)	0.79 [0.41, 1.54]
2 Positive for microbial agent	1	140	Odds Ratio (M-H, Fixed, 95% CI)	3.83 [1.87, 7.83]
3 Adverse reaction	1	140	Odds Ratio (M-H, Fixed, 95% CI)	2.0 [0.35, 11.29]
4 Cure rate	1	140	Odds Ratio (M-H, Fixed, 95% CI)	0.32 [0.11, 0.94]
5 Failure rate	1	140	Odds Ratio (M-H, Fixed, 95% CI)	6.81 [1.46, 31.70]

Comparison 26. Oxacillin ceftriaxone versus co-amoxyclavulanic acid

Outcome or subgroup title	No. of studies	No. of participants	Statistical method	Effect size
1 Median age (months) with IQR			Other data	No numeric data
2 Male sex	1	104	Odds Ratio (M-H, Random, 95% CI)	0.70 [0.32, 1.54]
3 Mean number of days before admission	1	104	Mean Difference (IV, Random, 95% CI)	-0.90 [-2.28, 0.48]
4 Received antibiotics before enrolment	1	104	Odds Ratio (M-H, Random, 95% CI)	1.17 [0.50, 2.76]
5 Failure rates	1	104	Odds Ratio (M-H, Random, 95% CI)	0.98 [0.33, 2.92]
6 Mean time for improvement in tachypnoea	1	104	Mean Difference (IV, Random, 95% CI)	-1.0 [-1.89, -0.11]
7 Mean length of stay	1	104	Mean Difference (IV, Random, 95% CI)	-3.40 [-5.46, -1.34]

Comparison 27. Oral versus parenteral antibiotics for treatment of severe pneumonia

Outcome or subgroup title	No. of studies	No. of participants	Statistical method	Effect size
1 Male sex	5	4164	Odds Ratio (M-H, Random, 95% CI)	1.06 [0.94, 1.21]
2 Age below 12 months	4	3961	Odds Ratio (M-H, Random, 95% CI)	0.95 [0.69, 1.30]
3 Received antibiotics in the past week	3	3942	Odds Ratio (M-H, Random, 95% CI)	1.14 [0.86, 1.52]
4 Children with wheezing	2	3739	Odds Ratio (M-H, Random, 95% CI)	1.09 [0.70, 1.68]
5 RSV positivity	2	1634	Odds Ratio (M-H, Random, 95% CI)	1.04 [0.82, 1.31]
6 Failure rates on day 3	3	3942	Odds Ratio (M-H, Random, 95% CI)	0.95 [0.78, 1.15]
7 Failure rates on day 6	6	4331	Odds Ratio (M-H, Random, 95% CI)	0.84 [0.56, 1.24]
8 Failure rate in children below 5 years of age	3	3870	Odds Ratio (M-H, Random, 95% CI)	0.91 [0.76, 1.09]
9 Failure rates in children receiving oral amoxicillin or injectable antibiotics	4	4112	Odds Ratio (M-H, Random, 95% CI)	0.92 [0.77, 1.10]
10 Failure rate in children receiving cotrimoxazole or injectable penicillin	2	219	Odds Ratio (M-H, Random, 95% CI)	0.31 [0.03, 3.29]
11 Failure rate in children treated with oral or parenteral antibiotics on ambulatory basis	4	2426	Odds Ratio (M-H, Random, 95% CI)	0.56 [0.24, 1.32]
12 Failure rate after removing one study	2	2240	Odds Ratio (M-H, Random, 95% CI)	1.11 [0.44, 2.83]
13 Hospitalisation	3	458	Odds Ratio (M-H, Random, 95% CI)	1.13 [0.38, 3.34]
14 Relapse rates	2	2076	Odds Ratio (M-H, Random, 95% CI)	1.28 [0.34, 4.82]
15 Death rates	3	3942	Odds Ratio (M-H, Random, 95% CI)	0.15 [0.03, 0.87]
16 Lost to follow-up	1	2037	Odds Ratio (M-H, Random, 95% CI)	0.45 [0.17, 1.20]
17 Cure rate	2	334	Odds Ratio (M-H, Random, 95% CI)	5.05 [1.19, 21.33]

18 Failure rates in radiographically confirmed-pneumonia	2	373	Odds Ratio (M-H, Random, 95% CI)	1.33 [0.41, 4.29]
19 Death rates after removing one study	2	2240	Odds Ratio (M-H, Fixed, 95% CI)	0.25 [0.03, 2.21]

Comparison 28. Co-trimoxazole versus co-amoxyclavulanic acid

Outcome or subgroup title	No. of studies	No. of participants	Statistical method	Effect size
1 Children below 1 year of age	2	1232	Odds Ratio (M-H, Random, 95% CI)	117.90 [16.39, 848.37]
2 Male sex	2	1232	Odds Ratio (M-H, Random, 95% CI)	0.54 [0.33, 0.88]
3 Failure rate	2	1232	Odds Ratio (M-H, Random, 95% CI)	12.98 [3.18, 53.06]

Comparison 29. Amoxycillin versus cefpodoxime

Outcome or subgroup title	No. of studies	No. of participants	Statistical method	Effect size
1 Age in months	1	284	Mean Difference (IV, Random, 95% CI)	0.0 [0.0, 0.0]
2 Male sex	1	51	Odds Ratio (M-H, Random, 95% CI)	1.71 [0.07, 44.09]
3 Response/cure rate	1	238	Odds Ratio (M-H, Random, 95% CI)	0.20 [0.08, 0.53]

Comparison 30. Amoxycillin versus chloramphenicol

Outcome or subgroup title	No. of studies	No. of participants	Statistical method	Effect size
1 Age (mean/median)	2	1032	Mean Difference (IV, Random, 95% CI)	-6.60 [-10.52, -2.68]
2 Male sex	2	1032	Odds Ratio (M-H, Random, 95% CI)	2.34 [1.55, 3.53]
3 Cure rate	1	796	Odds Ratio (M-H, Random, 95% CI)	4.26 [2.57, 7.08]
4 Failure rates	2	1065	Odds Ratio (M-H, Random, 95% CI)	0.64 [0.41, 1.00]

Analysis 1.1. Comparison 1 Azithromycin versus erythromycin, Outcome 1 Mean age (months).

Review: Antibiotics for community-acquired pneumonia in children

Comparison: 1 Azithromycin versus erythromycin

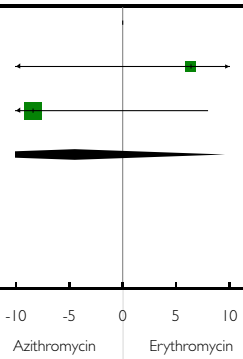
Outcome: 1 Mean age (months)

Study or subgroup	Azithromycin N	Mean(SD)	Erythromycin N	Mean(SD)	Mean Difference IV,Random,95% CI	Mean Difference IV,Random,95% CI
Harris 1998	156	0 (0)	69	0 (0)		0.0 [0.0, 0.0]
Kogan 2003	33	62.6 (53.6)	26	56.2 (52.8)		6.40 [-20.92, 33.72]
Roord 1996	45	58.8 (37.2)	40	67.2 (39.6)		-8.40 [-24.79, 7.99]
Total (95% CI)	**234**		**135**			**-4.48 [-18.54, 9.57]**

Heterogeneity: $Tau^2 = 0.0$; $Chi^2 = 0.83$, df = 1 (P = 0.36); $I^2 = 0.0\%$

Test for overall effect: Z = 0.62 (P = 0.53)

Test for subgroup differences: Not applicable



Analysis 1.2. Comparison 1 Azithromycin versus erythromycin, Outcome 2 Male sex.

Review: Antibiotics for community-acquired pneumonia in children

Comparison: 1 Azithromycin versus erythromycin

Outcome: 2 Male sex

Study or subgroup	Azithromycin n/N	Erythromycin n/N	Odds Ratio M-H,Random,95% CI	Weight	Odds Ratio M-H,Random,95% CI
Harris 1998	153/285	83/135		71.6 %	0.73 [0.48, 1.10]
Kogan 2003	17/33	14/26		11.8 %	0.91 [0.33, 2.55]
Roord 1996	28/45	22/40		16.6 %	1.35 [0.57, 3.21]
Total (95% CI)	**363**	**201**		**100.0 %**	**0.83 [0.58, 1.18]**

Total events: 198 (Azithromycin), 119 (Erythromycin)

Heterogeneity: $Tau^2 = 0.0$; $Chi^2 = 1.63$, df = 2 (P = 0.44); $I^2 = 0.0\%$

Test for overall effect: Z = 1.06 (P = 0.29)

Test for subgroup differences: Not applicable

Analysis 1.3. Comparison 1 Azithromycin versus erythromycin, Outcome 3 Wheezing present.

Review: Antibiotics for community-acquired pneumonia in children

Comparison: 1 Azithromycin versus erythromycin

Outcome: 3 Wheezing present

Study or subgroup	Azithromycin n/N	Erythromycin n/N	Odds Ratio M-H,Random,95% CI	Weight	Odds Ratio M-H,Random,95% CI
Harris 1998	82/285	51/135		56.2 %	0.67 [0.43, 1.03]
Kogan 2003	22/33	11/26		43.8 %	2.73 [0.94, 7.89]
Total (95% CI)	**318**	**161**		**100.0 %**	**1.23 [0.31, 4.87]**

Total events: 104 (Azithromycin), 62 (Erythromycin)

Heterogeneity: $Tau^2 = 0.82$; $Chi^2 = 5.81$, df = 1 (P = 0.02); $I^2 = 83\%$

Test for overall effect: Z = 0.30 (P = 0.76)

Test for subgroup differences: Not applicable

Analysis 1.4. Comparison 1 Azithromycin versus erythromycin, Outcome 4 Cure rate.

Review: Antibiotics for community-acquired pneumonia in children

Comparison: 1 Azithromycin versus erythromycin

Outcome: 4 Cure rate

Study or subgroup	Azithromycin n/N	Erythromycin n/N	Odds Ratio M-H,Random,95% CI	Weight	Odds Ratio M-H,Random,95% CI
Harris 1998	115/152	52/67		51.0 %	0.90 [0.45, 1.78]
Kogan 2003	33/33	21/26		8.0 %	17.14 [0.90, 325.93]
Roord 1996	31/45	27/40		41.0 %	1.07 [0.43, 2.66]
Total (95% CI)	**230**	**133**		**100.0 %**	**1.22 [0.50, 2.94]**

Total events: 179 (Azithromycin), 100 (Erythromycin)

Heterogeneity: $Tau^2 = 0.28$; $Chi^2 = 3.80$, df = 2 (P = 0.15); $I^2 = 47\%$

Test for overall effect: Z = 0.44 (P = 0.66)

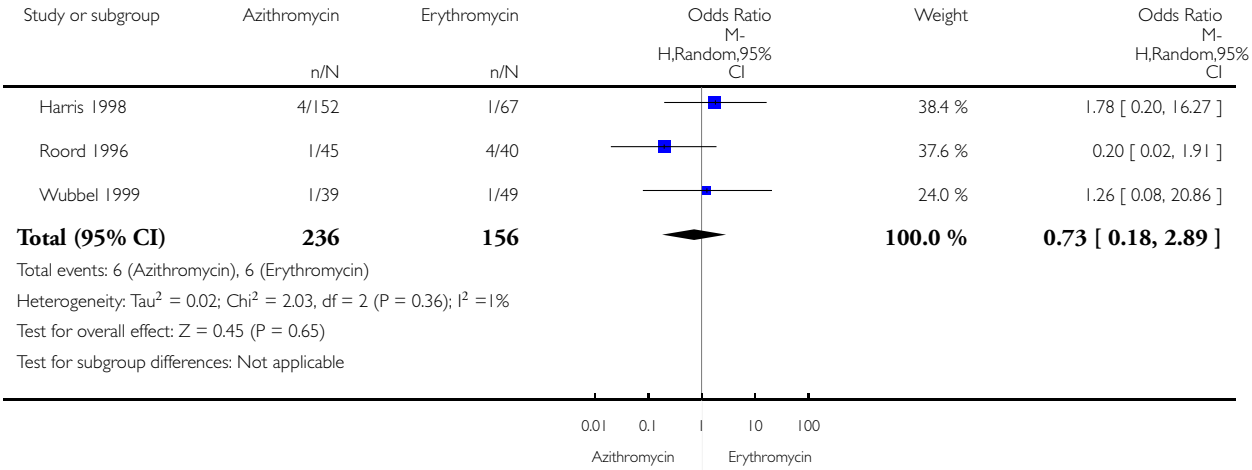
Test for subgroup differences: Not applicable

Analysis 1.5. Comparison 1 Azithromycin versus erythromycin, Outcome 5 Failure rate.

Review: Antibiotics for community-acquired pneumonia in children

Comparison: 1 Azithromycin versus erythromycin

Outcome: 5 Failure rate

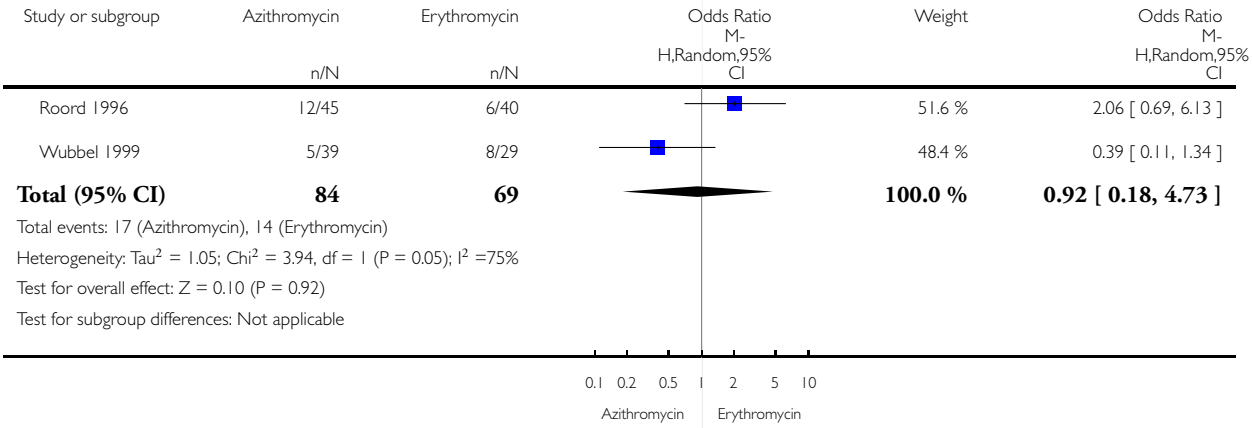


Analysis 1.6. Comparison 1 Azithromycin versus erythromycin, Outcome 6 Side effects.

Review: Antibiotics for community-acquired pneumonia in children

Comparison: 1 Azithromycin versus erythromycin

Outcome: 6 Side effects



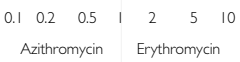
Analysis 1.7. Comparison 1 Azithromycin versus erythromycin, Outcome 7 Organisms identified by serology or nasopharyngeal cultures.

Review: Antibiotics for community-acquired pneumonia in children

Comparison: 1 Azithromycin versus erythromycin

Outcome: 7 Organisms identified by serology or nasopharyngeal cultures

Study or subgroup	Azithromycin n/N	Erythromycin n/N	Odds Ratio M-H,Random,95% CI	Weight	Odds Ratio M-H,Random,95% CI
Harris 1998	103/156	43/69		39.5 %	1.18 [0.65, 2.12]
Kogan 2003	14/33	20/26		27.1 %	0.22 [0.07, 0.69]
Roord 1996	24/44	20/40		33.4 %	1.20 [0.51, 2.83]
Total (95% CI)	**233**	**135**		**100.0 %**	**0.75 [0.30, 1.87]**
Total events: 141 (Azithromycin), 83 (Erythromycin)					
Heterogeneity: $Tau^2 = 0.46$; $Chi^2 = 7.01$, df = 2 (P = 0.03); $I^2 = 71\%$					
Test for overall effect: Z = 0.61 (P = 0.54)					
Test for subgroup differences: Not applicable					



Analysis 1.8. Comparison 1 Azithromycin versus erythromycin, Outcome 8 Cure rate in radiographically confirmed pneumonia.

Review: Antibiotics for community-acquired pneumonia in children

Comparison: 1 Azithromycin versus erythromycin

Outcome: 8 Cure rate in radiographically confirmed pneumonia

Study or subgroup	Azithromycin n/N	Erythromycin n/N	Odds Ratio M-H,Random,95% CI	Weight	Odds Ratio M-H,Random,95% CI
Kogan 2003	20/33	12/26		87.9 %	1.79 [0.63, 5.08]
Wubbel 1999	1/39	1/49		12.1 %	1.26 [0.08, 20.86]
Total (95% CI)	**72**	**75**		**100.0 %**	**1.72 [0.65, 4.56]**

Total events: 21 (Azithromycin), 13 (Erythromycin)

Heterogeneity: $Tau^2 = 0.0$; $Chi^2 = 0.05$, df = 1 (P = 0.82); $I^2 = 0.0\%$

Test for overall effect: Z = 1.09 (P = 0.28)

Test for subgroup differences: Not applicable

Analysis 1.9. Comparison 1 Azithromycin versus erythromycin, Outcome 9 Failure rate in radiographically confirmed pneumonia.

Review: Antibiotics for community-acquired pneumonia in children

Comparison: 1 Azithromycin versus erythromycin

Outcome: 9 Failure rate in radiographically confirmed pneumonia

Study or subgroup	Azithromycin n/N	Erythromycin n/N	Odds Ratio M-H,Random,95% CI	Weight	Odds Ratio M-H,Random,95% CI
Kogan 2003	13/33	14/26		87.9 %	0.56 [0.20, 1.58]
Wubbel 1999	1/39	1/49		12.1 %	1.26 [0.08, 20.86]
Total (95% CI)	**72**	**75**		**100.0 %**	**0.62 [0.23, 1.63]**

Total events: 14 (Azithromycin), 15 (Erythromycin)

Heterogeneity: $Tau^2 = 0.0$; $Chi^2 = 0.29$, df = 1 (P = 0.59); $I^2 = 0.0\%$

Test for overall effect: Z = 0.98 (P = 0.33)

Test for subgroup differences: Not applicable

Analysis 2.1. Comparison 2 Clarithromycin versus erythromycin, Outcome 1 Age below 5 years.

Review: Antibiotics for community-acquired pneumonia in children

Comparison: 2 Clarithromycin versus erythromycin

Outcome: 1 Age below 5 years

Study or subgroup	Clarithromycin n/N	Erythromycin n/N	Odds Ratio M-H,Random,95% CI	Weight	Odds Ratio M-H,Random,95% CI
Block 1995	45/133	45/127		100.0 %	0.93 [0.56, 1.55]
Total (95% CI)	**133**	**127**		**100.0 %**	**0.93 [0.56, 1.55]**

Total events: 45 (Clarithromycin), 45 (Erythromycin)

Heterogeneity: not applicable

Test for overall effect: Z = 0.27 (P = 0.79)

Test for subgroup differences: Not applicable

Analysis 2.2. Comparison 2 Clarithromycin versus erythromycin, Outcome 2 Cure rates.

Review: Antibiotics for community-acquired pneumonia in children

Comparison: 2 Clarithromycin versus erythromycin

Outcome: 2 Cure rates

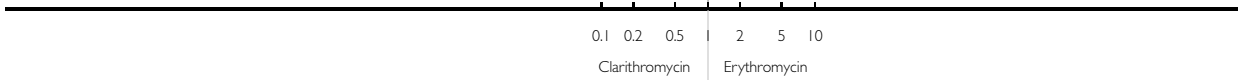
Study or subgroup	Clarithromycin n/N	Erythromycin n/N	Odds Ratio M-H,Random,95% CI	Weight	Odds Ratio M-H,Random,95% CI
Block 1995	104/124	84/110		100.0 %	1.61 [0.84, 3.08]
Total (95% CI)	**124**	**110**		**100.0 %**	**1.61 [0.84, 3.08]**

Total events: 104 (Clarithromycin), 84 (Erythromycin)

Heterogeneity: not applicable

Test for overall effect: Z = 1.44 (P = 0.15)

Test for subgroup differences: Not applicable



Analysis 2.3. Comparison 2 Clarithromycin versus erythromycin, Outcome 3 Clinical success rate.

Review: Antibiotics for community-acquired pneumonia in children

Comparison: 2 Clarithromycin versus erythromycin

Outcome: 3 Clinical success rate

Study or subgroup	Clarithromycin n/N	Erythromycin n/N	Odds Ratio M-H,Random,95% CI	Weight	Odds Ratio M-H,Random,95% CI
Block 1995	121/124	105/110		100.0 %	1.92 [0.45, 8.23]
Total (95% CI)	**124**	**110**		**100.0 %**	**1.92 [0.45, 8.23]**

Total events: 121 (Clarithromycin), 105 (Erythromycin)

Heterogeneity: not applicable

Test for overall effect: Z = 0.88 (P = 0.38)

Test for subgroup differences: Not applicable

Analysis 2.4. Comparison 2 Clarithromycin versus erythromycin, Outcome 4 Failure rate.

Review: Antibiotics for community-acquired pneumonia in children

Comparison: 2 Clarithromycin versus erythromycin

Outcome: 4 Failure rate

Study or subgroup	Clarithromycin n/N	Erythromycin n/N	Odds Ratio M-H,Random,95% CI	Weight	Odds Ratio M-H,Random,95% CI
Block 1995	3/124	5/110		100.0 %	0.52 [0.12, 2.23]
Total (95% CI)	**124**	**110**		**100.0 %**	**0.52 [0.12, 2.23]**

Total events: 3 (Clarithromycin), 5 (Erythromycin)

Heterogeneity: not applicable

Test for overall effect: Z = 0.88 (P = 0.38)

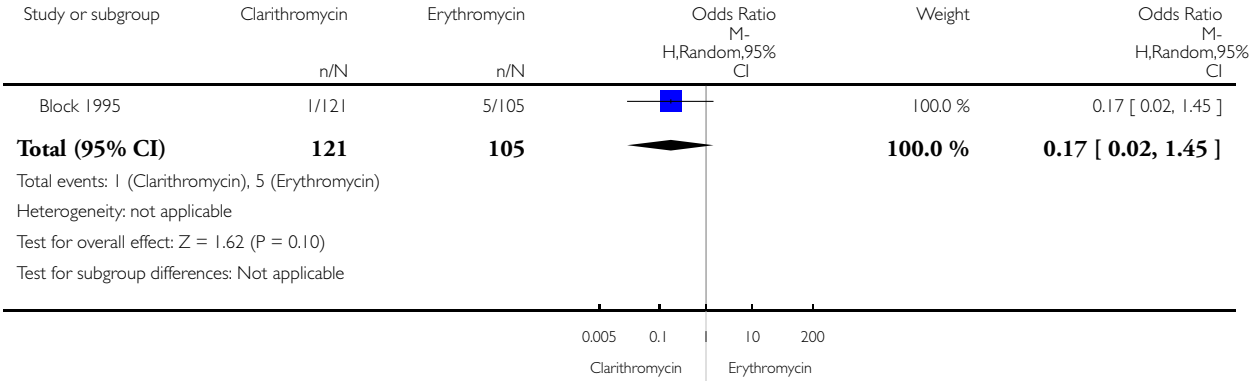
Test for subgroup differences: Not applicable

Analysis 2.5. Comparison 2 Clarithromycin versus erythromycin, Outcome 5 Relapse rate.

Review: Antibiotics for community-acquired pneumonia in children

Comparison: 2 Clarithromycin versus erythromycin

Outcome: 5 Relapse rate

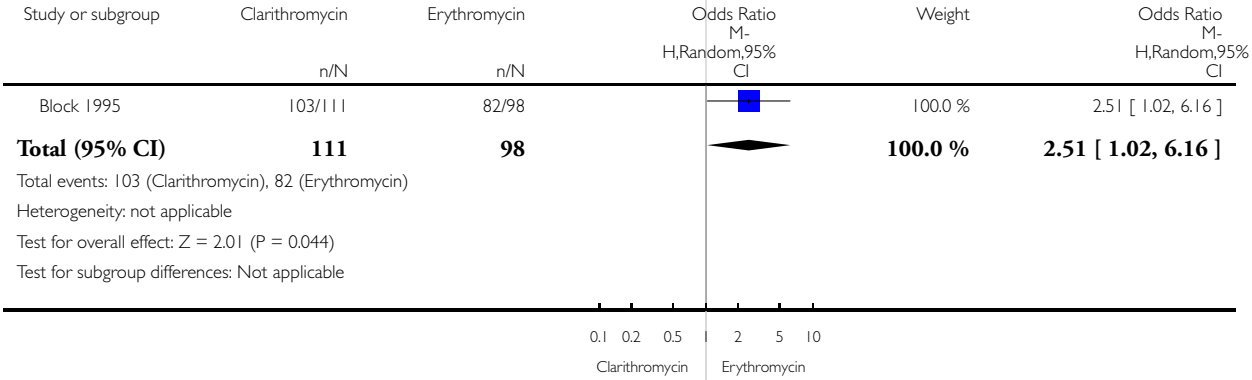


Analysis 2.6. Comparison 2 Clarithromycin versus erythromycin, Outcome 6 Radiologic resolution.

Review: Antibiotics for community-acquired pneumonia in children

Comparison: 2 Clarithromycin versus erythromycin

Outcome: 6 Radiologic resolution

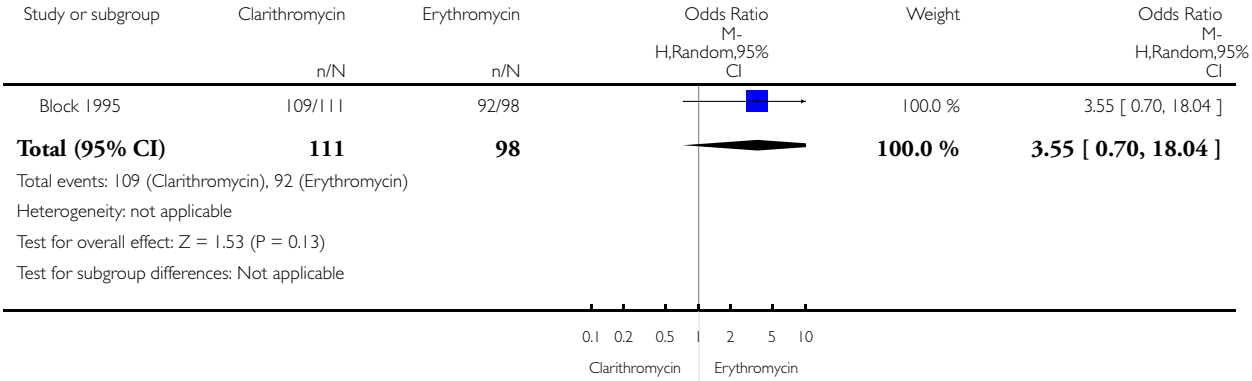


Analysis 2.7. Comparison 2 Clarithromycin versus erythromycin, Outcome 7 Radiologic success.

Review: Antibiotics for community-acquired pneumonia in children

Comparison: 2 Clarithromycin versus erythromycin

Outcome: 7 Radiologic success

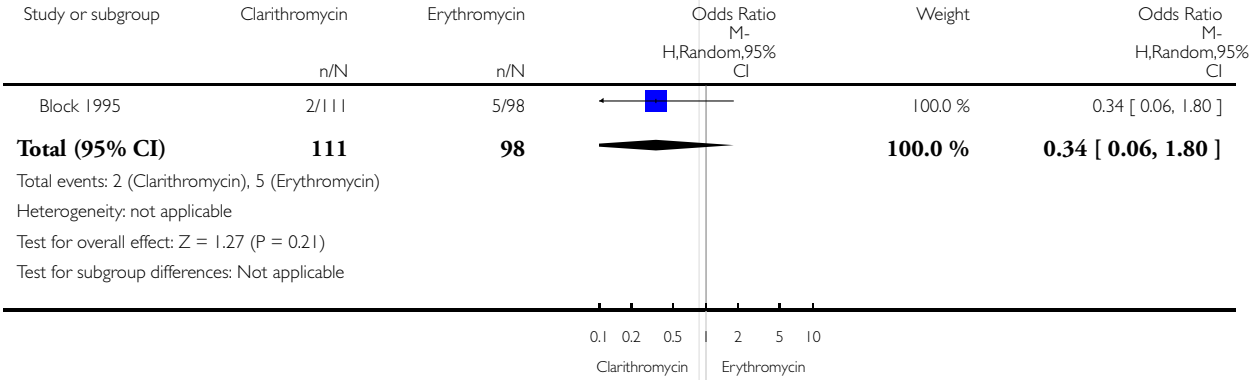


Analysis 2.8. Comparison 2 Clarithromycin versus erythromycin, Outcome 8 Radiologic failure.

Review: Antibiotics for community-acquired pneumonia in children

Comparison: 2 Clarithromycin versus erythromycin

Outcome: 8 Radiologic failure

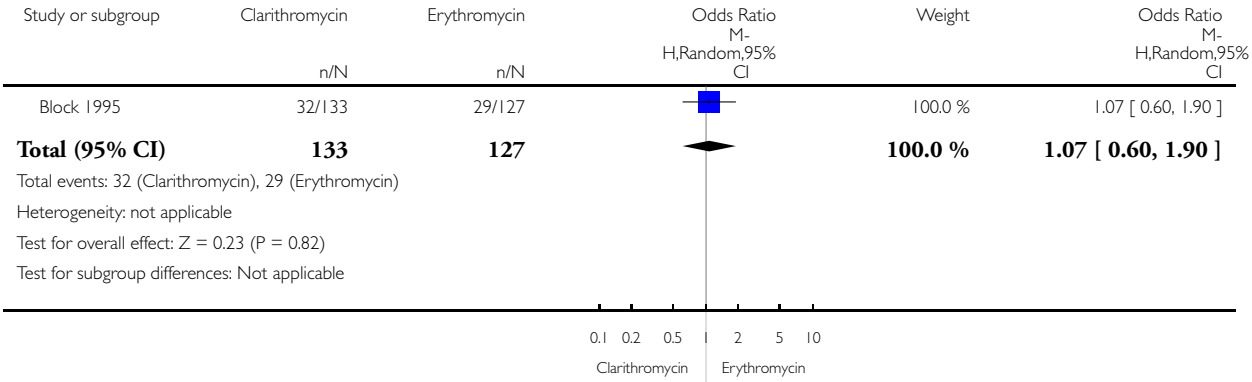


Analysis 2.9. Comparison 2 Clarithromycin versus erythromycin, Outcome 9 Adverse events.

Review: Antibiotics for community-acquired pneumonia in children

Comparison: 2 Clarithromycin versus erythromycin

Outcome: 9 Adverse events

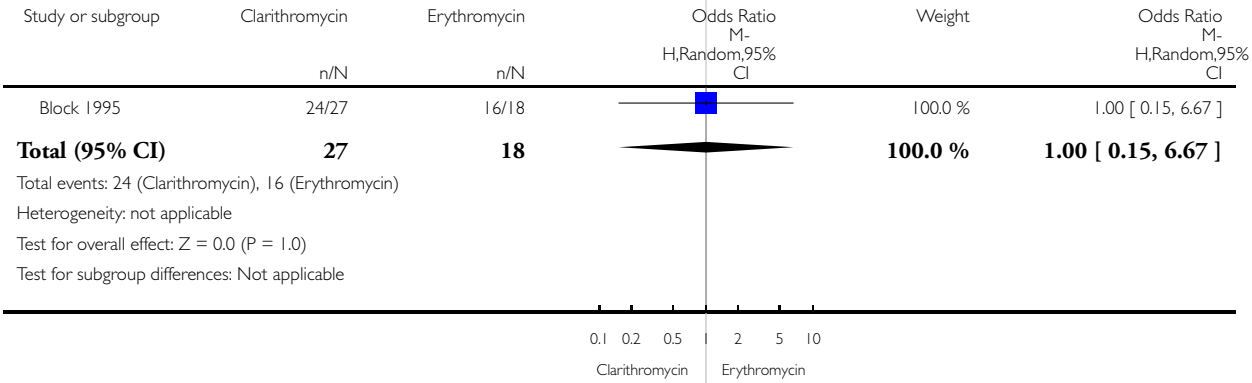


Analysis 2.10. Comparison 2 Clarithromycin versus erythromycin, Outcome 10 Bacteriologic response.

Review: Antibiotics for community-acquired pneumonia in children

Comparison: 2 Clarithromycin versus erythromycin

Outcome: 10 Bacteriologic response



Analysis 3.1. Comparison 3 Azithromycin versus co-amoxyclavulanic acid, Outcome 1 Cure rate.

Review: Antibiotics for community-acquired pneumonia in children

Comparison: 3 Azithromycin versus co-amoxyclavulanic acid

Outcome: 1 Cure rate

Study or subgroup	Azithromycin n/N	Co-amoxyclavulanic acid n/N	Odds Ratio M-H,Random,95% CI	Weight	Odds Ratio M-H,Random,95% CI
Harris 1998	84/125	42/63		100.0 %	1.02 [0.54, 1.95]
Total (95% CI)	**125**	**63**		**100.0 %**	**1.02 [0.54, 1.95]**

Total events: 84 (Azithromycin), 42 (Co-amoxyclavulanic acid)

Heterogeneity: not applicable

Test for overall effect: Z = 0.07 (P = 0.94)

Test for subgroup differences: Not applicable

Analysis 3.2. Comparison 3 Azithromycin versus co-amoxyclavulanic acid, Outcome 2 Failure rate.

Review: Antibiotics for community-acquired pneumonia in children

Comparison: 3 Azithromycin versus co-amoxyclavulanic acid

Outcome: 2 Failure rate

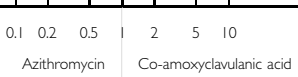
Study or subgroup	Azithromycin n/N	Co-amoxyclavulanic acid n/N	Odds Ratio M-H,Random,95% CI	Weight	Odds Ratio M-H,Random,95% CI
Harris 1998	11/125	4/63		80.8 %	1.42 [0.43, 4.66]
Wubbel 1999	1/39	2/49		19.2 %	0.62 [0.05, 7.08]
Total (95% CI)	**164**	**112**		**100.0 %**	**1.21 [0.42, 3.53]**

Total events: 12 (Azithromycin), 6 (Co-amoxyclavulanic acid)

Heterogeneity: $Tau^2 = 0.0$; $Chi^2 = 0.36$, df = 1 (P = 0.55); $I^2 = 0.0\%$

Test for overall effect: Z = 0.36 (P = 0.72)

Test for subgroup differences: Not applicable

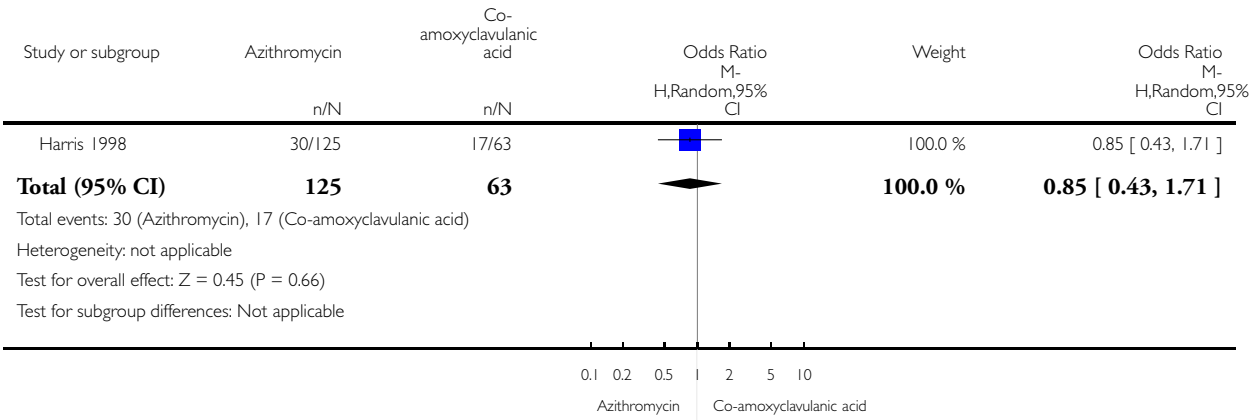


Analysis 3.3. Comparison 3 Azithromycin versus co-amoxyclavulanic acid, Outcome 3 Improved.

Review: Antibiotics for community-acquired pneumonia in children

Comparison: 3 Azithromycin versus co-amoxyclavulanic acid

Outcome: 3 Improved



Analysis 3.4. Comparison 3 Azithromycin versus co-amoxyclavulanic acid, Outcome 4 Side effects.

Review: Antibiotics for community-acquired pneumonia in children

Comparison: 3 Azithromycin versus co-amoxyclavulanic acid

Outcome: 4 Side effects

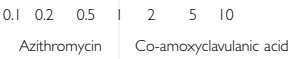
Study or subgroup	Azithromycin n/N	Co-amoxyclavulanic acid n/N	Odds Ratio M-H,Random,95% CI	Weight	Odds Ratio M-H,Random,95% CI
Harris 1998	14/125	19/63		54.2 %	0.29 [0.13, 0.63]
Wubbel 1999	5/39	33/49		45.8 %	0.07 [0.02, 0.22]
Total (95% CI)	**164**	**112**		**100.0 %**	**0.15 [0.04, 0.61]**

Total events: 19 (Azithromycin), 52 (Co-amoxyclavulanic acid)

Heterogeneity: $Tau^2 = 0.76$; $Chi^2 = 4.19$, df = 1 (P = 0.04); $I^2 = 76\%$

Test for overall effect: Z = 2.66 (P = 0.0078)

Test for subgroup differences: Not applicable



Analysis 3.5. Comparison 3 Azithromycin versus co-amoxyclavulanic acid, Outcome 5 Organisms isolated.

Review: Antibiotics for community-acquired pneumonia in children

Comparison: 3 Azithromycin versus co-amoxyclavulanic acid

Outcome: 5 Organisms isolated

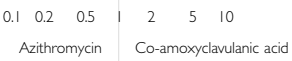
Study or subgroup	Azithromycin n/N	Co-amoxyclavulanic acid n/N	Odds Ratio M-H,Random,95% CI	Weight	Odds Ratio M-H,Random,95% CI
Harris 1998	5/125	2/63		100.0 %	1.27 [0.24, 6.74]
Total (95% CI)	**125**	**63**		**100.0 %**	**1.27 [0.24, 6.74]**

Total events: 5 (Azithromycin), 2 (Co-amoxyclavulanic acid)

Heterogeneity: not applicable

Test for overall effect: Z = 0.28 (P = 0.78)

Test for subgroup differences: Not applicable

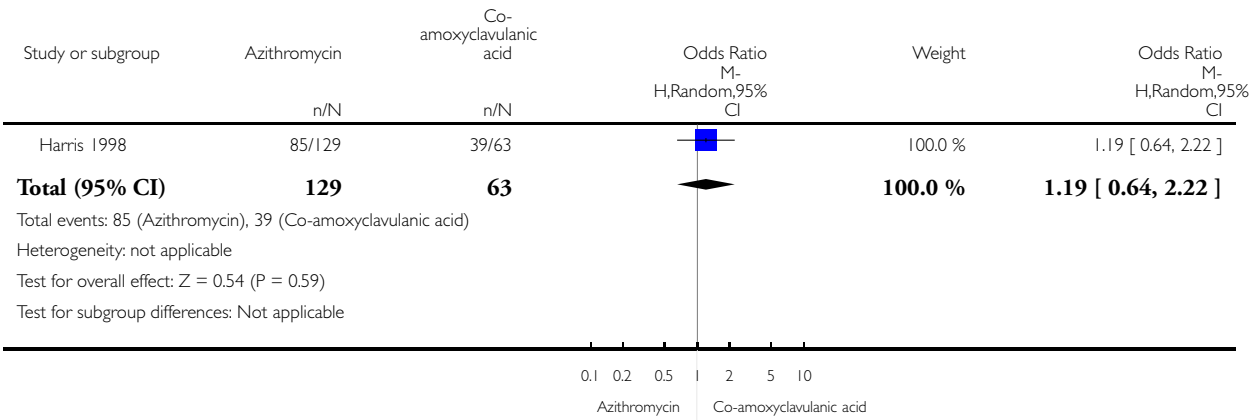


Analysis 3.6. Comparison 3 Azithromycin versus co-amoxyclavulanic acid, Outcome 6 Mycoplasma serology positive.

Review: Antibiotics for community-acquired pneumonia in children

Comparison: 3 Azithromycin versus co-amoxyclavulanic acid

Outcome: 6 Mycoplasma serology positive

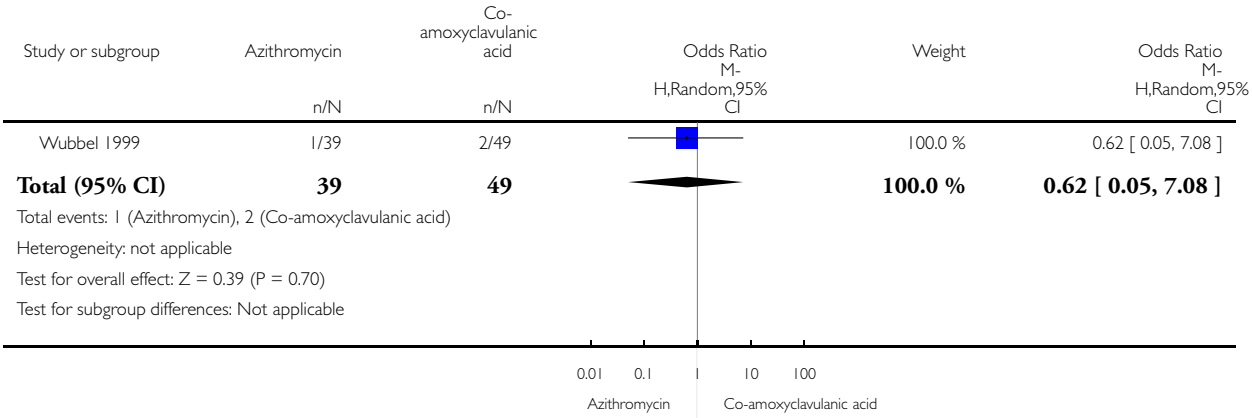


Analysis 3.7. Comparison 3 Azithromycin versus co-amoxyclavulanic acid, Outcome 7 Failure rates in radiographically confirmed pneumonia.

Review: Antibiotics for community-acquired pneumonia in children

Comparison: 3 Azithromycin versus co-amoxyclavulanic acid

Outcome: 7 Failure rates in radiographically confirmed pneumonia

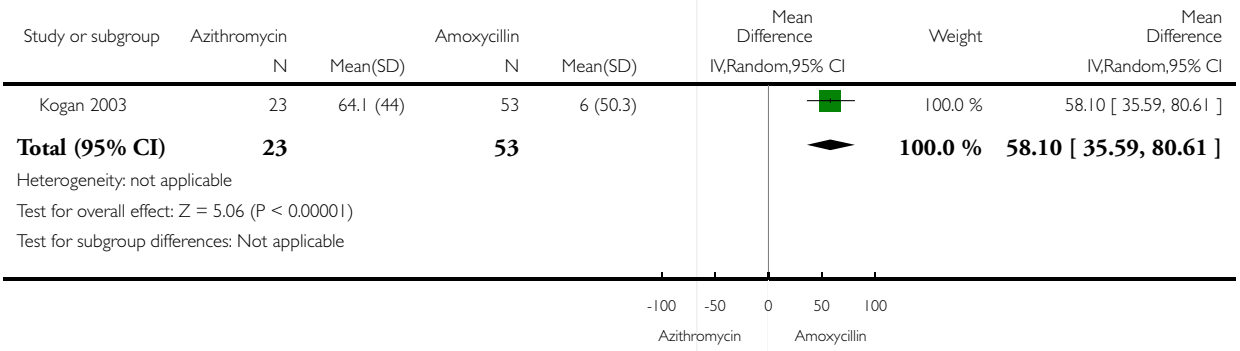


Analysis 4.1. Comparison 4 Azithromycin versus amoxycillin, Outcome 1 Age in months.

Review: Antibiotics for community-acquired pneumonia in children

Comparison: 4 Azithromycin versus amoxycillin

Outcome: 1 Age in months



Analysis 4.2. Comparison 4 Azithromycin versus amoxycillin, Outcome 2 Duration of illness.

Review: Antibiotics for community-acquired pneumonia in children

Comparison: 4 Azithromycin versus amoxycillin

Outcome: 2 Duration of illness

Study or subgroup	Azithromycin N	Mean(SD)	Amoxycillin N	Mean(SD)	Mean Difference IV,Random,95% CI	Weight	Mean Difference IV,Random,95% CI
Kogan 2003	23	3.6 (2.3)	24	3.7 (2.6)		100.0 %	-0.10 [-1.50, 1.30]
Total (95% CI)	**23**		**24**			**100.0 %**	**-0.10 [-1.50, 1.30]**

Heterogeneity: not applicable

Test for overall effect: Z = 0.14 (P = 0.89)

Test for subgroup differences: Not applicable

Analysis 4.3. Comparison 4 Azithromycin versus amoxycillin, Outcome 3 Wheezing present.

Review: Antibiotics for community-acquired pneumonia in children

Comparison: 4 Azithromycin versus amoxycillin

Outcome: 3 Wheezing present

Study or subgroup	Azithromycin n/N	Amoxycillin n/N	Odds Ratio M-H,Random,95% CI	Weight	Odds Ratio M-H,Random,95% CI
Kogan 2003	17/23	14/24		100.0 %	2.02 [0.59, 6.96]
Total (95% CI)	**23**	**24**		**100.0 %**	**2.02 [0.59, 6.96]**

Total events: 17 (Azithromycin), 14 (Amoxycillin)

Heterogeneity: not applicable

Test for overall effect: Z = 1.12 (P = 0.26)

Test for subgroup differences: Not applicable

Analysis 4.4. Comparison 4 Azithromycin versus amoxycillin, Outcome 4 Cure rate clinical.

Review: Antibiotics for community-acquired pneumonia in children

Comparison: 4 Azithromycin versus amoxycillin

Outcome: 4 Cure rate clinical

Study or subgroup	Azithromycin n/N	Amoxycillin n/N	Odds Ratio M-H,Random,95% CI	Odds Ratio M-H,Random,95% CI
Kogan 2003	23/23	24/24		0.0 [0.0, 0.0]
Total (95% CI)	**23**	**24**		**0.0 [0.0, 0.0]**

Total events: 23 (Azithromycin), 24 (Amoxycillin)
Heterogeneity: not applicable
Test for overall effect: Z = 0.0 (P < 0.00001)
Test for subgroup differences: Not applicable

Analysis 4.5. Comparison 4 Azithromycin versus amoxycillin, Outcome 5 Cure rate radiological.

Review: Antibiotics for community-acquired pneumonia in children

Comparison: 4 Azithromycin versus amoxycillin

Outcome: 5 Cure rate radiological

Study or subgroup	Azithromycin n/N	Amoxycillin n/N	Odds Ratio M-H,Random,95% CI	Weight	Odds Ratio M-H,Random,95% CI
Kogan 2003	19/23	15/24		100.0 %	2.85 [0.73, 11.09]
Total (95% CI)	**23**	**24**		**100.0 %**	**2.85 [0.73, 11.09]**

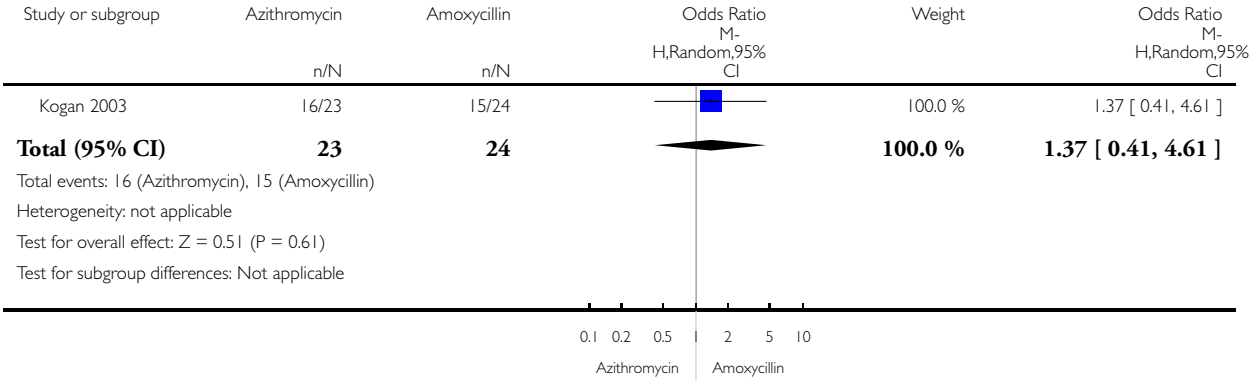
Total events: 19 (Azithromycin), 15 (Amoxycillin)
Heterogeneity: not applicable
Test for overall effect: Z = 1.51 (P = 0.13)
Test for subgroup differences: Not applicable

Analysis 4.6. Comparison 4 Azithromycin versus amoxycillin, Outcome 6 Fever day 7.

Review: Antibiotics for community-acquired pneumonia in children

Comparison: 4 Azithromycin versus amoxycillin

Outcome: 6 Fever day 7

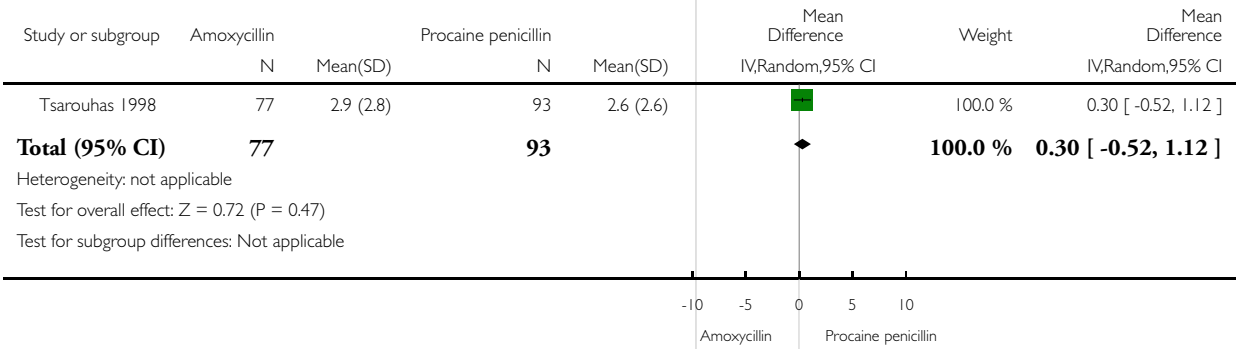


Analysis 5.1. Comparison 5 Amoxycillin versus procaine penicillin, Outcome 1 Median age.

Review: Antibiotics for community-acquired pneumonia in children

Comparison: 5 Amoxycillin versus procaine penicillin

Outcome: 1 Median age

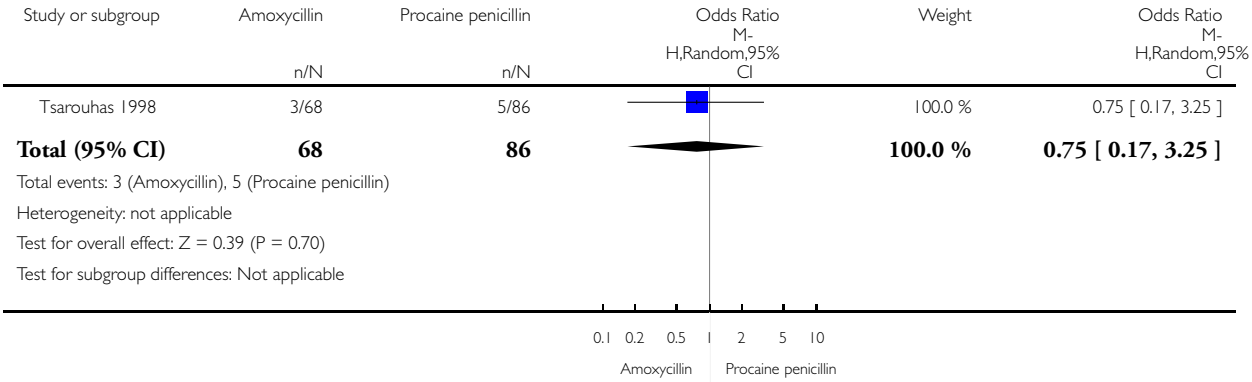


Analysis 5.2. Comparison 5 Amoxycillin versus procaine penicillin, Outcome 2 Failure rate.

Review: Antibiotics for community-acquired pneumonia in children

Comparison: 5 Amoxycillin versus procaine penicillin

Outcome: 2 Failure rate

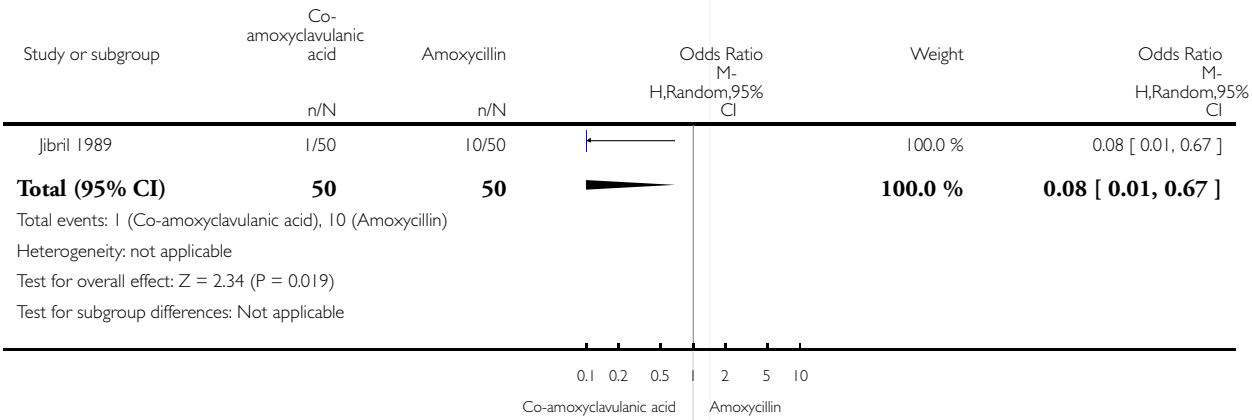


Analysis 6.1. Comparison 6 Co-amoxyclavulanic acid versus amoxycillin, Outcome 1 Poor or no response.

Review: Antibiotics for community-acquired pneumonia in children

Comparison: 6 Co-amoxyclavulanic acid versus amoxycillin

Outcome: 1 Poor or no response



Analysis 6.2. Comparison 6 Co-amoxyclavulanic acid versus amoxycillin, Outcome 2 Cure rate.

Review: Antibiotics for community-acquired pneumonia in children

Comparison: 6 Co-amoxyclavulanic acid versus amoxycillin

Outcome: 2 Cure rate

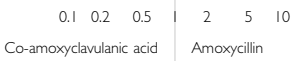
Study or subgroup	Co-amoxyclavulanic acid n/N	Amoxycillin n/N	Odds Ratio M-H,Random,95% CI	Weight	Odds Ratio M-H,Random,95% CI
Jibril 1989	47/50	30/50		100.0 %	10.44 [2.85, 38.21]
Total (95% CI)	**50**	**50**		**100.0 %**	**10.44 [2.85, 38.21]**

Total events: 47 (Co-amoxyclavulanic acid), 30 (Amoxycillin)

Heterogeneity: not applicable

Test for overall effect: Z = 3.55 (P = 0.00039)

Test for subgroup differences: Not applicable



Analysis 6.3. Comparison 6 Co-amoxyclavulanic acid versus amoxycillin, Outcome 3 Complications.

Review: Antibiotics for community-acquired pneumonia in children

Comparison: 6 Co-amoxyclavulanic acid versus amoxycillin

Outcome: 3 Complications

Study or subgroup	Co-amoxyclavulanic acid n/N	Amoxycillin n/N	Odds Ratio M-H,Random,95% CI	Weight	Odds Ratio M-H,Random,95% CI
Jibril 1989	2/50	0/50		100.0 %	5.21 [0.24, 111.24]
Total (95% CI)	**50**	**50**		**100.0 %**	**5.21 [0.24, 111.24]**

Total events: 2 (Co-amoxyclavulanic acid), 0 (Amoxycillin)

Heterogeneity: not applicable

Test for overall effect: Z = 1.06 (P = 0.29)

Test for subgroup differences: Not applicable

Analysis 6.4. Comparison 6 Co-amoxyclavulanic acid versus amoxycillin, Outcome 4 Age (months).

Review: Antibiotics for community-acquired pneumonia in children

Comparison: 6 Co-amoxyclavulanic acid versus amoxycillin

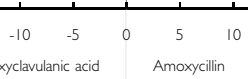
Outcome: 4 Age (months)

Study or subgroup	Co-amoxyclavulanic acid N	Mean(SD)	Amoxycillin N	Mean(SD)	Mean Difference IV,Random,95% CI	Weight	Mean Difference IV,Random,95% CI
Jibril 1989	50	63.6 (32.28)	50	58.8 (33.48)		100.0 %	4.80 [-8.09, 17.69]
Total (95% CI)	**50**		**50**			**100.0 %**	**4.80 [-8.09, 17.69]**

Heterogeneity: not applicable

Test for overall effect: Z = 0.73 (P = 0.47)

Test for subgroup differences: Not applicable

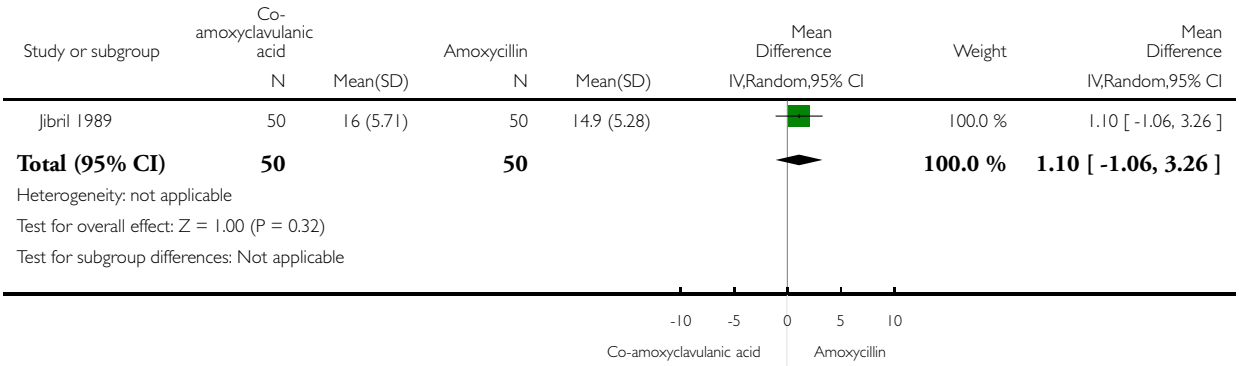


Analysis 6.5. Comparison 6 Co-amoxyclavulanic acid versus amoxycillin, Outcome 5 Weight.

Review: Antibiotics for community-acquired pneumonia in children

Comparison: 6 Co-amoxyclavulanic acid versus amoxycillin

Outcome: 5 Weight

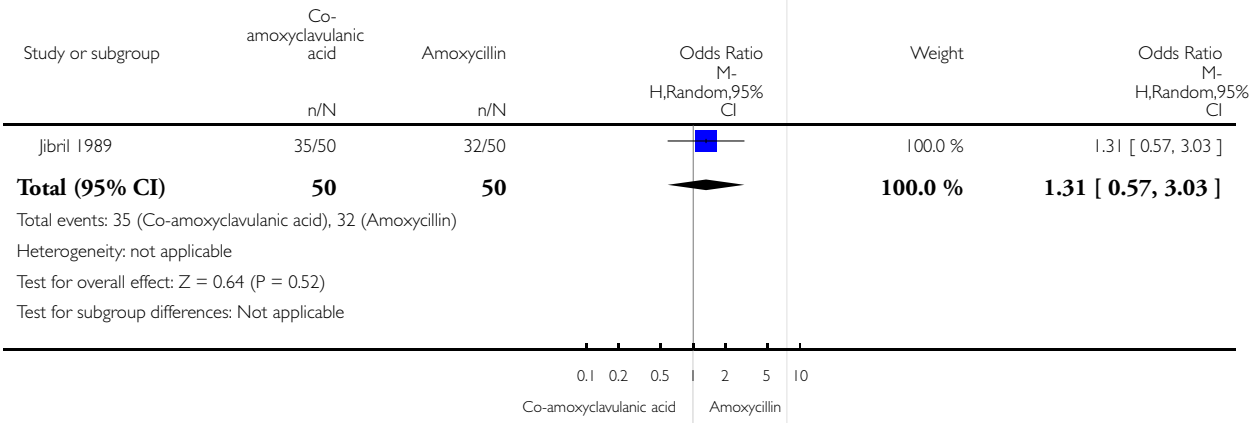


Analysis 6.6. Comparison 6 Co-amoxyclavulanic acid versus amoxycillin, Outcome 6 Male sex.

Review: Antibiotics for community-acquired pneumonia in children

Comparison: 6 Co-amoxyclavulanic acid versus amoxycillin

Outcome: 6 Male sex

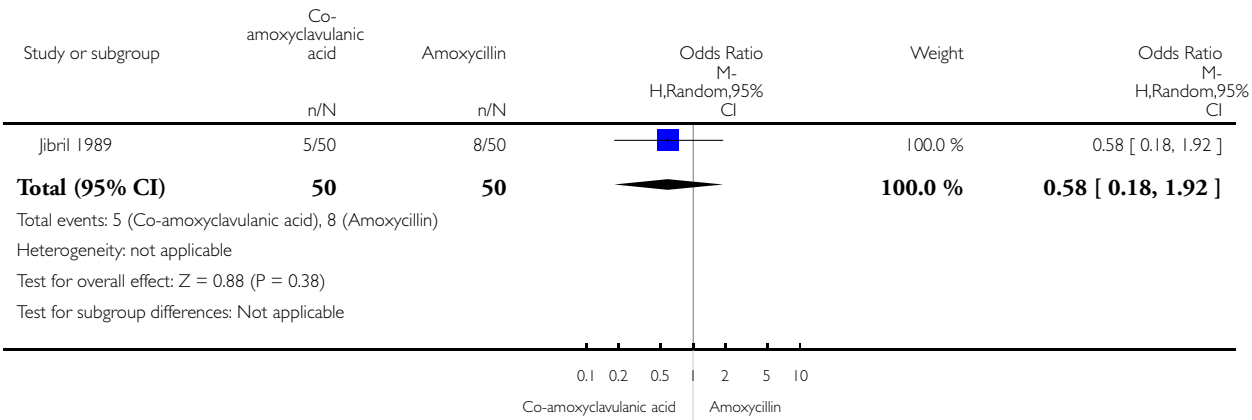


Analysis 6.7. Comparison 6 Co-amoxyclavulanic acid versus amoxycillin, Outcome 7 Wheeze present.

Review: Antibiotics for community-acquired pneumonia in children

Comparison: 6 Co-amoxyclavulanic acid versus amoxycillin

Outcome: 7 Wheeze present

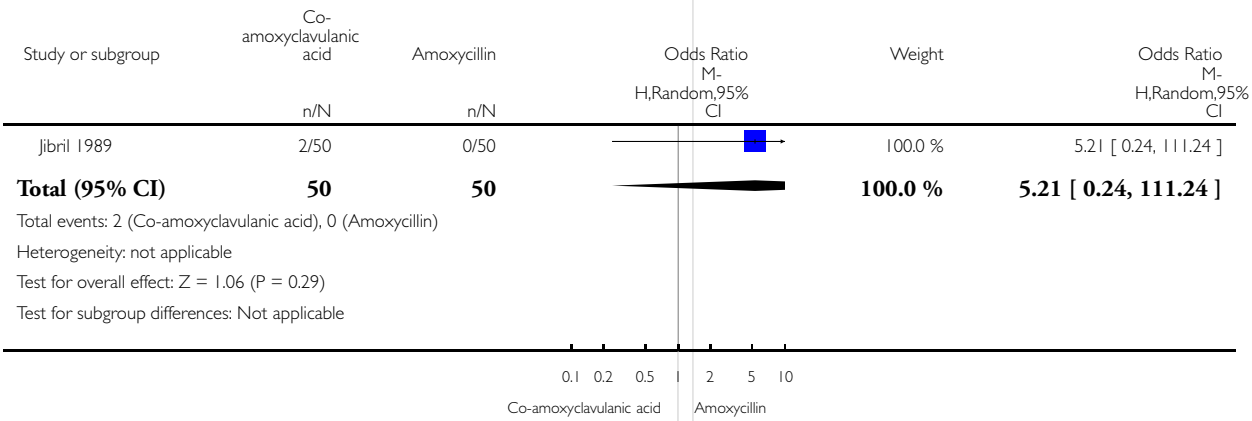


Analysis 6.8. Comparison 6 Co-amoxyclavulanic acid versus amoxycillin, Outcome 8 Side effects.

Review: Antibiotics for community-acquired pneumonia in children

Comparison: 6 Co-amoxyclavulanic acid versus amoxycillin

Outcome: 8 Side effects



Analysis 7.1. Comparison 7 Co-trimoxazole versus amoxycillin, Outcome 1 Age less than 1 year.

Review: Antibiotics for community-acquired pneumonia in children

Comparison: 7 Co-trimoxazole versus amoxycillin

Outcome: 1 Age less than 1 year

Study or subgroup	Co-trimoxazole n/N	Amoxycillin n/N	Odds Ratio M-H,Random,95% CI	Weight	Odds Ratio M-H,Random,95% CI
Awasthi 2008	43/138	38/135		20.0 %	1.16 [0.69, 1.94]
CATCHUP 2002	372/734	360/745		48.1 %	1.10 [0.90, 1.35]
Straus 1998	227/398	127/197		31.9 %	0.73 [0.51, 1.04]
Total (95% CI)	**1270**	**1077**		**100.0 %**	**0.97 [0.74, 1.29]**

Total events: 642 (Co-trimoxazole), 525 (Amoxycillin)

Heterogeneity: $Tau^2 = 0.03$; $Chi^2 = 4.12$, df = 2 (P = 0.13); $I^2 = 51\%$

Test for overall effect: Z = 0.18 (P = 0.86)

Test for subgroup differences: Not applicable

Analysis 7.2. Comparison 7 Co-trimoxazole versus amoxycillin, Outcome 2 Male sex.

Review: Antibiotics for community-acquired pneumonia in children

Comparison: 7 Co-trimoxazole versus amoxycillin

Outcome: 2 Male sex

Study or subgroup	Co-trimoxazole n/N	Amoxycillin n/N	Odds Ratio M-H,Random,95% CI	Weight	Odds Ratio M-H,Random,95% CI
Awasthi 2008	71/129	74/130		11.8 %	0.93 [0.57, 1.51]
CATCHUP 2002	362/734	435/730		66.7 %	0.66 [0.54, 0.81]
Straus 1998	246/398	137/197		21.5 %	0.71 [0.49, 1.02]
Total (95% CI)	**1261**	**1057**		**100.0 %**	**0.70 [0.59, 0.83]**

Total events: 679 (Co-trimoxazole), 646 (Amoxycillin)

Heterogeneity: $Tau^2 = 0.0$; $Chi^2 = 1.57$, df = 2 (P = 0.46); $I^2 = 0.0\%$

Test for overall effect: Z = 4.18 (P = 0.000029)

Test for subgroup differences: Not applicable

Analysis 7.3. Comparison 7 Co-trimoxazole versus amoxycillin, Outcome 3 Mean Z score for weight.

Review: Antibiotics for community-acquired pneumonia in children

Comparison: 7 Co-trimoxazole versus amoxycillin

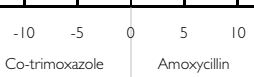
Outcome: 3 Mean Z score for weight

Study or subgroup	Co-trimoxazole N	Mean(SD)	Amoxycillin N	Mean(SD)	Mean Difference IV,Random,95% CI	Mean Difference IV,Random,95% CI
CATCHUP 2002	741	-0.94 (0)	730	-1.11 (0)		0.0 [0.0, 0.0]
Straus 1998	398	-0.45 (1.28)	197	-0.39 (1.21)		-0.06 [-0.27, 0.15]
Total (95% CI)	**1139**		**927**			**-0.06 [-0.27, 0.15]**

Heterogeneity: $Tau^2 = 0.0$; $Chi^2 = 0.0$, df = 0 (P = 1.00); $I^2 = 0.0\%$

Test for overall effect: Z = 0.56 (P = 0.58)

Test for subgroup differences: Not applicable



Analysis 7.4. Comparison 7 Co-trimoxazole versus amoxycillin, Outcome 4 Non-severe pneumonia.

Review: Antibiotics for community-acquired pneumonia in children

Comparison: 7 Co-trimoxazole versus amoxycillin

Outcome: 4 Non-severe pneumonia

Study or subgroup	Co-trimoxazole n/N	Amoxycillin n/N	Odds Ratio M-H,Random,95% CI	Weight	Odds Ratio M-H,Random,95% CI
Straus 1998	195/398	98/197		100.0 %	0.97 [0.69, 1.37]
Total (95% CI)	**398**	**197**		**100.0 %**	**0.97 [0.69, 1.37]**

Total events: 195 (Co-trimoxazole), 98 (Amoxycillin)

Heterogeneity: not applicable

Test for overall effect: Z = 0.17 (P = 0.86)

Test for subgroup differences: Not applicable

Analysis 7.5. Comparison 7 Co-trimoxazole versus amoxycillin, Outcome 5 Received antibiotics in previous week.

Review: Antibiotics for community-acquired pneumonia in children

Comparison: 7 Co-trimoxazole versus amoxycillin

Outcome: 5 Received antibiotics in previous week

Study or subgroup	Co-trimoxazole n/N	Amoxycillin n/N	Odds Ratio M-H,Random,95% CI	Weight	Odds Ratio M-H,Random,95% CI
Straus 1998	102/398	67/197		100.0 %	0.67 [0.46, 0.97]
Total (95% CI)	**398**	**197**		**100.0 %**	**0.67 [0.46, 0.97]**

Total events: 102 (Co-trimoxazole), 67 (Amoxycillin)

Heterogeneity: not applicable

Test for overall effect: Z = 2.13 (P = 0.033)

Test for subgroup differences: Not applicable

Analysis 7.6. Comparison 7 Co-trimoxazole versus amoxycillin, Outcome 6 Severe pneumonia.

Review: Antibiotics for community-acquired pneumonia in children

Comparison: 7 Co-trimoxazole versus amoxycillin

Outcome: 6 Severe pneumonia

Study or subgroup	Co-trimoxazole n/N	Amoxycillin n/N	Odds Ratio M-H,Random,95% CI	Weight	Odds Ratio M-H,Random,95% CI
Straus 1998	203/398	99/197		100.0 %	1.03 [0.73, 1.45]
Total (95% CI)	**398**	**197**		**100.0 %**	**1.03 [0.73, 1.45]**

Total events: 203 (Co-trimoxazole), 99 (Amoxycillin)

Heterogeneity: not applicable

Test for overall effect: Z = 0.17 (P = 0.86)

Test for subgroup differences: Not applicable

Analysis 7.7. Comparison 7 Co-trimoxazole versus amoxycillin, Outcome 7 Failure rate in non-severe pneumonia.

Review: Antibiotics for community-acquired pneumonia in children

Comparison: 7 Co-trimoxazole versus amoxycillin

Outcome: 7 Failure rate in non-severe pneumonia

Study or subgroup	Co-trimoxazole n/N	Amoxycillin n/N	Odds Ratio M-H,Random,95% CI	Weight	Odds Ratio M-H,Random,95% CI
Awasthi 2008	2/19	3/18		1.7 %	0.59 [0.09, 4.01]
CATCHUP 2002	139/734	117/725		86.6 %	1.21 [0.93, 1.59]
Straus 1998	25/195	12/96		11.7 %	1.03 [0.49, 2.15]
Total (95% CI)	**948**	**839**		**100.0 %**	**1.18 [0.91, 1.51]**

Total events: 166 (Co-trimoxazole), 132 (Amoxycillin)

Heterogeneity: $Tau^2 = 0.0$; $Chi^2 = 0.68$, df = 2 (P = 0.71); $I^2 = 0.0\%$

Test for overall effect: Z = 1.26 (P = 0.21)

Test for subgroup differences: Not applicable

Analysis 7.8. Comparison 7 Co-trimoxazole versus amoxycillin, Outcome 8 Failure rate severe pneumonia clinical diagnosis.

Review: Antibiotics for community-acquired pneumonia in children

Comparison: 7 Co-trimoxazole versus amoxycillin

Outcome: 8 Failure rate severe pneumonia clinical diagnosis

Study or subgroup	Co-trimoxazole n/N	Amoxycillin n/N	Odds Ratio M-H,Random,95% CI	Weight	Odds Ratio M-H,Random,95% CI
Straus 1998	56/203	18/99		100.0 %	1.71 [0.94, 3.11]
Total (95% CI)	**203**	**99**		**100.0 %**	**1.71 [0.94, 3.11]**
Total events: 56 (Co-trimoxazole), 18 (Amoxycillin)					
Heterogeneity: not applicable					
Test for overall effect: Z = 1.77 (P = 0.076)					
Test for subgroup differences: Not applicable					

Analysis 7.9. Comparison 7 Co-trimoxazole versus amoxycillin, Outcome 9 Failure rate radiological positive pneumonia.

Review: Antibiotics for community-acquired pneumonia in children

Comparison: 7 Co-trimoxazole versus amoxycillin

Outcome: 9 Failure rate radiological positive pneumonia

Study or subgroup	Co-trimoxazole n/N	Amoxycillin n/N	Odds Ratio M-H,Random,95% CI	Weight	Odds Ratio M-H,Random,95% CI
Straus 1998	35/102	10/51		100.0 %	2.14 [0.96, 4.78]
Total (95% CI)	**102**	**51**		**100.0 %**	**2.14 [0.96, 4.78]**
Total events: 35 (Co-trimoxazole), 10 (Amoxycillin)					
Heterogeneity: not applicable					
Test for overall effect: Z = 1.86 (P = 0.063)					
Test for subgroup differences: Not applicable					

Analysis 7.10. Comparison 7 Co-trimoxazole versus amoxycillin, Outcome 10 Failure rate radiological negative pneumonia.

Review: Antibiotics for community-acquired pneumonia in children

Comparison: 7 Co-trimoxazole versus amoxycillin

Outcome: 10 Failure rate radiological negative pneumonia

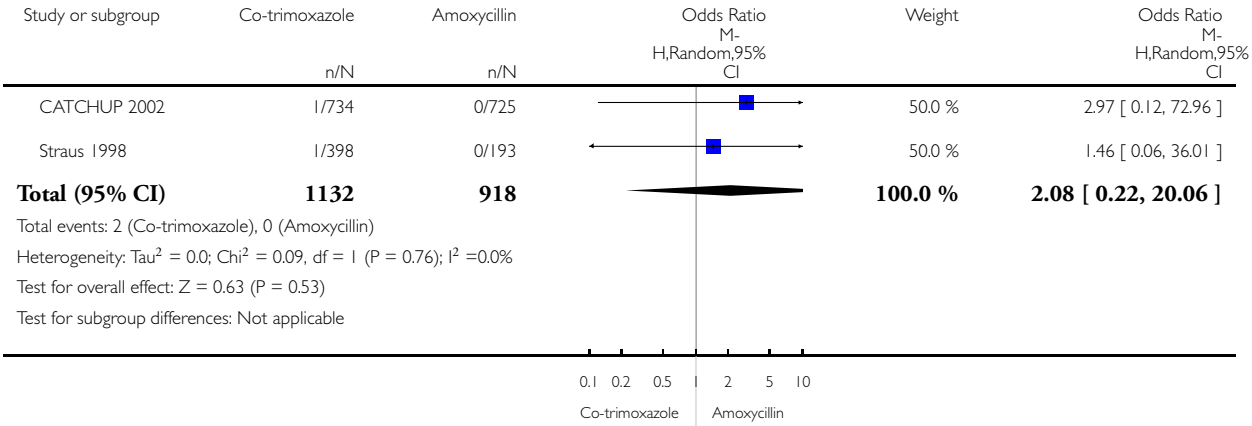
Study or subgroup	Co-trimoxazole n/N	Amoxycillin n/N	Odds Ratio M-H,Random,95% CI	Weight	Odds Ratio M-H,Random,95% CI
Straus 1998	54/283	17/141		100.0 %	1.72 [0.96, 3.09]
Total (95% CI)	**283**	**141**		**100.0 %**	**1.72 [0.96, 3.09]**
Total events: 54 (Co-trimoxazole), 17 (Amoxycillin)					
Heterogeneity: not applicable					
Test for overall effect: Z = 1.81 (P = 0.070)					
Test for subgroup differences: Not applicable					

Analysis 7.11. Comparison 7 Co-trimoxazole versus amoxycillin, Outcome 11 Death rate.

Review: Antibiotics for community-acquired pneumonia in children

Comparison: 7 Co-trimoxazole versus amoxycillin

Outcome: 11 Death rate

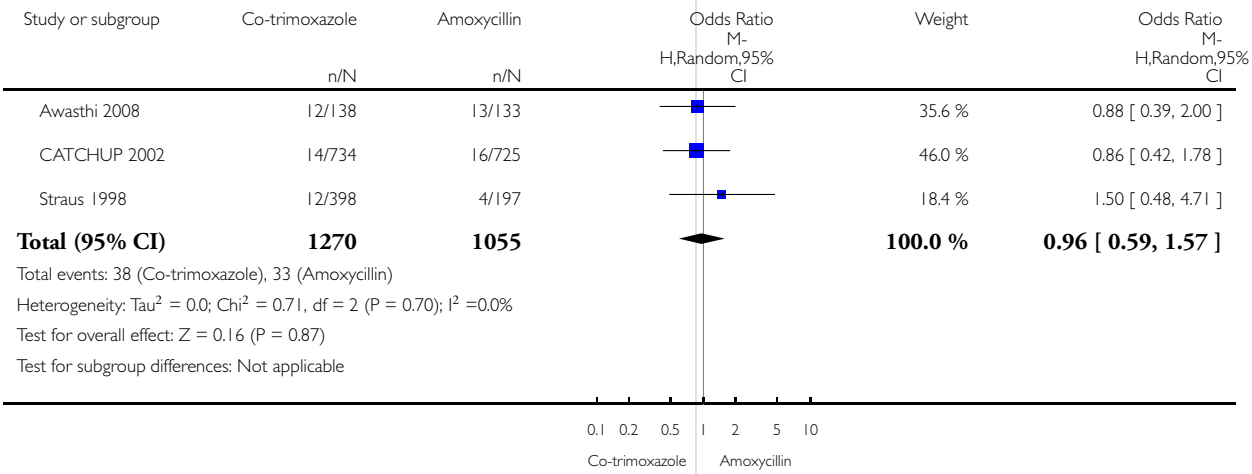


Analysis 7.12. Comparison 7 Co-trimoxazole versus amoxycillin, Outcome 12 Lost to follow-up.

Review: Antibiotics for community-acquired pneumonia in children

Comparison: 7 Co-trimoxazole versus amoxycillin

Outcome: 12 Lost to follow-up



Analysis 7.13. Comparison 7 Co-trimoxazole versus amoxycillin, Outcome 13 Wheeze positive.

Review: Antibiotics for community-acquired pneumonia in children

Comparison: 7 Co-trimoxazole versus amoxycillin

Outcome: 13 Wheeze positive

Study or subgroup	Co-trimoxazole n/N	Amoxycillin n/N	Odds Ratio M-H,Random,95% CI	Weight	Odds Ratio M-H,Random,95% CI
CATCHUP 2002	37/741	47/730		100.0 %	0.76 [0.49, 1.19]
Total (95% CI)	**741**	**730**		**100.0 %**	**0.76 [0.49, 1.19]**

Total events: 37 (Co-trimoxazole), 47 (Amoxycillin)

Heterogeneity: not applicable

Test for overall effect: Z = 1.19 (P = 0.23)

Test for subgroup differences: Not applicable

Analysis 7.14. Comparison 7 Co-trimoxazole versus amoxycillin, Outcome 14 Cure rate.

Review: Antibiotics for community-acquired pneumonia in children

Comparison: 7 Co-trimoxazole versus amoxycillin

Outcome: 14 Cure rate

Study or subgroup	Co-trimoxazole n/N	Amoxycillin n/N	Odds Ratio M-H,Random,95% CI	Weight	Odds Ratio M-H,Random,95% CI
Awasthi 2008	125/138	116/135		34.9 %	1.57 [0.74, 3.33]
CATCHUP 2002	595/734	608/725		65.1 %	0.82 [0.63, 1.08]
Total (95% CI)	**872**	**860**		**100.0 %**	**1.03 [0.56, 1.89]**

Total events: 720 (Co-trimoxazole), 724 (Amoxycillin)

Heterogeneity: $Tau^2 = 0.13$; $Chi^2 = 2.54$, df = 1 (P = 0.11); $I^2 = 61\%$

Test for overall effect: Z = 0.10 (P = 0.92)

Test for subgroup differences: Not applicable

Analysis 7.15. Comparison 7 Co-trimoxazole versus amoxycillin, Outcome 15 Change of antibiotics.

Review: Antibiotics for community-acquired pneumonia in children

Comparison: 7 Co-trimoxazole versus amoxycillin

Outcome: 15 Change of antibiotics

Study or subgroup	Co-trimoxazole n/N	Amoxycillin n/N	Odds Ratio M-H,Random,95% CI	Weight	Odds Ratio M-H,Random,95% CI
CATCHUP 2002	121/734	98/725		100.0 %	1.26 [0.95, 1.69]
Total (95% CI)	**734**	**725**		**100.0 %**	**1.26 [0.95, 1.69]**

Total events: 121 (Co-trimoxazole), 98 (Amoxycillin)

Heterogeneity: not applicable

Test for overall effect: Z = 1.58 (P = 0.11)

Test for subgroup differences: Not applicable

Analysis 7.16. Comparison 7 Co-trimoxazole versus amoxycillin, Outcome 16 Failure rates after excluding study by Awasthi 2008.

Review: Antibiotics for community-acquired pneumonia in children

Comparison: 7 Co-trimoxazole versus amoxycillin

Outcome: 16 Failure rates after excluding study by Awasthi 2008

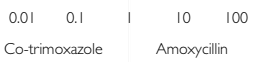
Study or subgroup	Co-trimoxazole n/N	Amoxycillin n/N	Odds Ratio M-H,Random,95% CI	Weight	Odds Ratio M-H,Random,95% CI
CATCHUP 2002	139/734	117/725		88.1 %	1.21 [0.93, 1.59]
Straus 1998	25/195	12/96		11.9 %	1.03 [0.49, 2.15]
Total (95% CI)	**929**	**821**		**100.0 %**	**1.19 [0.92, 1.53]**

Total events: 164 (Co-trimoxazole), 129 (Amoxycillin)

Heterogeneity: $Tau^2 = 0.0$; $Chi^2 = 0.17$, df = 1 (P = 0.68); $I^2 = 0.0\%$

Test for overall effect: Z = 1.34 (P = 0.18)

Test for subgroup differences: Not applicable



Analysis 8.1. Comparison 8 Co-trimoxazole versus procaine penicillin, Outcome 1 Age less than 1 year.

Review: Antibiotics for community-acquired pneumonia in children

Comparison: 8 Co-trimoxazole versus procaine penicillin

Outcome: 1 Age less than 1 year

Study or subgroup	Co-trimoxazole n/N	Procaine penicillin n/N	Odds Ratio M-H,Random,95% CI	Weight	Odds Ratio M-H,Random,95% CI
Keeley 1990	148/303	134/311		87.2 %	1.26 [0.92, 1.73]
Sidal 1994	16/46	16/63		12.8 %	1.57 [0.68, 3.60]
Total (95% CI)	**349**	**374**		**100.0 %**	**1.30 [0.96, 1.75]**

Total events: 164 (Co-trimoxazole), 150 (Procaine penicillin)

Heterogeneity: $Tau^2 = 0.0$; $Chi^2 = 0.23$, df = 1 (P = 0.63); $I^2 = 0.0\%$

Test for overall effect: Z = 1.71 (P = 0.086)

Test for subgroup differences: Not applicable

Analysis 8.2. Comparison 8 Co-trimoxazole versus procaine penicillin, Outcome 2 Age 1 to 5 years.

Review: Antibiotics for community-acquired pneumonia in children

Comparison: 8 Co-trimoxazole versus procaine penicillin

Outcome: 2 Age 1 to 5 years

Study or subgroup	Co-trimoxazole n/N	Procaine penicillin n/N	Odds Ratio M-H,Random,95% CI	Weight	Odds Ratio M-H,Random,95% CI
Keeley 1990	142/303	159/311		100.0 %	0.84 [0.61, 1.16]
Total (95% CI)	**303**	**311**		**100.0 %**	**0.84 [0.61, 1.16]**

Total events: 142 (Co-trimoxazole), 159 (Procaine penicillin)

Heterogeneity: not applicable

Test for overall effect: Z = 1.06 (P = 0.29)

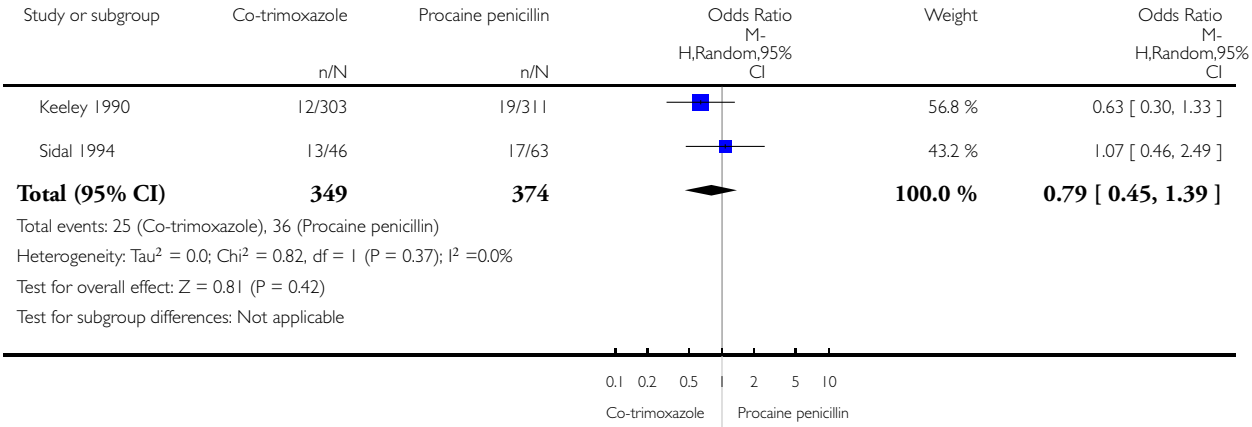
Test for subgroup differences: Not applicable

Analysis 8.3. Comparison 8 Co-trimoxazole versus procaine penicillin, Outcome 3 Age 5 to 12 years.

Review: Antibiotics for community-acquired pneumonia in children

Comparison: 8 Co-trimoxazole versus procaine penicillin

Outcome: 3 Age 5 to 12 years

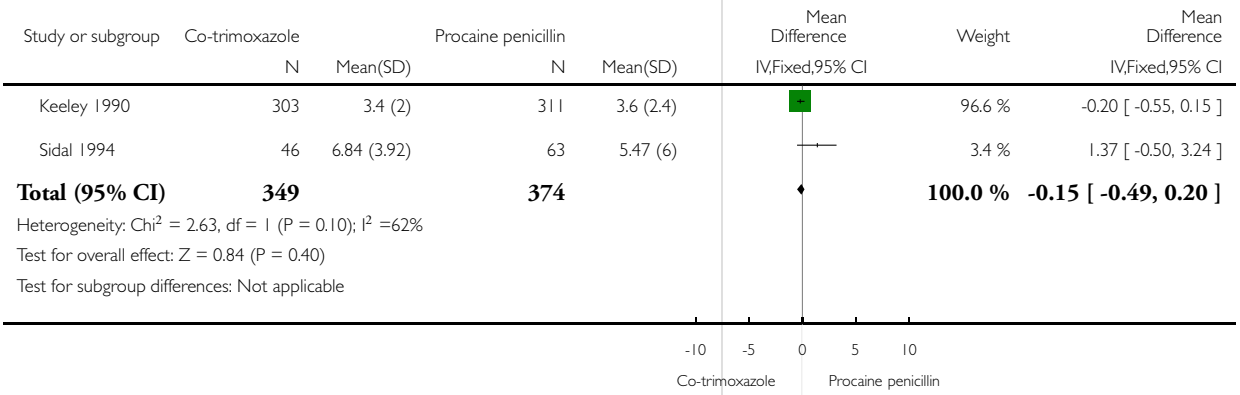


Analysis 8.4. Comparison 8 Co-trimoxazole versus procaine penicillin, Outcome 4 Duration of illness in days.

Review: Antibiotics for community-acquired pneumonia in children

Comparison: 8 Co-trimoxazole versus procaine penicillin

Outcome: 4 Duration of illness in days



Analysis 8.5. Comparison 8 Co-trimoxazole versus procaine penicillin, Outcome 5 Male sex.

Review: Antibiotics for community-acquired pneumonia in children

Comparison: 8 Co-trimoxazole versus procaine penicillin

Outcome: 5 Male sex

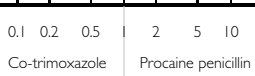
Study or subgroup	Co-trimoxazole n/N	Procaine penicillin n/N	Odds Ratio M-H,Random,95% CI	Weight	Odds Ratio M-H,Random,95% CI
Keeley 1990	153/303	163/311		100.0 %	0.93 [0.67, 1.27]
Total (95% CI)	**303**	**311**		**100.0 %**	**0.93 [0.67, 1.27]**

Total events: 153 (Co-trimoxazole), 163 (Procaine penicillin)

Heterogeneity: not applicable

Test for overall effect: Z = 0.48 (P = 0.63)

Test for subgroup differences: Not applicable



Analysis 8.6. Comparison 8 Co-trimoxazole versus procaine penicillin, Outcome 6 Cure rate.

Review: Antibiotics for community-acquired pneumonia in children

Comparison: 8 Co-trimoxazole versus procaine penicillin

Outcome: 6 Cure rate

Study or subgroup	Co-trimoxazole n/N	Procaine penicillin n/N	Odds Ratio M-H,Random,95% CI	Weight	Odds Ratio M-H,Random,95% CI
Keeley 1990	288/303	261/311		54.6 %	3.68 [2.02, 6.71]
Sidal 1994	40/46	58/63		45.4 %	0.57 [0.16, 2.01]
Total (95% CI)	**349**	**374**		**100.0 %**	**1.58 [0.26, 9.69]**

Total events: 328 (Co-trimoxazole), 319 (Procaine penicillin)

Heterogeneity: $Tau^2 = 1.47$; $Chi^2 = 6.86$, df = 1 (P = 0.01); $I^2 = 85\%$

Test for overall effect: Z = 0.50 (P = 0.62)

Test for subgroup differences: Not applicable

Analysis 8.7. Comparison 8 Co-trimoxazole versus procaine penicillin, Outcome 7 Hospitalisation rate.

Review: Antibiotics for community-acquired pneumonia in children

Comparison: 8 Co-trimoxazole versus procaine penicillin

Outcome: 7 Hospitalisation rate

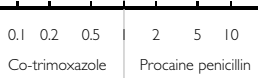
Study or subgroup	Co-trimoxazole n/N	Procaine penicillin n/N	Odds Ratio M-H,Random,95% CI	Weight	Odds Ratio M-H,Random,95% CI
Keeley 1990	12/303	5/311		100.0 %	2.52 [0.88, 7.25]
Total (95% CI)	**303**	**311**		**100.0 %**	**2.52 [0.88, 7.25]**

Total events: 12 (Co-trimoxazole), 5 (Procaine penicillin)

Heterogeneity: not applicable

Test for overall effect: Z = 1.72 (P = 0.086)

Test for subgroup differences: Not applicable

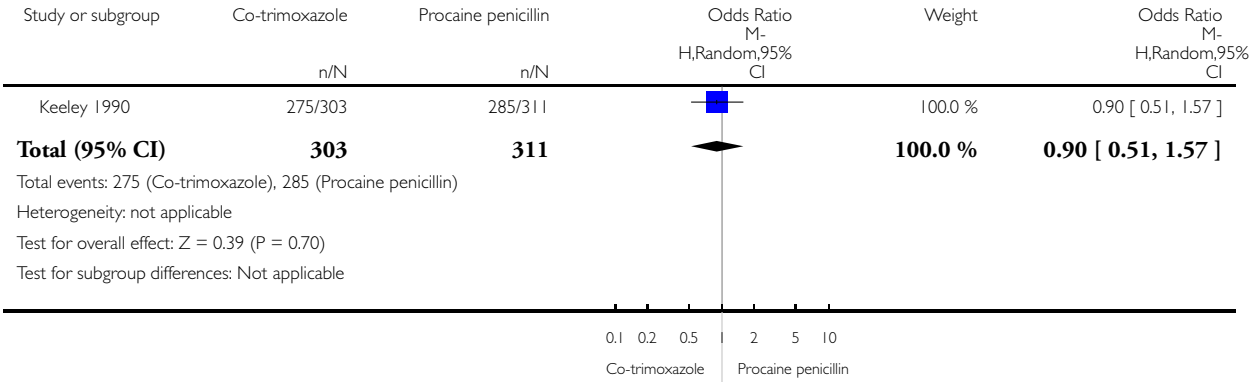


Analysis 8.8. Comparison 8 Co-trimoxazole versus procaine penicillin, Outcome 8 Well at end of follow-up.

Review: Antibiotics for community-acquired pneumonia in children

Comparison: 8 Co-trimoxazole versus procaine penicillin

Outcome: 8 Well at end of follow-up

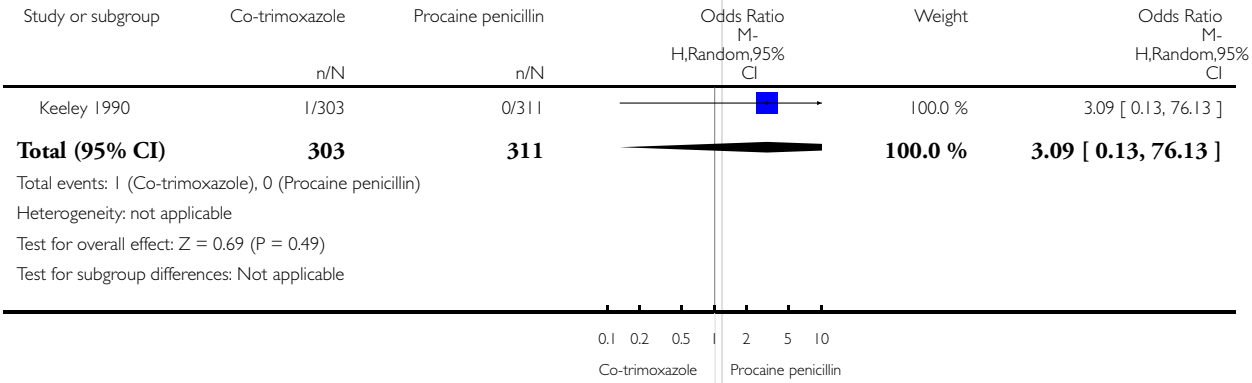


Analysis 8.9. Comparison 8 Co-trimoxazole versus procaine penicillin, Outcome 9 Death.

Review: Antibiotics for community-acquired pneumonia in children

Comparison: 8 Co-trimoxazole versus procaine penicillin

Outcome: 9 Death

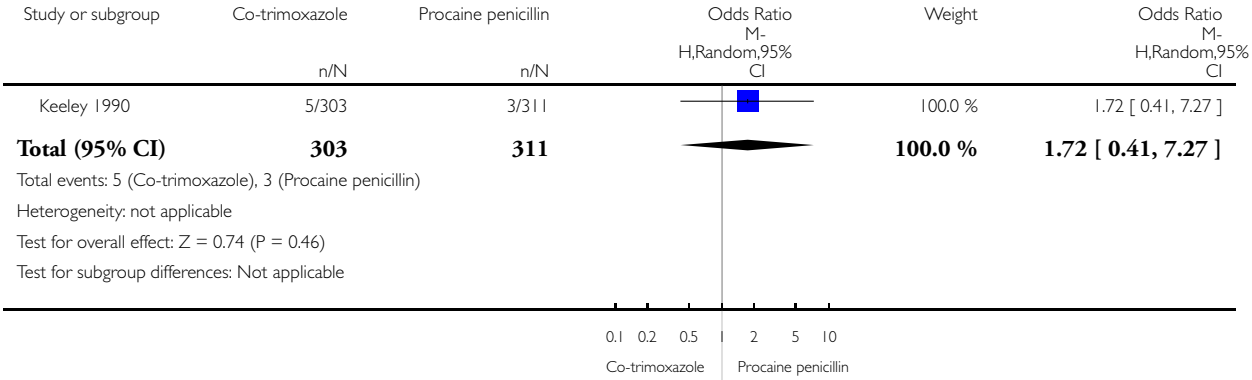


Analysis 8.10. Comparison 8 Co-trimoxazole versus procaine penicillin, Outcome 10 Treatment failure.

Review: Antibiotics for community-acquired pneumonia in children

Comparison: 8 Co-trimoxazole versus procaine penicillin

Outcome: 10 Treatment failure

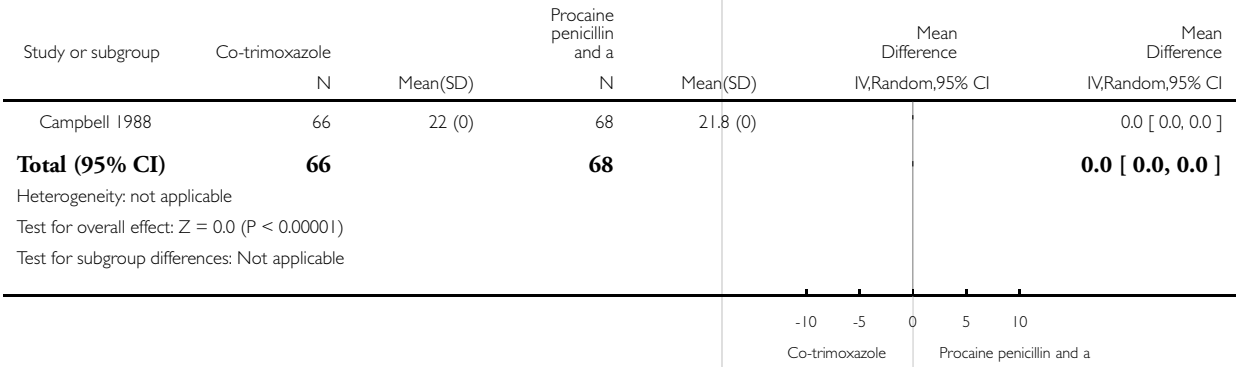


Analysis 9.1. Comparison 9 Co-trimoxazole versus procaine penicillin and ampicillin, Outcome 1 Mean age in months.

Review: Antibiotics for community-acquired pneumonia in children

Comparison: 9 Co-trimoxazole versus procaine penicillin and ampicillin

Outcome: 1 Mean age in months

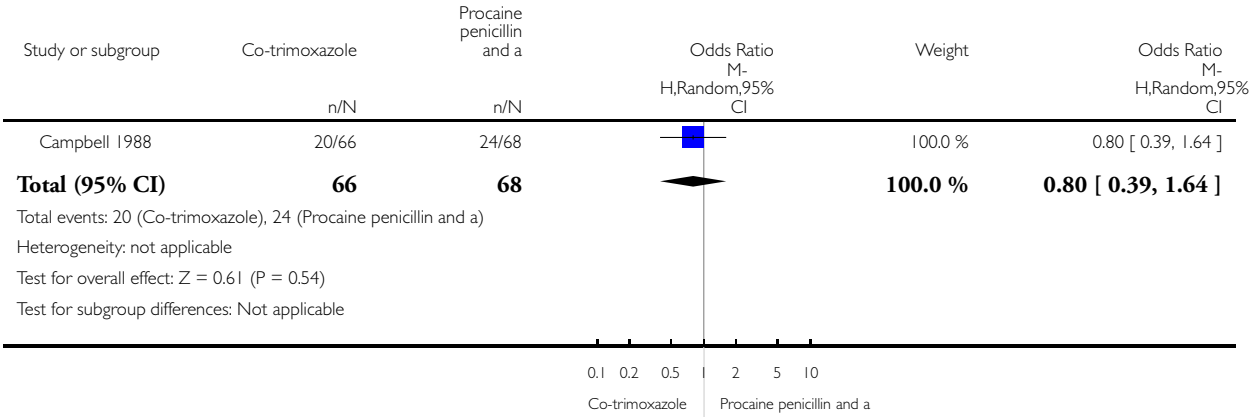


Analysis 9.2. Comparison 9 Co-trimoxazole versus procaine penicillin and ampicillin, Outcome 2 Age less than 1 year.

Review: Antibiotics for community-acquired pneumonia in children

Comparison: 9 Co-trimoxazole versus procaine penicillin and ampicillin

Outcome: 2 Age less than 1 year

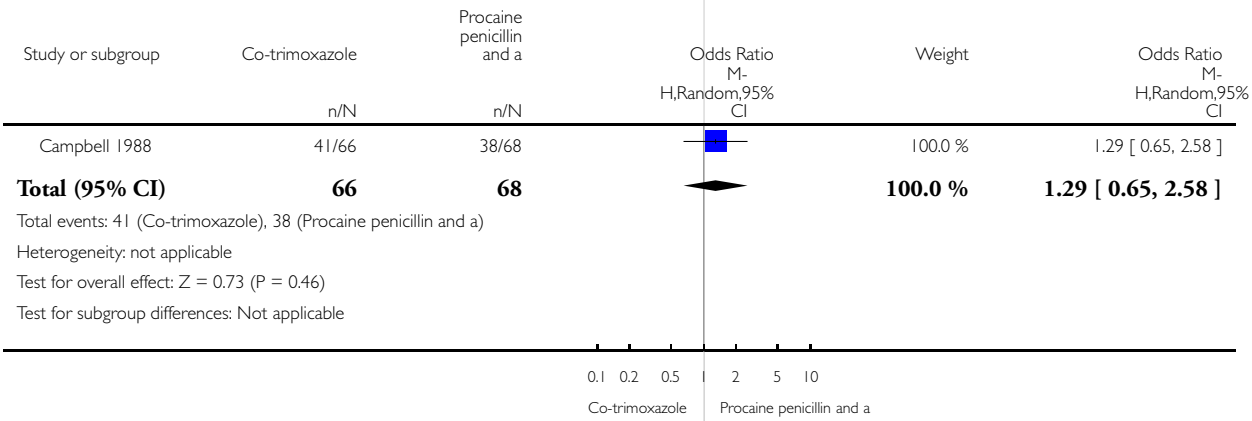


Analysis 9.3. Comparison 9 Co-trimoxazole versus procaine penicillin and ampicillin, Outcome 3 Male sex.

Review: Antibiotics for community-acquired pneumonia in children

Comparison: 9 Co-trimoxazole versus procaine penicillin and ampicillin

Outcome: 3 Male sex

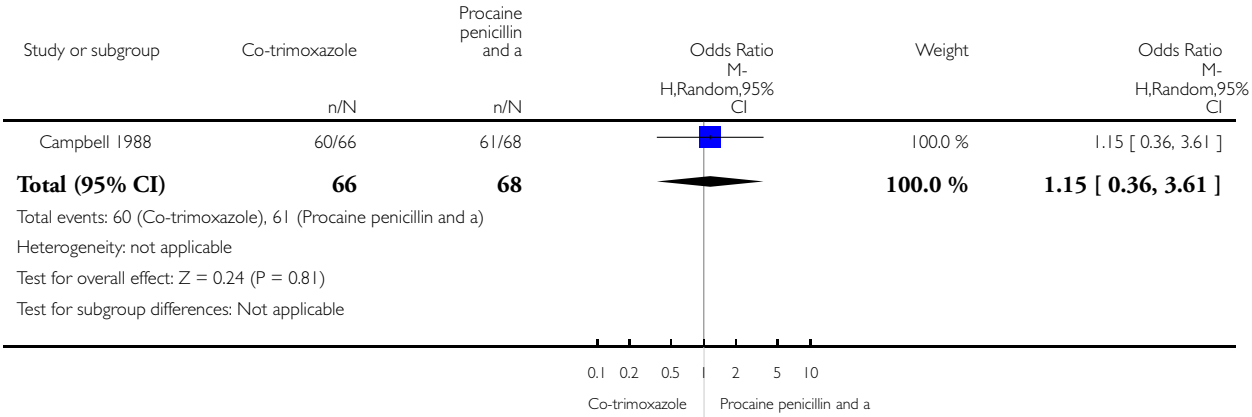


Analysis 9.4. Comparison 9 Co-trimoxazole versus procaine penicillin and ampicillin, Outcome 4 Cure rate.

Review: Antibiotics for community-acquired pneumonia in children

Comparison: 9 Co-trimoxazole versus procaine penicillin and ampicillin

Outcome: 4 Cure rate



Analysis 9.5. Comparison 9 Co-trimoxazole versus procaine penicillin and ampicillin, Outcome 5 Hospitalisation rate.

Review: Antibiotics for community-acquired pneumonia in children

Comparison: 9 Co-trimoxazole versus procaine penicillin and ampicillin

Outcome: 5 Hospitalisation rate

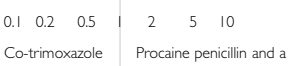
Study or subgroup	Co-trimoxazole n/N	Procaine penicillin and a n/N	Odds Ratio M-H,Random,95% CI	Weight	Odds Ratio M-H,Random,95% CI
Campbell 1988	3/66	2/68		100.0 %	1.57 [0.25, 9.72]
Total (95% CI)	**66**	**68**		**100.0 %**	**1.57 [0.25, 9.72]**

Total events: 3 (Co-trimoxazole), 2 (Procaine penicillin and a)

Heterogeneity: not applicable

Test for overall effect: Z = 0.49 (P = 0.63)

Test for subgroup differences: Not applicable



Analysis 9.6. Comparison 9 Co-trimoxazole versus procaine penicillin and ampicillin, Outcome 6 Death rate.

Review: Antibiotics for community-acquired pneumonia in children

Comparison: 9 Co-trimoxazole versus procaine penicillin and ampicillin

Outcome: 6 Death rate

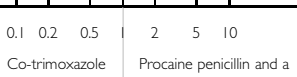
Study or subgroup	Co-trimoxazole n/N	Procaine penicillin and a n/N	Odds Ratio M-H,Random,95% CI	Weight	Odds Ratio M-H,Random,95% CI
Campbell 1988	0/66	2/68		100.0 %	0.20 [0.01, 4.25]
Total (95% CI)	**66**	**68**		**100.0 %**	**0.20 [0.01, 4.25]**

Total events: 0 (Co-trimoxazole), 2 (Procaine penicillin and a)

Heterogeneity: not applicable

Test for overall effect: Z = 1.03 (P = 0.30)

Test for subgroup differences: Not applicable



Analysis 10.1. Comparison 10 Cefpodoxime versus co-amoxyclavulanic acid, Outcome 1 Cure rate (response rate) at end of treatment.

Review: Antibiotics for community-acquired pneumonia in children

Comparison: 10 Cefpodoxime versus co-amoxyclavulanic acid

Outcome: 1 Cure rate (response rate) at end of treatment

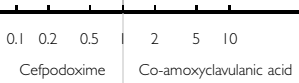
Study or subgroup	Cefpodoxime n/N	Co-amoxyclavulanic acid n/N	Odds Ratio M-H,Random,95% CI	Weight	Odds Ratio M-H,Random,95% CI
Klein 1995	179/188	87/90		100.0 %	0.69 [0.18, 2.60]
Total (95% CI)	**188**	**90**		**100.0 %**	**0.69 [0.18, 2.60]**

Total events: 179 (Cefpodoxime), 87 (Co-amoxyclavulanic acid)

Heterogeneity: not applicable

Test for overall effect: Z = 0.56 (P = 0.58)

Test for subgroup differences: Not applicable



Analysis 10.2. Comparison 10 Cefpodoxime versus co-amoxyclavulanic acid, Outcome 2 Mean age (months).

Review: Antibiotics for community-acquired pneumonia in children

Comparison: 10 Cefpodoxime versus co-amoxyclavulanic acid

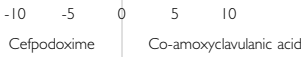
Outcome: 2 Mean age (months)

Study or subgroup	Cefpodoxime N	Mean(SD)	Co-amoxyclavulanic acid N	Mean(SD)	Mean Difference IV,Random,95% CI	Mean Difference IV,Random,95% CI
Klein 1995	234	31.32 (0)	114	37.2 (0)		0.0 [0.0, 0.0]
Total (95% CI)	**234**		**114**			**0.0 [0.0, 0.0]**

Heterogeneity: not applicable

Test for overall effect: Z = 0.0 (P < 0.00001)

Test for subgroup differences: Not applicable



Analysis 10.3. Comparison 10 Cefpodoxime versus co-amoxyclavulanic acid, Outcome 3 Adverse effects.

Review: Antibiotics for community-acquired pneumonia in children

Comparison: 10 Cefpodoxime versus co-amoxyclavulanic acid

Outcome: 3 Adverse effects

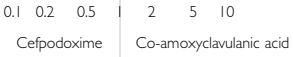
Study or subgroup	Cefpodoxime n/N	Co-amoxyclavulanic acid n/N	Odds Ratio M-H,Random,95% CI	Weight	Odds Ratio M-H,Random,95% CI
Klein 1995	7/188	7/90		100.0 %	0.46 [0.16, 1.35]
Total (95% CI)	**188**	**90**		**100.0 %**	**0.46 [0.16, 1.35]**

Total events: 7 (Cefpodoxime), 7 (Co-amoxyclavulanic acid)

Heterogeneity: not applicable

Test for overall effect: Z = 1.42 (P = 0.16)

Test for subgroup differences: Not applicable



Analysis 10.4. Comparison 10 Cefpodoxime versus co-amoxyclavulanic acid, Outcome 4 Age in years.

Review: Antibiotics for community-acquired pneumonia in children

Comparison: 10 Cefpodoxime versus co-amoxyclavulanic acid

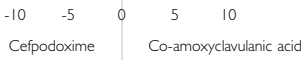
Outcome: 4 Age in years

Study or subgroup	Cefpodoxime N	Mean(SD)	Co-amoxyclavulanic acid N	Mean(SD)	Mean Difference IV,Random,95% CI	Mean Difference IV,Random,95% CI
Klein 1995	234	1.8 (0)	114	3.1 (0)		0.0 [0.0, 0.0]
Total (95% CI)	**234**		**114**			**0.0 [0.0, 0.0]**

Heterogeneity: not applicable

Test for overall effect: Z = 0.0 (P < 0.00001)

Test for subgroup differences: Not applicable



Analysis 10.5. Comparison 10 Cefpodoxime versus co-amoxyclavulanic acid, Outcome 5 Follow-up.

Review: Antibiotics for community-acquired pneumonia in children

Comparison: 10 Cefpodoxime versus co-amoxyclavulanic acid

Outcome: 5 Follow-up

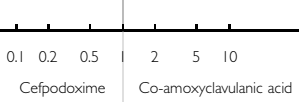
Study or subgroup	Cefpodoxime n/N	Co-amoxyclavulanic acid n/N	Odds Ratio M-H,Random,95% CI	Weight	Odds Ratio M-H,Random,95% CI
Klein 1995	172/188	87/90		100.0 %	0.37 [0.11, 1.31]
Total (95% CI)	**188**	**90**		**100.0 %**	**0.37 [0.11, 1.31]**

Total events: 172 (Cefpodoxime), 87 (Co-amoxyclavulanic acid)

Heterogeneity: not applicable

Test for overall effect: Z = 1.54 (P = 0.12)

Test for subgroup differences: Not applicable

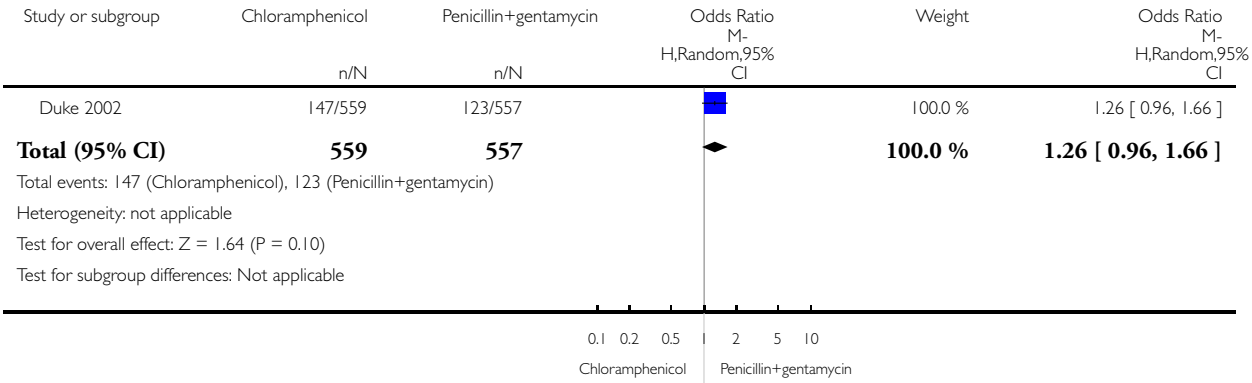


Analysis 11.1. Comparison 11 Chloramphenicol versus penicillin plus gentamicin, Outcome 1 Adverse events.

Review: Antibiotics for community-acquired pneumonia in children

Comparison: 11 Chloramphenicol versus penicillin plus gentamicin

Outcome: 1 Adverse events

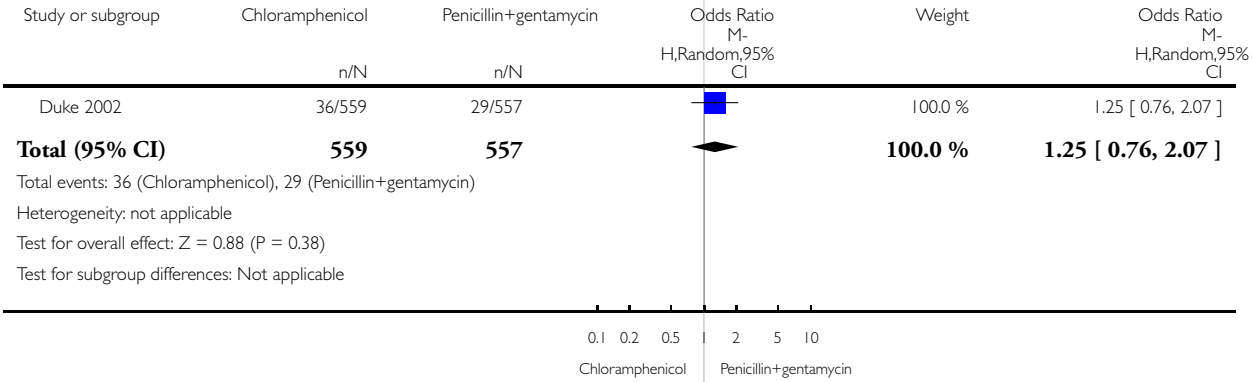


Analysis 11.2. Comparison 11 Chloramphenicol versus penicillin plus gentamicin, Outcome 2 Death.

Review: Antibiotics for community-acquired pneumonia in children

Comparison: 11 Chloramphenicol versus penicillin plus gentamicin

Outcome: 2 Death



Analysis 11.3. Comparison 11 Chloramphenicol versus penicillin plus gentamicin, Outcome 3 Change of antibiotics.

Review: Antibiotics for community-acquired pneumonia in children

Comparison: 11 Chloramphenicol versus penicillin plus gentamicin

Outcome: 3 Change of antibiotics

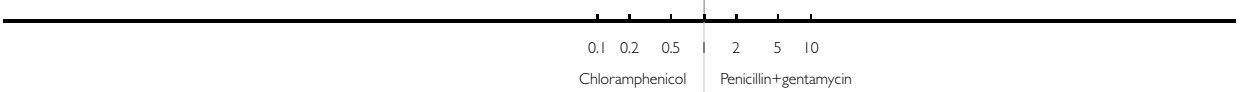
Study or subgroup	Chloramphenicol n/N	Penicillin+gentamycin n/N	Odds Ratio M-H,Random,95% CI	Weight	Odds Ratio M-H,Random,95% CI
Duke 2002	49/559	60/557		100.0 %	0.80 [0.54, 1.18]
Total (95% CI)	**559**	**557**		**100.0 %**	**0.80 [0.54, 1.18]**

Total events: 49 (Chloramphenicol), 60 (Penicillin+gentamycin)

Heterogeneity: not applicable

Test for overall effect: Z = 1.13 (P = 0.26)

Test for subgroup differences: Not applicable



Analysis 11.4. Comparison 11 Chloramphenicol versus penicillin plus gentamicin, Outcome 4 Readmission before 30 days.

Review: Antibiotics for community-acquired pneumonia in children

Comparison: 11 Chloramphenicol versus penicillin plus gentamicin

Outcome: 4 Readmission before 30 days

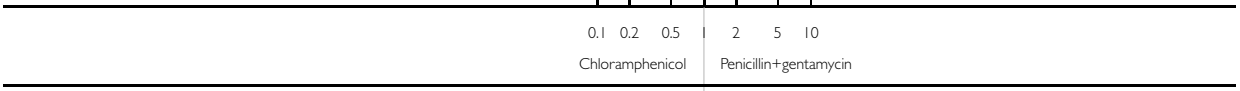
Study or subgroup	Chloramphenicol n/N	Penicillin+gentamycin n/N	Odds Ratio M-H,Random,95% CI	Weight	Odds Ratio M-H,Random,95% CI
Duke 2002	50/559	32/557		100.0 %	1.61 [1.02, 2.55]
Total (95% CI)	**559**	**557**		**100.0 %**	**1.61 [1.02, 2.55]**

Total events: 50 (Chloramphenicol), 32 (Penicillin+gentamycin)

Heterogeneity: not applicable

Test for overall effect: Z = 2.03 (P = 0.042)

Test for subgroup differences: Not applicable



Analysis 11.5. Comparison 11 Chloramphenicol versus penicillin plus gentamicin, Outcome 5 Absconded.

Review: Antibiotics for community-acquired pneumonia in children

Comparison: 11 Chloramphenicol versus penicillin plus gentamicin

Outcome: 5 Absconded

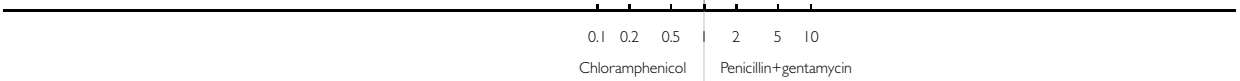
Study or subgroup	Chloramphenicol n/N	Penicillin+gentamycin n/N	Odds Ratio M-H,Random,95% CI	Weight	Odds Ratio M-H,Random,95% CI
Duke 2002	44/559	34/557		100.0 %	1.31 [0.83, 2.09]
Total (95% CI)	**559**	**557**		**100.0 %**	**1.31 [0.83, 2.09]**

Total events: 44 (Chloramphenicol), 34 (Penicillin+gentamycin)

Heterogeneity: not applicable

Test for overall effect: Z = 1.15 (P = 0.25)

Test for subgroup differences: Not applicable



Analysis 11.6. Comparison 11 Chloramphenicol versus penicillin plus gentamicin, Outcome 6 Age (months).

Review: Antibiotics for community-acquired pneumonia in children

Comparison: 11 Chloramphenicol versus penicillin plus gentamicin

Outcome: 6 Age (months)

Study or subgroup	Chloramphenicol N	Mean(SD)	Penicillin+gentamycin N	Mean(SD)	Mean Difference IV,Random,95% CI	Mean Difference IV,Random,95% CI
Duke 2002	559	6.1 (0)	557	5.9 (0)		0.0 [0.0, 0.0]
Total (95% CI)	**559**		**557**			**0.0 [0.0, 0.0]**

Heterogeneity: not applicable

Test for overall effect: Z = 0.0 (P < 0.00001)

Test for subgroup differences: Not applicable

Analysis 11.7. Comparison 11 Chloramphenicol versus penicillin plus gentamicin, Outcome 7 Culture positive.

Review: Antibiotics for community-acquired pneumonia in children

Comparison: 11 Chloramphenicol versus penicillin plus gentamicin

Outcome: 7 Culture positive

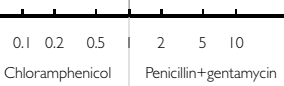
Study or subgroup	Chloramphenicol n/N	Penicillin+gentamycin n/N	Odds Ratio M-H,Random,95% CI	Weight	Odds Ratio M-H,Random,95% CI
Duke 2002	67/559	77/557		100.0 %	0.85 [0.60, 1.21]
Total (95% CI)	**559**	**557**		**100.0 %**	**0.85 [0.60, 1.21]**

Total events: 67 (Chloramphenicol), 77 (Penicillin+gentamycin)

Heterogeneity: not applicable

Test for overall effect: Z = 0.92 (P = 0.36)

Test for subgroup differences: Not applicable



Analysis 11.8. Comparison 11 Chloramphenicol versus penicillin plus gentamicin, Outcome 8 Male sex.

Review: Antibiotics for community-acquired pneumonia in children

Comparison: 11 Chloramphenicol versus penicillin plus gentamicin

Outcome: 8 Male sex

Study or subgroup	Chloramphenicol n/N	Penicillin+gentamycin n/N	Odds Ratio M-H,Random,95% CI	Weight	Odds Ratio M-H,Random,95% CI
Duke 2002	324/559	340/557		100.0 %	0.88 [0.69, 1.12]
Total (95% CI)	**559**	**557**		**100.0 %**	**0.88 [0.69, 1.12]**

Total events: 324 (Chloramphenicol), 340 (Penicillin+gentamycin)

Heterogeneity: not applicable

Test for overall effect: Z = 1.05 (P = 0.29)

Test for subgroup differences: Not applicable

Analysis 11.9. Comparison 11 Chloramphenicol versus penicillin plus gentamicin, Outcome 9 Received antibiotics in previous 1 week.

Review: Antibiotics for community-acquired pneumonia in children

Comparison: 11 Chloramphenicol versus penicillin plus gentamicin

Outcome: 9 Received antibiotics in previous 1 week

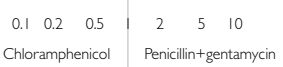
Study or subgroup	Chloramphenicol n/N	Penicillin+gentamycin n/N	Odds Ratio M-H,Random,95% CI	Weight	Odds Ratio M-H,Random,95% CI
Duke 2002	212/559	217/557		100.0 %	0.96 [0.75, 1.22]
Total (95% CI)	**559**	**557**		**100.0 %**	**0.96 [0.75, 1.22]**

Total events: 212 (Chloramphenicol), 217 (Penicillin+gentamycin)

Heterogeneity: not applicable

Test for overall effect: Z = 0.35 (P = 0.72)

Test for subgroup differences: Not applicable

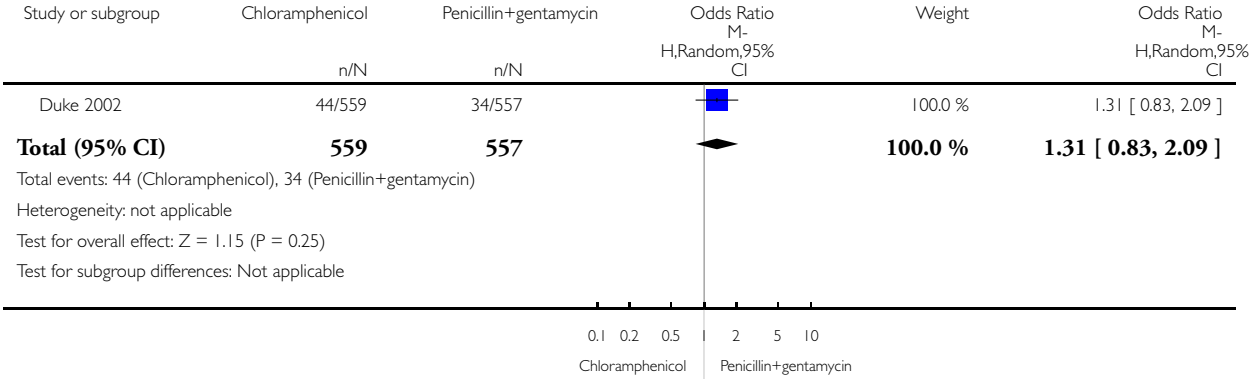


Analysis 11.10. Comparison 11 Chloramphenicol versus penicillin plus gentamicin, Outcome 10 Lost to follow-up.

Review: Antibiotics for community-acquired pneumonia in children

Comparison: 11 Chloramphenicol versus penicillin plus gentamicin

Outcome: 10 Lost to follow-up

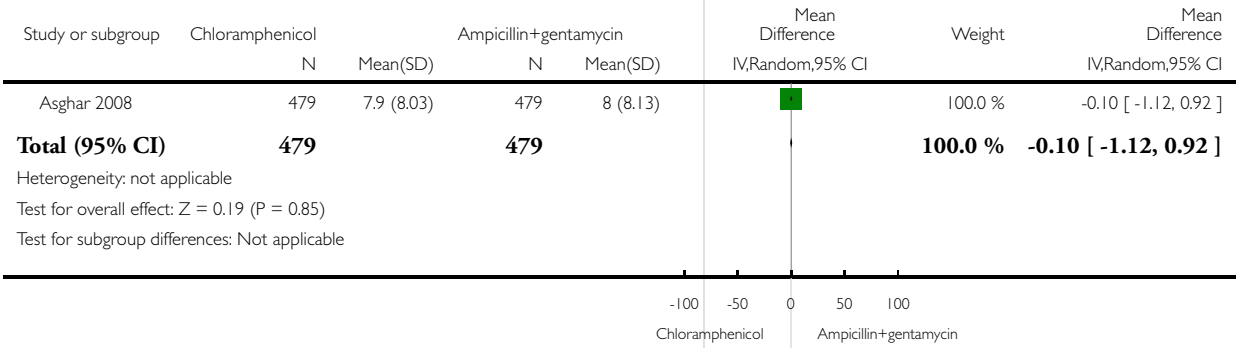


Analysis 12.1. Comparison 12 Chloramphenicol with ampicillin and gentamicin, Outcome 1 Mean age.

Review: Antibiotics for community-acquired pneumonia in children

Comparison: 12 Chloramphenicol with ampicillin and gentamicin

Outcome: 1 Mean age



Analysis 12.2. Comparison 12 Chloramphenicol with ampicillin and gentamicin, Outcome 2 Male sex.

Review: Antibiotics for community-acquired pneumonia in children

Comparison: 12 Chloramphenicol with ampicillin and gentamicin

Outcome: 2 Male sex

Study or subgroup	Chloramphenicol n/N	Ampicillin+gentamycin n/N	Odds Ratio M-H,Random,95% CI	Weight	Odds Ratio M-H,Random,95% CI
Asghar 2008	285/479	303/479		100.0 %	0.85 [0.66, 1.11]
Total (95% CI)	**479**	**479**		**100.0 %**	**0.85 [0.66, 1.11]**

Total events: 285 (Chloramphenicol), 303 (Ampicillin+gentamycin)

Heterogeneity: not applicable

Test for overall effect: Z = 1.19 (P = 0.23)

Test for subgroup differences: Not applicable

Analysis 12.3. Comparison 12 Chloramphenicol with ampicillin and gentamicin, Outcome 3 Number received antibiotics in past 7 days.

Review: Antibiotics for community-acquired pneumonia in children

Comparison: 12 Chloramphenicol with ampicillin and gentamicin

Outcome: 3 Number received antibiotics in past 7 days

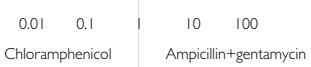
Study or subgroup	Chloramphenicol n/N	Ampicillin+gentamycin n/N	Odds Ratio M-H,Random,95% CI	Weight	Odds Ratio M-H,Random,95% CI
Asghar 2008	154/477	167/473		100.0 %	0.87 [0.67, 1.14]
Total (95% CI)	**477**	**473**		**100.0 %**	**0.87 [0.67, 1.14]**

Total events: 154 (Chloramphenicol), 167 (Ampicillin+gentamycin)

Heterogeneity: not applicable

Test for overall effect: Z = 0.98 (P = 0.33)

Test for subgroup differences: Not applicable



Analysis 12.4. Comparison 12 Chloramphenicol with ampicillin and gentamicin, Outcome 4 Failure rates on day 5.

Review: Antibiotics for community-acquired pneumonia in children

Comparison: 12 Chloramphenicol with ampicillin and gentamicin

Outcome: 4 Failure rates on day 5

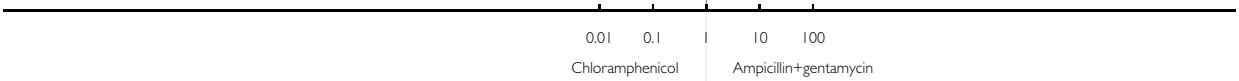
Study or subgroup	Chloramphenicol n/N	Ampicillin+gentamycin n/N	Odds Ratio M-H,Random,95% CI	Weight	Odds Ratio M-H,Random,95% CI
Asghar 2008	77/479	54/479		100.0 %	1.51 [1.04, 2.19]
Total (95% CI)	**479**	**479**		**100.0 %**	**1.51 [1.04, 2.19]**

Total events: 77 (Chloramphenicol), 54 (Ampicillin+gentamycin)

Heterogeneity: not applicable

Test for overall effect: Z = 2.15 (P = 0.031)

Test for subgroup differences: Not applicable



Analysis 12.5. Comparison 12 Chloramphenicol with ampicillin and gentamicin, Outcome 5 Failure rates on day 10.

Review: Antibiotics for community-acquired pneumonia in children

Comparison: 12 Chloramphenicol with ampicillin and gentamicin

Outcome: 5 Failure rates on day 10

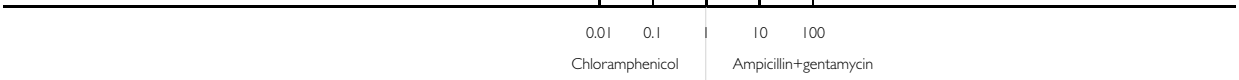
Study or subgroup	Chloramphenicol n/N	Ampicillin+gentamycin n/N	Odds Ratio M-H,Random,95% CI	Weight	Odds Ratio M-H,Random,95% CI
Asghar 2008	92/479	67/479		100.0 %	1.46 [1.04, 2.06]
Total (95% CI)	**479**	**479**		**100.0 %**	**1.46 [1.04, 2.06]**

Total events: 92 (Chloramphenicol), 67 (Ampicillin+gentamycin)

Heterogeneity: not applicable

Test for overall effect: Z = 2.16 (P = 0.031)

Test for subgroup differences: Not applicable



Analysis 12.6. Comparison 12 Chloramphenicol with ampicillin and gentamicin, Outcome 6 Failure rates on day 21.

Review: Antibiotics for community-acquired pneumonia in children

Comparison: 12 Chloramphenicol with ampicillin and gentamicin

Outcome: 6 Failure rates on day 21

Study or subgroup	Chloramphenicol n/N	Ampicillin+gentamycin n/N	Odds Ratio M-H,Random,95% CI	Weight	Odds Ratio M-H,Random,95% CI
Asghar 2008	103/479	77/479		100.0 %	1.43 [1.03, 1.98]
Total (95% CI)	**479**	**479**		**100.0 %**	**1.43 [1.03, 1.98]**

Total events: 103 (Chloramphenicol), 77 (Ampicillin+gentamycin)

Heterogeneity: not applicable

Test for overall effect: Z = 2.14 (P = 0.032)

Test for subgroup differences: Not applicable

Analysis 12.7. Comparison 12 Chloramphenicol with ampicillin and gentamicin, Outcome 7 Need for change in antibiotics (day 5).

Review: Antibiotics for community-acquired pneumonia in children

Comparison: 12 Chloramphenicol with ampicillin and gentamicin

Outcome: 7 Need for change in antibiotics (day 5)

Study or subgroup	Chloramphenicol n/N	Ampicillin+gentamycin n/N	Odds Ratio M-H,Random,95% CI	Weight	Odds Ratio M-H,Random,95% CI
Asghar 2008	45/479	26/479		100.0 %	1.81 [1.10, 2.98]
Total (95% CI)	**479**	**479**		**100.0 %**	**1.81 [1.10, 2.98]**

Total events: 45 (Chloramphenicol), 26 (Ampicillin+gentamycin)

Heterogeneity: not applicable

Test for overall effect: Z = 2.32 (P = 0.021)

Test for subgroup differences: Not applicable

Analysis 12.8. Comparison 12 Chloramphenicol with ampicillin and gentamicin, Outcome 8 Need for change in antibiotics (day 10).

Review: Antibiotics for community-acquired pneumonia in children

Comparison: 12 Chloramphenicol with ampicillin and gentamicin

Outcome: 8 Need for change in antibiotics (day 10)

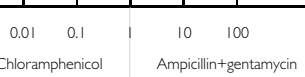
Study or subgroup	Chloramphenicol n/N	Ampicillin+gentamycin n/N	Odds Ratio M-H,Random,95% CI	Weight	Odds Ratio M-H,Random,95% CI
Asghar 2008	57/479	35/479		100.0 %	1.71 [1.10, 2.66]
Total (95% CI)	**479**	**479**		**100.0 %**	**1.71 [1.10, 2.66]**

Total events: 57 (Chloramphenicol), 35 (Ampicillin+gentamycin)

Heterogeneity: not applicable

Test for overall effect: Z = 2.39 (P = 0.017)

Test for subgroup differences: Not applicable



Analysis 12.9. Comparison 12 Chloramphenicol with ampicillin and gentamicin, Outcome 9 Need for change in antibiotics (day 21).

Review: Antibiotics for community-acquired pneumonia in children

Comparison: 12 Chloramphenicol with ampicillin and gentamicin

Outcome: 9 Need for change in antibiotics (day 21)

Study or subgroup	Chloramphenicol n/N	Ampicillin+gentamycin n/N	Odds Ratio M-H,Random,95% CI	Weight	Odds Ratio M-H,Random,95% CI
Asghar 2008	64/479	41/479		100.0 %	1.65 [1.09, 2.49]
Total (95% CI)	**479**	**479**		**100.0 %**	**1.65 [1.09, 2.49]**

Total events: 64 (Chloramphenicol), 41 (Ampicillin+gentamycin)

Heterogeneity: not applicable

Test for overall effect: Z = 2.36 (P = 0.018)

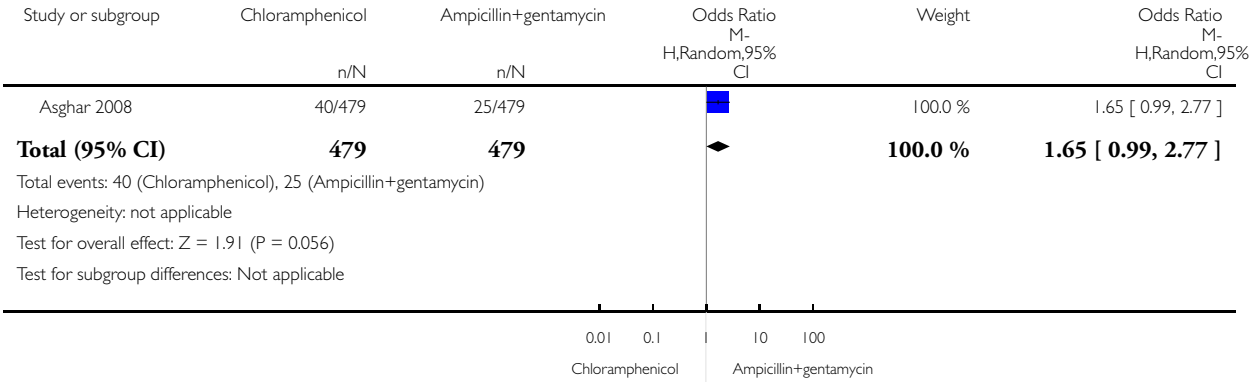
Test for subgroup differences: Not applicable

Analysis 12.10. Comparison 12 Chloramphenicol with ampicillin and gentamicin, Outcome 10 Death rates.

Review: Antibiotics for community-acquired pneumonia in children

Comparison: 12 Chloramphenicol with ampicillin and gentamicin

Outcome: 10 Death rates

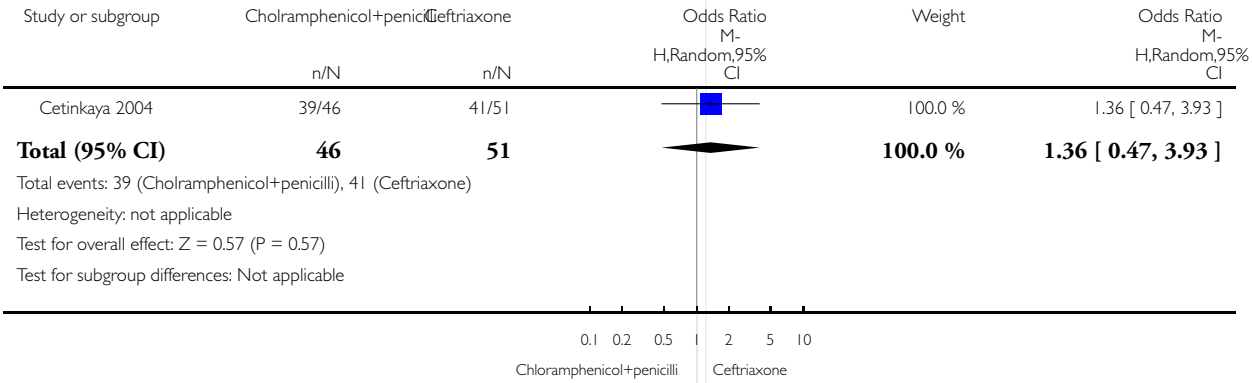


Analysis 13.1. Comparison 13 Chloramphenicol plus penicillin versus ceftriaxone, Outcome 1 Cure rates.

Review: Antibiotics for community-acquired pneumonia in children

Comparison: 13 Chloramphenicol plus penicillin versus ceftriaxone

Outcome: 1 Cure rates

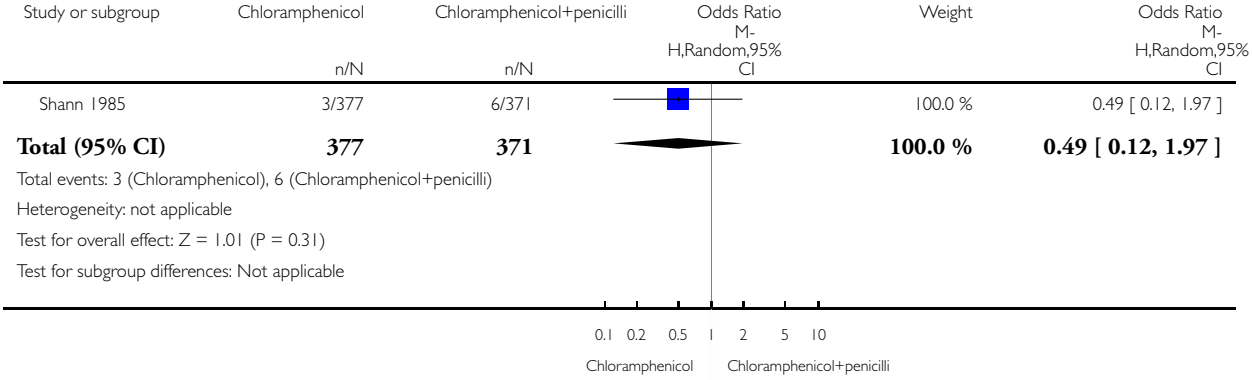


Analysis 14.1. Comparison 14 Chloramphenicol versus chloramphenicol plus penicillin, Outcome 1 Need for change of antibiotics.

Review: Antibiotics for community-acquired pneumonia in children

Comparison: 14 Chloramphenicol versus chloramphenicol plus penicillin

Outcome: 1 Need for change of antibiotics

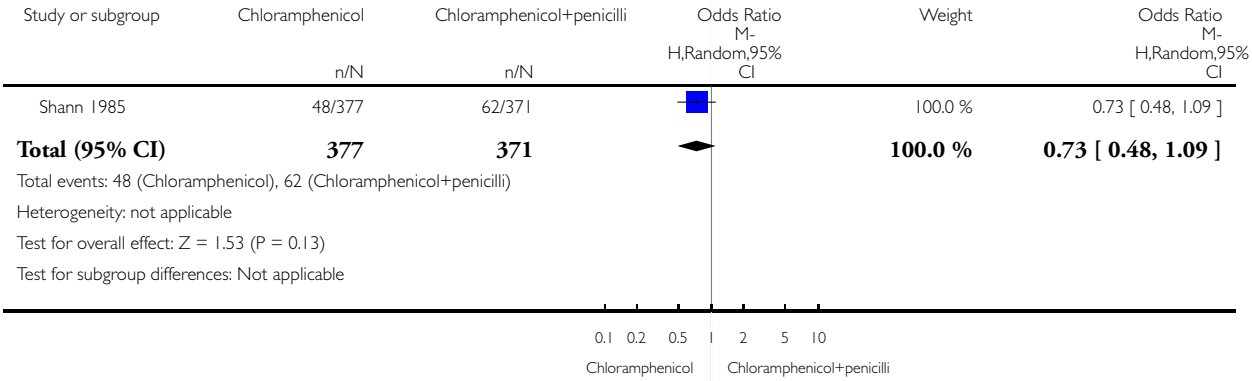


Analysis 14.2. Comparison 14 Chloramphenicol versus chloramphenicol plus penicillin, Outcome 2 Death rates.

Review: Antibiotics for community-acquired pneumonia in children

Comparison: 14 Chloramphenicol versus chloramphenicol plus penicillin

Outcome: 2 Death rates

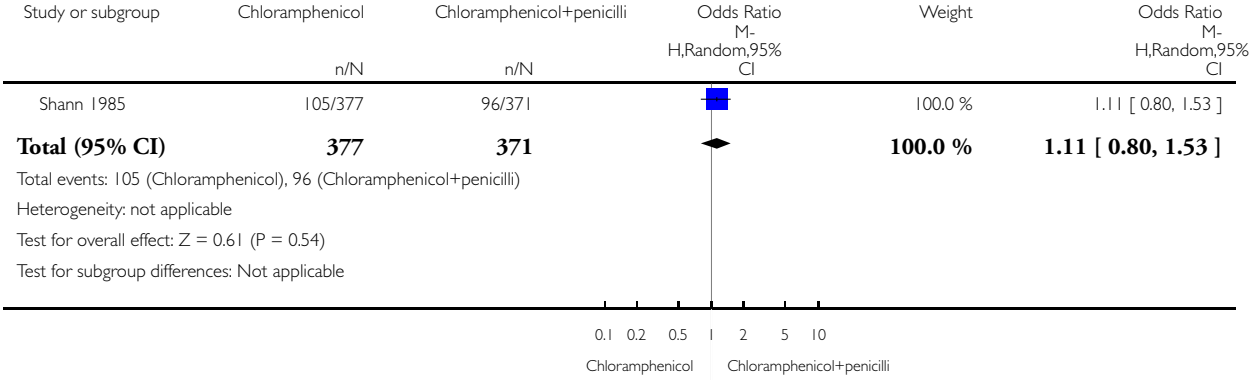


Analysis 14.3. Comparison 14 Chloramphenicol versus chloramphenicol plus penicillin, Outcome 3 Lost to follow-up.

Review: Antibiotics for community-acquired pneumonia in children

Comparison: 14 Chloramphenicol versus chloramphenicol plus penicillin

Outcome: 3 Lost to follow-up

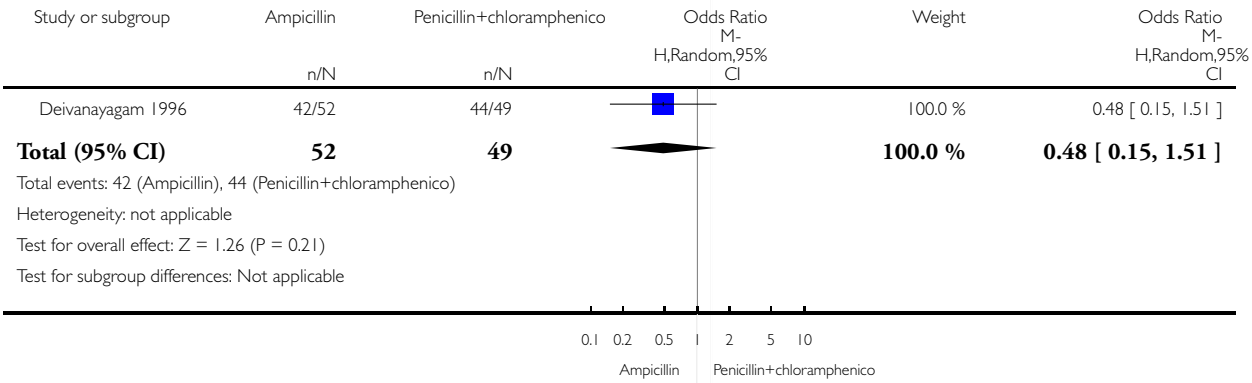


Analysis 15.1. Comparison 15 Ampicillin alone versus penicillin with chloramphenicol, Outcome 1 Cure rates.

Review: Antibiotics for community-acquired pneumonia in children

Comparison: 15 Ampicillin alone versus penicillin with chloramphenicol

Outcome: 1 Cure rates

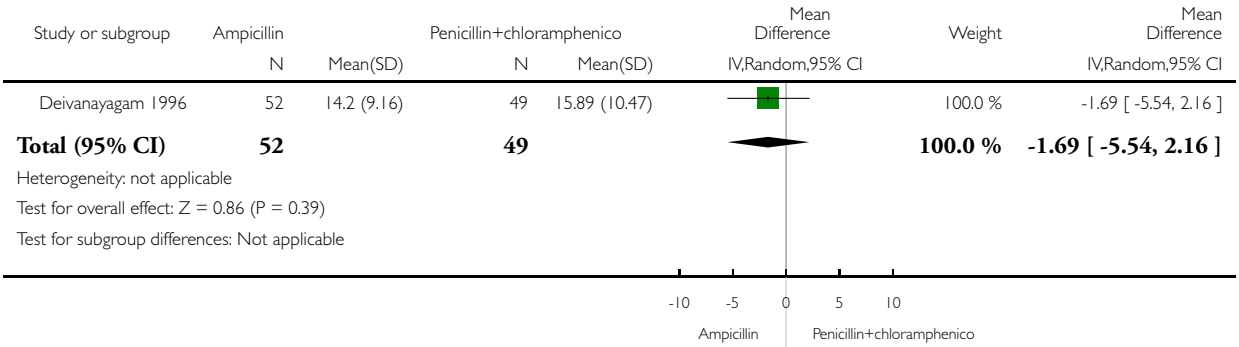


Analysis 15.2. Comparison 15 Ampicillin alone versus penicillin with chloramphenicol, Outcome 2 Age (months).

Review: Antibiotics for community-acquired pneumonia in children

Comparison: 15 Ampicillin alone versus penicillin with chloramphenicol

Outcome: 2 Age (months)

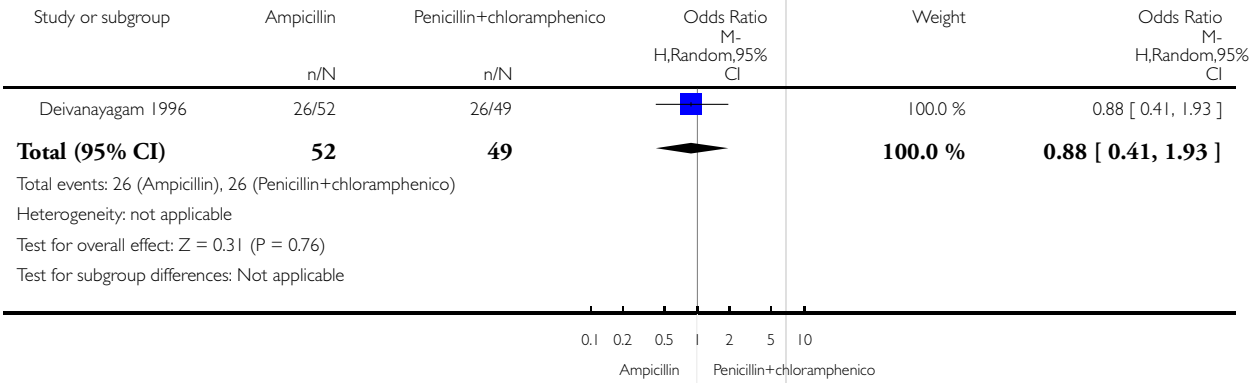


Analysis 15.3. Comparison 15 Ampicillin alone versus penicillin with chloramphenicol, Outcome 3 Male sex.

Review: Antibiotics for community-acquired pneumonia in children

Comparison: 15 Ampicillin alone versus penicillin with chloramphenicol

Outcome: 3 Male sex



Analysis 15.4. Comparison 15 Ampicillin alone versus penicillin with chloramphenicol, Outcome 4 Duration of hospital stay.

Review: Antibiotics for community-acquired pneumonia in children

Comparison: 15 Ampicillin alone versus penicillin with chloramphenicol

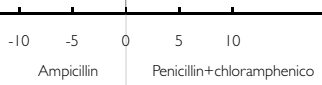
Outcome: 4 Duration of hospital stay

Study or subgroup	Ampicillin		Penicillin+chloramphenico		Mean Difference	Weight	Mean Difference
	N	Mean(SD)	N	Mean(SD)	IV,Random,95% CI		IV,Random,95% CI
Deivanayagam 1996	52	6.19 (2.78)	49	6.29 (2.5)		100.0 %	-0.10 [-1.13, 0.93]
Total (95% CI)	**52**		**49**			**100.0 %**	**-0.10 [-1.13, 0.93]**

Heterogeneity: not applicable

Test for overall effect: Z = 0.19 (P = 0.85)

Test for subgroup differences: Not applicable



Analysis 15.5. Comparison 15 Ampicillin alone versus penicillin with chloramphenicol, Outcome 5 Grade 2 to 4 malnutrition.

Review: Antibiotics for community-acquired pneumonia in children

Comparison: 15 Ampicillin alone versus penicillin with chloramphenicol

Outcome: 5 Grade 2 to 4 malnutrition

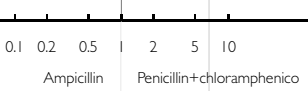
Study or subgroup	Ampicillin	Penicillin+chloramphenico	Odds Ratio M-H,Random,95% CI	Weight	Odds Ratio M-H,Random,95% CI
	n/N	n/N			
Deivanayagam 1996	26/52	26/49		100.0 %	0.88 [0.41, 1.93]
Total (95% CI)	**52**	**49**		**100.0 %**	**0.88 [0.41, 1.93]**

Total events: 26 (Ampicillin), 26 (Penicillin+chloramphenico)

Heterogeneity: not applicable

Test for overall effect: Z = 0.31 (P = 0.76)

Test for subgroup differences: Not applicable



Analysis 16.1. Comparison 16 Benzathine penicillin versus procaine penicillin, Outcome 1 Cure rate.

Review: Antibiotics for community-acquired pneumonia in children

Comparison: 16 Benzathine penicillin versus procaine penicillin

Outcome: 1 Cure rate

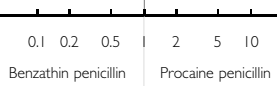
Study or subgroup	Benzathin penicillin n/N	Procaine penicillin n/N	Odds Ratio M-H,Random,95% CI	Weight	Odds Ratio M-H,Random,95% CI
Camargos 1997	84/93	78/83		33.0 %	0.60 [0.19, 1.86]
Sidal 1994	16/42	35/63		67.0 %	0.49 [0.22, 1.09]
Total (95% CI)	**135**	**146**		**100.0 %**	**0.53 [0.27, 1.01]**

Total events: 100 (Benzathin penicillin), 113 (Procaine penicillin)

Heterogeneity: $Tau^2 = 0.0$; $Chi^2 = 0.08$, df = 1 (P = 0.78); $I^2 = 0.0\%$

Test for overall effect: Z = 1.94 (P = 0.053)

Test for subgroup differences: Not applicable



Analysis 16.2. Comparison 16 Benzathine penicillin versus procaine penicillin, Outcome 2 Failure rate.

Review: Antibiotics for community-acquired pneumonia in children

Comparison: 16 Benzathine penicillin versus procaine penicillin

Outcome: 2 Failure rate

Study or subgroup	Benzathin penicillin n/N	Procaine penicillin n/N	Odds Ratio M-H,Random,95% CI	Weight	Odds Ratio M-H,Random,95% CI
Camargos 1997	7/93	4/83		47.2 %	1.61 [0.45, 5.70]
Sidal 1994	14/42	5/63		52.8 %	5.80 [1.90, 17.71]
Total (95% CI)	**135**	**146**		**100.0 %**	**3.17 [0.90, 11.11]**

Total events: 21 (Benzathin penicillin), 9 (Procaine penicillin)

Heterogeneity: $Tau^2 = 0.45$; $Chi^2 = 2.22$, df = 1 (P = 0.14); $I^2 = 55\%$

Test for overall effect: Z = 1.80 (P = 0.072)

Test for subgroup differences: Not applicable

Analysis 16.3. Comparison 16 Benzathine penicillin versus procaine penicillin, Outcome 3 Male sex.

Review: Antibiotics for community-acquired pneumonia in children

Comparison: 16 Benzathine penicillin versus procaine penicillin

Outcome: 3 Male sex

Study or subgroup	Benzathin penicillin n/N	Procaine penicillin n/N	Odds Ratio M-H,Random,95% CI	Weight	Odds Ratio M-H,Random,95% CI
Camargos 1997	56/93	47/83		64.9 %	1.16 [0.64, 2.11]
Sidal 1994	27/42	41/63		35.1 %	0.97 [0.43, 2.19]
Total (95% CI)	**135**	**146**		**100.0 %**	**1.09 [0.67, 1.76]**

Total events: 83 (Benzathin penicillin), 88 (Procaine penicillin)

Heterogeneity: $Tau^2 = 0.0$; $Chi^2 = 0.12$, df = 1 (P = 0.72); $I^2 = 0.0\%$

Test for overall effect: Z = 0.34 (P = 0.73)

Test for subgroup differences: Not applicable

Analysis 16.4. Comparison 16 Benzathine penicillin versus procaine penicillin, Outcome 4 Age between 2 to 6 years.

Review: Antibiotics for community-acquired pneumonia in children

Comparison: 16 Benzathine penicillin versus procaine penicillin

Outcome: 4 Age between 2 to 6 years

Study or subgroup	Benzathin penicillin n/N	Procaine penicillin n/N	Odds Ratio M-H,Random,95% CI	Weight	Odds Ratio M-H,Random,95% CI
Camargos 1997	58/93	42/83		52.6 %	1.62 [0.89, 2.95]
Sidal 1994	24/62	30/63		47.4 %	0.69 [0.34, 1.41]
Total (95% CI)	**155**	**146**		**100.0 %**	**1.08 [0.47, 2.48]**

Total events: 82 (Benzathin penicillin), 72 (Procaine penicillin)

Heterogeneity: $Tau^2 = 0.24$; $Chi^2 = 3.17$, df = 1 (P = 0.08); $I^2 = 68\%$

Test for overall effect: Z = 0.19 (P = 0.85)

Test for subgroup differences: Not applicable

Analysis 16.5. Comparison 16 Benzathine penicillin versus procaine penicillin, Outcome 5 Age between 7 to 12 years.

Review: Antibiotics for community-acquired pneumonia in children

Comparison: 16 Benzathine penicillin versus procaine penicillin

Outcome: 5 Age between 7 to 12 years

Study or subgroup	Benzathin penicillin n/N	Procaine penicillin n/N	Odds Ratio M-H,Random,95% CI	Weight	Odds Ratio M-H,Random,95% CI
Camargos 1997	35/93	41/83		71.5 %	0.62 [0.34, 1.13]
Sidal 1994	7/62	17/63		28.5 %	0.34 [0.13, 0.90]
Total (95% CI)	**155**	**146**		**100.0 %**	**0.52 [0.31, 0.88]**

Total events: 42 (Benzathin penicillin), 58 (Procaine penicillin)

Heterogeneity: $Tau^2 = 0.00$; $Chi^2 = 1.02$, df = 1 (P = 0.31); $I^2 = 2\%$

Test for overall effect: Z = 2.45 (P = 0.014)

Test for subgroup differences: Not applicable

Analysis 16.6. Comparison 16 Benzathine penicillin versus procaine penicillin, Outcome 6 Lost to follow-up.

Review: Antibiotics for community-acquired pneumonia in children

Comparison: 16 Benzathine penicillin versus procaine penicillin

Outcome: 6 Lost to follow-up

Study or subgroup	Benzathin penicillin n/N	Procaine penicillin n/N	Odds Ratio M-H,Random,95% CI	Weight	Odds Ratio M-H,Random,95% CI
Camargos 1997	2/93	1/83		100.0 %	1.80 [0.16, 20.25]
Total (95% CI)	**93**	**83**		**100.0 %**	**1.80 [0.16, 20.25]**

Total events: 2 (Benzathin penicillin), 1 (Procaine penicillin)

Heterogeneity: not applicable

Test for overall effect: Z = 0.48 (P = 0.63)

Test for subgroup differences: Not applicable

Analysis 16.7. Comparison 16 Benzathine penicillin versus procaine penicillin, Outcome 7 Failure rates in radiographically confirmed pneumonia.

Review: Antibiotics for community-acquired pneumonia in children

Comparison: 16 Benzathine penicillin versus procaine penicillin

Outcome: 7 Failure rates in radiographically confirmed pneumonia

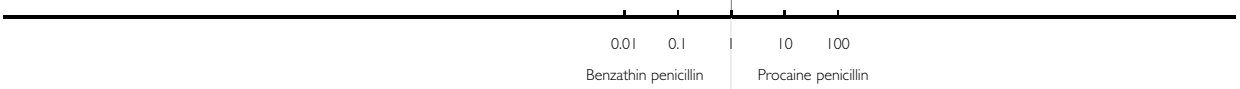
Study or subgroup	Benzathin penicillin n/N	Procaine penicillin n/N	Odds Ratio M-H,Random,95% CI	Weight	Odds Ratio M-H,Random,95% CI
Camargos 1997	7/93	4/83		100.0 %	1.61 [0.45, 5.70]
Total (95% CI)	**93**	**83**		**100.0 %**	**1.61 [0.45, 5.70]**

Total events: 7 (Benzathin penicillin), 4 (Procaine penicillin)

Heterogeneity: not applicable

Test for overall effect: Z = 0.74 (P = 0.46)

Test for subgroup differences: Not applicable



Analysis 17.1. Comparison 17 Amoxycillin versus penicillin, Outcome 1 Nasopharyngeal aspirates for S. pneumoniae.

Review: Antibiotics for community-acquired pneumonia in children

Comparison: 17 Amoxycillin versus penicillin

Outcome: 1 Nasopharyngeal aspirates for *S. pneumoniae*

Study or subgroup	Amoxycillin n/N	Penicillin n/N	Odds Ratio M-H,Random,95% CI	Weight	Odds Ratio M-H,Random,95% CI
Addo-Yobo 2004	201/743	217/743		100.0 %	0.90 [0.72, 1.13]
Total (95% CI)	**743**	**743**		**100.0 %**	**0.90 [0.72, 1.13]**

Total events: 201 (Amoxycillin), 217 (Penicillin)

Heterogeneity: not applicable

Test for overall effect: Z = 0.92 (P = 0.36)

Test for subgroup differences: Not applicable

Analysis 17.2. Comparison 17 Amoxycillin versus penicillin, Outcome 2 Age less than 1 year.

Review: Antibiotics for community-acquired pneumonia in children

Comparison: 17 Amoxycillin versus penicillin

Outcome: 2 Age less than 1 year

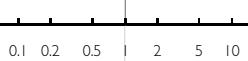
Study or subgroup	Amoxycillin n/N	Penicillin n/N	Odds Ratio M-H,Random,95% CI	Weight	Odds Ratio M-H,Random,95% CI
Addo-Yobo 2004	532/857	513/845		100.0 %	1.06 [0.87, 1.29]
Total (95% CI)	**857**	**845**		**100.0 %**	**1.06 [0.87, 1.29]**

Total events: 532 (Amoxycillin), 513 (Penicillin)

Heterogeneity: not applicable

Test for overall effect: Z = 0.58 (P = 0.56)

Test for subgroup differences: Not applicable

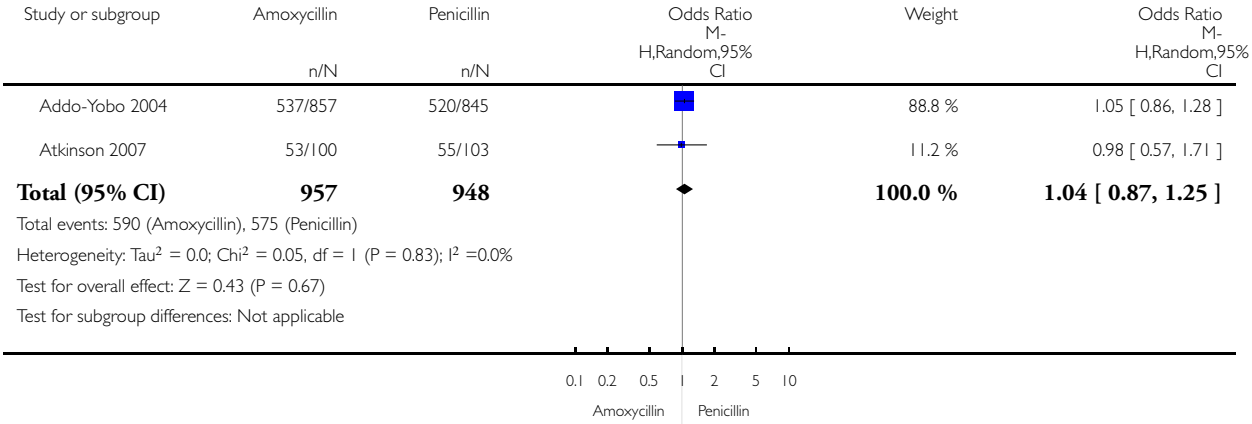


Analysis 17.3. Comparison 17 Amoxycillin versus penicillin, Outcome 3 Male sex.

Review: Antibiotics for community-acquired pneumonia in children

Comparison: 17 Amoxycillin versus penicillin

Outcome: 3 Male sex

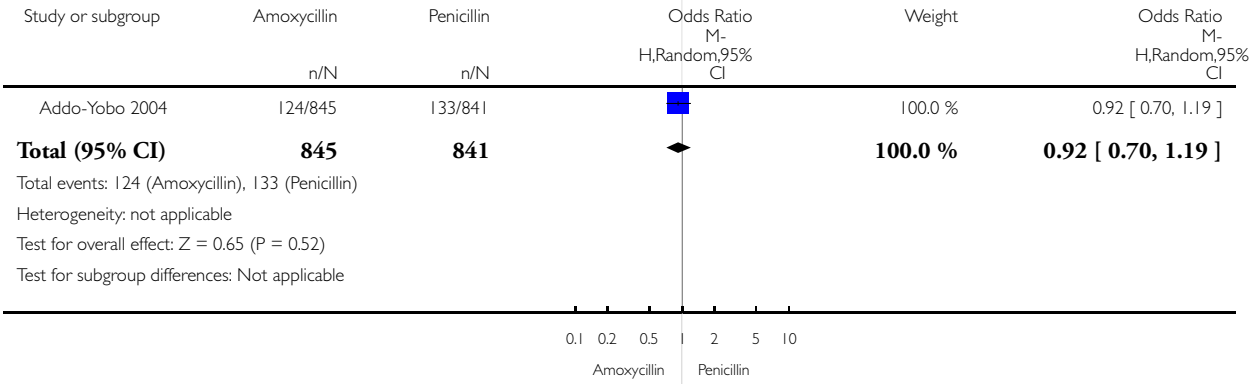


Analysis 17.4. Comparison 17 Amoxycillin versus penicillin, Outcome 4 Weight below 2 Z score (indicating severe malnutrition).

Review: Antibiotics for community-acquired pneumonia in children

Comparison: 17 Amoxycillin versus penicillin

Outcome: 4 Weight below 2 Z score (indicating severe malnutrition)



Analysis 17.5. Comparison 17 Amoxycillin versus penicillin, Outcome 5 Breast fed.

Review: Antibiotics for community-acquired pneumonia in children

Comparison: 17 Amoxycillin versus penicillin

Outcome: 5 Breast fed

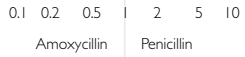
Study or subgroup	Amoxycillin n/N	Penicillin n/N	Odds Ratio M-H,Random,95% CI	Weight	Odds Ratio M-H,Random,95% CI
Addo-Yobo 2004	561/857	531/845		100.0 %	1.12 [0.92, 1.37]
Total (95% CI)	**857**	**845**		**100.0 %**	**1.12 [0.92, 1.37]**

Total events: 561 (Amoxycillin), 531 (Penicillin)

Heterogeneity: not applicable

Test for overall effect: Z = 1.13 (P = 0.26)

Test for subgroup differences: Not applicable

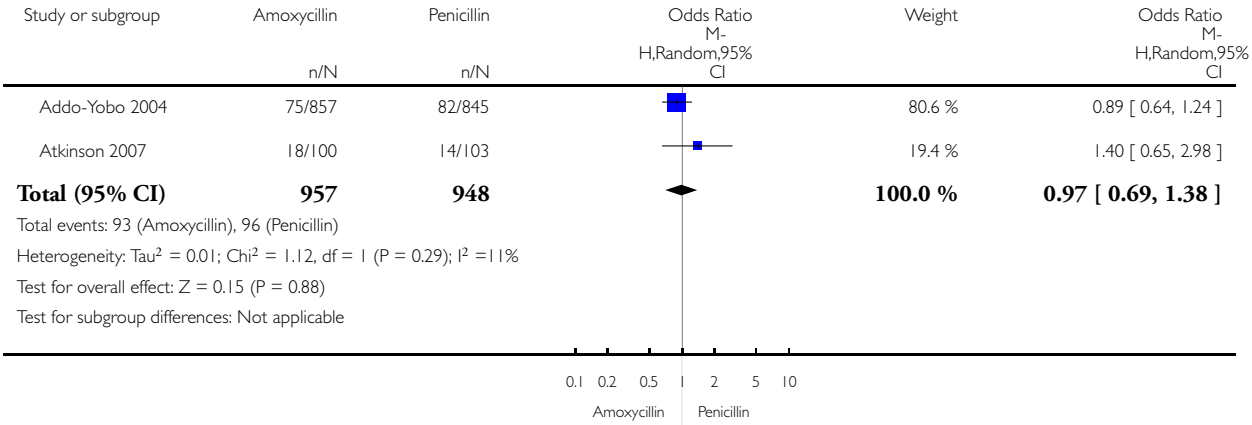


Analysis 17.6. Comparison 17 Amoxycillin versus penicillin, Outcome 6 Received antibiotics in last 7 days.

Review: Antibiotics for community-acquired pneumonia in children

Comparison: 17 Amoxycillin versus penicillin

Outcome: 6 Received antibiotics in last 7 days

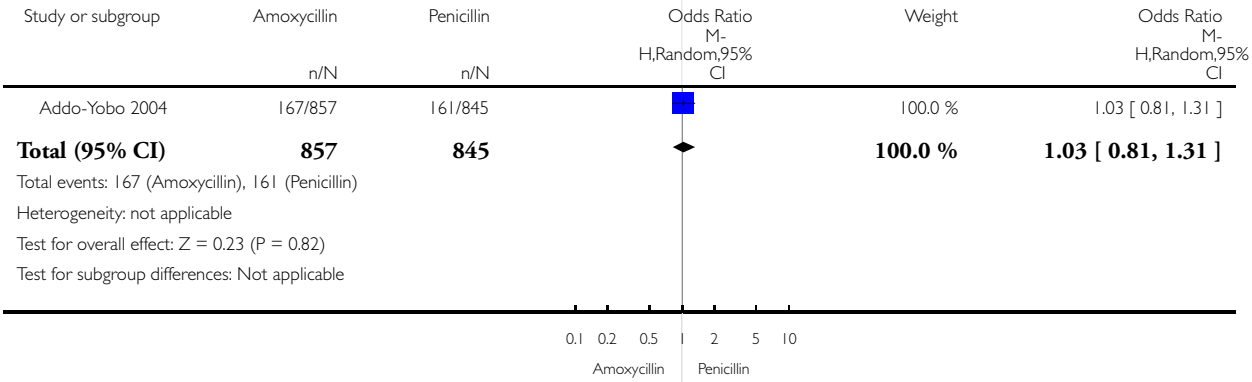


Analysis 17.7. Comparison 17 Amoxycillin versus penicillin, Outcome 7 Failure rate at 48 hours.

Review: Antibiotics for community-acquired pneumonia in children

Comparison: 17 Amoxycillin versus penicillin

Outcome: 7 Failure rate at 48 hours

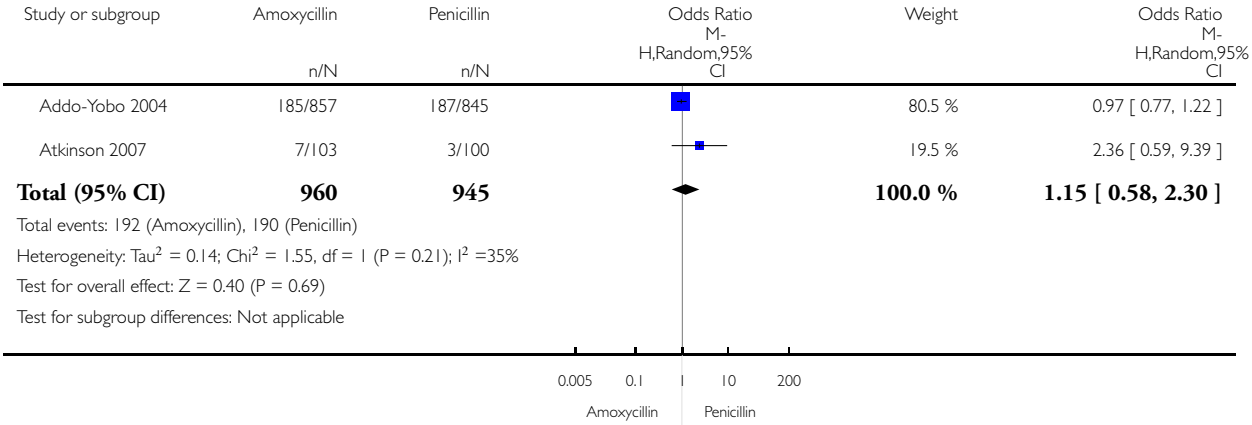


Analysis 17.8. Comparison 17 Amoxycillin versus penicillin, Outcome 8 Failure rate on day 5.

Review: Antibiotics for community-acquired pneumonia in children

Comparison: 17 Amoxycillin versus penicillin

Outcome: 8 Failure rate on day 5

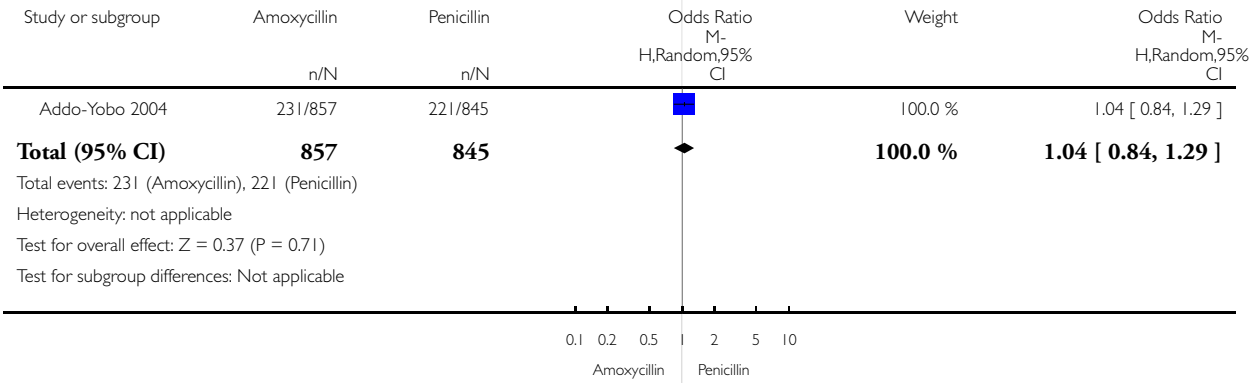


Analysis 17.9. Comparison 17 Amoxycillin versus penicillin, Outcome 9 Failure rate on day 14.

Review: Antibiotics for community-acquired pneumonia in children

Comparison: 17 Amoxycillin versus penicillin

Outcome: 9 Failure rate on day 14

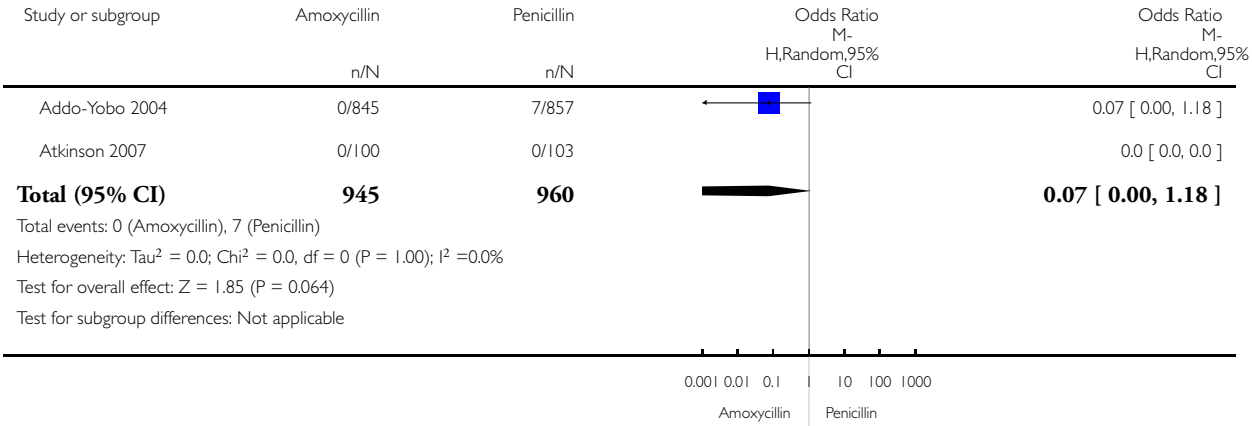


Analysis 17.10. Comparison 17 Amoxycillin versus penicillin, Outcome 10 Death rates.

Review: Antibiotics for community-acquired pneumonia in children

Comparison: 17 Amoxycillin versus penicillin

Outcome: 10 Death rates

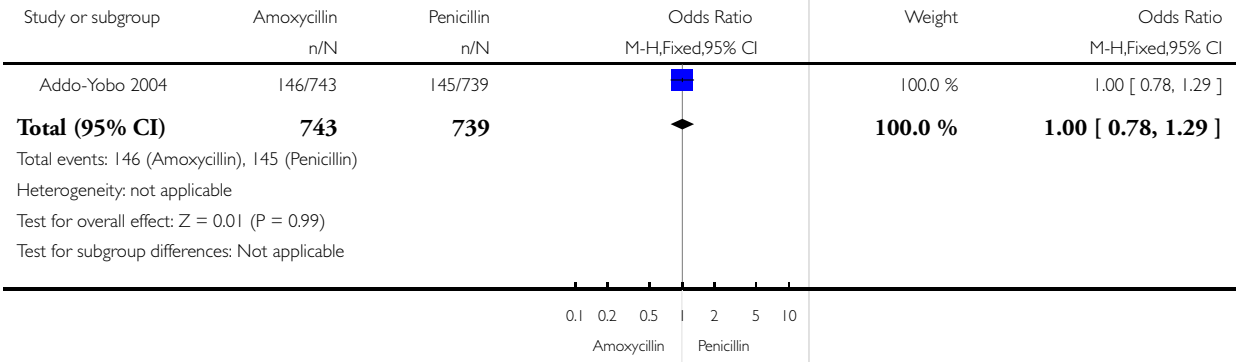


Analysis 17.11. Comparison 17 Amoxycillin versus penicillin, Outcome 11 Nasopharyngeal H. influenzae.

Review: Antibiotics for community-acquired pneumonia in children

Comparison: 17 Amoxycillin versus penicillin

Outcome: 11 Nasopharyngeal *H. influenzae*



Analysis 17.12. Comparison 17 Amoxycillin versus penicillin, Outcome 12 Respiratory syncytial virus (RSV) in nasopharyngeal swabs.

Review: Antibiotics for community-acquired pneumonia in children

Comparison: 17 Amoxycillin versus penicillin

Outcome: 12 Respiratory syncytial virus (RSV) in nasopharyngeal swabs

Study or subgroup	Amoxycillin n/N	Penicillin n/N	Odds Ratio M-H,Random,95% CI	Weight	Odds Ratio M-H,Random,95% CI
Addo-Yobo 2004	192/769	183/759		97.1 %	1.05 [0.83, 1.32]
Atkinson 2007	4/100	5/103		2.9 %	0.82 [0.21, 3.13]
Total (95% CI)	**869**	**862**		**100.0 %**	**1.04 [0.83, 1.31]**

Total events: 196 (Amoxycillin), 188 (Penicillin)

Heterogeneity: $Tau^2 = 0.0$; $Chi^2 = 0.13$, df = 1 (P = 0.72); $I^2 = 0.0\%$

Test for overall effect: Z = 0.33 (P = 0.74)

Test for subgroup differences: Not applicable

Analysis 17.13. Comparison 17 Amoxycillin versus penicillin, Outcome 13 Mean age.

Review: Antibiotics for community-acquired pneumonia in children

Comparison: 17 Amoxycillin versus penicillin

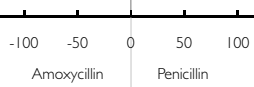
Outcome: 13 Mean age

Study or subgroup	Amoxycillin N	Mean(SD)	Penicillin N	Mean(SD)	Mean Difference IV,Random,95% CI	Mean Difference IV,Random,95% CI
Atkinson 2007	100	2.4 (0)	103	2.5 (0)		0.0 [0.0, 0.0]
Total (95% CI)	**100**		**103**			**0.0 [0.0, 0.0]**

Heterogeneity: not applicable

Test for overall effect: Z = 0.0 (P < 0.00001)

Test for subgroup differences: Not applicable



Analysis 17.14. Comparison 17 Amoxycillin versus penicillin, Outcome 14 Blood culture positive for S. pneumoniae.

Review: Antibiotics for community-acquired pneumonia in children

Comparison: 17 Amoxycillin versus penicillin

Outcome: 14 Blood culture positive for *S. pneumoniae*

Study or subgroup	Amoxycillin n/N	Penicillin n/N	Odds Ratio M-H,Random,95% CI	Weight	Odds Ratio M-H,Random,95% CI
Atkinson 2007	1/100	3/103		100.0 %	0.34 [0.03, 3.29]
Total (95% CI)	**100**	**103**		**100.0 %**	**0.34 [0.03, 3.29]**

Total events: 1 (Amoxycillin), 3 (Penicillin)

Heterogeneity: not applicable

Test for overall effect: Z = 0.94 (P = 0.35)

Test for subgroup differences: Not applicable

Analysis 17.15. Comparison 17 Amoxycillin versus penicillin, Outcome 15 Failure rate on day 5 in radiographically confirmed pneumonia.

Review: Antibiotics for community-acquired pneumonia in children

Comparison: 17 Amoxycillin versus penicillin

Outcome: 15 Failure rate on day 5 in radiographically confirmed pneumonia

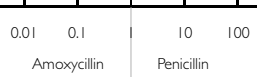
Study or subgroup	Amoxycillin n/N	Penicillin n/N	Odds Ratio M-H,Random,95% CI	Weight	Odds Ratio M-H,Random,95% CI
Atkinson 2007	7/103	3/100		100.0 %	2.36 [0.59, 9.39]
Total (95% CI)	**103**	**100**		**100.0 %**	**2.36 [0.59, 9.39]**

Total events: 7 (Amoxycillin), 3 (Penicillin)

Heterogeneity: not applicable

Test for overall effect: Z = 1.22 (P = 0.22)

Test for subgroup differences: Not applicable



Analysis 18.1. Comparison 18 Amoxycillin with IV ampicillin, Outcome 1 Age below one year.

Review: Antibiotics for community-acquired pneumonia in children

Comparison: 18 Amoxycillin with IV ampicillin

Outcome: 1 Age below one year

Study or subgroup	Amoxycillin n/N	Ampicillin n/N	Odds Ratio M-H,Random,95% CI	Weight	Odds Ratio M-H,Random,95% CI
Hazir 2008	653/1025	658/1012		100.0 %	0.94 [0.79, 1.13]
Total (95% CI)	**1025**	**1012**		**100.0 %**	**0.94 [0.79, 1.13]**

Total events: 653 (Amoxycillin), 658 (Ampicillin)

Heterogeneity: not applicable

Test for overall effect: Z = 0.62 (P = 0.54)

Test for subgroup differences: Not applicable

Analysis 18.2. Comparison 18 Amoxycillin with IV ampicillin, Outcome 2 Male sex.

Review: Antibiotics for community-acquired pneumonia in children

Comparison: 18 Amoxycillin with IV ampicillin

Outcome: 2 Male sex

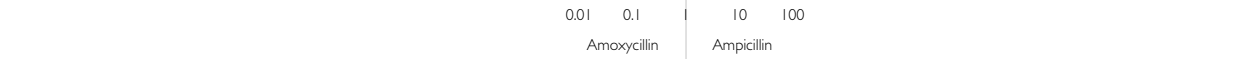
Study or subgroup	Amoxycillin n/N	Ampicillin n/N	Odds Ratio M-H,Random,95% CI	Weight	Odds Ratio M-H,Random,95% CI
Hazir 2008	630/1025	602/1012		100.0 %	1.09 [0.91, 1.30]
Total (95% CI)	**1025**	**1012**		**100.0 %**	**1.09 [0.91, 1.30]**

Total events: 630 (Amoxycillin), 602 (Ampicillin)

Heterogeneity: not applicable

Test for overall effect: Z = 0.91 (P = 0.36)

Test for subgroup differences: Not applicable



Analysis 18.3. Comparison 18 Amoxycillin with IV ampicillin, Outcome 3 Wheezing in infants.

Review: Antibiotics for community-acquired pneumonia in children

Comparison: 18 Amoxycillin with IV ampicillin

Outcome: 3 Wheezing in infants

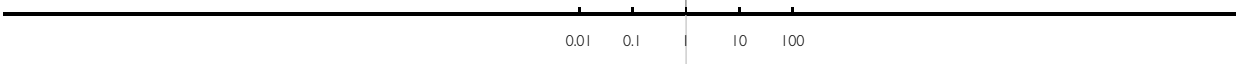
Study or subgroup	Amoxycillin n/N	Ampicillin n/N	Odds Ratio M-H,Random,95% CI	Weight	Odds Ratio M-H,Random,95% CI
Hazir 2008	535/653	536/658		100.0 %	1.03 [0.78, 1.37]
Total (95% CI)	**653**	**658**		**100.0 %**	**1.03 [0.78, 1.37]**

Total events: 535 (Amoxycillin), 536 (Ampicillin)

Heterogeneity: not applicable

Test for overall effect: Z = 0.22 (P = 0.83)

Test for subgroup differences: Not applicable



Analysis 18.4. Comparison 18 Amoxycillin with IV ampicillin, Outcome 4 Wheezing in age group one to five years.

Review: Antibiotics for community-acquired pneumonia in children

Comparison: 18 Amoxycillin with IV ampicillin

Outcome: 4 Wheezing in age group one to five years

Study or subgroup	Amoxycillin n/N	Ampicillin n/N	Odds Ratio M-H,Random,95% CI	Weight	Odds Ratio M-H,Random,95% CI
Hazir 2008	232/372	242/354		100.0 %	0.77 [0.56, 1.04]
Total (95% CI)	**372**	**354**		**100.0 %**	**0.77 [0.56, 1.04]**

Total events: 232 (Amoxycillin), 242 (Ampicillin)

Heterogeneity: not applicable

Test for overall effect: Z = 1.69 (P = 0.090)

Test for subgroup differences: Not applicable

Analysis 18.5. Comparison 18 Amoxycillin with IV ampicillin, Outcome 5 Failure rates.

Review: Antibiotics for community-acquired pneumonia in children

Comparison: 18 Amoxycillin with IV ampicillin

Outcome: 5 Failure rates

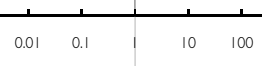
Study or subgroup	Amoxycillin n/N	Ampicillin n/N	Odds Ratio M-H,Random,95% CI	Weight	Odds Ratio M-H,Random,95% CI
Hazir 2008	77/1025	87/1012		100.0 %	0.86 [0.63, 1.19]
Total (95% CI)	**1025**	**1012**		**100.0 %**	**0.86 [0.63, 1.19]**

Total events: 77 (Amoxycillin), 87 (Ampicillin)

Heterogeneity: not applicable

Test for overall effect: Z = 0.90 (P = 0.37)

Test for subgroup differences: Not applicable

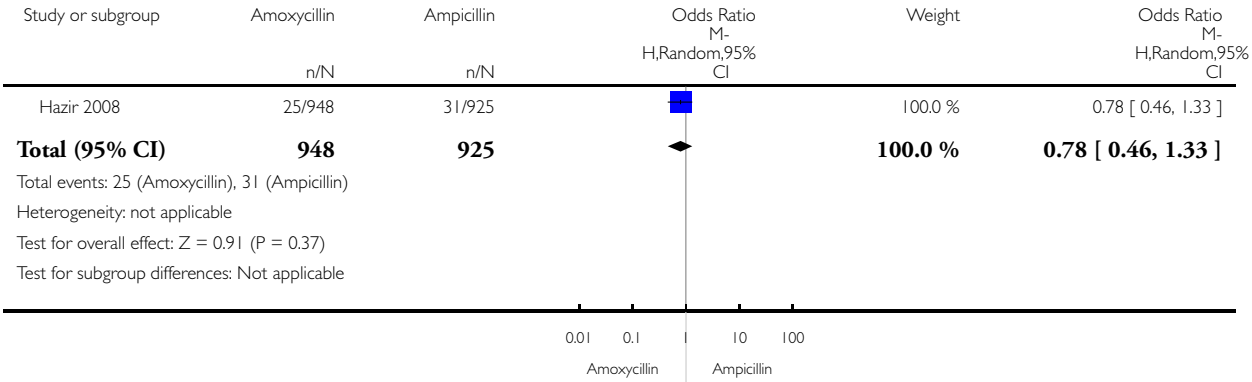


Analysis 18.6. Comparison 18 Amoxycillin with IV ampicillin, Outcome 6 Relapse rates.

Review: Antibiotics for community-acquired pneumonia in children

Comparison: 18 Amoxycillin with IV ampicillin

Outcome: 6 Relapse rates

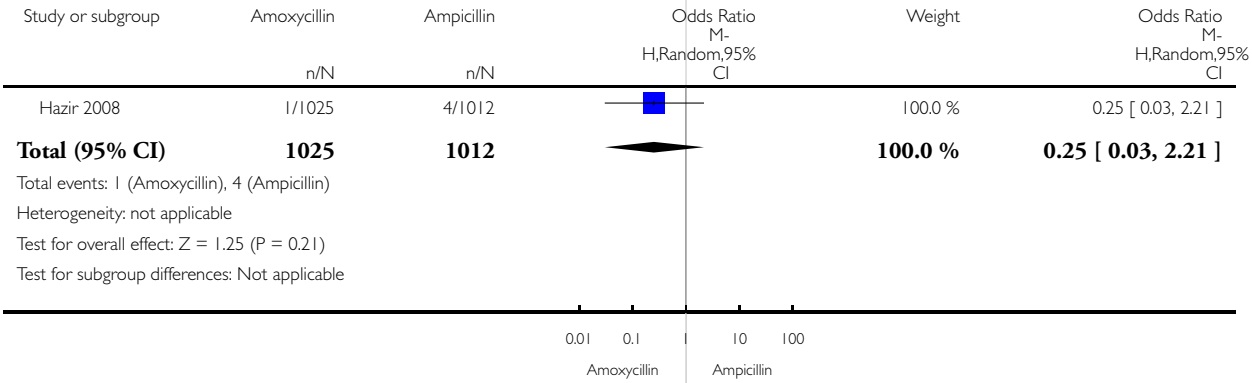


Analysis 18.7. Comparison 18 Amoxycillin with IV ampicillin, Outcome 7 Death rates.

Review: Antibiotics for community-acquired pneumonia in children

Comparison: 18 Amoxycillin with IV ampicillin

Outcome: 7 Death rates

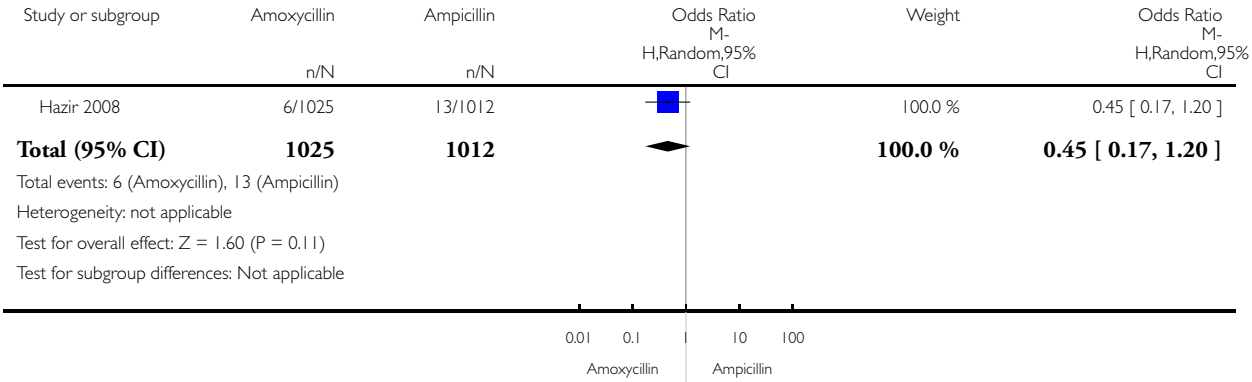


Analysis 18.8. Comparison 18 Amoxycillin with IV ampicillin, Outcome 8 Lost to follow-up.

Review: Antibiotics for community-acquired pneumonia in children

Comparison: 18 Amoxycillin with IV ampicillin

Outcome: 8 Lost to follow-up

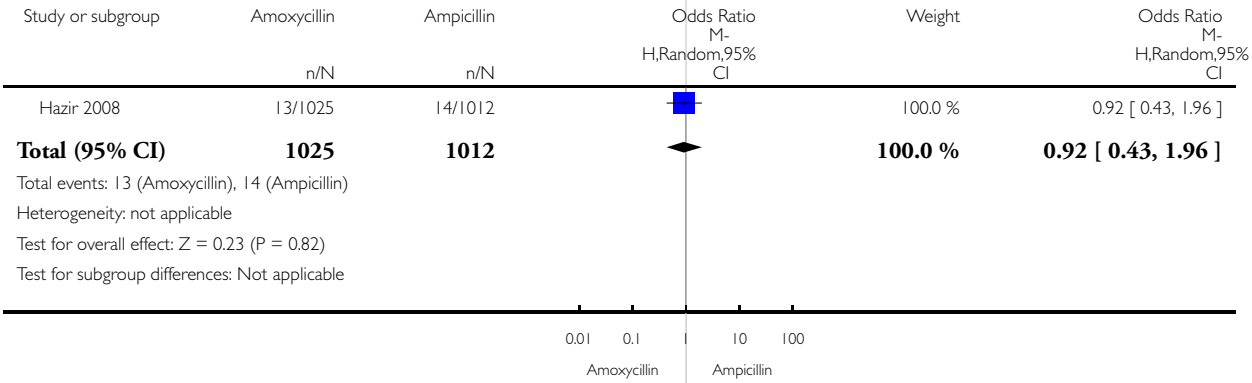


Analysis 18.9. Comparison 18 Amoxycillin with IV ampicillin, Outcome 9 Protocol violation.

Review: Antibiotics for community-acquired pneumonia in children

Comparison: 18 Amoxycillin with IV ampicillin

Outcome: 9 Protocol violation



Analysis 19.1. Comparison 19 Amoxycillin with cefuroxime, Outcome 1 Mean age in months.

Review: Antibiotics for community-acquired pneumonia in children

Comparison: 19 Amoxycillin with cefuroxime

Outcome: 1 Mean age in months

Study or subgroup	Amoxycillin N	Mean(SD)	Cefuroxime N	Mean(SD)	Mean Difference IV,Random,95% CI	Weight	Mean Difference IV,Random,95% CI
Aurangzeb 2003	43	12.79 (16.47)	41	8.32 (10.72)		100.0 %	4.47 [-1.45, 10.39]
Total (95% CI)	**43**		**41**			**100.0 %**	**4.47 [-1.45, 10.39]**

Heterogeneity: not applicable

Test for overall effect: Z = 1.48 (P = 0.14)

Test for subgroup differences: Not applicable

Analysis 19.2. Comparison 19 Amoxycillin with cefuroxime, Outcome 2 Male sex.

Review: Antibiotics for community-acquired pneumonia in children

Comparison: 19 Amoxycillin with cefuroxime

Outcome: 2 Male sex

Study or subgroup	Amoxycillin n/N	Cefuroxime n/N	Odds Ratio M-H,Random,95% CI	Weight	Odds Ratio M-H,Random,95% CI
Aurangzeb 2003	35/43	41/42		100.0 %	0.11 [0.01, 0.90]
Total (95% CI)	**43**	**42**		**100.0 %**	**0.11 [0.01, 0.90]**

Total events: 35 (Amoxycillin), 41 (Cefuroxime)

Heterogeneity: not applicable

Test for overall effect: Z = 2.06 (P = 0.039)

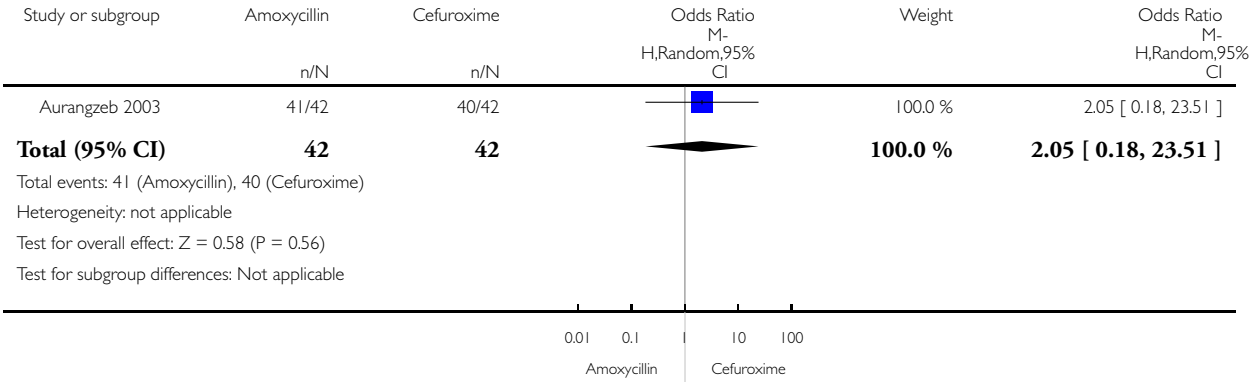
Test for subgroup differences: Not applicable

Analysis 19.3. Comparison 19 Amoxycillin with cefuroxime, Outcome 3 Cure rates.

Review: Antibiotics for community-acquired pneumonia in children

Comparison: 19 Amoxycillin with cefuroxime

Outcome: 3 Cure rates

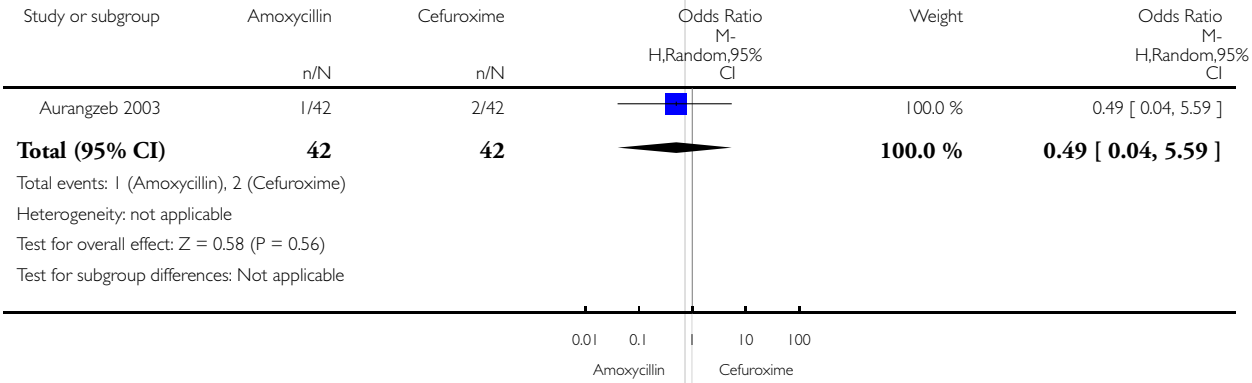


Analysis 19.4. Comparison 19 Amoxycillin with cefuroxime, Outcome 4 Failure rates.

Review: Antibiotics for community-acquired pneumonia in children

Comparison: 19 Amoxycillin with cefuroxime

Outcome: 4 Failure rates



Analysis 20.1. Comparison 20 Amoxycillin with clarithromycin, Outcome 1 Mean age.

Review: Antibiotics for community-acquired pneumonia in children

Comparison: 20 Amoxycillin with clarithromycin

Outcome: 1 Mean age

Study or subgroup	Amoxycillin N	Mean(SD)	Clarithromycin N	Mean(SD)	Mean Difference IV,Random,95% CI	Weight	Mean Difference IV,Random,95% CI
Aurangzeb 2003	43	12.79 (16.47)	42	15.95 (17.12)		100.0 %	-3.16 [-10.30, 3.98]
Total (95% CI)	**43**		**42**			**100.0 %**	**-3.16 [-10.30, 3.98]**

Heterogeneity: not applicable

Test for overall effect: Z = 0.87 (P = 0.39)

Test for subgroup differences: Not applicable

Analysis 20.2. Comparison 20 Amoxycillin with clarithromycin, Outcome 2 Male sex.

Review: Antibiotics for community-acquired pneumonia in children

Comparison: 20 Amoxycillin with clarithromycin

Outcome: 2 Male sex

Study or subgroup	Amoxycillin n/N	Clarithromycin n/N	Odds Ratio M-H,Random,95% CI	Weight	Odds Ratio M-H,Random,95% CI
Aurangzeb 2003	35/43	31/42		100.0 %	1.55 [0.55, 4.35]
Total (95% CI)	**43**	**42**		**100.0 %**	**1.55 [0.55, 4.35]**

Total events: 35 (Amoxycillin), 31 (Clarithromycin)

Heterogeneity: not applicable

Test for overall effect: Z = 0.84 (P = 0.40)

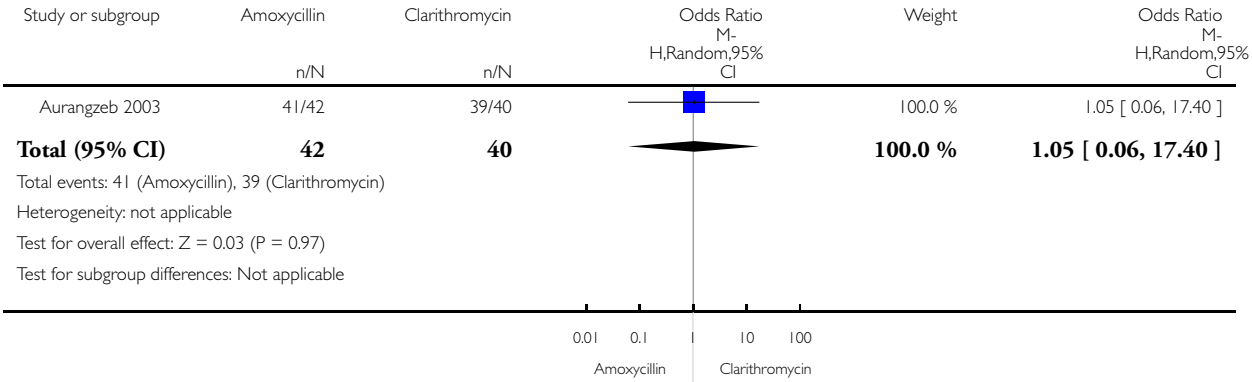
Test for subgroup differences: Not applicable

Analysis 20.3. Comparison 20 Amoxycillin with clarithromycin, Outcome 3 Cure rates.

Review: Antibiotics for community-acquired pneumonia in children

Comparison: 20 Amoxycillin with clarithromycin

Outcome: 3 Cure rates

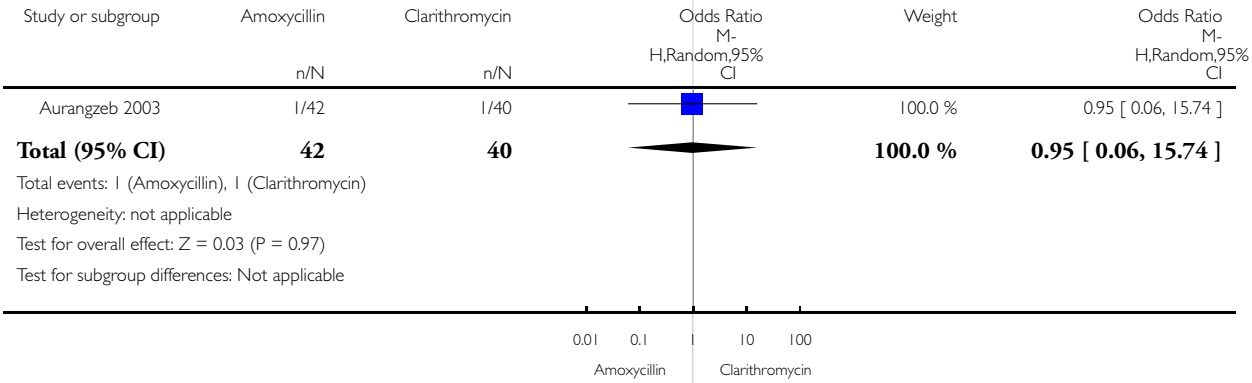


Analysis 20.4. Comparison 20 Amoxycillin with clarithromycin, Outcome 4 Failure rates.

Review: Antibiotics for community-acquired pneumonia in children

Comparison: 20 Amoxycillin with clarithromycin

Outcome: 4 Failure rates

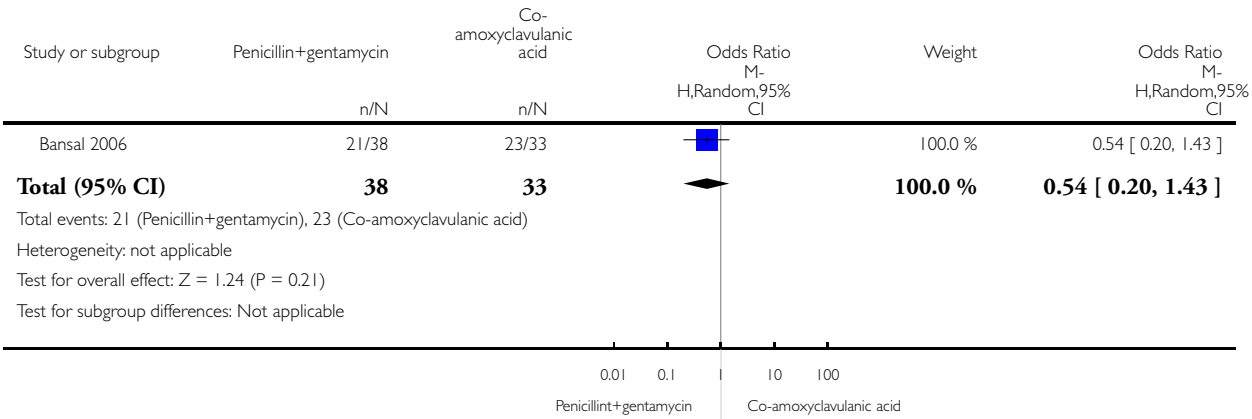


Analysis 21.1. Comparison 21 Penicillin and gentamycin with co-amoxyclavulanic acid, Outcome 1 Number of children less than 1 year age.

Review: Antibiotics for community-acquired pneumonia in children

Comparison: 21 Penicillin and gentamycin with co-amoxyclavulanic acid

Outcome: 1 Number of children less than 1 year age

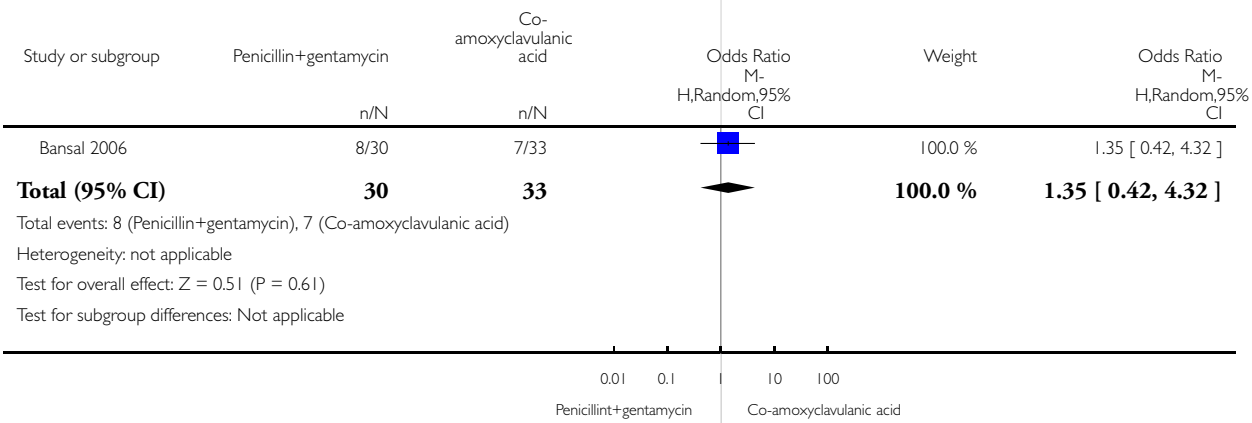


Analysis 21.2. Comparison 21 Penicillin and gentamycin with co-amoxyclavulanic acid, Outcome 2 Male sex.

Review: Antibiotics for community-acquired pneumonia in children

Comparison: 21 Penicillin and gentamycin with co-amoxyclavulanic acid

Outcome: 2 Male sex

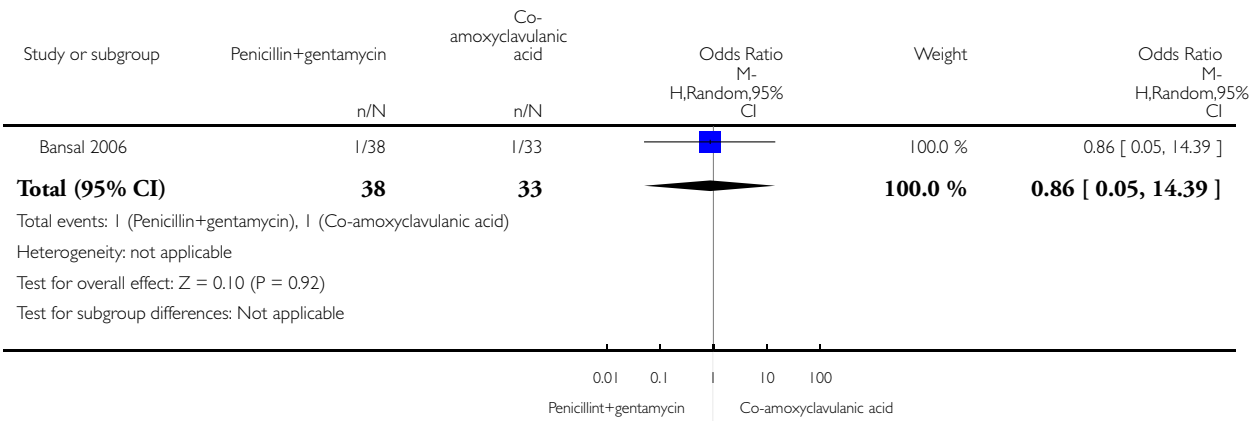


Analysis 21.3. Comparison 21 Penicillin and gentamycin with co-amoxyclavulanic acid, Outcome 3 Failure rates.

Review: Antibiotics for community-acquired pneumonia in children

Comparison: 21 Penicillin and gentamycin with co-amoxyclavulanic acid

Outcome: 3 Failure rates



Analysis 22.1. Comparison 22 Levofloxacin with comparator (co-amoxyclavulanic acid/ceftriaxone), Outcome 1 Mean age.

Review: Antibiotics for community-acquired pneumonia in children

Comparison: 22 Levofloxacin with comparator (co-amoxyclavulanic acid/ceftriaxone)

Outcome: 1 Mean age

Study or subgroup	Levofloxacin N	Mean(SD)	Comparator N	Mean(SD)	Mean Difference IV,Random,95% CI	Weight	Mean Difference IV,Random,95% CI
Bradley 2007	529	5.52 (4.01)	180	5.47 (4.12)		100.0 %	0.05 [-0.64, 0.74]
Total (95% CI)	**529**		**180**			**100.0 %**	**0.05 [-0.64, 0.74]**

Heterogeneity: not applicable

Test for overall effect: Z = 0.14 (P = 0.89)

Test for subgroup differences: Not applicable

Analysis 22.2. Comparison 22 Levofloxacin with comparator (co-amoxyclavulanic acid/ceftriaxone), Outcome 2 Male sex.

Review: Antibiotics for community-acquired pneumonia in children

Comparison: 22 Levofloxacin with comparator (co-amoxyclavulanic acid/ceftriaxone)

Outcome: 2 Male sex

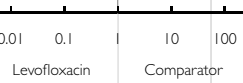
Study or subgroup	Levofloxacin n/N	Comparator n/N	Odds Ratio M-H,Random,95% CI	Weight	Odds Ratio M-H,Random,95% CI
Bradley 2007	266/529	92/180		100.0 %	0.97 [0.69, 1.36]
Total (95% CI)	**529**	**180**		**100.0 %**	**0.97 [0.69, 1.36]**

Total events: 266 (Levofloxacin), 92 (Comparator)

Heterogeneity: not applicable

Test for overall effect: Z = 0.19 (P = 0.85)

Test for subgroup differences: Not applicable



Analysis 22.3. Comparison 22 Levofloxacin with comparator (co-amoxyclavulanic acid/ceftriaxone), Outcome 3 Numbers received antibiotics in past 1 week.

Review: Antibiotics for community-acquired pneumonia in children

Comparison: 22 Levofloxacin with comparator (co-amoxyclavulanic acid/ceftriaxone)

Outcome: 3 Numbers received antibiotics in past 1 week

Study or subgroup	Levofloxacin n/N	Comparator n/N	Odds Ratio M-H,Random,95% CI	Weight	Odds Ratio M-H,Random,95% CI
Bradley 2007	142/529	51/180		100.0 %	0.93 [0.64, 1.35]
Total (95% CI)	**529**	**180**		**100.0 %**	**0.93 [0.64, 1.35]**

Total events: 142 (Levofloxacin), 51 (Comparator)

Heterogeneity: not applicable

Test for overall effect: Z = 0.39 (P = 0.70)

Test for subgroup differences: Not applicable

Analysis 22.4. Comparison 22 Levofloxacin with comparator (co-amoxyclavulanic acid/ceftriaxone), Outcome 4 Cure rates.

Review: Antibiotics for community-acquired pneumonia in children

Comparison: 22 Levofloxacin with comparator (co-amoxyclavulanic acid/ceftriaxone)

Outcome: 4 Cure rates

Study or subgroup	Levofloxacin n/N	Comparator n/N	Odds Ratio M-H,Random,95% CI	Weight	Odds Ratio M-H,Random,95% CI
Bradley 2007	382/405	126/134		100.0 %	1.05 [0.46, 2.42]
Total (95% CI)	**405**	**134**		**100.0 %**	**1.05 [0.46, 2.42]**

Total events: 382 (Levofloxacin), 126 (Comparator)

Heterogeneity: not applicable

Test for overall effect: Z = 0.13 (P = 0.90)

Test for subgroup differences: Not applicable

Analysis 23.1. Comparison 23 Cefuroxime with clarithromycin, Outcome 1 Mean age.

Review: Antibiotics for community-acquired pneumonia in children

Comparison: 23 Cefuroxime with clarithromycin

Outcome: 1 Mean age

Study or subgroup	Cefuroxime N	Mean(SD)	Clarithromycin N	Mean(SD)	Mean Difference IV,Random,95% CI	Weight	Mean Difference IV,Random,95% CI
Aurangzeb 2003	41	8.32 (10.72)	42	15.35 (17.12)		100.0 %	-7.03 [-13.16, -0.90]
Total (95% CI)	**41**		**42**			**100.0 %**	**-7.03 [-13.16, -0.90]**

Heterogeneity: not applicable

Test for overall effect: Z = 2.25 (P = 0.025)

Test for subgroup differences: Not applicable

Analysis 23.2. Comparison 23 Cefuroxime with clarithromycin, Outcome 2 Male sex.

Review: Antibiotics for community-acquired pneumonia in children

Comparison: 23 Cefuroxime with clarithromycin

Outcome: 2 Male sex

Study or subgroup	Cefuroxime n/N	Clarithromycin n/N	Odds Ratio M-H,Random,95% CI	Weight	Odds Ratio M-H,Random,95% CI
Aurangzeb 2003	41/42	31/42		100.0 %	14.55 [1.78, 118.76]
Total (95% CI)	**42**	**42**		**100.0 %**	**14.55 [1.78, 118.76]**

Total events: 41 (Cefuroxime), 31 (Clarithromycin)

Heterogeneity: not applicable

Test for overall effect: Z = 2.50 (P = 0.012)

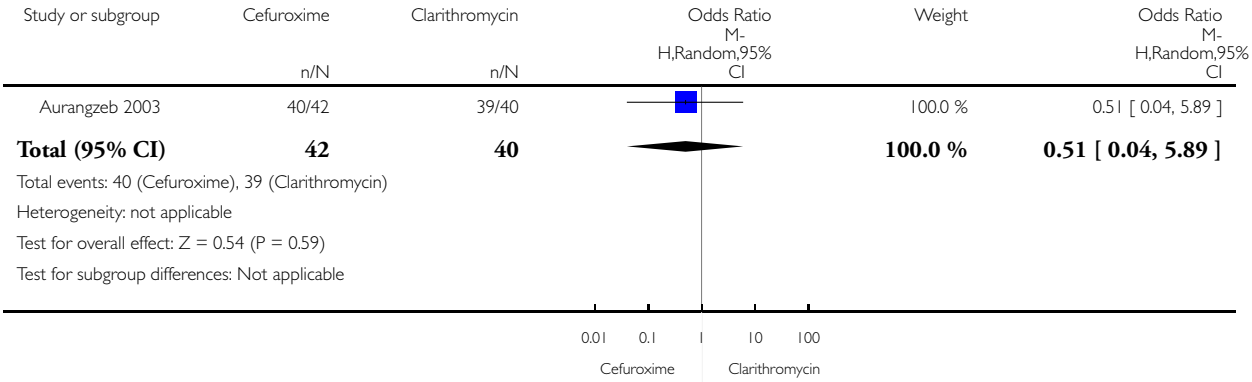
Test for subgroup differences: Not applicable

Analysis 23.3. Comparison 23 Cefuroxime with clarithromycin, Outcome 3 Cure rates.

Review: Antibiotics for community-acquired pneumonia in children

Comparison: 23 Cefuroxime with clarithromycin

Outcome: 3 Cure rates

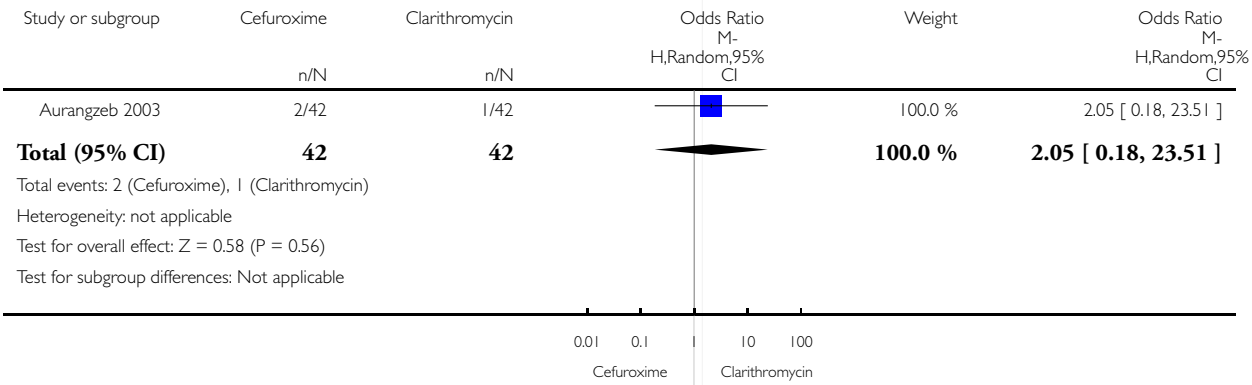


Analysis 23.4. Comparison 23 Cefuroxime with clarithromycin, Outcome 4 Failure rates.

Review: Antibiotics for community-acquired pneumonia in children

Comparison: 23 Cefuroxime with clarithromycin

Outcome: 4 Failure rates

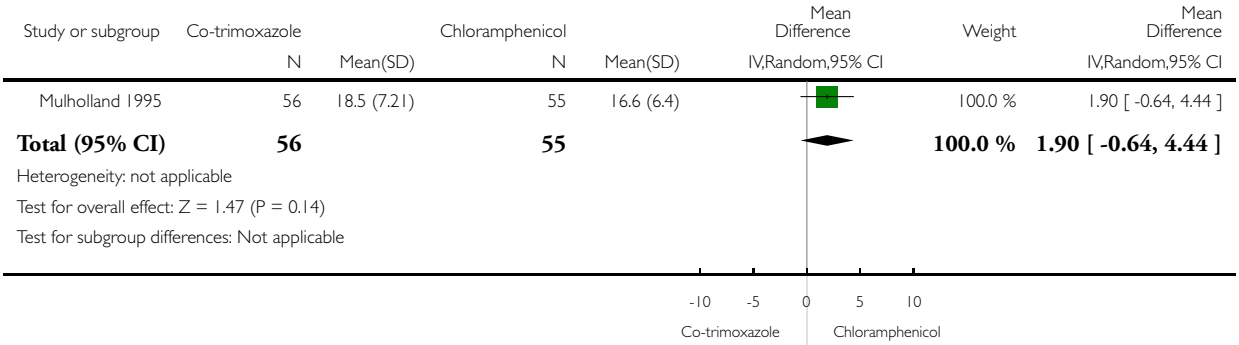


Analysis 24.1. Comparison 24 Co-trimoxazole versus chloramphenicol, Outcome 1 Age in months.

Review: Antibiotics for community-acquired pneumonia in children

Comparison: 24 Co-trimoxazole versus chloramphenicol

Outcome: 1 Age in months

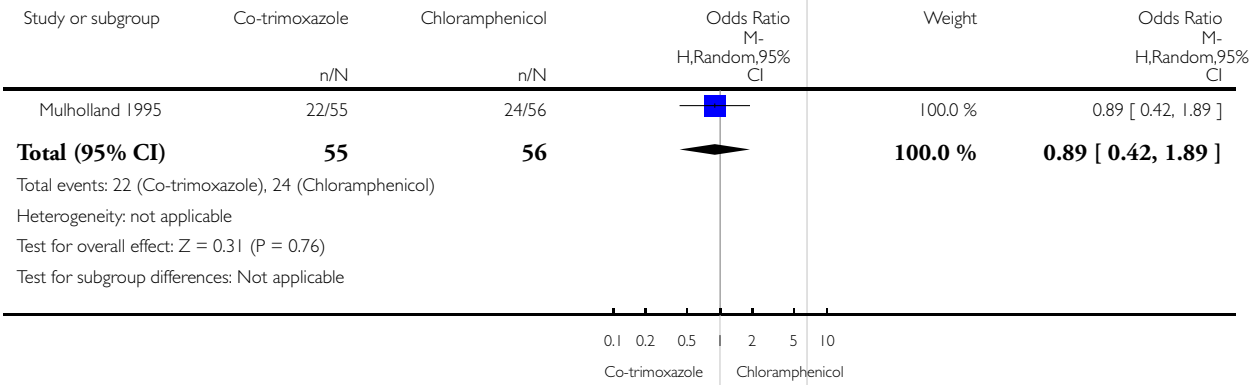


Analysis 24.2. Comparison 24 Co-trimoxazole versus chloramphenicol, Outcome 2 Male sex.

Review: Antibiotics for community-acquired pneumonia in children

Comparison: 24 Co-trimoxazole versus chloramphenicol

Outcome: 2 Male sex

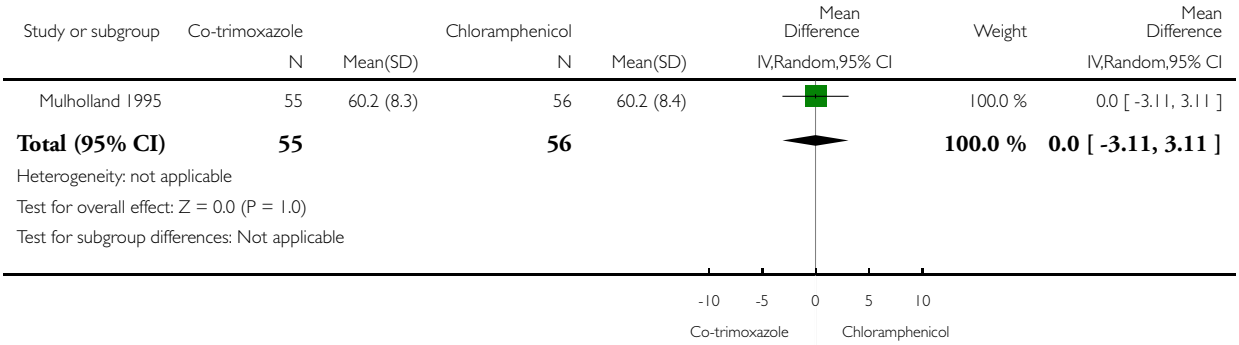


Analysis 24.3. Comparison 24 Co-trimoxazole versus chloramphenicol, Outcome 3 Weight for age.

Review: Antibiotics for community-acquired pneumonia in children

Comparison: 24 Co-trimoxazole versus chloramphenicol

Outcome: 3 Weight for age

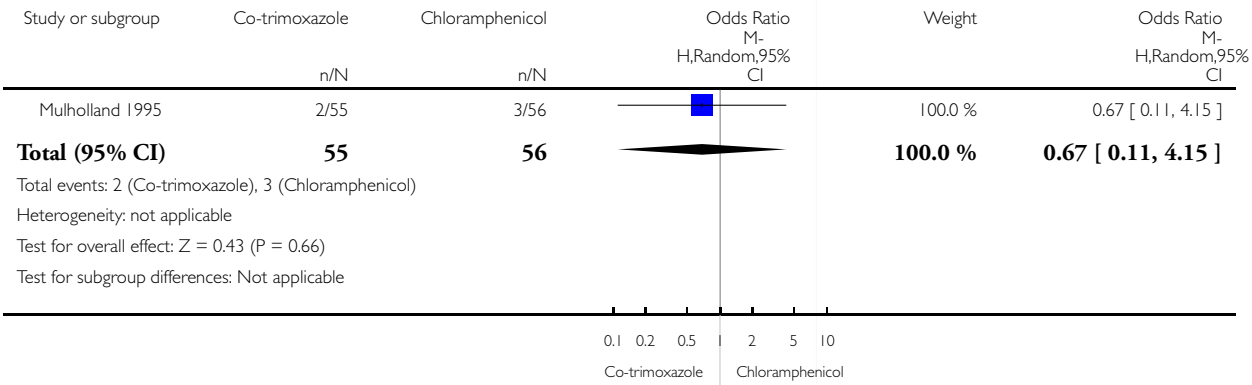


Analysis 24.4. Comparison 24 Co-trimoxazole versus chloramphenicol, Outcome 4 Wheezing positive.

Review: Antibiotics for community-acquired pneumonia in children

Comparison: 24 Co-trimoxazole versus chloramphenicol

Outcome: 4 Wheezing positive

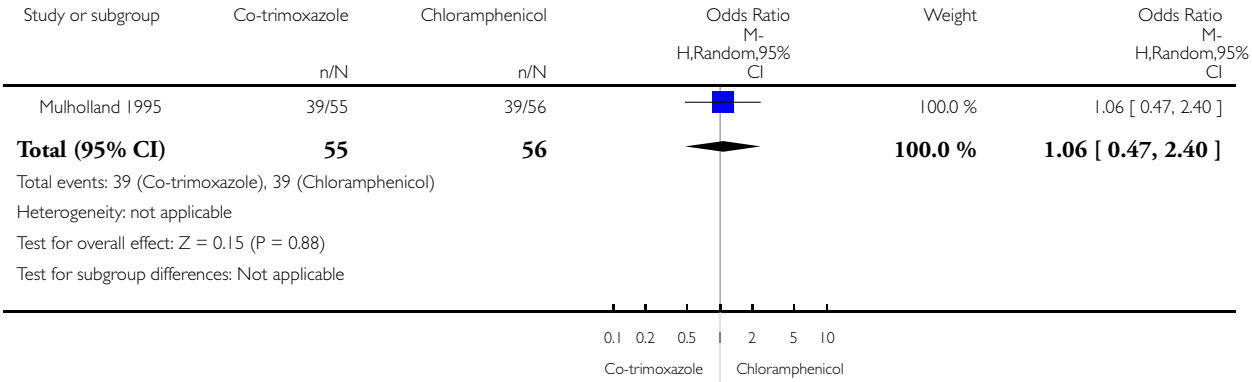


Analysis 24.5. Comparison 24 Co-trimoxazole versus chloramphenicol, Outcome 5 Cure rate.

Review: Antibiotics for community-acquired pneumonia in children

Comparison: 24 Co-trimoxazole versus chloramphenicol

Outcome: 5 Cure rate

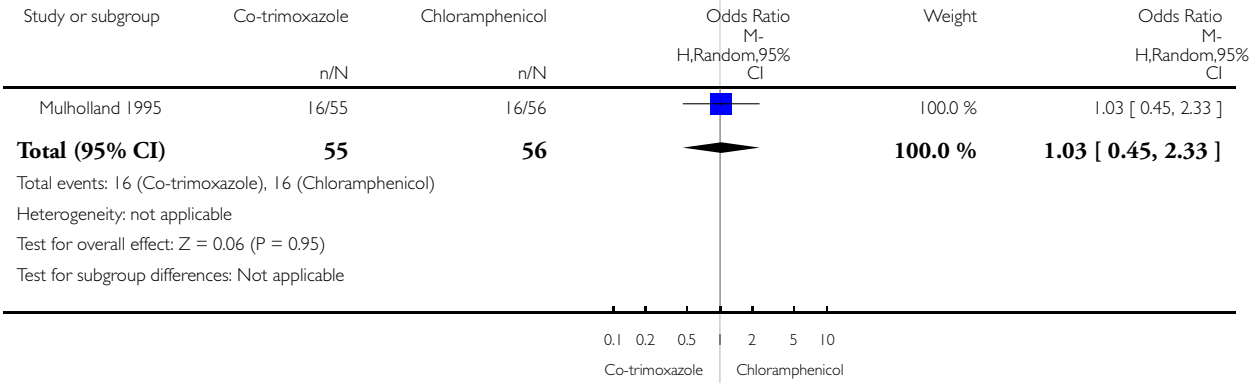


Analysis 24.6. Comparison 24 Co-trimoxazole versus chloramphenicol, Outcome 6 Failure rate.

Review: Antibiotics for community-acquired pneumonia in children

Comparison: 24 Co-trimoxazole versus chloramphenicol

Outcome: 6 Failure rate

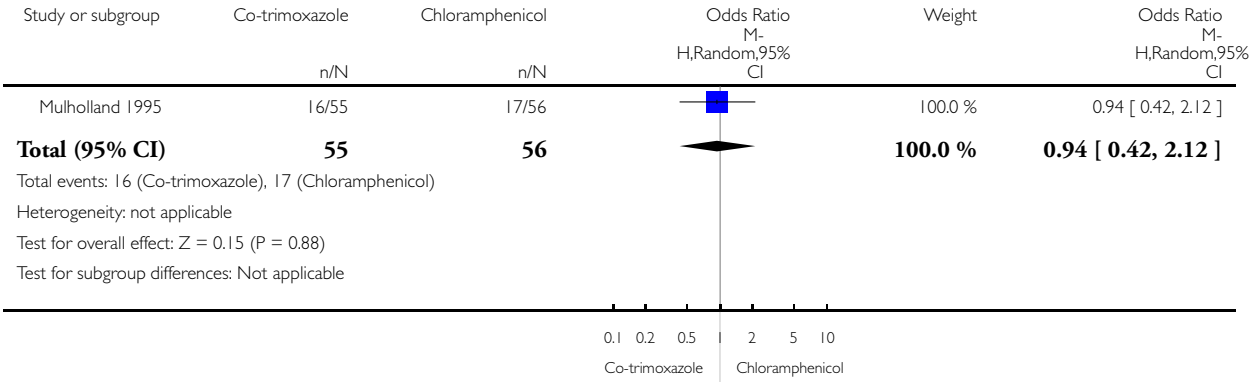


Analysis 24.7. Comparison 24 Co-trimoxazole versus chloramphenicol, Outcome 7 Excluded.

Review: Antibiotics for community-acquired pneumonia in children

Comparison: 24 Co-trimoxazole versus chloramphenicol

Outcome: 7 Excluded

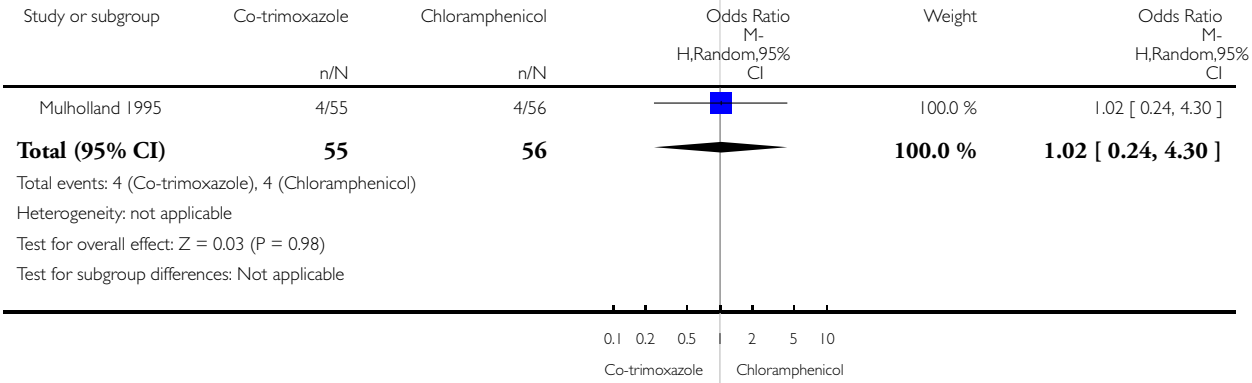


Analysis 24.8. Comparison 24 Co-trimoxazole versus chloramphenicol, Outcome 8 Relapse rate.

Review: Antibiotics for community-acquired pneumonia in children

Comparison: 24 Co-trimoxazole versus chloramphenicol

Outcome: 8 Relapse rate



Analysis 24.9. Comparison 24 Co-trimoxazole versus chloramphenicol, Outcome 9 Need for change in antibiotics.

Review: Antibiotics for community-acquired pneumonia in children

Comparison: 24 Co-trimoxazole versus chloramphenicol

Outcome: 9 Need for change in antibiotics

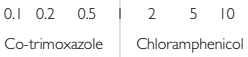
Study or subgroup	Co-trimoxazole n/N	Chloramphenicol n/N	Odds Ratio M-H,Random,95% CI	Weight	Odds Ratio M-H,Random,95% CI
Mulholland 1995	8/55	6/56		100.0 %	1.42 [0.46, 4.40]
Total (95% CI)	**55**	**56**		**100.0 %**	**1.42 [0.46, 4.40]**

Total events: 8 (Co-trimoxazole), 6 (Chloramphenicol)

Heterogeneity: not applicable

Test for overall effect: Z = 0.61 (P = 0.54)

Test for subgroup differences: Not applicable



Analysis 24.10. Comparison 24 Co-trimoxazole versus chloramphenicol, Outcome 10 Death rate.

Review: Antibiotics for community-acquired pneumonia in children

Comparison: 24 Co-trimoxazole versus chloramphenicol

Outcome: 10 Death rate

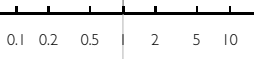
Study or subgroup	Co-trimoxazole n/N	Chloramphenicol n/N	Odds Ratio M-H,Random,95% CI	Weight	Odds Ratio M-H,Random,95% CI
Mulholland 1995	8/55	4/56		100.0 %	2.21 [0.63, 7.83]
Total (95% CI)	**55**	**56**		**100.0 %**	**2.21 [0.63, 7.83]**

Total events: 8 (Co-trimoxazole), 4 (Chloramphenicol)

Heterogeneity: not applicable

Test for overall effect: Z = 1.23 (P = 0.22)

Test for subgroup differences: Not applicable

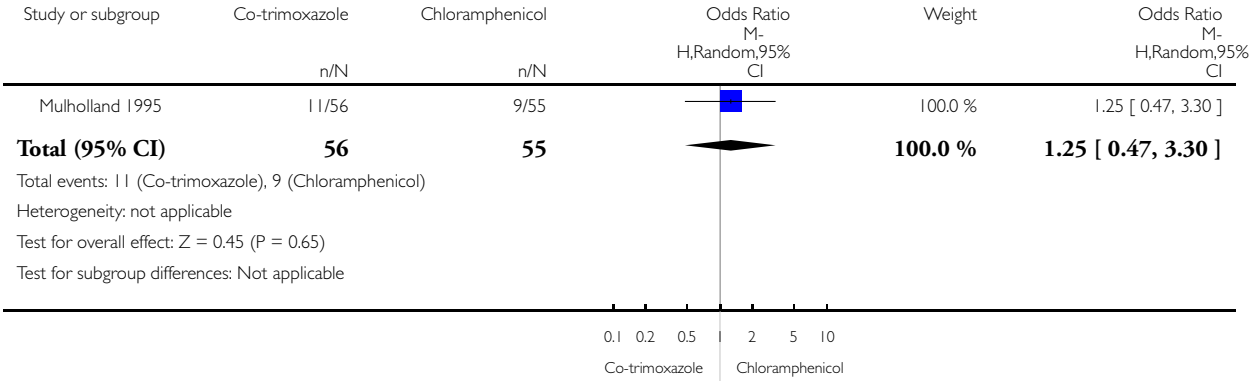


Analysis 24.11. Comparison 24 Co-trimoxazole versus chloramphenicol, Outcome 11 Organisms isolated on blood culture or lung puncture.

Review: Antibiotics for community-acquired pneumonia in children

Comparison: 24 Co-trimoxazole versus chloramphenicol

Outcome: 11 Organisms isolated on blood culture or lung puncture

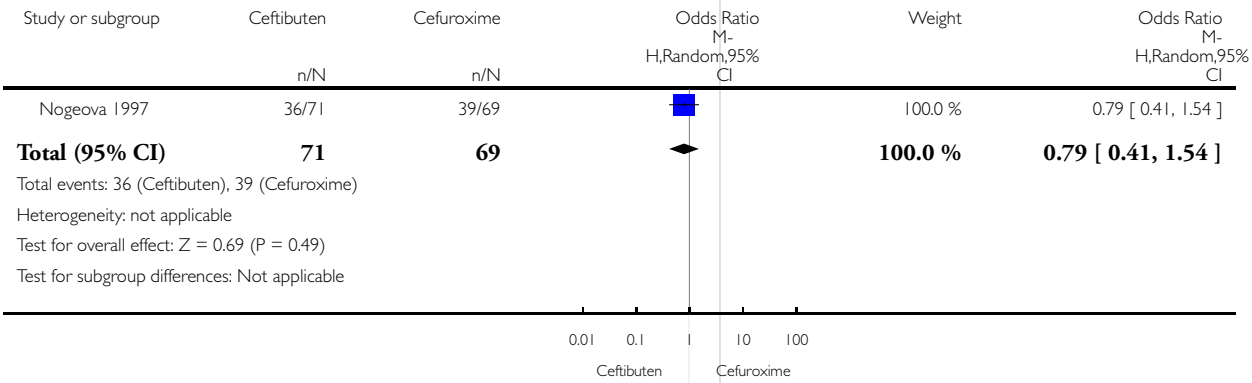


Analysis 25.1. Comparison 25 Ceftibuten versus cefuroxime, Outcome 1 Male sex.

Review: Antibiotics for community-acquired pneumonia in children

Comparison: 25 Ceftibuten versus cefuroxime

Outcome: 1 Male sex



Analysis 25.2. Comparison 25 Ceftibuten versus cefuroxime, Outcome 2 Positive for microbial agent.

Review: Antibiotics for community-acquired pneumonia in children

Comparison: 25 Ceftibuten versus cefuroxime

Outcome: 2 Positive for microbial agent

Study or subgroup	Ceftibuten n/N	Cefuroxime n/N	Odds Ratio M-H,Fixed,95% CI	Weight	Odds Ratio M-H,Fixed,95% CI
Nogeova 1997	53/71	30/69		100.0 %	3.83 [1.87, 7.83]
Total (95% CI)	**71**	**69**		**100.0 %**	**3.83 [1.87, 7.83]**

Total events: 53 (Ceftibuten), 30 (Cefuroxime)
Heterogeneity: not applicable
Test for overall effect: Z = 3.68 (P = 0.00024)
Test for subgroup differences: Not applicable

Analysis 25.3. Comparison 25 Ceftibuten versus cefuroxime, Outcome 3 Adverse reaction.

Review: Antibiotics for community-acquired pneumonia in children

Comparison: 25 Ceftibuten versus cefuroxime

Outcome: 3 Adverse reaction

Study or subgroup	Ceftibuten n/N	Cefuroxime n/N	Odds Ratio M-H,Fixed,95% CI	Weight	Odds Ratio M-H,Fixed,95% CI
Nogeova 1997	4/71	2/69		100.0 %	2.00 [0.35, 11.29]
Total (95% CI)	**71**	**69**		**100.0 %**	**2.00 [0.35, 11.29]**

Total events: 4 (Ceftibuten), 2 (Cefuroxime)
Heterogeneity: not applicable
Test for overall effect: Z = 0.78 (P = 0.43)
Test for subgroup differences: Not applicable

Analysis 25.4. Comparison 25 Ceftibuten versus cefuroxime, Outcome 4 Cure rate.

Review: Antibiotics for community-acquired pneumonia in children

Comparison: 25 Ceftibuten versus cefuroxime

Outcome: 4 Cure rate

Study or subgroup	Ceftibuten n/N	Cefuroxime n/N	Odds Ratio M-H,Fixed,95% CI	Weight	Odds Ratio M-H,Fixed,95% CI
Nogeova 1997	57/71	64/69		100.0 %	0.32 [0.11, 0.94]
Total (95% CI)	**71**	**69**		**100.0 %**	**0.32 [0.11, 0.94]**

Total events: 57 (Ceftibuten), 64 (Cefuroxime)
Heterogeneity: not applicable
Test for overall effect: Z = 2.08 (P = 0.038)
Test for subgroup differences: Not applicable

Analysis 25.5. Comparison 25 Ceftibuten versus cefuroxime, Outcome 5 Failure rate.

Review: Antibiotics for community-acquired pneumonia in children

Comparison: 25 Ceftibuten versus cefuroxime

Outcome: 5 Failure rate

Study or subgroup	Ceftibuten n/N	Cefuroxime n/N	Odds Ratio M-H,Fixed,95% CI	Weight	Odds Ratio M-H,Fixed,95% CI
Nogeova 1997	12/71	2/69		100.0 %	6.81 [1.46, 31.70]
Total (95% CI)	**71**	**69**		**100.0 %**	**6.81 [1.46, 31.70]**

Total events: 12 (Ceftibuten), 2 (Cefuroxime)
Heterogeneity: not applicable
Test for overall effect: Z = 2.45 (P = 0.014)
Test for subgroup differences: Not applicable

Analysis 26.1. Comparison 26 Oxacillin ceftriaxone versus co-amoxyclavulanic acid, Outcome 1 Median age (months) with IQR.

Median age (months) with IQR

Study	**Amoxicillin clavulanic acid group**	**Oxacillin+ ceftriaxone group**
Ribeiro 2011	11.5 (3 to 60)	10.5 (2 to 60)

Analysis 26.2. Comparison 26 Oxacillin ceftriaxone versus co-amoxyclavulanic acid, Outcome 2 Male sex.

Review: Antibiotics for community-acquired pneumonia in children

Comparison: 26 Oxacillin ceftriaxone versus co-amoxyclavulanic acid

Outcome: 2 Male sex

Study or subgroup	Co-amoxtclavulanic acid n/N	Oxacillin ceftrioxone n/N	Odds Ratio M-H,Random,95% CI	Weight	Odds Ratio M-H,Random,95% CI
Ribeiro 2011	29/56	29/48		100.0 %	0.70 [0.32, 1.54]
Total (95% CI)	**56**	**48**		**100.0 %**	**0.70 [0.32, 1.54]**

Total events: 29 (Co-amoxtclavulanic acid), 29 (Oxacillin ceftrioxone)

Heterogeneity: not applicable

Test for overall effect: Z = 0.88 (P = 0.38)

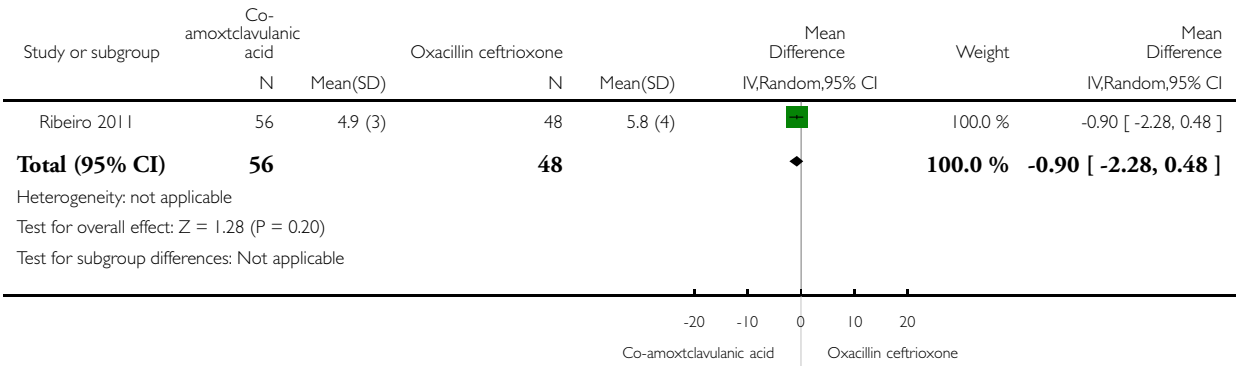
Test for subgroup differences: Not applicable

Analysis 26.3. Comparison 26 Oxacillin ceftriaxone versus co-amoxyclavulanic acid, Outcome 3 Mean number of days before admission.

Review: Antibiotics for community-acquired pneumonia in children

Comparison: 26 Oxacillin ceftriaxone versus co-amoxyclavulanic acid

Outcome: 3 Mean number of days before admission

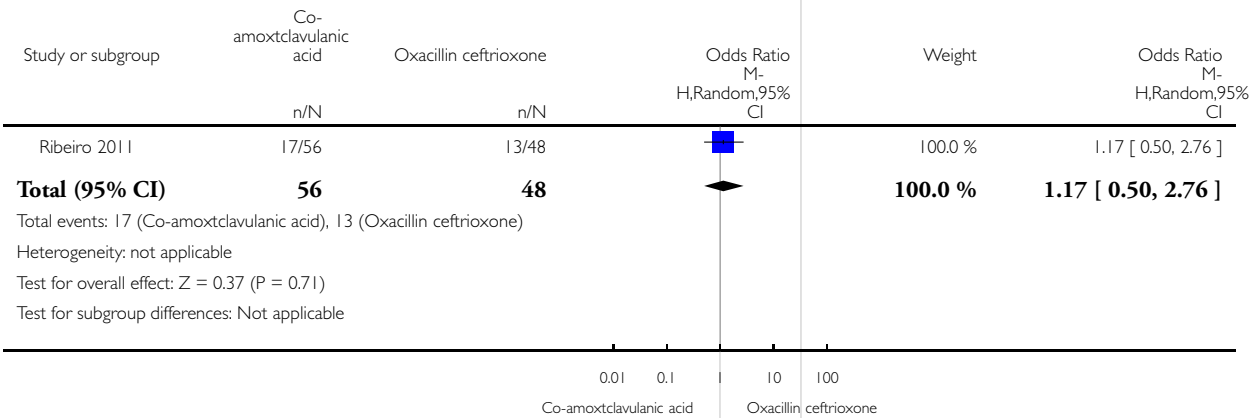


Analysis 26.4. Comparison 26 Oxacillin ceftriaxone versus co-amoxyclavulanic acid, Outcome 4 Received antibiotics before enrolment.

Review: Antibiotics for community-acquired pneumonia in children

Comparison: 26 Oxacillin ceftriaxone versus co-amoxyclavulanic acid

Outcome: 4 Received antibiotics before enrolment



Analysis 26.5. Comparison 26 Oxacillin ceftriaxone versus co-amoxyclavulanic acid, Outcome 5 Failure rates.

Review: Antibiotics for community-acquired pneumonia in children

Comparison: 26 Oxacillin ceftriaxone versus co-amoxyclavulanic acid

Outcome: 5 Failure rates

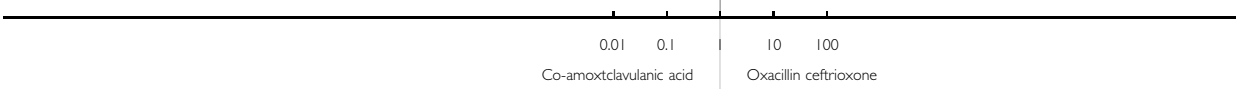
Study or subgroup	Co-amoxtclavulanic acid n/N	Oxacillin ceftrioxone n/N	Odds Ratio M-H,Random,95% CI	Weight	Odds Ratio M-H,Random,95% CI
Ribeiro 2011	8/56	7/48		100.0 %	0.98 [0.33, 2.92]
Total (95% CI)	**56**	**48**		**100.0 %**	**0.98 [0.33, 2.92]**

Total events: 8 (Co-amoxtclavulanic acid), 7 (Oxacillin ceftrioxone)

Heterogeneity: not applicable

Test for overall effect: Z = 0.04 (P = 0.97)

Test for subgroup differences: Not applicable



Analysis 26.6. Comparison 26 Oxacillin ceftriaxone versus co-amoxyclavulanic acid, Outcome 6 Mean time for improvement in tachypnoea.

Review: Antibiotics for community-acquired pneumonia in children

Comparison: 26 Oxacillin ceftriaxone versus co-amoxyclavulanic acid

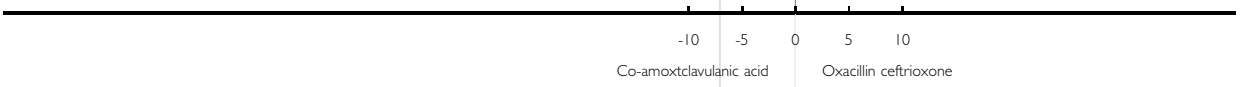
Outcome: 6 Mean time for improvement in tachypnoea

Study or subgroup	Co-amoxtclavulanic acid N	Mean(SD)	Oxacillin ceftrioxone N	Mean(SD)	Mean Difference IV,Random,95% CI	Weight	Mean Difference IV,Random,95% CI
Ribeiro 2011	56	4.8 (2.2)	48	5.8 (2.4)		100.0 %	-1.00 [-1.89, -0.11]
Total (95% CI)	**56**		**48**			**100.0 %**	**-1.00 [-1.89, -0.11]**

Heterogeneity: not applicable

Test for overall effect: Z = 2.20 (P = 0.028)

Test for subgroup differences: Not applicable



Analysis 26.7. Comparison 26 Oxacillin ceftriaxone versus co-amoxyclavulanic acid, Outcome 7 Mean length of stay.

Review: Antibiotics for community-acquired pneumonia in children

Comparison: 26 Oxacillin ceftriaxone versus co-amoxyclavulanic acid

Outcome: 7 Mean length of stay

Study or subgroup	Co-amoxtclavulanic acid N	Mean(SD)	Oxacillin ceftrioxone N	Mean(SD)	Mean Difference IV,Random,95% CI	Weight	Mean Difference IV,Random,95% CI
Ribeiro 2011	56	11 (6.2)	48	14.4 (4.5)		100.0 %	-3.40 [-5.46, -1.34]
Total (95% CI)	**56**		**48**			**100.0 %**	**-3.40 [-5.46, -1.34]**

Heterogeneity: not applicable

Test for overall effect: Z = 3.23 (P = 0.0012)

Test for subgroup differences: Not applicable

Analysis 27.1. Comparison 27 Oral versus parenteral antibiotics for treatment of severe pneumonia, Outcome 1 Male sex.

Review: Antibiotics for community-acquired pneumonia in children

Comparison: 27 Oral versus parenteral antibiotics for treatment of severe pneumonia

Outcome: 1 Male sex

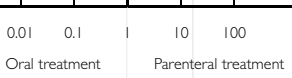
Study or subgroup	Oral treatment n/N	Parenteral treatment n/N	Odds Ratio M-H,Random,95% CI	Weight	Odds Ratio M-H,Random,95% CI
Addo-Yobo 2004	537/857	520/845		40.4 %	1.05 [0.86, 1.28]
Atkinson 2007	53/100	55/103		5.1 %	0.98 [0.57, 1.71]
Campbell 1988	41/66	38/68		3.3 %	1.29 [0.65, 2.58]
Hazir 2008	630/1025	602/1012		49.1 %	1.09 [0.91, 1.30]
Sidal 1994	27/46	27/42		2.1 %	0.79 [0.33, 1.87]
Total (95% CI)	**2094**	**2070**		**100.0 %**	**1.06 [0.94, 1.21]**

Total events: 1288 (Oral treatment), 1242 (Parenteral treatment)

Heterogeneity: $Tau^2 = 0.0$; $Chi^2 = 0.92$, df = 4 (P = 0.92); $I^2 = 0.0\%$

Test for overall effect: Z = 0.98 (P = 0.32)

Test for subgroup differences: Not applicable



Analysis 27.2. Comparison 27 Oral versus parenteral antibiotics for treatment of severe pneumonia, Outcome 2 Age below 12 months.

Review: Antibiotics for community-acquired pneumonia in children

Comparison: 27 Oral versus parenteral antibiotics for treatment of severe pneumonia

Outcome: 2 Age below 12 months

Study or subgroup	Oral treatment n/N	Parenteral treatment n/N	Odds Ratio M-H,Random,95% CI	Weight	Odds Ratio M-H,Random,95% CI
Addo-Yobo 2004	532/857	513/845		38.6 %	1.06 [0.87, 1.29]
Campbell 1988	20/66	13/68		11.8 %	1.84 [0.83, 4.10]
Hazir 2008	653/1025	658/1012		39.4 %	0.94 [0.79, 1.13]
Sidal 1994	16/46	27/42		10.3 %	0.30 [0.12, 0.71]
Total (95% CI)	**1994**	**1967**		**100.0 %**	**0.95 [0.69, 1.30]**

Total events: 1221 (Oral treatment), 1211 (Parenteral treatment)

Heterogeneity: $Tau^2 = 0.06$; $Chi^2 = 10.31$, df = 3 (P = 0.02); $I^2 = 71\%$

Test for overall effect: Z = 0.33 (P = 0.74)

Test for subgroup differences: Not applicable

Analysis 27.3. Comparison 27 Oral versus parenteral antibiotics for treatment of severe pneumonia, Outcome 3 Received antibiotics in the past week.

Review: Antibiotics for community-acquired pneumonia in children

Comparison: 27 Oral versus parenteral antibiotics for treatment of severe pneumonia

Outcome: 3 Received antibiotics in the past week

Study or subgroup	Oral treatment n/N	Parenteral treatment n/N	Odds Ratio M-H,Random,95% CI	Weight	Odds Ratio M-H,Random,95% CI
Addo-Yobo 2004	75/857	82/845		36.4 %	0.89 [0.64, 1.24]
Atkinson 2007	18/100	14/103		11.6 %	1.40 [0.65, 2.98]
Hazir 2008	267/1025	216/1012		52.0 %	1.30 [1.06, 1.59]
Total (95% CI)	**1982**	**1960**		**100.0 %**	**1.14 [0.86, 1.52]**

Total events: 360 (Oral treatment), 312 (Parenteral treatment)

Heterogeneity: $Tau^2 = 0.03$; $Chi^2 = 3.79$, df = 2 (P = 0.15); $I^2 = 47\%$

Test for overall effect: Z = 0.92 (P = 0.36)

Test for subgroup differences: Not applicable

Analysis 27.4. Comparison 27 Oral versus parenteral antibiotics for treatment of severe pneumonia, Outcome 4 Children with wheezing.

Review: Antibiotics for community-acquired pneumonia in children

Comparison: 27 Oral versus parenteral antibiotics for treatment of severe pneumonia

Outcome: 4 Children with wheezing

Study or subgroup	Oral treatment n/N	Parenteral treatment n/N	Odds Ratio M-H,Random,95% CI	Weight	Odds Ratio M-H,Random,95% CI
Addo-Yobo 2004	72/857	52/845		43.8 %	1.40 [0.97, 2.03]
Hazir 2008	767/1025	778/1012		56.2 %	0.89 [0.73, 1.10]
Total (95% CI)	**1882**	**1857**		**100.0 %**	**1.09 [0.70, 1.68]**

Total events: 839 (Oral treatment), 830 (Parenteral treatment)

Heterogeneity: $Tau^2 = 0.08$; $Chi^2 = 4.32$, df = 1 (P = 0.04); $I^2 = 77\%$

Test for overall effect: Z = 0.38 (P = 0.71)

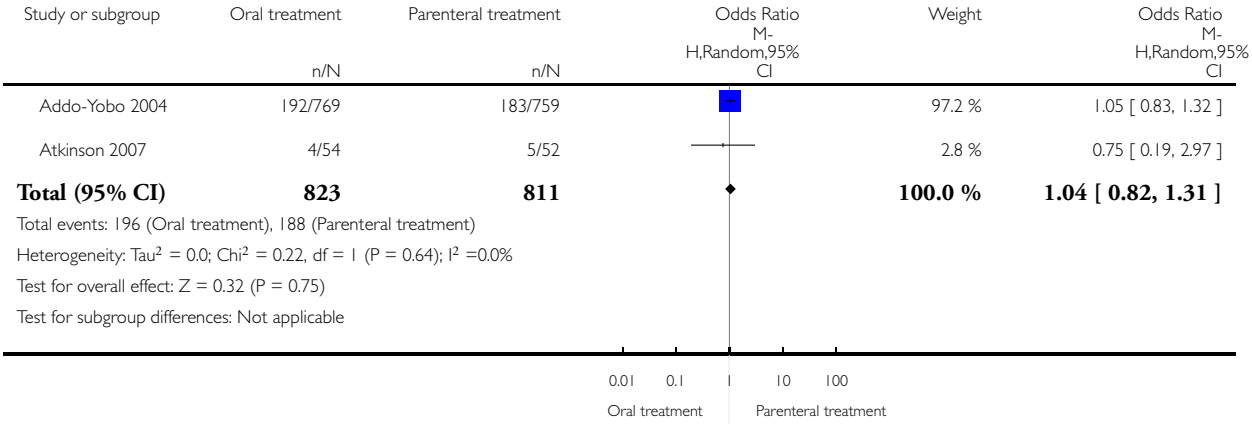
Test for subgroup differences: Not applicable

Analysis 27.5. Comparison 27 Oral versus parenteral antibiotics for treatment of severe pneumonia, Outcome 5 RSV positivity.

Review: Antibiotics for community-acquired pneumonia in children

Comparison: 27 Oral versus parenteral antibiotics for treatment of severe pneumonia

Outcome: 5 RSV positivity



Analysis 27.6. Comparison 27 Oral versus parenteral antibiotics for treatment of severe pneumonia, Outcome 6 Failure rates on day 3.

Review: Antibiotics for community-acquired pneumonia in children

Comparison: 27 Oral versus parenteral antibiotics for treatment of severe pneumonia

Outcome: 6 Failure rates on day 3

Study or subgroup	Oral treatment n/N	Parenteral treatment n/N	Odds Ratio M-H,Random,95% CI	Weight	Odds Ratio M-H,Random,95% CI
Addo-Yobo 2004	167/857	161/845		61.7 %	1.03 [0.81, 1.31]
Atkinson 2007	3/100	7/103		2.0 %	0.42 [0.11, 1.69]
Hazir 2008	77/1025	87/1012		36.3 %	0.86 [0.63, 1.19]
Total (95% CI)	**1982**	**1960**		**100.0 %**	**0.95 [0.78, 1.15]**

Total events: 247 (Oral treatment), 255 (Parenteral treatment)

Heterogeneity: $Tau^2 = 0.00$; $Chi^2 = 2.07$, df = 2 (P = 0.36); $I^2 = 3\%$

Test for overall effect: Z = 0.53 (P = 0.60)

Test for subgroup differences: Not applicable

Analysis 27.7. Comparison 27 Oral versus parenteral antibiotics for treatment of severe pneumonia, Outcome 7 Failure rates on day 6.

Review: Antibiotics for community-acquired pneumonia in children

Comparison: 27 Oral versus parenteral antibiotics for treatment of severe pneumonia

Outcome: 7 Failure rates on day 6

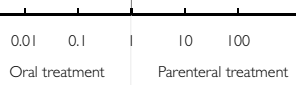
Study or subgroup	Oral treatment n/N	Parenteral treatment n/N	Odds Ratio M-H,Random,95% CI	Weight	Odds Ratio M-H,Random,95% CI
Addo-Yobo 2004	185/857	187/845		38.2 %	0.97 [0.77, 1.22]
Atkinson 2007	7/103	3/100		6.9 %	2.36 [0.59, 9.39]
Campbell 1988	5/66	5/65		7.7 %	0.98 [0.27, 3.57]
Hazir 2008	89/1025	105/1012		35.2 %	0.82 [0.61, 1.11]
Sidal 1994	2/46	14/42		5.6 %	0.09 [0.02, 0.43]
Tsarouhas 1998	3/77	5/93		6.3 %	0.71 [0.16, 3.09]
Total (95% CI)	**2174**	**2157**		**100.0 %**	**0.84 [0.56, 1.24]**

Total events: 291 (Oral treatment), 319 (Parenteral treatment)

Heterogeneity: $Tau^2 = 0.09$; $Chi^2 = 11.11$, df = 5 (P = 0.05); $I^2 = 55\%$

Test for overall effect: Z = 0.89 (P = 0.37)

Test for subgroup differences: Not applicable



Analysis 27.8. Comparison 27 Oral versus parenteral antibiotics for treatment of severe pneumonia, Outcome 8 Failure rate in children below 5 years of age.

Review: Antibiotics for community-acquired pneumonia in children

Comparison: 27 Oral versus parenteral antibiotics for treatment of severe pneumonia

Outcome: 8 Failure rate in children below 5 years of age

Study or subgroup	Oral treatment n/N	Parenteral treatment n/N	Odds Ratio M-H,Random,95% CI	Weight	Odds Ratio M-H,Random,95% CI
Addo-Yobo 2004	185/857	187/845		61.3 %	0.97 [0.77, 1.22]
Campbell 1988	5/66	5/65		1.9 %	0.98 [0.27, 3.57]
Hazir 2008	89/1025	105/1012		36.8 %	0.82 [0.61, 1.11]
Total (95% CI)	**1948**	**1922**		**100.0 %**	**0.91 [0.76, 1.09]**

Total events: 279 (Oral treatment), 297 (Parenteral treatment)

Heterogeneity: $Tau^2 = 0.0$; $Chi^2 = 0.76$, df = 2 (P = 0.69); $I^2 = 0.0\%$

Test for overall effect: Z = 1.00 (P = 0.32)

Test for subgroup differences: Not applicable

Analysis 27.9. Comparison 27 Oral versus parenteral antibiotics for treatment of severe pneumonia, Outcome 9 Failure rates in children receiving oral amoxicillin or injectable antibiotics.

Review: Antibiotics for community-acquired pneumonia in children

Comparison: 27 Oral versus parenteral antibiotics for treatment of severe pneumonia

Outcome: 9 Failure rates in children receiving oral amoxicillin or injectable antibiotics

Study or subgroup	Oral treatment n/N	Parenteral treatment n/N	Odds Ratio M-H,Random,95% CI	Weight	Odds Ratio M-H,Random,95% CI
Addo-Yobo 2004	185/857	187/845		60.5 %	0.97 [0.77, 1.22]
Atkinson 2007	7/103	3/100		1.7 %	2.36 [0.59, 9.39]
Hazir 2008	89/1025	105/1012		36.3 %	0.82 [0.61, 1.11]
Tsarouhas 1998	3/77	5/93		1.5 %	0.71 [0.16, 3.09]
Total (95% CI)	**2062**	**2050**		**100.0 %**	**0.92 [0.77, 1.10]**

Total events: 284 (Oral treatment), 300 (Parenteral treatment)

Heterogeneity: $Tau^2 = 0.0$; $Chi^2 = 2.65$, df = 3 (P = 0.45); $I^2 = 0.0\%$

Test for overall effect: Z = 0.89 (P = 0.37)

Test for subgroup differences: Not applicable

Analysis 27.10. Comparison 27 Oral versus parenteral antibiotics for treatment of severe pneumonia, Outcome 10 Failure rate in children receiving cotrimoxazole or injectable penicillin.

Review: Antibiotics for community-acquired pneumonia in children

Comparison: 27 Oral versus parenteral antibiotics for treatment of severe pneumonia

Outcome: 10 Failure rate in children receiving cotrimoxazole or injectable penicillin

Study or subgroup	Oral treatment n/N	Parenteral treatment n/N	Odds Ratio M-H,Random,95% CI	Weight	Odds Ratio M-H,Random,95% CI
Campbell 1988	5/66	5/65		51.7 %	0.98 [0.27, 3.57]
Sidal 1994	2/46	14/42		48.3 %	0.09 [0.02, 0.43]
Total (95% CI)	**112**	**107**		**100.0 %**	**0.31 [0.03, 3.29]**

Total events: 7 (Oral treatment), 19 (Parenteral treatment)

Heterogeneity: $Tau^2 = 2.37$; $Chi^2 = 5.45$, df = 1 (P = 0.02); $I^2 = 82\%$

Test for overall effect: Z = 0.97 (P = 0.33)

Test for subgroup differences: Not applicable

Analysis 27.11. Comparison 27 Oral versus parenteral antibiotics for treatment of severe pneumonia, Outcome 11 Failure rate in children treated with oral or parenteral antibiotics on ambulatory basis.

Review: Antibiotics for community-acquired pneumonia in children

Comparison: 27 Oral versus parenteral antibiotics for treatment of severe pneumonia

Outcome: 11 Failure rate in children treated with oral or parenteral antibiotics on ambulatory basis

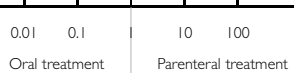
Study or subgroup	Oral treatment n/N	Parenteral treatment n/N	Odds Ratio M-H,Random,95% CI	Weight	Odds Ratio M-H,Random,95% CI
Campbell 1988	5/66	5/65		21.9 %	0.98 [0.27, 3.57]
Hazir 2008	89/1025	105/1012		41.1 %	0.82 [0.61, 1.11]
Sidal 1994	2/46	14/42		17.9 %	0.09 [0.02, 0.43]
Tsarouhas 1998	3/77	5/93		19.1 %	0.71 [0.16, 3.09]
Total (95% CI)	**1214**	**1212**		**100.0 %**	**0.56 [0.24, 1.32]**

Total events: 99 (Oral treatment), 129 (Parenteral treatment)

Heterogeneity: $Tau^2 = 0.44$; $Chi^2 = 7.65$, df = 3 (P = 0.05); $I^2 = 61\%$

Test for overall effect: Z = 1.32 (P = 0.19)

Test for subgroup differences: Not applicable

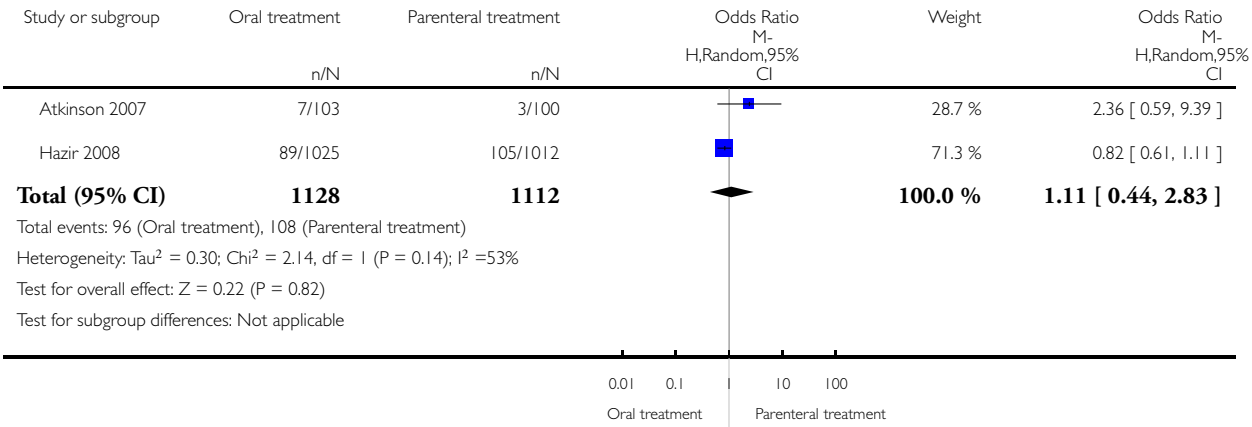


Analysis 27.12. Comparison 27 Oral versus parenteral antibiotics for treatment of severe pneumonia, Outcome 12 Failure rate after removing one study.

Review: Antibiotics for community-acquired pneumonia in children

Comparison: 27 Oral versus parenteral antibiotics for treatment of severe pneumonia

Outcome: 12 Failure rate after removing one study

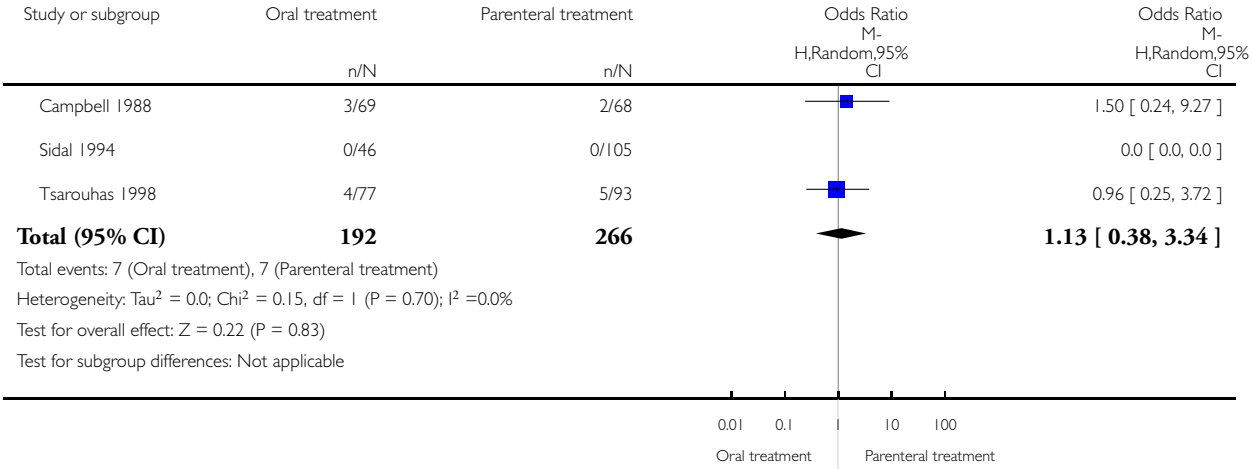


Analysis 27.13. Comparison 27 Oral versus parenteral antibiotics for treatment of severe pneumonia, Outcome 13 Hospitalisation.

Review: Antibiotics for community-acquired pneumonia in children

Comparison: 27 Oral versus parenteral antibiotics for treatment of severe pneumonia

Outcome: 13 Hospitalisation

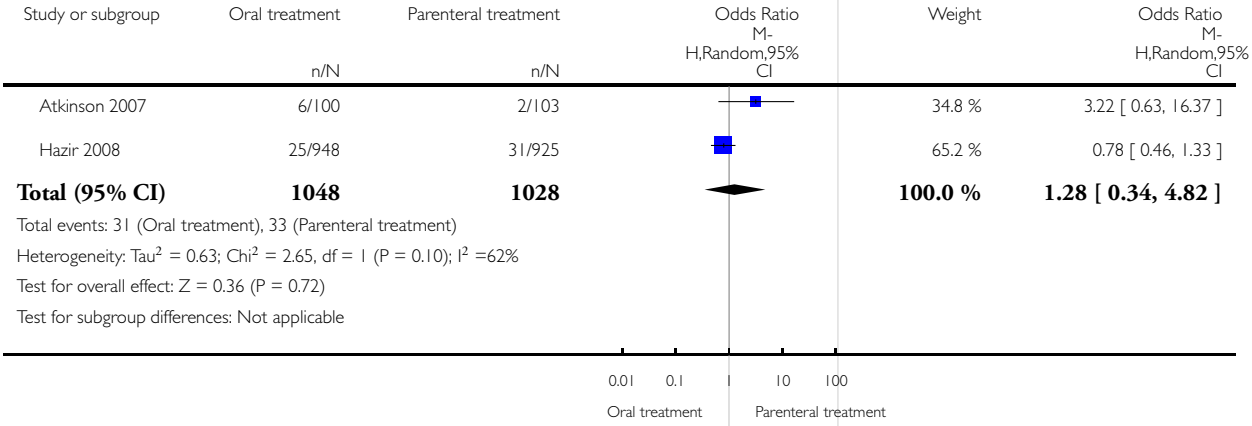


Analysis 27.14. Comparison 27 Oral versus parenteral antibiotics for treatment of severe pneumonia, Outcome 14 Relapse rates.

Review: Antibiotics for community-acquired pneumonia in children

Comparison: 27 Oral versus parenteral antibiotics for treatment of severe pneumonia

Outcome: 14 Relapse rates



Analysis 27.15. Comparison 27 Oral versus parenteral antibiotics for treatment of severe pneumonia, Outcome 15 Death rates.

Review: Antibiotics for community-acquired pneumonia in children

Comparison: 27 Oral versus parenteral antibiotics for treatment of severe pneumonia

Outcome: 15 Death rates

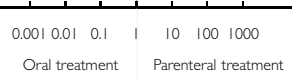
Study or subgroup	Oral treatment n/N	Parenteral treatment n/N	Odds Ratio M-H,Random,95% CI	Odds Ratio M-H,Random,95% CI
Addo-Yobo 2004	0/845	7/857		0.07 [0.00, 1.18]
Atkinson 2007	0/100	0/103		0.0 [0.0, 0.0]
Hazir 2008	1/1025	4/1012		0.25 [0.03, 2.21]
Total (95% CI)	**1970**	**1972**		**0.15 [0.03, 0.87]**

Total events: 1 (Oral treatment), 11 (Parenteral treatment)

Heterogeneity: $Tau^2 = 0.0$; $Chi^2 = 0.53$, df = 1 (P = 0.47); $I^2 = 0.0\%$

Test for overall effect: Z = 2.12 (P = 0.034)

Test for subgroup differences: Not applicable



Analysis 27.16. Comparison 27 Oral versus parenteral antibiotics for treatment of severe pneumonia, Outcome 16 Lost to follow-up.

Review: Antibiotics for community-acquired pneumonia in children

Comparison: 27 Oral versus parenteral antibiotics for treatment of severe pneumonia

Outcome: 16 Lost to follow-up

Study or subgroup	Oral treatment n/N	Parenteral treatment n/N	Odds Ratio M-H,Random,95% CI	Weight	Odds Ratio M-H,Random,95% CI
Hazir 2008	6/1025	13/1012		100.0 %	0.45 [0.17, 1.20]
Total (95% CI)	**1025**	**1012**		**100.0 %**	**0.45 [0.17, 1.20]**

Total events: 6 (Oral treatment), 13 (Parenteral treatment)

Heterogeneity: not applicable

Test for overall effect: Z = 1.60 (P = 0.11)

Test for subgroup differences: Not applicable

Analysis 27.17. Comparison 27 Oral versus parenteral antibiotics for treatment of severe pneumonia, Outcome 17 Cure rate.

Review: Antibiotics for community-acquired pneumonia in children

Comparison: 27 Oral versus parenteral antibiotics for treatment of severe pneumonia

Outcome: 17 Cure rate

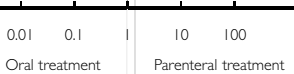
Study or subgroup	Oral treatment n/N	Parenteral treatment n/N	Odds Ratio M-H,Random,95% CI	Weight	Odds Ratio M-H,Random,95% CI
Atkinson 2007	123/126	113/120		53.1 %	2.54 [0.64, 10.06]
Sidal 1994	44/46	28/42		46.9 %	11.00 [2.32, 52.11]
Total (95% CI)	**172**	**162**		**100.0 %**	**5.05 [1.19, 21.33]**

Total events: 167 (Oral treatment), 141 (Parenteral treatment)

Heterogeneity: $Tau^2 = 0.52$; $Chi^2 = 1.93$, df = 1 (P = 0.16); $I^2 = 48\%$

Test for overall effect: Z = 2.20 (P = 0.028)

Test for subgroup differences: Not applicable



Analysis 27.18. Comparison 27 Oral versus parenteral antibiotics for treatment of severe pneumonia, Outcome 18 Failure rates in radiographically confirmed-pneumonia.

Review: Antibiotics for community-acquired pneumonia in children

Comparison: 27 Oral versus parenteral antibiotics for treatment of severe pneumonia

Outcome: 18 Failure rates in radiographically confirmed-pneumonia

Study or subgroup	Oral treatment n/N	Parenteral treatment n/N	Odds Ratio M-H,Random,95% CI	Weight	Odds Ratio M-H,Random,95% CI
Atkinson 2007	7/103	3/100		52.1 %	2.36 [0.59, 9.39]
Tsarouhas 1998	3/77	5/93		47.9 %	0.71 [0.16, 3.09]
Total (95% CI)	**180**	**193**		**100.0 %**	**1.33 [0.41, 4.29]**

Total events: 10 (Oral treatment), 8 (Parenteral treatment)

Heterogeneity: $Tau^2 = 0.19$; $Chi^2 = 1.35$, df = 1 (P = 0.24); $I^2 = 26\%$

Test for overall effect: Z = 0.48 (P = 0.63)

Test for subgroup differences: Not applicable

Analysis 27.19. Comparison 27 Oral versus parenteral antibiotics for treatment of severe pneumonia, Outcome 19 Death rates after removing one study.

Review: Antibiotics for community-acquired pneumonia in children

Comparison: 27 Oral versus parenteral antibiotics for treatment of severe pneumonia

Outcome: 19 Death rates after removing one study

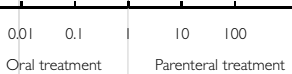
Study or subgroup	Oral treatment n/N	Parenteral treatment n/N	Odds Ratio M-H,Fixed,95% CI	Odds Ratio M-H,Fixed,95% CI
Atkinson 2007	0/100	0/103		0.0 [0.0, 0.0]
Hazir 2008	1/1025	4/1012		0.25 [0.03, 2.21]
Total (95% CI)	**1125**	**1115**		**0.25 [0.03, 2.21]**

Total events: 1 (Oral treatment), 4 (Parenteral treatment)

Heterogeneity: $Chi^2 = 0.0$, df = 0 (P = 1.00); $I^2 = 0.0\%$

Test for overall effect: Z = 1.25 (P = 0.21)

Test for subgroup differences: Not applicable



Analysis 28.1. Comparison 28 Co-trimoxazole versus co-amoxyclavulanic acid, Outcome 1 Children below 1 year of age.

Review: Antibiotics for community-acquired pneumonia in children

Comparison: 28 Co-trimoxazole versus co-amoxyclavulanic acid

Outcome: 1 Children below 1 year of age

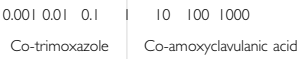
Study or subgroup	Co-trimoxazole n/N	Co-amoxyclavulanic acid n/N	Odds Ratio M-H,Random,95% CI	Weight	Odds Ratio M-H,Random,95% CI
CATCHUP 2002	372/734	0/50		50.1 %	103.79 [6.38, 1688.47]
Straus 1998	227/398	0/50		49.9 %	133.98 [8.21, 2186.87]
Total (95% CI)	**1132**	**100**		**100.0 %**	**117.90 [16.39, 848.37]**

Total events: 599 (Co-trimoxazole), 0 (Co-amoxyclavulanic acid)

Heterogeneity: $Tau^2 = 0.0$; $Chi^2 = 0.02$, df = 1 (P = 0.90); $I^2 = 0.0\%$

Test for overall effect: Z = 4.74 (P < 0.00001)

Test for subgroup differences: Not applicable



Analysis 28.2. Comparison 28 Co-trimoxazole versus co-amoxyclavulanic acid, Outcome 2 Male sex.

Review: Antibiotics for community-acquired pneumonia in children

Comparison: 28 Co-trimoxazole versus co-amoxyclavulanic acid

Outcome: 2 Male sex

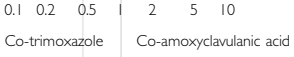
Study or subgroup	Co-trimoxazole n/N	Co-amoxyclavulanic acid n/N	Odds Ratio M-H,Random,95% CI	Weight	Odds Ratio M-H,Random,95% CI
CATCHUP 2002	362/734	35/50		51.0 %	0.42 [0.22, 0.78]
Straus 1998	246/398	35/50		49.0 %	0.69 [0.37, 1.31]
Total (95% CI)	**1132**	**100**		**100.0 %**	**0.54 [0.33, 0.88]**

Total events: 608 (Co-trimoxazole), 70 (Co-amoxyclavulanic acid)

Heterogeneity: $Tau^2 = 0.03$; $Chi^2 = 1.25$, df = 1 (P = 0.26); $I^2 = 20\%$

Test for overall effect: Z = 2.46 (P = 0.014)

Test for subgroup differences: Not applicable



Analysis 28.3. Comparison 28 Co-trimoxazole versus co-amoxyclavulanic acid, Outcome 3 Failure rate.

Review: Antibiotics for community-acquired pneumonia in children

Comparison: 28 Co-trimoxazole versus co-amoxyclavulanic acid

Outcome: 3 Failure rate

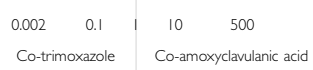
Study or subgroup	Co-trimoxazole n/N	Co-amoxyclavulanic acid n/N	Odds Ratio M-H,Random,95% CI	Weight	Odds Ratio M-H,Random,95% CI
CATCHUP 2002	139/734	1/50		50.1 %	11.45 [1.57, 83.61]
Straus 1998	92/398	1/50		49.9 %	14.73 [2.01, 108.15]
Total (95% CI)	**1132**	**100**		**100.0 %**	**12.98 [3.18, 53.06]**

Total events: 231 (Co-trimoxazole), 2 (Co-amoxyclavulanic acid)

Heterogeneity: $Tau^2 = 0.0$; $Chi^2 = 0.03$, df = 1 (P = 0.86); $I^2 = 0.0\%$

Test for overall effect: Z = 3.57 (P = 0.00036)

Test for subgroup differences: Not applicable



Analysis 29.1. Comparison 29 Amoxycillin versus cefpodoxime, Outcome 1 Age in months.

Review: Antibiotics for community-acquired pneumonia in children

Comparison: 29 Amoxycillin versus cefpodoxime

Outcome: 1 Age in months

Study or subgroup	Amoxycillin N	Mean(SD)	Cefpodoxime N	Mean(SD)	Mean Difference IV,Random,95% CI	Mean Difference IV,Random,95% CI
Jibril 1989	50	58.8 (0)	234	21.6 (0)		0.0 [0.0, 0.0]
Total (95% CI)	**50**		**234**			**0.0 [0.0, 0.0]**

Heterogeneity: not applicable

Test for overall effect: Z = 0.0 (P < 0.00001)

Test for subgroup differences: Not applicable

Analysis 29.2. Comparison 29 Amoxycillin versus cefpodoxime, Outcome 2 Male sex.

Review: Antibiotics for community-acquired pneumonia in children

Comparison: 29 Amoxycillin versus cefpodoxime

Outcome: 2 Male sex

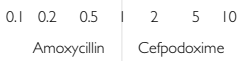
Study or subgroup	Amoxycillin n/N	Cefpodoxime n/N	Odds Ratio M-H,Random,95% CI	Weight	Odds Ratio M-H,Random,95% CI
Jibril 1989	18/50	0/1		100.0 %	1.71 [0.07, 44.09]
Total (95% CI)	**50**	**1**		**100.0 %**	**1.71 [0.07, 44.09]**

Total events: 18 (Amoxycillin), 0 (Cefpodoxime)

Heterogeneity: not applicable

Test for overall effect: Z = 0.32 (P = 0.75)

Test for subgroup differences: Not applicable

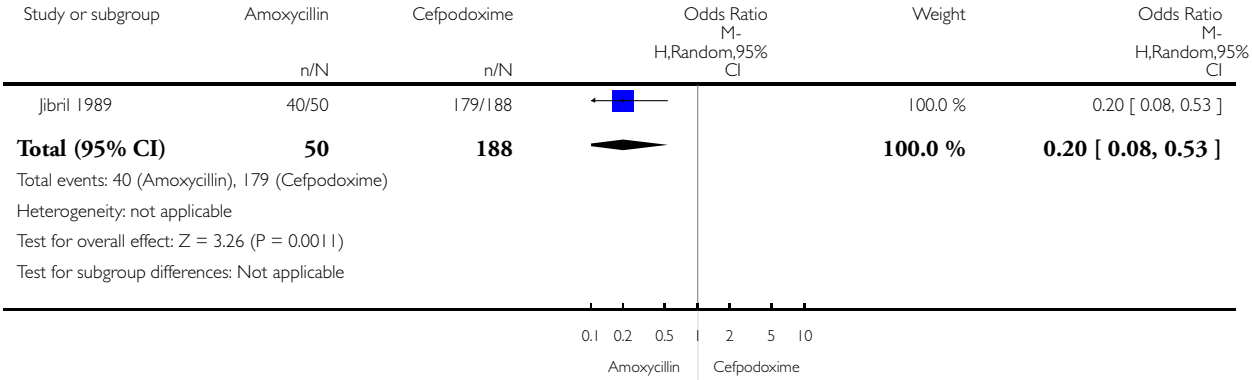


Analysis 29.3. Comparison 29 Amoxycillin versus cefpodoxime, Outcome 3 Response/cure rate.

Review: Antibiotics for community-acquired pneumonia in children

Comparison: 29 Amoxycillin versus cefpodoxime

Outcome: 3 Response/cure rate

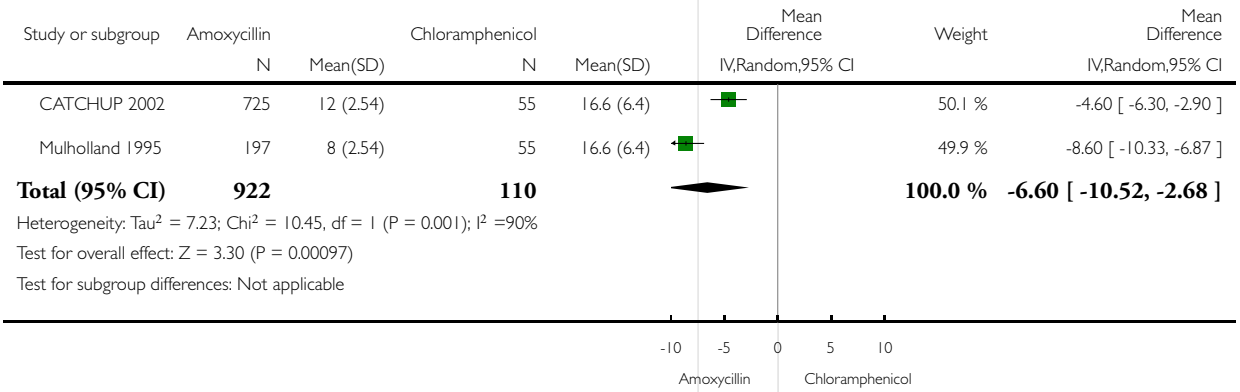


Analysis 30.1. Comparison 30 Amoxycillin versus chloramphenicol, Outcome 1 Age (mean/median).

Review: Antibiotics for community-acquired pneumonia in children

Comparison: 30 Amoxycillin versus chloramphenicol

Outcome: 1 Age (mean/median)



Analysis 30.2. Comparison 30 Amoxycillin versus chloramphenicol, Outcome 2 Male sex.

Review: Antibiotics for community-acquired pneumonia in children

Comparison: 30 Amoxycillin versus chloramphenicol

Outcome: 2 Male sex

Study or subgroup	Amoxycillin n/N	Chloramphenicol n/N	Odds Ratio M-H,Random,95% CI	Weight	Odds Ratio M-H,Random,95% CI
CATCHUP 2002	435/725	24/55		55.1 %	1.94 [1.11, 3.37]
Straus 1998	137/197	24/55		44.9 %	2.95 [1.60, 5.45]
Total (95% CI)	**922**	**110**		**100.0 %**	**2.34 [1.55, 3.53]**

Total events: 572 (Amoxycillin), 48 (Chloramphenicol)

Heterogeneity: $Tau^2 = 0.0$; $Chi^2 = 0.99$, df = 1 (P = 0.32); $I^2 = 0.0\%$

Test for overall effect: Z = 4.06 (P = 0.000050)

Test for subgroup differences: Not applicable

Analysis 30.3. Comparison 30 Amoxycillin versus chloramphenicol, Outcome 3 Cure rate.

Review: Antibiotics for community-acquired pneumonia in children

Comparison: 30 Amoxycillin versus chloramphenicol

Outcome: 3 Cure rate

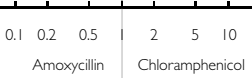
Study or subgroup	Amoxycillin n/N	Chloramphenicol n/N	Odds Ratio M-H,Random,95% CI	Weight	Odds Ratio M-H,Random,95% CI
CATCHUP 2002	608/725	39/71		100.0 %	4.26 [2.57, 7.08]
Total (95% CI)	**725**	**71**		**100.0 %**	**4.26 [2.57, 7.08]**

Total events: 608 (Amoxycillin), 39 (Chloramphenicol)

Heterogeneity: not applicable

Test for overall effect: Z = 5.60 (P < 0.00001)

Test for subgroup differences: Not applicable

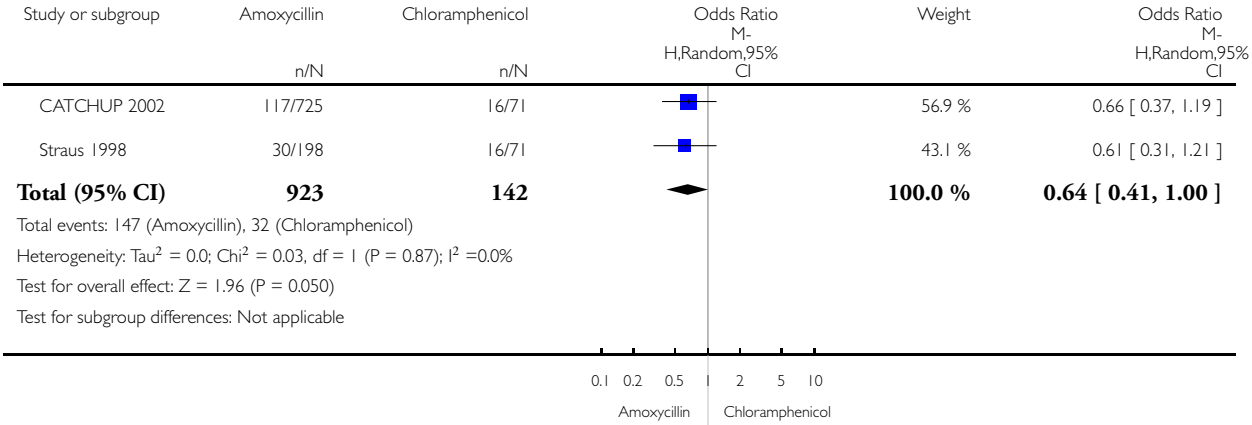


Analysis 30.4. Comparison 30 Amoxycillin versus chloramphenicol, Outcome 4 Failure rates.

Review: Antibiotics for community-acquired pneumonia in children

Comparison: 30 Amoxycillin versus chloramphenicol

Outcome: 4 Failure rates



ADDITIONAL TABLES

Table 1. Bacterial isolation

Study/total tested	*S. pneumoniae*	*H. influenzae*	*Staphylococcus*	Others
Asghar 2008/958	22	8	47	33
Bansal 2006/71	3	2	0	0
Block 1995/122	2	2	0	0
Bradley 2007/709	21	7	0	3
Camargos 1997/90	6	0	0	0
Duke 2002/1116	4	10	10	36
Harris 1998/351	5	2	0	0
Klein 1995/348	14	28	0	17
Kogan 2003/47	7	0	0	4
Mulholland 1995/111	10	2	0	8

Table 1. Bacterial isolation (*Continued*)

Nogeova 1997/140	24	21	11	22
Roord 1996/95	11	19	1	13
Straus 1998/595	79	49	0	0
Wubbel 1999/129	35	0	0	0
Total/4882 (12%)	236 (4.8%)	150 (3.0%)	69 (1.4%)	136 (2.8%)
Out of total bacterial isolates (591)	236/591 (40%)	150/591 (25%)	69/591 (12%)	136/591 (23%)

APPENDICES

Appendix 1. Previous search strategy

We searched the Cochrane Central Register of Controlled Trials (CENTRAL) (*The Cochrane Library* 2009, Issue 2), which contains the Acute Respiratory Infections Group's Specialised Register, MEDLINE (1966 to September 2009) and EMBASE (1990 to September 2009). There were no language or publication restrictions. We combined the MEDLINE search with the Cochrane Highly Sensitive Search Strategy for identifying randomised trials in MEDLINE: sensitivity- and precision-maximising version (2008 revision); Ovid format (Lefebvre 2008).

MEDLINE (OVID)

1 exp PNEUMONIA/
2 pneumonia
3 or/1-2
4 exp Anti-Bacterial Agents/
5 antibiotic$
6 or/4-5
7 exp CHILD/
8 exp INFANT/
9 (children or infant$ or pediatric or paediatric)
10 or/7-9
11 3 and 6 and 10

EMBASE (WebSPIRS)

#1 explode 'pneumonia-' / all subheadings in DEM,DER,DRM,DRR
#2 (pneumonia in ti) or (pneumonia in ab)
#3 #1 or #2
#4 'antibiotic-agent' / all subheadings in DEM,DER,DRM,DRR
#5 (antibiotic* in ti) or (antibiotic* in ab)
#6 #4 or #5

#7 'child-' / all subheadings in DEM,DER,DRM,DRR
#8 (child in ti) or (child in ab)
#9 (children in ti) or (children in ab)
#10 'infant-' / all subheadings in DEM,DER,DRM,DRR
#11 (infant* in ti) or (infant* in ab)
#12 #7 or #8 or #9 or #10 or #11
#13 #3 and #6 and #12
#14 explode 'randomized-controlled-trial' / all subheadings
#15 explode 'controlled-study' / all subheadings
#16 explode 'single-blind-procedure' / all subheadings
#17 explode 'double-blind-procedure' / all subheadings
#18 explode 'crossover-procedure' / all subheadings
#19 explode 'phase-3-clinical-trial' / all subheadings
#20 (randomi?ed controlled trial in ti) or (randomi?ed controlled trial in ab)
#21 ((random* or placebo* or double-blind*)in ti) or ((random* or placebo* or double-blind*)in ab)
#22 (controlled clinical trial* in ti) or (controlled clinical trial* in ab)
#23 #14 or #15 or #16 or #17 or 318 or #19 or #290 or #21 or #22
#24 (nonhuman in der) not ((human in der) and (nonhuman in der))
#25 #23 not #24
#26 #13 and #25

Appendix 2. EMBASE search strategy

#9 #7 AND #8
#8 'randomized controlled trial'/exp OR 'single blind procedure'/exp OR 'double blind procedure'/exp OR 'crossover procedure'/exp OR (random*:ab,ti OR placebo*:ab,ti OR factorial*:ab,ti OR crossover*:ab,ti OR 'cross over':ab,ti OR 'cross-over':ab,ti OR volunteer*:ab,ti OR assign*:ab,ti OR allocat*:ab,ti OR ((singl* OR doubl*) NEAR/1 blind*):ab,ti
#7 #1 AND #6
#6 #2 OR #3 OR #4 OR #5
#5 kindergar*:ab,ti OR highschool*:ab,ti OR (school* NEAR/1 (nursery OR primary OR secondary OR elementary OR high)):ab,ti
#4 (school NEAR/2 (age* OR child*)):ab,ti
#3 infant*:ab,ti OR infanc*:ab,ti OR baby*:ab,ti OR babies:ab,ti OR newborn*:ab,ti OR child*:ab,ti OR schoolchild*:ab,ti OR preschool*:ab,ti OR kid:ab,ti OR kids:ab,ti OR toddler*:ab,ti OR adolescen*:ab,ti OR teen*:ab,ti OR boy*:ab,ti OR girl*:ab,ti OR minor*:ab,ti OR puberty:ab,ti OR pediatric*:ab,ti OR paediatric*:ab,ti
#2 'infant'/exp OR 'child'/exp OR 'adolescent'/exp OR 'pediatrics'/exp OR 'juvenile'/exp OR 'puberty'/exp
#1
#1.9 #1.4 AND #1.8
#1.8 #1.5 OR #1.6 OR #1.7
#1.7 amoxycillin:ab,ti OR amoxicillin:ab,ti OR ampicillin:ab,ti OR azithromycin:ab,ti OR augmentin:ab,ti OR benzylpenicillin:ab,ti OR 'b-lactam':ab,ti OR 'beta-lactam':ab,ti OR 'beta-lactams':ab,ti OR clarithromycin:ab,ti OR cefuroxime:ab,ti OR cotrimoxazole:ab,ti OR 'co-trimoxazole':ab,ti OR cefotaxime:ab,ti OR ceftriaxone:ab,ti OR ceftrioxone:ab,ti OR cefditoren:ab,ti OR chloramphenicol:ab,ti OR cefpodixime:ab,ti OR cephradine:ab,ti OR cephalexin:ab,ti OR cefetanet:ab,ti OR cefaclor:ab,ti OR cephalosporin*:ab,ti OR erythromycin:ab,ti OR gentamicin:ab,ti OR genamycin:ab,ti OR levofloxacin:ab,ti OR minocyclin:ab,ti OR moxifloxacin:ab,ti OR peniclin*:ab,ti OR quinolone*:ab,ti OR roxithromycin:ab,ti OR sulphamethoxazole:ab,ti OR sulfamethoxazole:ab,ti OR trimethoprim:ab,ti
#1.6 antibiotic*:ab,ti
#1.5 'antibiotic agent'/exp
#1.4 #1.1 OR #1.2 OR #1.3
#1.3 'community-acquired-pneumonia':ab,ti OR bronchopneumon*:ab,ti OR pleuropneumon*:ab,ti OR cap:ab,ti
#1.2 pneumon*:ab,ti
#1.1 'pneumonia'/exp

Appendix 3. CINAHL (Ebsco) search strategy

S37 S35 and S36
S36 S11 and S20
S35 S22 or S23 or S24 or S25 or S26 or S27 or S28 or S29 or S30 or S31 or S32 or S33 or S34
S34 TI school* OR AB school*
S33 TI (nursery school* or kindergar* or primary school* or secondary school* or elementary school* or high school* or highschool*) OR AB (nursery school* or kindergar* or primary school* or secondary school* or elementary school* or high school* or highschool*)
S32 (MH "Schools") OR (MH "Schools, Elementary") OR (MH "Schools, Middle") OR (MH "Schools, Nursery") OR (MH "Schools, Secondary") OR (MH "Schools, Special") 8229 Edit S32
S31 TI (pediatric* or paediatric*) OR AB (pediatric* or paediatric*)
S30 (MH "Pediatrics+")
S29 TI (minor* or pubert* or pubescen*) OR AB (minor* or pubert* or pubescen*)
S28 (MH "Puberty")
S27 (adoles* or teen* or boy* or girl*) OR (adoles* or teen* or boy* or girl*)
S26 (MH "Adolescence+")
S25 TI (child* or schoolchild* or school age* or preschool* or kid or kids or toddler*) OR AB (child* or schoolchild* or school age* or preschool* or kid or kids or toddler*)
S24 (MH "Child+")
S23 TI (infant* or infancy or newborn* or baby* or babies or neonat* or preterm* or prematur*) OR AB (infant* or infancy or newborn* or baby* or babies or neonat* or preterm* or prematur*) 66234
S22 (MH "Infant+")
S21 (S11 and S20)
S20 S12 or S13 or S14 or S15 or S16 or S17 or S18 or S19
S19 (MH "Placebos")
S18 (MH "Quantitative Studies")
S17 TI placebo* OR AB placebo*
S16 TI random* OR AB random*
S15 TI (singl* blind* or doubl* blind* or tripl* blind* or trebl* blind* or singl* mask* or doubl* mask* or trebl* mask* or tripl* mask*) OR AB (singl* blind* or doubl* blind* or tripl* blind* or trebl* blind* or singl* mask* or doubl* mask* or trebl* mask* or tripl* mask*)
S14 TI clinic* trial* OR AB clinic* trial*
S13 PT clinical trial
S12 (MH "Clinical Trials+")
S11 S9 and S10
S10 S5 or S6 or S7 or S8
S9 S1 or S2 or S3 or S4
S8 AB amoxycillin* or amoxicillin* or ampicillin* or azithromycin* or augmentin* or benzylpenicillin* or b-lactam* or beta-lactam* or clarithromycin* or ceftriaxone* or cefuroxime* or cotrimoxazole* or
co-trimoxazole* or co-amoxyclavulanic acid or cefotaxime* or ceftriaxone* or ceftrioxone* or cefditoren* or chloramphenicol* or cefpodioxime* or cephradine* or cephalexin* or cefaclor* or cefetamet* or cephalosporin* or erythromycin* or gentamicin* or gentamycin* or levofloxacin* or macrolide* or minocyclin* or moxifloxacin* or penicillin* or quinolone* or roxithromycin* or sulphamethoxazole* or sulfamethoxazole* or tetracycline* or trimethoprim*
S7 TI amoxycillin* or amoxicillin* or ampicillin* or azithromycin* or augmentin* or benzylpenicillin* or b-lactam* or beta-lactam* or clarithromycin* or ceftriaxone* or cefuroxime* or cotrimoxazole* or
co-trimoxazole* or co-amoxyclavulanic acid or cefotaxime* or ceftriaxone* or ceftrioxone* or cefditoren* or chloramphenicol* or cefpodioxime* or cephradine* or cephalexin* or cefaclor* or cefetamet* or cephalosporin* or erythromycin* or gentamicin* or gentamycin* or levofloxacin* or macrolide* or minocyclin* or moxifloxacin* or penicillin* or quinolone* or roxithromycin* or sulphamethoxazole* or sulfamethoxazole* or tetracycline* or trimethoprim*
S6 TI (antibiotic* or antibacter* or anti-bacter*) OR AB (antibiotic* or antibacter* or anti-bacter*)
S5 (MH "Antibiotics+")
S4 TI cap OR AB cap
S3 TI (bronchopneumon* or pleuropneumon*) OR AB (bronchopneumon* or pleuropneumon*)
S2 TI pneumon* OR AB pneumon*

S1 (MH “Pneumonia+”)

Appendix 4. Web of Science (Thomson ISI) search strategy

# 6	113	#4 AND #3 Refined by: Publication Years=(2011 OR 2012) *Databases=SCI-EXPANDED, CPCI-S Timespan=All Years* *Lemmatization=On*
# 5	796	#4 AND #3 *Databases=SCI-EXPANDED, CPCI-S Timespan=All Years* *Lemmatization=On*
# 4	1,302,084	Topic=(random* or placebo* or allocat* or crossover* or “cross over” or ((singl* or doubl*) NEAR/1 blind*)) OR Title=(trial) *Databases=SCI-EXPANDED, CPCI-S Timespan=All Years* *Lemmatization=On*
# 3	5,848	#2 AND #1 *Databases=SCI-EXPANDED, CPCI-S Timespan=All Years* *Lemmatization=On*
# 2	1,414,126	Topic=(infant* or infancy or newborn* or baby or babies or neonat* or preterm* or prematur* or child* or schoolchild* or “school age*” or preschool* or kid or kids or toddler* or adoles* or teen* or boy* or girl* or pediatric* or paediatric*) *Databases=SCI-EXPANDED, CPCI-S Timespan=All Years* *Lemmatization=On*
# 1	29,498	Topic=(pneumon* or bronchopneumon* or pleuropneumon* or cap) AND Topic=(antibiotic* or amoxycillin* or amoxicillin* or ampicillin* or azithromycin* or augmentin* or benzylpenicillin* or b-lactam* or beta-lactam* or clarithromycin* or ceftriaxone* or cefuroxime* or cotrimoxazole* or co-trimoxazole* or co-amoxyclavulanic acid or cefotaxime* or ceftriaxone* or ceftrioxone* or cefditoren* or chloramphenicol* or cefpodoxime* or cephradine* or cephalexin* or cefaclor* or cefetamet* or cephalosporin* or erythromycin* or gentamicin* or gentamycin* or levofloxacin* or macrolide* or minocyclin* or moxifloxacin* or penicillin* or quinolone* or roxithromycin* or sulphamethoxazole* or sulfamethoxazole* or tetracyclin* or trimethoprim*) *Databases=SCI-EXPANDED, CPCI-S Timespan=All Years* *Lemmatization=On*

Appendix 5. LILACS (Brieme) search strategy

> Search > (MH:pneumonia OR Neumonía OR MH:C08.381.677$ OR MH:C08.730.610$ OR Pulmonía OR "Inflamación Experimental del Pulmón" OR "Inflamación del Pulmón" OR "Neumonía Lobar" OR Neumonitis OR "Inflamación Pulmonar" OR "Inflamação Experimental dos Pulmões" OR "Inflamação do Pulmão" OR "Pneumonia Lobar" OR Pneumonite OR "Inflamação Pulmonar" OR Pulmonia OR bronchopneumon$ OR Bronconeumonía OR Broncopneumonia OR Pleuropneumonia OR Pleuroneumonía OR Pleuropneumonia) AND (MH:"Anti-Bacterial Agents" OR antibiotic$ OR Antibacterianos OR Antibióticos OR MH:D27.505.954.122.085$ OR MH:amoxicillin OR amoxicillin$ OR Amoxicilina OR MH:ampicillin OR Ampicilina OR ampicillin$ OR MH:Azithromycin OR Azitromicina OR azithromycin$ OR augmentin$ OR benzylpenillin OR MH:"penicillin g" OR "penicilina g" OR MH:"beta-lactams" OR "beta-lactams" OR "beta-lactamas" OR MH:clarithromycin OR claritromicina OR clarithromycin OR MH:ceftriaxone OR ceftriaxone OR ceftriaxona OR MH:cefroxime OR cefroxime$ OR cefuroxima OR cotrimoxazol$ OR "Trimethoprim-Sulfamethoxazole Combination" OR "Combinación Trimetoprim-Sulfametoxazol" OR "Combinação Trimetoprima-sulfametoxazol" OR "co-amoxyclavulanic acid" OR cefotaxime OR MH:cefotaxime OR cefotaxima OR MH:ceftriaxone OR ceftriaxone OR ceftriaxona OR ceftrioxone OR cefditoren$ OR chloramphenicol OR cloranfenicol OR MH:chloramphenicol OR cefpodixime OR MH:cephradine OR cephradin$ OR cefradina OR MH:cephalexin OR cefalexina OR cephalexin$ OR cefaclor OR MH:cefaclor OR cefetamet OR cephalosporin$ OR MH:cephalosporins OR cefalosporinas OR MH:erythromycin OR erythromycin OR eritomicina OR MH:gentamicins OR gentamicin$ OR gentamycin$ OR Gentamicinas OR levofloxacin OR MH:ofloxacin OR ofloxacin$ OR MH:macrolides OR macrolide$ OR Macrólidos OR Macrolídeos OR minocyclin$ OR MH:minocycline OR Minociclina OR moxifloxacin OR penicillin$ OR MH:penicillins OR penicilinas OR
MH:quinolones OR quinolon$ OR roxithromycin OR MH:roxithromycin OR roxitromicina OR MH:sulfamethoxazole OR sulfamethoxazole$ OR sulphamethoxazole OR Sulfametoxazol OR MH:tetracyclines OR tetracycline$ OR Tetraciclinas OR MH:trimethoprim OR trimetoprim OR trimetoprima) > clinical˙trials

WHAT'S NEW

Last assessed as up-to-date: 7 November 2012.

Date	Event	Description
7 November 2012	New search has been performed	Searches updated. We included two new trials (Nogeova 1997; Ribeiro 2011) and excluded three new trials (Ambroggio 2012; Bari 2011; Soofi 2012).
7 November 2012	New citation required and conclusions have changed	We have added conclusions about treatment of severe pneumonia with oral antibiotics and a comparison of antibiotics in radiographically confirmed pneumonia

HISTORY

Protocol first published: Issue 3, 2004

Review first published: Issue 3, 2006

Date	Event	Description
4 January 2010	New citation required and conclusions have changed	Seven new studies included and we have added new information on ambulatory treatment for severe pneumonia and the superiority of ampicillin/penicillin with gentamycin instead of chloramphenicol for the treatment of very severe pneumonia to the conclusions
18 September 2009	New search has been performed	Searches conducted.
1 August 2009	Amended	Converted to new review format.
6 January 2006	New citation required and major changes	Search conducted.

CONTRIBUTIONS OF AUTHORS

Dr Sushil K Kabra (SK) and Dr Rakesh Lodha (RL) jointly prepared and edited the review.

Dr RM Pandey (RP) contributed to the sections on data extraction, data analysis, quality assessment and statistical methods, in addition to editing the review.

DECLARATIONS OF INTEREST

One of the authors (Kabra) was co-author of one study (Awasthi 2008) included in the review. Other two authors do not have any competing conflicts of interest.

SOURCES OF SUPPORT

Internal sources

- All India Institute of Medical Sciences, New Delhi, India.

External sources

- No sources of support supplied

DIFFERENCES BETWEEN PROTOCOL AND REVIEW

In the protocol we decided to include studies with an outcome in the form of cure rates. However, there were a few studies that did not report cure rates. We therefore decided to include studies that gave either cure rates or treatment failure rates as one of the outcomes.

INDEX TERMS

Medical Subject Headings (MeSH)

Amoxicillin [therapeutic use]; Anti-Bacterial Agents [*therapeutic use]; Chloramphenicol [therapeutic use]; Community-Acquired Infections [drug therapy]; Drug Therapy, Combination [methods]; Gentamicins [therapeutic use]; Penicillins [therapeutic use]; Pneumonia, Bacterial [*drug therapy]; Randomized Controlled Trials as Topic; Trimethoprim-Sulfamethoxazole Combination [therapeutic use]

MeSH check words

Adolescent; Child; Humans