

## Recommendations for treatment of childhood non-severe pneumonia

	Study location	Age	Study design	Outcome measure	Antimicrobial agents (number with outcome/total)	Conclusions	
<b>Comparisons of antimicrobial agents</b>							
	Hazir et al (2008) <sup>1</sup>	Pakistan	3–59 months	Randomised, open label	Treatment failure at day 6	Ampicillin at 48 h + amoxicillin at 3 days: 889/976; amoxicillin at 5 days: 911/988	Home treatment with high-dose oral amoxicillin is equivalent to currently recommended hospitalisation and parenteral ampicillin for treatment of severe pneumonia without underlying complications
	Bradley et al (2007) <sup>2</sup>	Multicentre, international	6–59 months	Randomised, open label	Clinical cure at 10–17 days after completion of therapy	Levofloxacin: 211/247; amoxicillin–clavulanic acid or ceftriaxone: 71/87	In children treated either in hospital or as an outpatient for community-acquired pneumonia, levofloxacin was as well-tolerated and as effective as standard-of-care antibiotics in infants and children
	Atkinson et al (2007) <sup>3</sup>	USA	6 months to 16 years	Randomised	Treatment failure	Amoxicillin (by mouth): 3/98; benyl penicillin: 7/98	In children hospitalised with radiographically confirmed pneumonia, there was no significant difference in outcome in children receiving each treatment
	Lu et al (2006) <sup>4</sup>	China	..	Randomised, open label	Favourable treatment response	Cefaclor: 94/110; amoxicillin–clavulanic acid: 91/110	For children with lower respiratory tract infections, there is no significant difference between the two treatments
	Bansal et al (2006) <sup>5</sup>	India	2–59 months	Randomised, open label	Relapse of pneumonia within 2 weeks, persistence of danger signs at 48 h or deterioration	Amoxicillin–clavulanic acid: 1/23; penicillin and gentamicin: 1/21	In children with severe or very severe radiographically confirmed hypoxemic pneumonia, there was no significant difference between the two treatments
	Hasali et al (2005) <sup>6</sup>	Malaysia	2 months to 5 years	Randomised, open label	Improvement of signs and symptoms	Ampicillin (intravenous): 20/20; ampicillin and gentamicin: 20/20	In children hospitalised with severe pneumonia, there were significant differences in time to desired outcome, favouring the ampicillin group, but all children recovered
	Cetinkaya et al (2004) <sup>7</sup>	Turkey	2–24 months	Randomised, double blind	Cure: “all symptoms and signs related to pneumonia had completely disappeared”	Penicillin G + chloramphenicol: 39/46; ceftriaxone: 41/51	For children with severe pneumonia, both treatments are successful regimens for treatment of severe pneumonia
	Addo-Yobo et al (2004) <sup>8</sup>	Multicentre, international	3–59 months	Randomised, open label	Treatment failure up to 48 h based on clinical signs	Amoxicillin: 161/857; penicillin G: 167/845	For children with severe pneumonia, penicillin and amoxicillin are equivalent
	Aurangzeb and Hameed (2003) <sup>9</sup>	Pakistan	2–72 months	Randomised	Clinical improvement	Amoxicillin: 41/43; cefuroxime: 40/41; clarithromycin: 39/41	For children with severe pneumonia, all antibiotics had similar outcomes, although amoxicillin was significantly less expensive
	Kogan et al (2003) <sup>10</sup>	Chile	1 month to 14 years	Randomised	Classic pneumonia: A=No fever at day 3; B=Improvement of ≥75% of radiographic baseline on day 7 Atypical pneumonia: A=Number of days with cough; B=Improvement of ≥75% of radiographic baseline on day 14	Classic pneumonia (A, B): azithromycin, (21,19)/23; amoxicillin, (21,15)/24; atypical pneumonia (A, B): azithromycin, (3-6 days, 33)/33; erythromycin, (5-5 days, 21)/26	For children with severe pneumonia, there is no difference in treatment except with duration of cough in the atypical group
	Duke et al (2002) <sup>11</sup>	Papua New Guinea	1 month to 5 years	Randomised, open label	Treatment failure on management	Chloramphenicol: 147/559; penicillin and gentamicin: 123/557	For children with very severe pneumonia, for both treatment groups resulted in good outcomes
	CATCHUP et al (2002) <sup>12</sup>	Pakistan	2–59 months	Randomised, double blind	Treatment failure on clinical signs on days 3 or 5	Amoxicillin: 117/725; co-trimoxazole: 139/734	For children with non-severe pneumonia, both treatments are equally effective
	Ferwerda et al (2001) <sup>13</sup>	Netherlands	3 months to 12 years	Randomised, double blind	Clinical cure at follow-up (day 10–13 after initiation of therapy)	Azithromycin: 41/56; amoxicillin–clavulanic acid: 37/54	For children with radiographically confirmed pneumonia, there was no significant difference between treatments, although azithromycin was better tolerated
	Vuori-Holopainen et al (2001) <sup>14</sup>	Finland	3 months to 15 years	Randomised, open label	“Uneventful recovery”	Procaine penicillin: 41/41; Cefuroxime (intravenously): 30/31	For children with pneumonia (study included children with other diagnosis), there was no significant difference between the two outcomes
	Boulesteix et al (2000) <sup>15</sup>	France	3 months to 15 years	Randomised	Clinical and radiological response	Cefuroxime: 37/40; cefpodoxime: 41/44	In children hospitalised with radiographically confirmed pneumonia, there was no significant difference in treatment between the two treatments

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Wubbel et al (1999) <sup>16</sup>	USA	6 months to 16 years (results given only for ≤5-year olds)	Randomised, not blinded	Treatment failure: persistence or progression after 3 days of treatment	Azithromycin: 1/39; amoxicillin-clavulanic acid: 2/49	For the children with radiographically confirmed pneumonia, there was no significant differences between the two treatment groups
Harris et al (1998) <sup>17</sup>	USA	6 months to 16 years (results given only for ≤5 year olds)	Randomised, double blind	Treatment failure: persistence or progression after 3 days of treatment	Azithromycin: 41/125; amoxicillin-clavulanic acid: 21/63	For children with radiographically confirmed pneumonia, there was no significant difference between the two treatment groups
Tsarouhas et al (1998) <sup>18</sup>	USA	6 months to 18 years	Randomised, evaluator blinded	Temperature, respiratory rate, and general appearance score	Amoxicillin: 3/90; penicillin G: 5/71	No significant difference between intramuscular and oral treatments at 24–36 h
Straus et al (1998) <sup>19</sup>	Pakistan	2–59 months	Randomised, double blind, placebo (for dosing)	Inpatient: clinical failure; outpatient: signs of clinical pneumonia at follow-up	Co-trimoxazole: 92/398; amoxicillin: 30/197	For children with severe pneumonia, co-trimoxazole was statistically less effective than amoxicillin For children with non-severe pneumonia, co-trimoxazole was as effective
Carmargos et al (1997) <sup>20</sup>	Brazil	2–12 years	Randomised, single blind	Lack of progressive radiographic improvement on days 2, 7, and 14	Benzathine penicillin: 7/91; procaine penicillin: 4/82	For children with radiographically confirmed pneumonia, there was no significant difference between treatment groups
Roord et al (1996) <sup>21</sup>	Netherlands	2–16 years	Randomised, open label	Resolution of clinical signs and symptoms of lower respiratory tract infection	Azithromycin: 43/44; erythromycin: 36/40	For children lower respiratory tract infections, azithromycin is as effective as erythromycin
Galova et al (1996) <sup>22</sup>	Slovak Republic	1 month to 16 years	Randomised	Clinical cure or improvement at 72 h or 14 days	Azithromycin: 85/89; ceftibuten: 62/74	In children with community-acquired respiratory tract infections, azithromycin had improved clinical efficacy over ceftibuten
Deivanayagam et al (1996) <sup>23</sup>	India	5 months to 4 years	Randomised	Treatment failure: no clinical improvement at 72 h with regard to fever, tachypnea, or chest findings.	Ampicillin: 19/52; penicillin and chloramphenicol: 5/49	In hospitalised children with clinical and radiographic pneumonia, there was no significant difference in outcome between treatment groups
Block et al (1995) <sup>24</sup>	USA	3–12 years	Randomised	No change or worsening of signs and symptoms	Clarithromycin: 3/124; erythromycin: 5/110	For children with chest radiographically confirmed pneumonia, there was no significant difference in outcome between the treatments
Mulholland et al (1995) <sup>25</sup>	Gambia	0–5 years	Randomised, double blind	Failure of therapy: death, evidence of pneumonia day 7 of treatment or at outpatient review (usually 2 weeks after initiation of therapy).	Co-trimoxazole: 16/73; chloramphenicol: 16/71	For malnourished children with pneumonia there was no significant difference in outcome between the two treatments
Keeley et al (1990) <sup>26</sup>	Zimbabwe	3 months to 12 years	Randomised, open label	Presentation to hospital between day 2 and 14 from start of therapy with pneumonia and radiological signs of pneumonia	Co-trimoxazole: 5/303; penicillin: 3/311	For children with non-severe pneumonia there was no significant difference in outcome between the two treatment groups
Jibril et al (1989) <sup>27</sup>	Nigeria	2–12 years	Randomised, open label	Physician assessment of good or excellent response	Amoxicillin: 31/50; amoxicillin-clavulanic acid: 45/50	In children with bacterial pneumonia there was a better response with amoxicillin-clavulanic acid than amoxicillin alone
Gatzola-Karaveli et al (1989) <sup>28</sup>	Switzerland	2–14 years	Randomised, open label	No apparent or incomplete clinical response to therapy or appearance of complications	Cefetamet (20 mg/kg daily): 0/11; cefetamet (40 mg/kg daily): 0/10; cefaclor (30 mg/kg daily): 1/10	In children hospitalised with lower respiratory tract infections, there was only one treatment failure in cefaclor, but none receiving either dose of cefetamet
Campbell et al (1988) <sup>29</sup>	Gambia	1 month to 4 years	Not randomised	Clinician at 14 days: outcome same or worse; mother at 14 days: no continuing problems.	Co-trimoxazole: clinician, 5/66; mother, 56/66; penicillin/ampicillin: clinician, 5/65; mother, 56/65	In children with severe pneumonia, there was no significant difference in either outcome (mother's or physician's assessment) between the two treatment groups
Shann et al (1985) <sup>30</sup>	Papua New Guinea	93% were <24 months	Randomised, open label, multicentre	Death or change of antibiotics	Chloramphenicol: 51/329; chloramphenicol and penicillin: 68/371	In children with severe pneumonia, there was no significant difference in outcome in children receiving each treatment

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Haffejee (1984) <sup>31</sup>	South Africa	0–10 years	Randomised, single blind	Complete recovery at end of therapy	Cefotaxime: 1/15; penicillin + gentamicin: 2/15	For children with pneumonia, there was no significant difference in outcome between the two groups. The larger study included other diagnoses, which showed greater complete recovery in children in children taking cefotaxime versus penicillin-gentamicin.
Friis et al (1984) <sup>32</sup>	Denmark	1 month to 6 years	Randomised, open label	Multiple outcomes measured, only radiological signs at 3 weeks	Antimicrobial treatment: 7/37; no antimicrobial (erythromycin if bacterial infection): 6/27	For children with hospitalised pneumonia, there was no significant difference in outcome if the child received antimicrobials (ampicillin if <12 months or penicillin if >12 months) or no antimicrobials (unless signs of bacterial infection then erythromycin was given).
Hofmann et al (1996) <sup>33</sup>	Germany	2–12 years	Randomised, open label	Presence of signs or symptoms of pneumonia on day 4 of therapy	Azithromycin: 5/54; cefaclor: 14/55	In non-hospitalised children with pneumonia, children treated with azithromycin had a lower proportion of signs or symptoms on day 4 than children treated with cefaclor.
Amir et al (1996) <sup>34</sup>	Israel	6 months to 5 years	Randomised, open label	No signs or symptoms of pneumonia after 11 days of therapy	Cefixime: 28/29; amoxicillin-clavulanic acid: 29/33	In children with radiographically confirmed pneumonia and receiving 2 days of ceftriaxone, their subsequent oral antibiotic use did not show a significant difference in outcome.
Syrogianopolous et al (1994) <sup>35</sup>	Greece		Randomised, open label	Successful treatment	Cefetamet (10 mg/kg): 80/81; cefetamet (20 mg/kg): 79/81; cefaclor (10 mg/kg): 71/75	In children with radiographically confirmed pneumonia, there was no significant difference between the three treatment outcomes.
Sidal et al (1994) <sup>36</sup>	Turkey	4 months to 14 years	Randomised, open label	Respiratory symptoms and fever after the day 3 of treatment abnormal breath sounds on day 10	Co-trimoxazole: 6/46; procaine penicillin: 5/63; benzathine then procaine penicillin: 14/42	In children with non-severe pneumonia, there was no significant difference in outcome between the co-trimoxazole and the procaine penicillin group, and benzathine penicillin was not effective. Co-trimoxazole was cost effective.
<b>Comparisons of dose and/or duration of the same antimicrobial agent</b>						
Hazir et al (2007) <sup>37</sup>	Pakistan	2–59 months	Randomised, double blind	Treatment failure on day 5: developed lower chest indrawing or danger signs	Amoxicillin (45 mg/kg daily): 417/437; amoxicillin (95 mg/kg daily): 414/439	Clinical outcome in children aged 2–59 months with non-severe pneumonia treated for 3 days is the same with standard and double-dose oral amoxicillin.
Rasmussen et al (2005) <sup>38</sup>	Pakistan	2–59 months	Randomised, double blind	Treatment failure: change of therapy, death, or loss to follow-up.	Co-trimoxazole (4 mg/kg trimethoprim dose): 112/578; co-trimoxazole (8 mg/kg trimethoprim dose): 118/556	For children with non-severe pneumonia, there was no difference in outcome between 4 mg/kg and 8 mg/kg dose groups.
Agarwal et al (2004) <sup>39</sup>	India	2–59 months	Randomised, double blind, multicentre	Cure: defined as no danger signs or respiratory rate below age specific cut-off on day 5	Amoxicillin for 3 days: 980/1095; amoxicillin for 5 days: 983/1093	In children with non-severe pneumonia, there was no significant difference in cure between a 3 or 5 day duration of therapy, and therefore both are equally effective.
MASCOT (2002) <sup>40</sup>	Pakistan	2–59 months	Randomised, double blind, multicentre	Treatment failure: needed a change in antimicrobial therapy, developed severe disease, did not improve, or died	Amoxicillin for 3 days: 209/1000; amoxicillin for 5 days: 202/1000	In children with non-severe pneumonia, there was no significant difference between each treatment.
Peltola et al (2001) <sup>41</sup>	Finland	3 months to 15 years	Randomised, open label	Treatment failure: change of antibiotic therapy or recurrence with discontinuation of therapy	Cefuroxime or penicillin for 4 days: 3/34; cefuroxime or penicillin for 7 days: 1/38	In children with radiographically confirmed pneumonia, there was no significant difference between beta-lactam therapy (parental penicillin or cefuroxime) for 4 or 7 days. Study designed to test all severe illness, only cases with pneumonia are described here.
Ficnar et al (1997) <sup>42</sup>	Croatia	6 months to 12 years	Randomised, open label, multicentre	Treatment failure: no improvement in chest radiograph or no complete resolution of symptoms at day 5 after initiation of therapy	Azithromycin for 3 days: 2/65; azithromycin for 5 days: 3/81	For children with radiographically confirmed pneumonia, there was no significant difference between 3 or 5 days of therapy. Only cases with pneumonia are described here.
Bocczazzi et al (1998) <sup>43</sup>	Italy	2–12 years	Randomised, open label	Resolution of clinical signs and symptoms	Co-trimoxazole (4 mg/kg trimethoprim dose): 112/578; co-trimoxazole (8 mg/kg trimethoprim dose): 118/556	For children with non-severe pneumonia, there was no difference between 4 mg/kg and 8 mg/kg dose groups.
All included studies were randomised and had a clinical outcome.						
<b>Webtable: Summary of studies comparing antimicrobial agents for the treatment of childhood pneumonia</b>						

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