

So what's new in the SCAN primary care guidelines 2018 (paediatrics)?

- Focus on clearer advice on when to prescribe and when not to
- Pragmatism versus purism:
 - If children require Abs, use a drug that is palatable
 - Amoxicillin suspension instead of pen V
 - Cefalexin suspension versus flucloxacillin suspension –research study being planned
 - Azithromycin instead of clarithromycin
 - If children require Abs, avoid qds dosing
 - Amoxicillin 40mg/kg bd (max 1g/dose) – WHO dosing recommendation
 - Pen V tablets bd for older children with tonsillitis
- Reduce duration of Ab course where possible
 - Tonsillitis treatment course 7 days, not 10 days
- Adequate dosing – BNFC commonly underdoses!

What's the evidence supporting these changes?

- Palatability

Archives of
Disease in Childhood

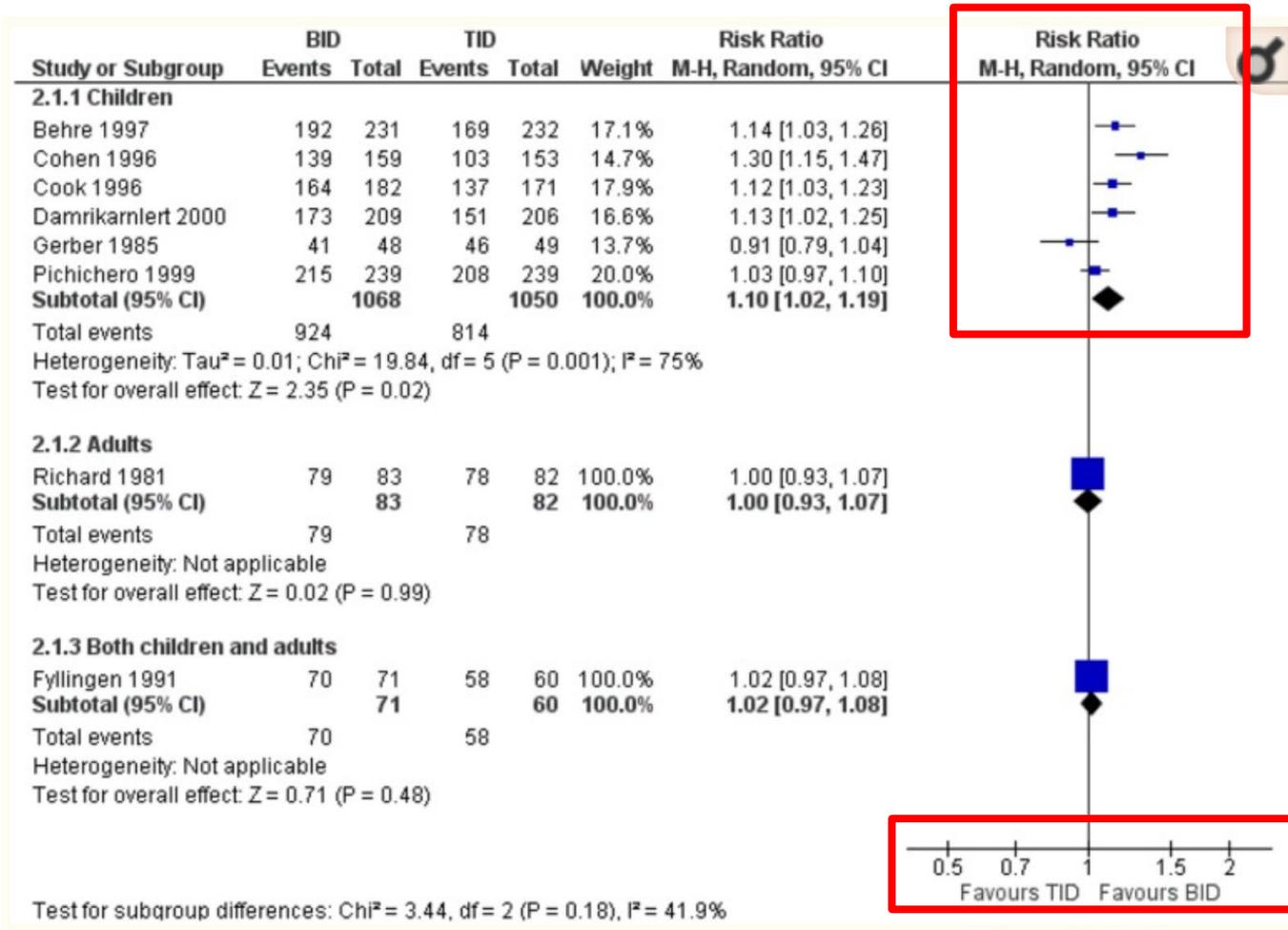
Prescribing for children – taste and palatability affect adherence to antibiotics: a review

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Arch Dis Child 2012;**97**:293–297. doi:10.1136/archdischild-2011-300909

Amoxicillin versus penicillin V
Cefalexin versus flucloxacillin

Dosing frequency and adherence



Felagas ME et al. Compliance with Once-Daily versus Twice or Thrice-Daily Administration of Antibiotic Regimens: A Meta-Analysis of Randomized Controlled Trials. PloS One 2015

BD dosing of pen V and amox - clinical efficacy (tonsillitis)

- Meta-analysis comparing overall cure rates between BID or once-daily (QD) versus more frequent dosing schedules in the treatment of streptococcal tonsillopharyngitis.
- A study was eligible for inclusion if it was a randomized clinical trial that compared the efficacies of different dosing frequencies of 10-day penicillin or amoxicillin in the treatment of streptococcal tonsillopharyngitis (6 studies met eligibility criteria).
- Results: BID dosing of 10-day penicillin is as efficacious as TDS/QID dosing regimens in the treatment of streptococcal tonsillopharyngitis. **This result also holds true in a subgroup analysis confined to pediatric cases. Similar findings with amoxicillin.**

Lan AJ. **The impact of dosing frequency on the efficacy of 10-day penicillin or amoxicillin therapy for streptococcal tonsillopharyngitis: A meta-analysis.**

[Pediatrics](#). 2000 Feb;105(2)

Amox versus penicillin V for tonsillitis— side-effects

- Mantra about avoiding ampicillin in tonsillitis due to risk of EBV rash: 80-100% risk of rash reported
- Risk of rash in children with confirmed EBV 29% with amoxicillin (23% in untreated children)¹
- EBV rare in children <12 years of age²
 - EBV accounts for as little as 1% of tonsillitis presenting to doctors³
- SCAN guidelines suggest amoxicillin suspension in young children (pen V tablets in older children)

1. Chovel-Senna A et al. Incidence of Rash After Amoxicillin Treatment in Children With Infectious Mononucleosis. [Pediatrics](#). 2013 May;131(5):e1424-7

2. Worrall GJ. Acute sore throat. *Can Fam Physician*. 2007 Nov; 53(11): 1961–1962

3. Hurt C et al. **Diagnostic evaluation of mononucleosis-like illnesses.** [Am J Med](#). 2007 Oct;120(10):911.e1-8

BD dosing of amox - clinical efficacy (pneumonia)

- 412 and 408 children 2-60 months of age with non-severe pneumonia received amoxicillin thrice or twice daily, respectively.
- Treatment failure was detected in 94 (22.8%) and 94 (23.0%) patients in intention-to-treat analysis (risk difference 0.2%; 95% CI: -5.5%-6.0%) and in 80 (20.1%) and 85 (21.3%) patients in per-protocol analysis (risk difference 1.2%; 95% CI: -4.4%-6.8%).
- Pneumonia was radiologically confirmed in 277 (33.8%) cases, among whom treatment failure was registered in 25/133 (18.8%) and 27/144 (18.8%) participants from the thrice and twice daily doses subgroups, respectively (risk difference -0.05%; 95% CI: -9.3%-9.2%).

Vilas-Boas AL et al; **Comparison of oral amoxicillin given thrice or twice daily to children between 2 and 59 months old with non-severe pneumonia: a randomized controlled trial.** [J Antimicrob Chemother.](#) 2014 Jul;69(7):1954-9

BD dosing of amox - clinical efficacy (Acute OM)

- Study comparing the clinical efficacy and side-effects of amoxycillin in two groups of children at the age of ≤ 6 years randomised to amoxycillin 40 mg/kg/day either two (n=180) or three times daily (n=187) for the clinical diagnosis of acute respiratory tract infections (**>80% of cases in both groups had acute OM**).
- **Results:** 82% of the patients with otitis media were cured in bd group vs 86% in tds group. Equivalence in terms of disappearance of the symptoms/improvement of the signs. Rate of side-effects same in both groups, 6.4% and 6.7% respectively.

Valtonen M et al. **Comparison of amoxycillin given two and three times a day in acute respiratory tract infections in children.** [Scand J Prim Health Care](#). 1986 Nov;4(4):201-4

Dosing frequency of amox – PK data

- Thirty-four children with upper or lower respiratory tract infections were randomly allocated to receive either a twice daily or three times daily dose of amoxicillin 50 mg /kg/day.
- On day 1, 16 of 27 children in the b.i.d. group and 11 of 26 children in the t.i.d. group had concentrations that were above 2.0 µg/ml for <50% of the dose interval
- On day 3, 18 of 31 children in the b.i.d. group and 8 of 31 children in the t.i.d. group had concentrations that were above 2.0 µg/ml for <50% of the dose interval.
- **Data supports dosing of 30-40mg/kg bd**

Fonseca W et al. Comparing Pharmacokinetics of Amoxicillin Given Twice or Three Times per Day to Children Older than 3 Months with Pneumonia. [Antimicrob Agents Chemother](#). 2003 Mar; 47(3): 997–1001

Choice of Ab and frequency of dosing

- Recognised by NICE- bd dosing in tonsillitis. Option of amoxicillin for children.
- WHO suggests bd dosing of amoxicillin in children: 40mg/kg (max 1g/dose) bd (WHO – (Guidelines for the management of common childhood illnesses. http://www.who.int/maternal_child_adolescent/documents/child_hospital_care/en/)

Duration of Abs for tonsillitis



The effect of short duration versus standard duration antibiotic therapy for streptococcal throat infection in children

Authors' conclusions:

Three to six days of oral antibiotics had comparable efficacy compared to the standard duration 10-day course of oral penicillin in treating children with acute GABHS pharyngitis. . In areas where the prevalence of rheumatic heart disease is still high, our results must be interpreted with caution.

SCAN guidelines = 7 day course (and avoids need for a second bottle to be dispensed)

Duration of antibiotics for tonsillitis if penicillin allergy

- Meta-analysis of randomized, controlled trials that involved bacteriological confirmation of GAS tonsillopharyngitis, random assignment to receive either azithromycin or a 10-day comparator antibiotic.
- In children, azithromycin administered at 60 mg/kg per course was superior to the 10-day courses of comparators ($P < .00001$), with bacterial failure occurring 5 times more often in patients receiving the 10-day courses of antibiotics.
- Azithromycin administered at 30 mg/kg per course was inferior to the 10-day courses of comparators ($P = .02$), with bacterial failure occurring 3 times more frequently in patients receiving azithromycin. **Three-day regimens were inferior to 5-day regimens ($P = .002$).**

SCAN guideline = azithromycin 10mg/kg for 5 days

Casey JR et al. Higher dosages of azithromycin are more effective in treatment of group A streptococcal tonsillopharyngitis. Clin Infect Dis 2005;40:1748-55

Azithromycin versus clarithromycin

- Differential selection of macrolide resistance: randomised, double-blind, placebo-controlled study of the effect of azithromycin (500 mg once daily for 3 days) and clarithromycin (500 mg twice daily for 7 days), was measured against placebo in four groups of volunteers by use of oral streptococci as model organisms (Malhotra-Kumar et al, 2007).
- Results: clearly defined effect on commensal pharyngeal streptococci was observed, with **both drugs selecting for macrolide resistance. Although azithromycin quantitatively selected for more persistent resistance, clarithromycin qualitatively selected for the higher resistance-conferring erm(B) gene. The acquisition of erm(B) represents a more efficient resistance mechanism for the organism. Not only does it confer increased resistance to the macrolide group of antibiotics, but it also induces resistance to clindamycin and tetracyclines.** This poses a heightened risk to public health. (Dancer, 2007).

SCAN guidelines = azithromycin due to benefits of once-daily dosing, fewer interactions and lower risk of selecting for ermB gene resistance. Consistency for resp tract infections and skin/soft tissue infections.

Cefalexin for treating skin/soft tissue infections

- RCT comparing cefalexin bd to dicloxacillin qds in adults with staph aureus skin infections (n=70)
- Results – no difference in treatment failures or recurrence
 - “Twice-daily therapy with cephalexin for staphylococcal skin and skin structure infections can be recommended with confidence.”

Cefalexin for treating skin/soft tissue infections

- RCT comparing oral cefalexin and IV cefazolin in adults with uncomplicated cellulitis (n=47)
- Results – no difference in rates of treatment failure

Aboltins CA et al. Oral versus parenteral antimicrobials for the treatment of cellulitis: a randomized non-inferiority trial. J Antimicrob Chemother. 2015 Feb;70(2):581-6

Dosing recommendations

The logo for 'thebmj' is displayed in white lowercase letters on a blue rectangular background.

Bielicki JA, Barker CI, Saxena S, Wong IC, Long PF, Sharland M. Not too little, not too much: problems of selecting oral antibiotic dose for children. *BMJ*. 2015 Nov 3;351:h5447.

Key messages

Methods for selecting dose of oral antibiotics in childhood must balance simplicity with accuracy

Although using exact weight is most accurate, it requires a recent weight and may not fit with fixed dose formulations

Age bands result in a substantial proportion of children receiving doses outside the recommended range and are context specific

Weight banded dose selection is transferable across populations and the most practical choice when up to date weight is available

Underdosing of oral Abs in children

- **Neonatal and Paediatric Pharmacokinetics of Antimicrobials Study (NAPPA study)**
 - PK study of penicillins in children suggests current BNFc doses results in subtherapeutic blood levels of co-amoxiclav (personal communication between Sanjay Patel and NAPPA study team)

Dosing recommendations SCAN versus BNFc

	SCAN	BNFc
Amoxicillin	40mg/kg bd (max 1g/dose) OR 3-11 months 250mg bd 1 year-4 years 500mg bd 5-11 years 750mg bd >12 years 1 gram bd	Up to 30mg/kg tds OR 1-11 months 125mg tds 1-4 years 250mg tds 5-11 years 500mg tds 12-17 years 500mg tds/1g tds
Penicillin V	Age 6-12 years 500mg bd Age >12 years 1 g bd	Age 6-11 years 250mg qds Age 12-17 years 500mg qds/1g qds
Cefalexin	12.5mg/kg 8 hourly (max 1g per dose). Double dose if severe infection OR 3-11 months 125mg tds 1 year-4 years 250mg tds 5-11 years 500mg tds >12 years 1 gram tds	12.5mg/kg bd 3-11 months 125mg bd 1 year-4 years 125mg tds 5-11 years 250mg tds >12 years 500mg tds (in severe infection up to 25mg/kg qds (age >12 year 1.5g qds) WHO dosing cefalexin 50 mg/kg/day PO divided in 2 or 4 doses