Summary of findings:

12 Antibiotics compared to placebo / no treatment / unproven therapy for children with otitis media with effusion

Patient or population: Children aged 0 to 15 years who have otitis media with effusion.

Setting: Primary health care

Intervention: Antibiotics (Studies used: amoxicillin (20-50 mg/kg/day in single or 3 divided doses for 14 days to 6 months), trimethoprim-sulfamethoxazole (8 mg and 40 mg/kg/day in 2-3 divided doses for 2-4 weeks) and amoxycillin/clavulanic acid (40 mg/kg/day in 3 divided doses (maximum 750 mg/day) for 2 weeks to 3 months).

Comparison: Placebo / No treatment / Unproven therapy.

Outcome № of participants (studies)	Relative effect (95% CI)	**Anticipated absolute effects (95% CI)**			Quality	What happens
		Without antibiotics	**With antibiotics**	**Difference**		
Hearing outcomes assessed with: pure tone average and speech reception threshold follow up: range 2 to 4 weeks № of participants: 784 (2 RCTs) [1,a,b]	Mandel 1987 reported no statistically significant differences in mean speech recognition threshold between antibiotic and placebo groups at 4 weeks. Mandel 1991 reported a statistically significant difference in the mean speech recognition threshold between antibiotic and placebo groups at 2 weeks (left and right ears). At 4 weeks a statistically significant result was only found in the right ears.				⊕◯◯◯ VERY LOW [c,d,e]	In children with OME treated with antibiotics compared to placebo / no treatment / unproven treatment there is possibly no improvement in hearing outcomes at 2-4 weeks. NNT Not Applicable
Complete resolution of OME assessed with: tympanometry +/- pneumatic otoscopy follow up: range 2 to 3 months № of participants: 484 (6 RCTs) [1,f]	**RR 2.00** (1.58 to 2.53)	24.7%	**49.3%** (39.0 to 62.4)	**24.7% more** (14.3 more to 37.7 more)	⊕⊕◯◯ LOW [e,g,h]	In children with OME treated with antibiotics compared to placebo / no treatment / unproven treatment there is possibly more resolution of OME at 2-3 months follow-up. NNT ~ 5
Complete resolution of OME (long term) assessed with: tympanometry +/- pneumatic otoscopy follow up: median 6 months № of participants: 606 (5 RCTs) [1,i]	**RR 1.75** (1.41 to 2.18)	25.5%	**44.5%** (35.9 to 55.5)	**19.1% more** (10.4 more to 30 more)	⊕⊕◯◯ LOW [e,j]	In children with OME treated with antibiotics compared to placebo / no treatment / unproven treatment there is possibly more resolution of OME at 6 months follow-up. NNT ~ 6
Adverse effects (diarrhoea, vomiting or skin rash) follow up: range 2 to 8 weeks № of participants: 742 (5 RCTs) [1,k]	**RR 2.15** (1.29 to 3.60)	4.5%	**9.7%** (5.8 to 16.2)	**5.2% more** (1.3 more to 11.7 more)	⊕⊕◯◯ LOW [e,l,m]	In children with OME treated with antibiotics compared to placebo / no treatment / unproven treatment there are possibly more adverse events at 2-8 weeks follow-up. NNH ~ 20
Tympanic membrane perforation assessed with: pneumatic otoscopy + tympanometry follow up: median 6 months № of participants: 103 (1 RCT) [1,n]	**RR 0.42** (0.18 to 1.01)	27.5%	**11.5%** (4.9 to 27.7)	15.9% fewer (NS) (22.5 fewer to 0.3 more)	⊕⊕◯◯ LOW [o]	In Aboriginal children with OME treated with antibiotics compared to placebo there is possibly a reduction in tympanic membrane perforation during therapy.

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Comparison: Placebo / No treatment / Unproven therapy.

Outcome № of participants (studies)	Relative effect (95% CI)	Anticipated absolute effects (95% CI)			Quality	What happens
		Without antibiotics	With antibiotics	Difference		
Insertion of tympanostomy tubes follow up: range 3 to 6 months № of participants: 121 (2 RCTs) [1,p]	**RR 0.90** (0.46 to 1.78)	18.5%	**16.7%** (8.5 to 33.0)	1.9% fewer (NS) (10 fewer to 14.4 more)	⊕⊕◯◯ LOW [e,q]	In children with OME treated with antibiotics compared to placebo / no treatment / unproven treatment there is possibly no reduction of TT insertion within 3 to 6 months. NNT Not Applicable

***The risk in the intervention group** (and its 95% confidence interval) is based on the assumed risk in the comparison group and the **relative effect** of the intervention (and its 95% CI).

CI: Confidence interval; **RR:** Risk ratio; **NS:** Not significant; **NNT**: Number needed to treat; **NNH**: Number needed to harm; **MD:** Mean difference; **TT**: tympanostomy tubes

GRADE Working Group grades of evidence
High quality: We are very confident that the true effect lies close to that of the estimate of the effect
Moderate quality: We are moderately confident in the effect estimate: The true effect is likely to be close to the estimate of the effect, but there is a possibility that it is substantially different
Low quality: Our confidence in the effect estimate is limited: The true effect may be substantially different from the estimate of the effect
Very low quality: We have very little confidence in the effect estimate: The true effect is likely to be substantially different from the estimate of effect

Explanations

a. Studies taken from: Cochrane Review, Venekamp 2016 (Mandel 1991, Mandel 1987)
b. Studies taken from: Cochrane Review, Venekamp 2016 (Mandel 1987, 1991)
c. Inconsistency: inconsistency of effect estimates across individual trials and incomplete outcome reporting
d. Indirectness: 4 week follow-up may be too early to detect important differences in hearing
e. Imprecision: Optimal information size not met
f. Studies taken from: Cochrane Review, Venekamp 2016 (Ardehali 2008, Chen 2013, Marchisio 1998, Podoshin 1990, Safak 2001, Schwartz 1982)
g. Risk of Bias: Performance bias across several studies, attrition bias (Podoshin), selection bias (Schwartz). However on sensitivity analysis same estimate of effect achieved. Not rated down
h. Indirectness: Different antibiotic regimens used, differing definitions for OME (Marchisio diagnosed OME >1 month of effusion vs other studies >3 months of effusion)
i. Studies taken from: Cochrane Review, Venekamp 2016 (Chuong 2008, Leach 2008, Otten 1990, Principi 1989, Thomsen 1989)
j. Risk of bias: Performance bias (lack blinding Chuong 2008) & attrition bias (Principi 1989, Thomsen 1989)
k. Studies taken from: Cochrane Review, Venekamp 2016 (Hemlin 1997, Marchisio 1998, Moller 1990, Thomsen 1989, van Balen 1996)
l. Risk of Bias: Attrition bias across several studies, differing baseline characteristics shown to be prognostic factor (van Balen)
m. Imprecision: Low event rate
n. Study taken from: Cochrane Review, Venekamp 2016 (Leach 2008)
o. Imprecision: Small, single study.
p. Studies taken from: Cochrane Review, Venekamp 2016 (Chen 2013, Choung 2008)
q. Risk of bias: Performance bias due to open label trials.

References

1. Venekamp RP, Burton MJ, van Dongen TM, van der Heijden GJ, van Zon A, Schilder AG. Antibiotics for otitis media with effusion in children. The Cochrane database of systematic reviews. 2016(6):Cd009163. Epub 2016/06/13. doi: 10.1002/14651858.CD009163.pub3. PubMed PMID: 27290722