Summary of findings:

1. Multivalent pneumococcal conjugate vaccines compared to placebo / other vaccine / no treatment for prevention of acute otitis media

**Patient or population:** Children aged 0-7 years.

**Setting:** Primary health care.

**Intervention:** Multivalent pneumococcal conjugate vaccines – 2 & 3 doses.

**Comparison:** Placebo / Other vaccine / No treatment.

<table>
<thead>
<tr>
<th>Outcome</th>
<th>Nr of participants (studies)</th>
<th>Relative effect (95% CI)</th>
<th>Anticipated absolute effects (95% CI)</th>
<th>Quality</th>
<th>What happens</th>
</tr>
</thead>
<tbody>
<tr>
<td>Risk of all-cause AOM (PCV 7 and PCV 10) assessed with: signs and symptoms of AOM and otoscopy follow up: range 2 to 2.75 years Nr of participants: 9258 (3 RCTs)</td>
<td>RR 0.93 (0.86 to 1.00)</td>
<td>22.3%</td>
<td>20.7% (19.2 to 22.3)</td>
<td>HIGH</td>
<td>In children vaccinated with PCV compared to no PCV there is less all cause AOM at ~2 years follow-up. NNV ~63</td>
</tr>
<tr>
<td>Risk of pneumococcal AOM (PCV 7 and PCV10) assessed with: signs and symptoms of AOM and otoscopy follow up: range 2.6 to 2.75 years Nr of participants: 7581 (2 RCTs)</td>
<td>RR 0.57 (0.39 to 0.83)</td>
<td>2.0%</td>
<td>1.1% (0.8 to 1.7)</td>
<td>HIGH</td>
<td>In children vaccinated with PCV compared to no PCV vaccine there is less pneumococcal AOM at ~2 years follow-up. NNV ~111</td>
</tr>
<tr>
<td>Risk of vaccine-specific AOM (PCV7, PCV10 and PCV 11) assessed with: signs and symptoms of AOM and otoscopy follow up: range 6 months to 2.75 years Nr of participants: 52079 (5 RCTs)</td>
<td>RR 0.51 (0.43 to 0.60)</td>
<td>1.5%</td>
<td>0.8% (0.6 to 0.9)</td>
<td>HIGH</td>
<td>In children vaccinated with PCV compared to no PCV vaccine there is less vaccine serotype pneumococcal AOM at ~2 years follow-up. NNV ~143</td>
</tr>
<tr>
<td>Risk of recurrent AOM (PCV7) assessed with: signs and symptoms of AOM and otoscopy follow up: 2 years Nr of participants: 1758 (2 RCTs)</td>
<td>RR 0.87 (0.72 to 1.05)</td>
<td>23.0%</td>
<td>20.0% (16.6 to 24.2)</td>
<td>MODERATE</td>
<td>In children vaccinated with PCV 7 compared to no PCV vaccine there are probably no fewer recurrent AOM episodes at 2 years follow-up. NNV Not Applicable</td>
</tr>
</tbody>
</table>
Summary of findings:

1. Multivalent pneumococcal conjugate vaccines compared to placebo / other vaccine / no treatment for prevention of acute otitis media

Patient or population: Children aged 0-7 years.

Setting: Primary health care.

Intervention: Multivalent pneumococcal conjugate vaccines – 2 & 3 doses.

Comparison: Placebo / Other vaccine / No treatment.

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<tbody>
<tr>
<td></td>
<td></td>
<td>Without multivalent pneumococcal conjugate vaccines</td>
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</tr>
<tr>
<td></td>
<td></td>
<td>With multivalent pneumococcal conjugate vaccines</td>
<td></td>
<td></td>
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<tr>
<td></td>
<td></td>
<td>Difference</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Insertion of tympanostomy tubes (PCV 7) follow up: range 2 years to 3.5 years</td>
<td>RR 0.80 (0.71 to 0.89)</td>
<td>3.1%</td>
<td>2.5% (2.2 to 2.8)</td>
<td>0.6% fewer (0.9 fewer to 0.3 fewer)</td>
</tr>
<tr>
<td>Outpatient antibiotic purchases (PCV 10) assessed with: national insurance register follow up: range 14 to 46 months</td>
<td>-</td>
<td>The mean outpatient antibiotic purchases was 1.55 purchases per person-year</td>
<td>-</td>
<td>MD 0.12 purchases per person-year fewer (0.01 fewer to 0.23 fewer)</td>
</tr>
</tbody>
</table>

*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; NNV: Number needed to vaccinate; MD: Mean difference

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

c. Inconsistency: Different vaccines used however low heterogeneity with pooled data.
d. Imprecision: Low event rate however large sample size.
f. Risk of Bias: Black 2000 stopped early for benefit, therefore high risk of over-estimation of effect. However in meta-analysis this trial only contributes 3% weight and removal does not effect estimate of effect. Not rated down.
h. Risk of bias: Lack of blinding. Parental threshold to consult ENT may be lower in children allocated to control treatment (no vaccination) than in those allocated to PCV, which may have introduced (detection) bias. Attrition bias (Gisselsson-Solen 2011).
k. Study: Palmu 2014

I. Indirectness: Data for indication not available for all purchases (indication only available for 52% purchases). Assumption made that certain specified antibiotics were prescribed for AOM. Secondary outcome.

References
# 2. Seasonal influenza vaccine compared to placebo / no treatment for prevention of acute otitis media

**Patient or population:** Children aged 6 months to 6 years of age.

**Setting:** Primary health care.

**Intervention:** Seasonal influenza vaccine [Studies used: Trivalent, Live, Cold Adapted Influenza Vaccine (CAIV-T) 1-2 doses for 1-2 years, Live Attenuated Influenza Vaccine (LAIV) intra-nasally 1-2 doses for 1-2 years, trivalent sub virion influenza virus vaccine 1-2 doses, CAIV 3 doses intra-nasally 60 days apart].

**Comparison:** Placebo / No treatment.

<table>
<thead>
<tr>
<th>Outcome No. of participants (studies)</th>
<th>Relative effect (95% CI)</th>
<th>Anticipated absolute effects (95% CI)</th>
<th>Quality</th>
<th>What happens</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>RR 0.80 (0.67 to 0.96)</td>
<td>26.4%</td>
<td>☢☢☢ MODERATE b,d</td>
<td>In children receiving seasonal influenza vaccine compared to placebo / no treatment there is probably less risk of OM during 6-18 months follow-up. NNV ~19</td>
</tr>
<tr>
<td>At least one episode of AOM assessed with: otoscopy +/- tympanometry follow up: range 6 to 18 months No of participants: 4736 (5 RCTs)</td>
<td>RR 1.15 (1.06 to 1.24)</td>
<td>17.4%</td>
<td>☢☢◯ MODERATE k</td>
<td>In children receiving seasonal influenza vaccine compared to placebo / no treatment there are probably more adverse events of fever. NNH ~39</td>
</tr>
<tr>
<td>AOM by season (respiratory and influenza season) assessed with: otoscopy +/- tympanometry follow up: median 6 months No of participants: 899 (2 RCTs)</td>
<td>RR 0.70 (0.59 to 0.83)</td>
<td>36.2%</td>
<td>☢☢◯ MODERATE e</td>
<td>In children receiving seasonal influenza vaccine compared to placebo / no treatment there is probably fewer antibiotic courses over 6-12 months follow-up. NNV ~10</td>
</tr>
</tbody>
</table>

### Notes:

- NNV = Number Needed to Vaccinate
- NNH = Number Needed to Harm

---

**Courses of antibiotics assessed with: number antibiotic prescriptions. follow up: range 6 to 12 months No of participants: 1223 (2 RCTs) **
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; NNV: Number needed to vaccinate; MD: Mean difference

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

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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

b. Risk of bias: Clements 1995 was a prospective cohort study where participants were not blinded, however outcome assessor blinded. Not rated down.
c. Inconsistency: High heterogeneity noted however estimate of effect in same direction.
d. Indirectness: Difference formulations and routes of vaccination given. Trivalent cold-adapted inactivated vaccine (CAIV), trivalent inactivated vaccines used in difference studies, given intramuscularly and intranasally. Not considered to have significant effect on results, therefore not rated down.
f. Inconsistency: Two trials with effect estimates in opposite directions. High heterogeneity precluded meta-analysis.
g. Imprecision: Optimal information size not reached.
i. Risk of Bias: Attrition bias in 2 studies (Swierkosz 1994, Bracco 2009)

References

### Summary of findings:

#### 3 Relative effect for association: breastfeeding compared to other feeding for prevention of otitis media

**Patient or population:** Children aged 0 to 8 years.

**Setting:** Community / Primary health care.

**Intervention:** Breastfeeding. Duration varied from 6 months to 8 years.

**Comparison:** Other feeding.

<table>
<thead>
<tr>
<th>Outcome</th>
<th>Nr of participants (studies)</th>
<th>Relative effect (95% CI)</th>
<th>Anticipated absolute effects (95% CI)</th>
<th>Quality</th>
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</tr>
</thead>
<tbody>
<tr>
<td></td>
<td></td>
<td></td>
<td>Without Breastfeeding / Never / “Less” Breastfeeding</td>
<td>With Breastfeeding / Ever / “More” Breastfeeding</td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td>Difference</td>
<td></td>
</tr>
<tr>
<td>Annual incidence rate of AOM episodes in the first two years of life - exclusive breastfeeding compared with nonexclusive breastfeeding for the first 6 months of life. assessed with: physician/doctor diagnosed AOM, parent/self-reported AOM, or AOM recorded on health-related databases. follow up: median 2 years</td>
<td>17735 (5 observational studies)</td>
<td>OR 0.57 (0.44 to 0.75)</td>
<td>No raw data available</td>
<td>🅸🥿🥿🥿 VERY LOW b,c</td>
<td>In children exclusively breastfed for first 6 months of life compared nonexclusive breastfeeding there are possibly fewer AOM episodes in first 2 years of life.</td>
</tr>
<tr>
<td>Annual incidence rate of AOM episodes in first two years of life - ever breast fed compared no never breast fed over those two years assessed with: physician/doctor diagnosed AOM, parent/self-reported AOM, or AOM recorded on health-related databases. follow up: median 2 years</td>
<td>19650 (5 observational studies)</td>
<td>OR 0.67 (0.56 to 0.80)</td>
<td>No raw data available</td>
<td>🅸🥿🥿🥿 VERY LOW b,c</td>
<td>In children breastfed compared to other feeding there are possibly fewer AOM episodes in first 2 years of life.</td>
</tr>
</tbody>
</table>
Summary of findings:

3 Relative effect for association: breastfeeding compared to other feeding for prevention of otitis media

Patient or population: Children aged 0 to 8 years.

Setting: Community / Primary health care.

Intervention: Breastfeeding. Duration varied from 6 months to 8 years.

Comparison: Other feeding.

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<tr>
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</tr>
</thead>
<tbody>
<tr>
<td>Annual incidence rate of AOM episodes in first two years of life: &quot;more&quot; versus &quot;less&quot; breastfeeding assessed with: physician/doctor diagnosed AOM, parent/self-reported AOM, or AOM recorded on health-related databases. follow up: median 2 years Ne of participants: 39380 (12 observational studies) 1,4</td>
<td>OR 0.67 (0.59 to 0.76)</td>
<td>No raw data available</td>
<td>☯◯◯◯ VERY LOW h</td>
<td>In children breastfed &quot;more&quot; compared to &quot;less&quot; there are possibly fewer AOM episodes in first 2 years of life. NNT not evaluable</td>
</tr>
<tr>
<td>Risk of AOM beyond two years of age: &quot;more&quot; versus &quot;less&quot; breastfeeding assessed with: physician/doctor diagnosed AOM, parent/self-reported AOM, or AOM recorded on health-related databases. follow up: range 2 to 8 years Ne of participants: 3943 (7 observational studies) 1,2</td>
<td>OR 1.03 (0.59 to 1.79)</td>
<td>No raw data available</td>
<td>☯◯◯◯ VERY LOW hh</td>
<td>In children breastfed &quot;more&quot; compared to &quot;less&quot; there is possibly no difference in long term outcomes of AOM. NNT not evaluable</td>
</tr>
</tbody>
</table>

*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

GRADE Working Group grades of evidence

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Explanations


b. Risk of Bias: Recall bias; some studies had mailed questionnaires which may lead to mis-classification of disease process.

c. Inconsistency: High heterogeneity noted with complete data.


f. Inconsistency: High heterogeneity noted with complete data.


h. Inconsistency: High heterogeneity

References

Summary of findings:

4. Hygiene promotion programs compared to no intervention for prevention of acute otitis media

Patient or population: Children with mean age of 3.5 years.

Setting: Primary health care / Community Day Care Centres.

Intervention: Hygiene promotion programs - The infection prevention program consisted of intensified handwashing, the use of an alcohol-based oily disinfectant, directions on the use of disposable towels, cleaning of the child-care centres and regular washing of the toys so that they were taken out of use for at least every other week. One healthy adult person always served food and tooth brushing was withdrawn. Attention was paid to diaper changing practices and the places where this was done. The personnel were encouraged to take sick leave at first appearance of symptoms (exact procedures and instructions given to the personnel are available on request). Duration was over 15 months.

Comparison: No intervention

<table>
<thead>
<tr>
<th>Outcome</th>
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<th>What happens</th>
</tr>
</thead>
<tbody>
<tr>
<td>Mean number of days with ear ache (symptom) per person year at risk &lt; 3 years of age assessed with: parental report follow up: median 8 months</td>
<td>-</td>
<td>The mean number of days with ear ache (symptom) per person year at risk &lt; 3 years of age was 6.8 per person year</td>
<td>MD 1.9 per person year fewer (1.43 fewer to 2.3 fewer)</td>
<td>LOW</td>
</tr>
<tr>
<td>Mean number of days with ear ache (symptom) per person year at risk &gt; 3 years of age assessed with: parental report follow up: median 8 months</td>
<td>-</td>
<td>The mean number of days with ear ache (symptom) per person year at risk &gt; 3 years of age was 2 per person year</td>
<td>MD 0.6 per person year fewer (0.5 fewer to 0.9 fewer)</td>
<td>LOW</td>
</tr>
</tbody>
</table>
Summary of findings:

4. Hygiene promotion programs compared to no intervention for prevention of acute otitis media

**Patient or population:** Children with mean age of 3.5 years.

**Setting:** Primary health care / Community Day Care Centres.

**Intervention:** Hygiene promotion programs - The infection prevention program consisted of intensified handwashing, the use of an alcohol-based oïlydisinfectant, directions on the use of disposable towels, cleaning of the child-care centres and regular washing of the toys, or if that was not possible, circulation of the toys so that they were taken out of use for at least every other week. One healthy adult person always served food and tooth brushing was withdrawn. Attention was paid to diaper changing practices and the places where this was done. The personnel were encouraged to take sick leave at first appearance of symptoms (exact procedures and instructions given to the personnel are available on request). Duration was over 15 months.

**Comparison:** No intervention

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</tr>
</thead>
<tbody>
<tr>
<td>Mean number of days with ear ache (infectious episode separated by at least 3 symptom free days) per person year at risk &lt;3 years of age assessed with: parental report follow up: median 8 months Ne of participants: 661 (1 RCT)</td>
<td>-</td>
<td>The mean number of days with ear ache (infectious episode separated by at least 3 symptom free days) per person year at risk &lt;3 years of age was 2 per person year</td>
<td>MD 0.4 per person year fewer (0.2 fewer to 0.7 fewer)</td>
<td>⬤ ⬤ ⬤ ⬤ LOW ⬤ ⬤</td>
</tr>
<tr>
<td>Mean number of days with ear ache (infectious episode separated by at least 3 symptom free days) per person year at risk &gt;3 years of age assessed with: parental report follow up: median 8 months Ne of participants: 861 (1 RCT)</td>
<td>-</td>
<td>The mean number of days with ear ache (infectious episode separated by at least 3 symptom free days) per person year at risk &gt;3 years of age was 0.7 per person year</td>
<td>MD 0.1 per person year fewer (0.02 fewer to 0.29 fewer)</td>
<td>⬤ ⬤ ⬤ ⬤ LOW ⬤ ⬤</td>
</tr>
</tbody>
</table>
Summary of findings:

4. Hygiene promotion programs compared to no intervention for prevention of acute otitis media

**Patient or population:** Children with mean age of 3.5 years.

**Setting:** Primary health care / Community Day Care Centres.

**Intervention:** Hygiene promotion programs - The infection prevention program consisted of intensified handwashing, the use of an alcohol-based oïlydisinfectant, directions on the use of disposable towels, cleaning of the child-care centres and regular washing of the toys, or if that was not possible, circulation of the toys so that they were taken out of use for at least every other week. One healthy adult person always served food and tooth brushing was withdrawn. Attention was paid to diaper changing practices and the places where this was done. The personnel were encouraged to take sick leave at first appearance of symptoms (exact procedures and instructions given to the personnel are available on request). Duration was over 15 months.

**Comparison:** No intervention

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<tr>
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</tr>
</thead>
<tbody>
<tr>
<td>Mean number of visits to a doctor because of an attack of acute otitis media (all ages) assessed with: parental report follow up: median 8 months</td>
<td>-</td>
<td>The mean number of visits to a doctor because of an attack of acute otitis media (all ages) was 1.5 visits/child/year</td>
<td>-</td>
<td>MD 0.4 visits/child/year fewer</td>
</tr>
</tbody>
</table>

*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

**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. Study: Uhari 1999
b. Risk of Bias: Noted that open label, however complete blinding difficult in study circumstances. Not rated down.
c. Indirectness: Otitis media not primary outcome. Only children in daycare centres studied. Ear ache used as a surrogate for middle ear disease.
d. Indirectness: Diagnostic criteria for otitis media not standardised (by parental report).

**References**

Summary of findings:

5. Relative effect for association: Parental counselling to restrict pacifier/dummy use compared to unrestricted pacifier/dummy use for prevention of acute otitis media

**Patient or population:** Children aged 0 to 7.24 years of age.

**Setting:** Primary health care / Day-care centres / Community.

**Intervention:** Parental counselling to restrict pacifier/dummy use (limit to moments of falling asleep after 6 months and discontinue use after 10 months of age). Single counselling session was provided.

**Comparison:** Unrestricted pacifier/dummy use.

<table>
<thead>
<tr>
<th>Outcome</th>
<th>Relative effect (95% CI)</th>
<th>Anticipated absolute effects (95% CI)</th>
<th>Quality</th>
<th>What happens</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td></td>
<td>Without Parental counselling to restrict pacifier/dummy use</td>
<td>With Parental counselling to restrict pacifier/dummy use</td>
<td>Difference</td>
</tr>
<tr>
<td>AOM per person-months at risk assessed with: parental report follow up: median 4.6 months Nr of participants: 484 (1 RCT) 1,8</td>
<td>Study in Finland found that with parental counselling against pacifier use there was a 29% lower occurrence of AOM/PMR in the intervention group. In the total series the occurrence of AOM/PMR was 33% higher in the group of children who used pacifier continuously than in those not using one or using it when falling asleep. 1,8</td>
<td>RR 0.49 (0.36 to 0.68) 21.6%</td>
<td>10.6% (7.8 to 14.7)</td>
<td>11.0% fewer (13.8 fewer to 6.9 fewer)</td>
</tr>
</tbody>
</table>

**Risk of rAOM (>3 episodes of AOM) assessed with: physician diagnosed AOM follow up: range 10 months to 5.6 years Nr of participants: 884 (2 observational studies) 2,3,7**

<table>
<thead>
<tr>
<th>Relative effect (95% CI)</th>
<th>Anticipated absolute effects (95% CI)</th>
<th>Quality</th>
<th>What happens</th>
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<tbody>
<tr>
<td>RR 0.49 (0.36 to 0.68)</td>
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<td>11.0% fewer (13.8 fewer to 6.9 fewer)</td>
</tr>
</tbody>
</table>

*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

**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. Study: Niemela 2000
b. Raw data not reported.
c. Risk of Bias: Nature of intervention makes blinding difficult.
d. Indirectness: Diagnosis of AOM was not made according predefined criteria or by trained staff but during routine visits to health care centres or private practices.
e. Imprecision: Single, small study
f. Studies: Rovers 2008 and Niemela 1995
g. Inconsistency: Pacifier use only measured at baseline in Rovers 2008. Diagnosis of AOM made by different physicians with differing pre-defined criteria. Short term follow-up in Niemela 1995 (median 10 months).
h. Imprecision: Optimal information size not reached.
i. Possible confounding: All children in Niemela 1995 attended daycare centres - not adjusted.

References
Summary of findings:

6. Relative effect of association: household tobacco smoke exposure compared to no household tobacco smoke exposure for prevention of acute otitis media

**Patient or population:** Children aged 0 to 18 years

**Setting:** Community / Primary health care.

**Intervention:** Household tobacco smoke exposure. Duration ranged from 6 months to 10 years.

**Comparison:** No household tobacco smoke exposure.

<table>
<thead>
<tr>
<th>Outcome</th>
<th>Relative effect (95% CI)</th>
<th>Anticipated absolute effects (95% CI)</th>
<th>Quality</th>
<th>What happens</th>
</tr>
</thead>
</table>
| Risk of middle ear infection (includes AOM, OME, recurrent otitis media, chronic otitis media) with any household member smoking assessed with: parental report / health record review follow up: median 2 years (37 observational studies) | OR 1.32 (1.20 to 1.45) | | | In children exposed to household smoking compared to no household smoking there is possibly an increased risk of OM during 2 years follow-up.
NNT not evaluable |
| Risk of middle ear infection (includes AOM, OME, recurrent otitis media, chronic otitis media) with postnatal maternal smoking assessed with: parental report / health record review follow up: range 6 months to 10 years (14 observational studies) | OR 1.53 (1.22 to 1.92) | | | In children exposed to postnatal maternal smoking compared to no smoking there is possibly an increased risk of OM between 6 months to 10 years of age.
NNT not evaluable |
### Summary of findings:

#### 6. Relative effect of association: household tobacco smoke exposure compared to no household tobacco smoke exposure for prevention of acute otitis media

**Patient or population:** Children aged 0 to 18 years

**Setting:** Community / Primary health care.

**Intervention:** Household tobacco smoke exposure. Duration ranged from 6 months to 10 years.

**Comparison:** No household tobacco smoke exposure.

<table>
<thead>
<tr>
<th>Outcome</th>
<th>Relative effect (95% CI)</th>
<th>Anticipated absolute effects (95% CI)</th>
<th>Quality</th>
<th>What happens</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td></td>
<td>Without household tobacco smoke exposure</td>
<td>With household tobacco smoke exposure</td>
<td>Difference</td>
</tr>
<tr>
<td>Risk of requiring surgery for middle ear disease with any household member smoking assessed with: parental report / health record review follow up: median 12 months (11 observational studies) ¹*</td>
<td>R 1.62 (1.31 to 1.98)</td>
<td></td>
<td>⚠️◯◯◯ VERY LOW ¹, ²</td>
<td>In children exposed to household smoking compared to no household smoking there is possibly an increased risk of requiring surgery for OM during 12 months follow-up.</td>
</tr>
<tr>
<td>Diagnosis of OM (AOM, OME, TM perforation with or without discharge) - observational study in Indigenous children, assessed with: ENT examination, otoscopy, pneumatic otoscopy and tympanometry follow up: median 12 months N° of participants: 80 (1 observational study)</td>
<td>OR 3.54 (1.68 to 7.47) ³</td>
<td>55.2% (67.4 to 90.2) ⁴</td>
<td>26.2% more (12.2 more to 35 more) ⚠️◯◯◯ VERY LOW ³</td>
<td>In Aboriginal children exposed to household tobacco smoke compared to no household tobacco smoke there are possibly more OM episodes at 12 months follow-up. NNT not evaluable</td>
</tr>
</tbody>
</table>
Summary of findings:

6. Relative effect of association: household tobacco smoke exposure compared to no household tobacco smoke exposure for prevention of acute otitis media

Patient or population: Children aged 0 to 18 years

Setting: Community / Primary health care.

Intervention: Household tobacco smoke exposure. Duration ranged from 6 months to 10 years.

Comparison: No household tobacco smoke exposure.

<table>
<thead>
<tr>
<th>Outcome No. of participants (studies)</th>
<th>Relative effect (95% CI)</th>
<th>Anticipated absolute effects (95% CI)</th>
<th>Quality</th>
<th>What happens</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td></td>
<td>Without household tobacco smoke exposure</td>
<td>With household tobacco smoke exposure</td>
<td>Difference</td>
</tr>
<tr>
<td>Post-operative tympanostomy tube otorrhoea with household smoking assessed with: parental report follow up: mean 323 days N of participants: 191 (1 observational study)</td>
<td>OR 2.310 (1.734 to 6.028)</td>
<td>45.3%</td>
<td>65.7% (58.9 to 83.3)</td>
<td>20.4% more (13.6 more to 38 more)</td>
</tr>
</tbody>
</table>

*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).

OR: Odds ratio; CI: Confidence interval; RR: Risk ratio; NS: Not significant; NNT: Number needed to treat; NNH: Number needed to harm

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
- b. Risk of Bias: Recall bias in some studies as AOM is by parental report.
f. Study: Jacoby 2008
h. Risk of Bias: Risk of reporter bias as tobacco smoke exposure recorded as per carer report.
i. Imprecision: Small, single study
j. Study: Bizzell 2017
k. Risk of Bias: Risk of recall bias as outcome based on parental report.
l. Imprecision: Small, single study.

References
Summary of findings:

7 Second-hand smoke prevention program compared to no intervention for prevention of acute otitis media

**Patient or population:** Australian Aboriginal and Maori children aged 4 to 12 months of age.

**Setting:** Community / Primary health care.

**Intervention:** Second-hand smoke (SHS) prevention program – three “behavioural coaching” face-to-face sessions for 3 months.

**Comparison:** No intervention.

<table>
<thead>
<tr>
<th>Outcome</th>
<th>Relative effect (95% CI)</th>
<th>Anticipated absolute effects (95% CI)</th>
<th>Quality</th>
<th>What happens</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td></td>
<td>Without intervention</td>
<td>With SHS prevention program</td>
<td>Difference</td>
</tr>
<tr>
<td>New episodes of otitis media assessed with: parental report and clinician review of medical record follow up: median 12 months</td>
<td>RR 1.13 (0.74 to 1.73)</td>
<td>64.2%</td>
<td>72.5% (47.5 to 100.0)</td>
<td>8.3% more (NS) (16.7 fewer to 46.9 more)</td>
</tr>
</tbody>
</table>

*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; SHS: Second Hand Smoke

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**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

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**Explanations**

a. Study: Walker 2015
b. Risk of Bias: Participants not blinded to intervention. Outcome assessors blinded.
c. Imprecision: Small, single study

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**References**

Summary of findings:

8. Probiotics compared to placebo for prevention of acute otitis media

Patient or population: Children aged 0 to 18 years.

Setting: Community / Primary health care.

Intervention: Probiotics (Studies used: Lactobacillus rhamnosus GG, multi-probiotic formula, Bifidobacterium animalis subsp. lactis BB-12). Duration varied from 3 to 12 months.

Comparison: Placebo.

<table>
<thead>
<tr>
<th>Outcome</th>
<th>Relative effect (95% CI)</th>
<th>Anticipated absolute effects (95% CI)</th>
<th>Quality</th>
<th>What happens</th>
</tr>
</thead>
<tbody>
<tr>
<td>Incidence of AOM during treatment with probiotics (Lactobacillus rhamnosus GG) assessed with: physician diagnosed AOM follow up: range 3 to 12 months</td>
<td>RR 0.76 (0.64 to 0.91)</td>
<td>24.4% 18.5% (15.6 to 22.2) 5.9% fewer (8.8 fewer to 2.2 fewer)</td>
<td>LOW i</td>
<td>In children receiving probiotics (LGG) compared to placebo there is possibly fewer episodes of AOM at 3-12 months follow-up. NNT –17</td>
</tr>
<tr>
<td>≥1 episodes of AOM during treatment with multi-probiotic formula in children aged 7-13 months at high risk of AOM assessed with: physician assessment follow up: median 1 year</td>
<td>RR 1.0 (0.8 to 1.2)</td>
<td>71.4% 71.4% (57.1 to 85.7) 0.0% fewer (NS) (14.3 fewer to 14.3 more)</td>
<td>LOW i</td>
<td>In children 7-13 months at high risk of AOM receiving probiotics (multi-probiotic formula) compared to placebo there is possibly no difference in AOM episodes during 1 year follow-up. NNT Not Applicable</td>
</tr>
<tr>
<td>Episodes of AOM (any) during treatment with Bifidobacterium animalis subsp. lactis BB-12 in well infants from 1 month of age assessed with: parental report of doctor diagnosed AOM follow up: median 8 months</td>
<td>RR 1.54 (0.62 to 3.87)</td>
<td>17.1% 26.4% (10.6 to 66.3) 9.3% more (NS) (6.5 fewer to 49.2 more)</td>
<td>VERY LOW h</td>
<td>In infants receiving probiotics (BB-12) compared to placebo there is possibly no reduction in AOM episodes during 8 months follow-up. NNT Not Applicable</td>
</tr>
</tbody>
</table>
### 8. Probiotics compared to placebo for prevention of acute otitis media

**Patient or population:** Children aged 0 to 18 years.

**Setting:** Community / Primary health care.

**Intervention:** Probiotics (Studies used: Lactobacillus rhamnosus GG, multi-probiotic formula, Bifidobacterium animalis subsp. lactis BB-12). Duration varied from 3 to 12 months.

**Comparison:** Placebo.

<table>
<thead>
<tr>
<th>Outcome (Nr of participants (studies))</th>
<th>Relative effect (95% CI)</th>
<th>Anticipated absolute effects (95% CI)</th>
<th>Quality</th>
<th>What happens</th>
</tr>
</thead>
<tbody>
<tr>
<td>Adverse events (gastrointestinal and dermatological) follow up: range 3 to 12 months</td>
<td>RR 0.88 (0.52 to 1.47)</td>
<td>Without probiotics: 24.2%</td>
<td>With probiotics: 21.3% (12.6 to 35.6)</td>
<td>⫷⫷⫷⫷  LOW</td>
</tr>
</tbody>
</table>

*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

**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 the effect

**Explanations**

- b. Indirectness: Differences in probiotic composition (however all contained Lactobacillus rhamnosus GG), Differences in regimens used. Poor definition of outcome measures between studies. However estimate if effect similar amongst studies. Not rated down.
- c. Imprecision: Optimal information size not reached. Low event rate with many studies reporting no adverse events.
- d. Defined as high risk if exposed to other children (day-care center attendance or with 2 siblings) and those with history of at least 1 episode of AOM before the current one.
- e. Study: Cohen 2013
- g. Study: Taipale 2011
- h. Risk of Bias: Recall bias
- i. Imprecision: Small single trial. Broad estimate of effect.
- j. Several other studies reported no differences in adverse events between probiotics and control groups however raw data not available.

**References**

Summary of findings:

9. Vitamin D supplementation compared to placebo for prevention of acute otitis media

Patient or population: Children aged 1 to 5 years who are otitis prone (defined as at least 3 episodes of AOM in the preceding 6 months or at least 4 episodes in the preceding 12 months, with the most recent episode in the previous 2–6 weeks)

Setting: Primary health care.

Intervention: Vitamin D supplementation (1000 IU per day of Vitamin D₃). Duration was for 4 months.

Comparison: Placebo.

<table>
<thead>
<tr>
<th>Outcome</th>
<th>Relative effect (95% CI)</th>
<th>Anticipated absolute effects (95% CI)</th>
<th>Quality</th>
<th>What happens</th>
</tr>
</thead>
<tbody>
<tr>
<td>&gt;1 AOM episode (includes AOMwP and AOMwoP) assessed with: fever, earache, irritability and otoscopy +/- tympanometry follow up: range 1 to 6 months</td>
<td>RR 0.68 (0.49 to 0.96)</td>
<td>65.5% (32.1 to 62.9)</td>
<td>21.0% fewer (33.4 fewer to 2.6 fewer)</td>
<td>LOW</td>
</tr>
<tr>
<td>&gt;1 episode of AOMwoP assessed with: fever, earache, irritability and otoscopy +/- tympanometry follow up: range 1 to 6 months</td>
<td>RR 0.34 (0.19 to 0.64)</td>
<td>50.0% (9.5 to 32.0)</td>
<td>33.0% fewer (40.5 fewer to 18 fewer)</td>
<td>LOW</td>
</tr>
<tr>
<td>Adverse Events (reported as “significant”, not defined)</td>
<td>not estimable</td>
<td>0.0% (0.0 to 0.0)</td>
<td>0.0% fewer (0 fewer to 0 fewer)</td>
<td>LOW</td>
</tr>
</tbody>
</table>

*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).*

Ct: Confidence interval; RR: Risk ratio; NS: Not significant; NNT: Number needed to treat; NNH: Number needed to harm; MD: Mean difference

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. Study: Marchisio 2013
b. Indirectness: Children studied during European winter (may not be applicable to warmer environments). Only children with rAOM studied.
c. Imprecision: Single, small study

References
Summary of findings:

10 Xylitol (administered as syrup, gum or lozenge) compared to placebo for prevention of acute otitis media

Patient or population: Children aged 6 months to 7 years.

Setting: Primary health care.

Intervention: Xylitol administered as syrup, gum or lozenge. (Studies used doses 5-10 grams per day, in 3-5 divided doses). Duration was for 2-3 months.

Comparison: Placebo.

<table>
<thead>
<tr>
<th>Outcome</th>
<th>Relative effect (95% CI)</th>
<th>Anticipated absolute effects (95% CI)</th>
<th>Quality</th>
<th>What happens</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td></td>
<td>Without xylitol (administered as syrup, gum or lozenge)</td>
<td>With xylitol (administered as syrup, gum or lozenge)</td>
<td>Difference</td>
</tr>
<tr>
<td>Final diagnosis of at least one episode of AOM assessed with: otoscopy / pneumatic otoscopy +/- tympanometry + signs / symptoms of AOM follow up: range 2 to 3 months</td>
<td>RR 0.75 (0.65 to 0.88)</td>
<td>29.9%</td>
<td>22.4% (19.4 to 26.3)</td>
<td>7.5% fewer (10.5 fewer to 3.6 fewer)</td>
</tr>
<tr>
<td>Final diagnosis of at least one episode of AOM - during respiratory infection assessed with: tympanometry + pneumatic otoscopy follow up: median 3 weeks</td>
<td>RR 1.13 (0.83 to 1.53)</td>
<td>11.5%</td>
<td>13.0% (9.5 to 17.6)</td>
<td>1.5% more (NS) (2 fewer to 6.1 more)</td>
</tr>
<tr>
<td>Final diagnosis of at least one episode of AOM - Otitis-prone children assessed with: physician diagnosed AOM on medical record and/or parental report follow up: median 3 months</td>
<td>RR 0.90 (0.67 to 1.21)</td>
<td>36.7%</td>
<td>33.1% (24.6 to 44.5)</td>
<td>3.7% fewer (NS) (12.1 fewer to 7.7 more)</td>
</tr>
</tbody>
</table>
10 Xylitol (administered as syrup, gum or lozenge) compared to placebo for prevention of acute otitis media

**Patient or population:** Children aged 6 months to 7 years.

**Setting:** Primary health care.

**Intervention:** Xylitol administered as syrup, gum or lozenge. (Studies used doses 5-10 grams per day, in 3-5 divided doses). Duration was for 2-3 months.

**Comparison:** Placebo.  

<table>
<thead>
<tr>
<th>Outcome (gastrointestinal related)</th>
<th>Relative effect (95% CI)</th>
<th>Anticipated absolute effects (95% CI)</th>
<th>Quality</th>
<th>What happens</th>
</tr>
</thead>
</table>
| Adverse events (gastrointestinal related) assessed with: parental report follow up: range 2 to 3 months | RR 1.43 (0.74 to 2.75) | Without xylitol (administered as syrup, gum or lozenge): 1.7%  
With xylitol (administered as syrup, gum or lozenge): 2.4% (1.3 to 4.7)  
Difference: 0.7% more (NS) (0.4 fewer to 3 more) | ☑️ ☑️ ☑️ MODERATE | In children receiving xylitol compared to placebo there is probably no more gastrointestinal-related adverse events at ~3 months follow-up. 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).

Ct: Confidence interval; RR: Risk ratio; NS: Not significant; NNT: Number needed to treat; NNH: Number needed to harm; MD: Mean difference

**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. Placebo was sucrose alternative (Uhari 1996), sorbitol (Vernacchio 2014) or low dose xylitol 0.5g (Uhari 1998, Hautalahti 2007, Tapiaienen 2002)  
c. Risk of Bias: Xylitol treatment syrup sweeter than control (so not truly blinded) but not considered sufficient to rate down.  
d. Inconsistency: High heterogeneity  
e. Indirectness: In one study mean age was 5 years and some children had already suffered AOM and undergone adenoidectomy. Not rated down.  
g. Indirectness: Xylitol syrup administered by parents once symptoms of respiratory tract infection occurred - this judgement was not standardised and parents may have different threshold for administration. Not rated down.  
h. Imprecision: Single study, optimal information size not reached. CI includes appreciable benefit and harm.  
i. Studies taken from: Cochrane Review, Azarpazhooh 2016 (Vernacchio 2014)  
j. Risk of Bias: Attrition bias.  
k. Indirectness: AOM diagnosed by different healthcare providers or by parental report (no consistency).  
l. Imprecision: 95% CIs are wide and imprecise. Moreover, there are few events and the CI includes appreciable benefit and harm.

**References**  
**11 Zinc supplementation compared to placebo for prevention of acute otitis media**

**Patient or population:** Children aged 0-31 months.

**Setting:** Primary health care.

**Intervention:** Zinc supplementation. (Studies used: 10-20mg elemental zinc daily) Duration was for 4-6 months.

**Comparison:** Placebo.

<table>
<thead>
<tr>
<th>Outcome</th>
<th>Nr of participants (studies)</th>
<th>Relative effect (95% CI)</th>
<th>Anticipated absolute effects (95% CI)</th>
<th>Quality</th>
<th>What happens</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td></td>
<td></td>
<td>Without Zinc supplementation</td>
<td>With Zinc supplementation</td>
<td>Difference</td>
</tr>
<tr>
<td>Any AOM assessed with: otoscopy +/- otorrhoea follow up: range 4 to 6 months Nr of participants: 3191 (2 RCTs)</td>
<td>RR 1.05 (0.82 to 1.36)</td>
<td>6.8%</td>
<td>7.2% (5.6 to 9.3)</td>
<td>0.3% more (NS) (1.2 fewer to 2.5 more)</td>
<td>MODERATE ‡‡</td>
</tr>
<tr>
<td>&gt;1 episode of definite otitis media assessed with: physician diagnosed AOM follow up: median 4 months Nr of participants: 2482 (1 RCT)</td>
<td>RR 1.08 (0.50 to 2.36)</td>
<td>1.0%</td>
<td>1.0% (0.5 to 2.3)</td>
<td>0.1% more (NS) (0.5 fewer to 1.3 more)</td>
<td>MODERATE ‡‡</td>
</tr>
<tr>
<td>Adverse events - discontinued supplement due to vomiting assessed with: parental report follow up: median 4 months Nr of participants: 2482 (1 RCT)</td>
<td>RR 17.00 (0.98 to 294.21)</td>
<td>0.0%</td>
<td>0.6% (0.0 to 0.0)</td>
<td>0.6% fewer (NS) (0 fewer to 0 fewer)</td>
<td>LOW ‡</td>
</tr>
<tr>
<td>Adverse events - Days with vomiting during intervention (per child for period of follow-up) assessed with: parental report follow up: median 4 months Nr of participants: 2482 (1 RCT)</td>
<td>1.7 days higher (1.31 higher to 2.09 higher)</td>
<td>Children receiving zinc supplements compared to placebo for prevention of AOM possibly experience more days with vomiting during 4 months follow up.</td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

*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.
Summary of findings:

### 11 Zinc supplementation compared to placebo for prevention of acute otitis media

**Patient or population:** Children aged 0-31 months.

**Setting:** Primary health care.

**Intervention:** Zinc supplementation. (Studies used: 10-20mg elemental zinc daily) Duration was for 4-6 months.

**Comparison:** Placebo.

<table>
<thead>
<tr>
<th>Outcome</th>
<th>Relative effect (95% CI)</th>
<th>Anticipated absolute effects (95% CI)</th>
<th>Quality</th>
<th>What happens</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Without Zinc supplementation</td>
<td>With Zinc supplementation</td>
<td>Difference</td>
<td></td>
</tr>
</tbody>
</table>

### 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

- c. Imprecision: Optimal information size not reached, small event rates
- d. Studies taken from: Cochrane Review, Gulani 2012 (Bhandari 2002)
- e. Imprecision: Wide estimate of effect

### References

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 amoxicillin/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.

<table>
<thead>
<tr>
<th>Outcome</th>
<th>Relative effect (95% CI)</th>
<th>Anticipated absolute effects (95% CI)</th>
<th>Quality</th>
<th>What happens</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Hearing outcomes assessed with:</strong> pure tone average and speech reception threshold follow up: range 2 to 4 weeks</td>
<td></td>
<td></td>
<td></td>
<td><strong>VERY LOW</strong></td>
</tr>
<tr>
<td><strong>Without antibiotics</strong></td>
<td><strong>With antibiotics</strong></td>
<td><strong>Difference</strong></td>
<td></td>
<td><strong>NNT Not Applicable</strong></td>
</tr>
<tr>
<td><strong>Number of participants (studies):</strong> 784 (2 RCTs)</td>
<td><strong>Number of participants:</strong> 784 (2 RCTs)</td>
<td><strong>Number of participants:</strong> 784 (2 RCTs)</td>
<td></td>
<td><strong>Number of participants:</strong> 784 (2 RCTs)</td>
</tr>
<tr>
<td><strong>RR 2.00</strong></td>
<td><strong>24.7%</strong></td>
<td><strong>49.3%</strong></td>
<td><strong>24.7% more</strong></td>
<td></td>
</tr>
<tr>
<td><strong>(1.58 to 2.53)</strong></td>
<td><strong>(39.0 to 62.4)</strong></td>
<td><strong>(14.3 more to 37.7 more)</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>Complete resolution of OME assessed with:</strong> tympanometry +/- pneumatic otoscopy follow up: range 2 to 3 months</td>
<td></td>
<td></td>
<td></td>
<td><strong>LOW</strong></td>
</tr>
<tr>
<td><strong>Number of participants (studies):</strong> 484 (6 RCTs)</td>
<td><strong>Number of participants:</strong> 484 (6 RCTs)</td>
<td><strong>Number of participants:</strong> 484 (6 RCTs)</td>
<td></td>
<td><strong>Number of participants:</strong> 484 (6 RCTs)</td>
</tr>
<tr>
<td><strong>RR 1.75</strong></td>
<td><strong>25.5%</strong></td>
<td><strong>44.5%</strong></td>
<td><strong>19.1% more</strong></td>
<td></td>
</tr>
<tr>
<td><strong>(1.41 to 2.18)</strong></td>
<td><strong>(35.9 to 55.5)</strong></td>
<td><strong>(10.4 more to 30 more)</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>Complete resolution of OME (long term) assessed with:</strong> tympanometry +/- pneumatic otoscopy follow up: median 6 months</td>
<td></td>
<td></td>
<td></td>
<td><strong>LOW</strong></td>
</tr>
<tr>
<td><strong>Number of participants (studies):</strong> 606 (5 RCTs)</td>
<td><strong>Number of participants:</strong> 606 (5 RCTs)</td>
<td><strong>Number of participants:</strong> 606 (5 RCTs)</td>
<td></td>
<td><strong>Number of participants:</strong> 606 (5 RCTs)</td>
</tr>
<tr>
<td><strong>RR 2.15</strong></td>
<td><strong>4.5%</strong></td>
<td><strong>9.7%</strong></td>
<td><strong>5.2% more</strong></td>
<td></td>
</tr>
<tr>
<td><strong>(1.29 to 3.60)</strong></td>
<td><strong>(5.8 to 16.2)</strong></td>
<td><strong>(1.3 more to 11.7 more)</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>Adverse effects</strong> (diarrhoea, vomiting or skin rash) follow up: range 2 to 8 weeks</td>
<td></td>
<td></td>
<td></td>
<td><strong>LOW</strong></td>
</tr>
<tr>
<td><strong>Number of participants (studies):</strong> 742 (5 RCTs)</td>
<td><strong>Number of participants:</strong> 742 (5 RCTs)</td>
<td><strong>Number of participants:</strong> 742 (5 RCTs)</td>
<td></td>
<td><strong>Number of participants:</strong> 742 (5 RCTs)</td>
</tr>
<tr>
<td><strong>RR 0.42</strong></td>
<td><strong>27.5%</strong></td>
<td><strong>11.5%</strong></td>
<td><strong>15.9% fewer</strong></td>
<td></td>
</tr>
<tr>
<td><strong>(0.18 to 1.01)</strong></td>
<td><strong>(4.9 to 27.7)</strong></td>
<td><strong>(NS)</strong></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

**Typanic membrane perforation assessed with:** pneumatic otoscopy + tympanometry follow up: median 6 months | | | | **LOW** |
| **Number of participants (studies):** 103 (1 RCT) | **Number of participants:** 103 (1 RCT) | | | **Number of participants:** 103 (1 RCT) |
| **RR 0.42** | **27.5%** | **11.5%** | **15.9% fewer** | | **LOW** |
| **(0.18 to 1.01)** | **(4.9 to 27.7)** | **(NS)** | | | |

In Aboriginal children with OME treated with antibiotics compared to placebo there is possibly a reduction in tympanic membrane perforation during therapy.
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 amoxicillin/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.

<table>
<thead>
<tr>
<th>Outcome</th>
<th>Relative effect (95% CI)</th>
<th>Anticipated absolute effects (95% CI)</th>
<th>Quality</th>
<th>What happens</th>
</tr>
</thead>
<tbody>
<tr>
<td>Insertion of tympanostomy tubes follow up: range 3 to 6 months</td>
<td>RR 0.90 (0.46 to 1.78)</td>
<td>18.5%</td>
<td>16.7% (8.5 to 33.0)</td>
<td>1.9% fewer (NS) (10 fewer to 14.4 more)</td>
</tr>
</tbody>
</table>

*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).

**Ct:** 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**

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
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)
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.
q. Risk of bias: Performance bias due to open label trials.

**References**

Summary of findings:

13. Tympanostomy tubes compared to no surgical intervention for otitis media with effusion

**Patient or population:** Children aged 6 months to 12 years with otitis media with effusion.

**Setting:** Hospital.

**Intervention:** Tympanostomy tubes (TTs) (Teflon biflanged, Donaldson and Bevel Bobbins ventilation tubes).

**Comparison:** No surgical intervention

<table>
<thead>
<tr>
<th>Outcome</th>
<th>Ne of participants (studies)</th>
<th>Relative effect (95% CI)</th>
<th>Anticipated absolute effects (95% CI)</th>
<th>Quality</th>
<th>What happens</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td></td>
<td>Without Tympanostomy tubes</td>
<td>With Tympanostomy tubes</td>
<td>Difference</td>
<td></td>
</tr>
<tr>
<td>By child hearing level assessed with: Binaural mean hearing level on pure tone audiometry 500-4000Hz follow up: median 3 months Ne of participants: 215 (1 RCT)</td>
<td>-</td>
<td>The mean by child hearing level was 26.3 dB HL</td>
<td>-</td>
<td><strong>MD 11.9 dB HL lower</strong> (9.6 lower to 14.2 lower)</td>
<td><img src="#" alt="MODERATE" /></td>
</tr>
<tr>
<td>By child hearing level assessed with: pure tone audiometry (500-4000Hz) or portable visual reinforcement audiometry follow up: range 6 to 9 months Ne of participants: 523 (3 RCTs)</td>
<td>-</td>
<td>The mean by child hearing level was 30.1 dB HL</td>
<td>-</td>
<td><strong>MD 4.2 dB HL lower</strong> (6 lower to 2.4 lower)</td>
<td><img src="#" alt="MODERATE" /></td>
</tr>
<tr>
<td>By child hearing level assessed with: pure tone audiometry (500-4000Hz) or portable visual reinforcement audiometry follow up: median 12 months Ne of participants: 328 (2 RCTs)</td>
<td>-</td>
<td>The mean by child hearing level was 27 dB HL</td>
<td>-</td>
<td><strong>MD 0.41 dB HL lower</strong> (NS) lower (2.37 lower to 1.54 higher)</td>
<td><img src="#" alt="MODERATE" /></td>
</tr>
</tbody>
</table>
Summary of findings:

### 13. Tympanostomy tubes compared to no surgical intervention for otitis media with effusion

**Patient or population:** Children aged 6 months to 12 years with otitis media with effusion.

**Setting:** Hospital.

**Intervention:** Tympanostomy tubes (TMs) (Teflon biflangeted, Donaldson and Bevel Bobbins ventilation tubes).

**Comparison:** No surgical intervention

<table>
<thead>
<tr>
<th>Outcome</th>
<th>Relative effect (95% CI)</th>
<th>Anticipated absolute effects (95% CI)</th>
<th>Quality</th>
<th>What happens</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td></td>
<td>Without Tympanostomy tubes</td>
<td>With Tympanostomy tubes</td>
<td>Difference</td>
</tr>
<tr>
<td></td>
<td></td>
<td>SMD 0.09 higher (NS)</td>
<td>MD 0.03 SD higher (NS)</td>
<td>+ + +</td>
</tr>
<tr>
<td></td>
<td></td>
<td>0.21 lower to 0.39 higher</td>
<td>0.42 lower to 0.49 higher</td>
<td></td>
</tr>
<tr>
<td>Comprehensive language development assessed with: Reynell test follow up: range 6 to 9 months</td>
<td>-</td>
<td>-</td>
<td>-</td>
<td>MODERATE</td>
</tr>
<tr>
<td>Expressive language development assessed with: Reynell, Schlichting follow up: range 6 to 9 months</td>
<td>-</td>
<td>-</td>
<td>MD 0.32 lower (0.46 lower to 0.17 lower)</td>
<td>VERY LOW</td>
</tr>
<tr>
<td>Time (proportion) with effusion in first year assessed with: otoscope and tympanometry</td>
<td>-</td>
<td>-</td>
<td>The mean time (proportion) with effusion in first year was 0.6</td>
<td>LOW</td>
</tr>
<tr>
<td>Quality of life assessed with: TAIQOL survey follow up: median 2 years</td>
<td>-</td>
<td>-</td>
<td>MD 0.32 lower (0.46 lower to 0.17 lower)</td>
<td>VERY LOW</td>
</tr>
<tr>
<td>Ne of participants (studies)</td>
<td>Ne of participants: 394 (3 RCTs)</td>
<td>Ne of participants: 393 (3 RCTs)</td>
<td>Ne of participants: 574 (3 RCTs)</td>
<td>Ne of participants: 187 (1 RCT)</td>
</tr>
</tbody>
</table>
### Summary of findings:

**13. Tymanostomy tubes compared to no surgical intervention for otitis media with effusion**

**Patient or population:** Children aged 6 months to 12 years with otitis media with effusion.

**Setting:** Hospital.

**Intervention:** Tymanostomy tubes (TTs) (Teflon biflanged, Donaldson and Bevel Bobbins ventilation tubes).

**Comparison:** No surgical intervention

<table>
<thead>
<tr>
<th>Outcome</th>
<th>Relative effect (95% CI)</th>
<th>Anticipated absolute effects (95% CI)</th>
<th>Quality</th>
<th>What happens</th>
</tr>
</thead>
<tbody>
<tr>
<td>Adverse effects – otorrhoea follow up: range 12 to 24 months</td>
<td>Rates of TTs otorhhoea vary widely between RCTs; MRC TARGET trial found a rate of 2% over 24 months (mean age 60 months) whilst Rovers 2000 reported a rate of 83% over 12 months (mean age 19.5 months). Best data in Australian children is from Jassar 2009 (cohort study); 36% across 213 Indigenous and non-Indigenous children in the NT 1996-2004.¹⁹</td>
<td>¹⁹</td>
<td>★★★★★ VERY LOW ¹⁹</td>
<td>In children with OME treated with TTs compared to no surgical intervention there is insufficient evidence to report on otorrhoea at 1 to 2 years.</td>
</tr>
</tbody>
</table>

*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; SMD: Standardised mean difference

**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.
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- **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.

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**Explanations**

- a. Study: MRC 2001
- b. Lower mean difference corresponds to better hearing outcome.
- c. Risk of Bias: Risk of selection bias however demographic, audiometric, tympanometric and otoscopic findings similar for randomised and non-randomised groups. Not rated down.
- d. Imprecision: Small studies, optimal information size not met.
- f. Risk of Bias: attrition bias , selective reporting noted. Not rated down.
- g. Indirectness: Only 1 frequency available for comparison in Maw 1999, whilst 4 frequency average measured in other studies. Not rated down.
- k. Risk of Bias: Ability to blind assessor as to the presence of a grommet or its sequelae is not possible.
- l. Inconsistency: High heterogeneity
- m. Study data: Rovers 2001
- n. Indirectness: TAIQOL is a generic quality of life measure which has not been validated for otitis media, whereas other specific otitis media quality of life measurements are now available.
- o. Study: Jassar 2009
- p. Indirectness: Data from Jassar 2009 included children with TT insertion for OME and RAOM.
Risk of Bias: Only those attending follow-up appointments included in analysis

Imprecision: Small study

References
### Summary of findings:

**14 Adenoidectomy +/- tympanostomy tubes compared to tympanostomy tubes alone or no surgery for otitis media with effusion**

**Patient or population:** Children aged 3 months to 18 years with otitis media with effusion

**Setting:** Hospital

**Intervention:** Adenoidectomy +/- tympanostomy tubes

**Comparison:** Tympanostomy tubes alone or no surgery

<table>
<thead>
<tr>
<th>Outcome</th>
<th>Relative effect (95% CI)</th>
<th>Anticipated absolute effects (95% CI)</th>
<th>Certainty</th>
<th>What happens</th>
</tr>
</thead>
<tbody>
<tr>
<td>Hearing outcome assessed with: mean binaural hearing level measured over 4 frequency average follow up: range 12 to 24 months</td>
<td>RR 0.77 (0.69 to 0.86)</td>
<td>69.6% (47.4 to 59.9)</td>
<td>MD 4.2 dB lower (2.6 lower to 5.7 lower)</td>
<td>MODERATE</td>
</tr>
<tr>
<td>Treatment Failure in children ≥4 years of age follow up: median 12 months</td>
<td>RR 0.98 (0.89 to 1.38)</td>
<td>29.7% (20.5 to 41.0)</td>
<td>0.6% fewer (NS) (9.2 fewer to 11.3 more)</td>
<td>LOW</td>
</tr>
<tr>
<td>Treatment Failure in children &lt; 4 years of age follow up: median 12 months</td>
<td>RR 2.29 (1.52 to 3.43)</td>
<td>17.0% (25.8 to 58.3)</td>
<td>21.9% more (8.8 more to 41.3 more)</td>
<td>LOW</td>
</tr>
<tr>
<td>Resolution of OME (randomised by ear) assessed with: tympanometry follow up: median 6 months</td>
<td>RR 0.29 (1.52 to 3.43)</td>
<td>38.9% (25.8 to 58.3)</td>
<td>21.9% more (8.8 more to 41.3 more)</td>
<td>LOW</td>
</tr>
</tbody>
</table>

### Notes:

- NNT: Number Needed to Treat
- CI: Confidence Interval
### Summary of findings:

**14 Adenoidectomy +/- tympanostomy tubes compared to tympanostomy tubes alone or no surgery for otitis media with effusion**

**Patient or population:** Children aged 3 months to 18 years with otitis media with effusion  
**Setting:** Hospital  
**Intervention:** Adenoidectomy +/- tympanostomy tubes  
**Comparison:** Tymanostomy tubes alone or no surgery

<table>
<thead>
<tr>
<th>Outcome</th>
<th>Relative effect (95% CI)</th>
<th>Anticipated absolute effects (95% CI)</th>
<th>Certainty</th>
<th>What happens</th>
</tr>
</thead>
</table>
| Resolution of OME assessed with: tympanometry follow up: median 12 months  
Ne of participants: 296  
(3 RCTs)  
| RR 2.33 (1.36 to 4.01) | 20.0%                  | 46.6% (27.2 to 80.2)                  | LOW       | In children with OME treated with adenoidectomy plus TTs compared to TTs alone is probably more resolution of OME at 12 months.  
NNT ~4.                                                                                                                                 |
| Complications of surgery (post-operative bleeding)  
Ne of participants: 508  
(2 RCTs)  
| RR 3.02 (0.32 to 28.87) | 0.0%                    | 0.0% (0.0 to 0.0)                      | LOW       | In children with OME treated with adenoidectomy plus TTs compared to TTs alone is possibly on complications post surgery. |
| Repeat tympanostomy tube surgery follow up: range 2 to 5 years  
Ne of participants: 879  
(4 RCTs)  
| RR 0.44 (0.35 to 0.54) | 38.3%                   | 16.9% (13.4 to 20.7)                   | MODERATE  | In children with OME treated with adenoidectomy plus TTs compared to TTs alone is possibly less repeat TTs surgery.  
NNT ~5.                                                                                                                                 |
| Repeat tympanostomy tube surgery follow up: range 1 to 5 years  
Ne of participants: 200  
(10 observational studies)  
| RR 0.54 (0.52 to 0.57) | 32.0%                   | 17.3% (16.6 to 18.2)                   | VERY LOW  | In children with OME treated with adenoidectomy plus TT compared to TT alone is possibly less repeat tympanostomy tube surgery.  
NNT ~7.                                                                                                                                 |

*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

**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. Study data taken from: MRC Multicentre Otitis Media Study Group 2012
b. Lower mean difference corresponds to better hearing outcome.
c. Imprecision: Small numbers. Optimal information size not reached.
d. Treatment failure defined as: ≥4 AOM episodes (including episodes of otorrhoea) per year, presence of effusion for ≥50% of the time (i.e. effusion for ≥6 months), need for additional surgery; hearing improved by < 10 dB.
f. Risk of Bias: Attribjon bias and Re-call bias (Nguyen 2004)
g. Publication Bias: 5 studies not included as individual patient data not supplied or unavailable, however there is no change is estimate of effect.
i. Studies taken from: Cochrane Review, van den Aardweg 2010 (Gates 1987) and MRC 2012
j. Imprecision: low event rate / rare event
l. Imprecision: Optimal information size not reached.
m. Meta-analysis (Mikals 2014) combined RCT and observational studies looking at children undergoing adenoidectomy & tympanostomy tubes vs tympanostomy tubes for recurrent acute otitis media, otitis media with effusion and hearing loss.
.n. Studies taken from: Mikals, 2014 (includes observational retrospective studies and RCT's)
o. No raw data available. Percentages extracted from published data (represented as rate %).
p. Inconsistency: High heterogeneity with lumping of data from a variety of studies which broad outcomes.

References
### Summary of findings:

#### 15. Autoinflation devices compared to watchful waiting for otitis media with effusion

**Patient or population:** Children aged 3 to 11 years with otitis media with effusion

**Setting:** Primary health care and Hospital

**Intervention:** Autoinflation devices (Otovent®; carnival blower + balloon and Politzer devices) for a duration of 1 week to 3 months (ranged across studies)

**Comparison:** Watchful waiting

<table>
<thead>
<tr>
<th>Outcome</th>
<th>Relative effect (95% CI)</th>
<th>Anticipated absolute effects (95% CI)</th>
<th>Certainty</th>
<th>What happens</th>
</tr>
</thead>
<tbody>
<tr>
<td>Hearing - average improvement &gt;= 10 dB assessed with: pure-tone audiogram (250 Hz to 2000 Hz) follow up: range 3 weeks to 3 months</td>
<td>Relative Risk 0.80 (0.22 to 2.88)</td>
<td>27.0% b 21.6% (5.9 to 77.8)</td>
<td>5.4% fewer (NS) (21.1 fewer to 50.8 more)</td>
<td>LOW d,d</td>
</tr>
<tr>
<td>Pure-tone threshold assessed with: pure-tone audiogram (250 Hz to 2000 Hz) follow up: median 7 weeks</td>
<td>-</td>
<td>-</td>
<td>MD 7.02 higher (NS) (6.92 lower to 20.96 higher)</td>
<td>LOW f,f</td>
</tr>
<tr>
<td>Tympanogram improvement - B to C1/A assessed with: tympanometry follow up: median 1 months</td>
<td>Relative risk 1.72 (1.23 to 2.40)</td>
<td>35.6% c 41.2% (43.8 to 85.5)</td>
<td>25.6% more (8.2 more to 49.8 more)</td>
<td>LOW c,c</td>
</tr>
<tr>
<td>Tympanogram improvement - B/C2 to C1/A assessed with: tympanometry follow up: median 1 months</td>
<td>Relative risk 1.48 (0.88 to 2.48)</td>
<td>35.6% c 52.7% (31.3 to 88.3)</td>
<td>17.1% more (4.3 fewer to 52.7 more)</td>
<td>LOW e,e</td>
</tr>
</tbody>
</table>
15. Autoinflation devices compared to watchful waiting for otitis media with effusion

**Patient or population:** Children aged 3 to 11 years with otitis media with effusion

**Setting:** Primary healthcare and Hospital

**Intervention:** Autoinflation devices (Otovent®, carnival blower + balloon and Politzer devices) for a duration of 1 week to 3 months (ranged across studies)

**Comparison:** Watchful waiting

### Summary of findings:

<table>
<thead>
<tr>
<th>Outcome</th>
<th>Anticipated absolute effects (95% CI)</th>
<th>Certainty</th>
<th>What happens</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Without Autoinflation</td>
<td>With Autoinflation</td>
<td>Difference</td>
</tr>
<tr>
<td>Tympanogram improvement - B/C2 to C1/A follow up: range 1 to 3 months</td>
<td>Relative Risk 1.27 (1.07 to 1.49)</td>
<td>38.3% 48.7% (41.0 to 57.1)</td>
<td>10.4% more (2.7 more to 18.8 more)</td>
</tr>
<tr>
<td>Adverse effects - Nosebleeds and Ear Pain assessed with: parental report follow up: median 3 months</td>
<td>Relative Risk 0.90 (0.55 to 1.45)</td>
<td>16.3% 14.6% (8.9 to 23.6)</td>
<td>1.6% fewer (NS) (7.3 fewer to 7.3 more)</td>
</tr>
<tr>
<td>Disease specific quality of life assessed with: standardised change in OMQ-14 score follow up: mean 3 months</td>
<td>-</td>
<td>-</td>
<td>SMD 0.42 SD lower (0.63 lower to 0.22 lower)</td>
</tr>
</tbody>
</table>

*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; MD: Mean difference; RR: Risk ratio; SMD: Standardised mean difference; NS: Not significant; NNT: Number needed to treat; NNH: Number needed to harm

**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**

b. Raw data not available from Cochrane Review. Baseline risk taken from watchful waiting group in Brooker 1992
c. Risk of Bias: Blinding not possible of participants. Unclear blinding of outcome assessors.
d. Imprecision: Broad estimate of effect. Includes benefit and harm.
f. Risk of Bias: Lack of binding of participants, however audiologists blinded to otologic findings (Arick 2005), Unclear binding Fraser 1977. Not rated down.
g. Inconsistency: High heterogeneity. Not rated down.
h. Imprecision: Optimal information size not reached. Broad estimate of effect.
j. Raw data not available from Cochrane Review. Baseline risk taken from watchful waiting group in Williamson 2015
k. Indirectness: Tympanostomy is a surrogate for functional hearing. Not rated down.
n. Study: Williamson 2015
o. Risk of Bias: Lack of participant blinding. Tinnitus and nosebleed reported anecdotally.
q. Lower score denotes better QOL.
r. Risk of Bias: Lack of participant blinding.

References
### Summary of findings:

#### 16. Topical / intranasal steroids compared to placebo for otitis media with effusion

**Patient or population:** Children aged 2 to 12 years with otitis media with effusion.

**Setting:** Primary health care.

**Intervention:** Topical / Intranasal steroids (Studies used: Aerosolised dexamethasone 1 spray each nostril, 3 times a day and mometasone furoate 50 - 200 mcg once daily.) Duration was for 3 to 16 weeks.

**Comparison:** Placebo.

<table>
<thead>
<tr>
<th>Outcome</th>
<th>No of participants (studies)</th>
<th>Relative effect (95% CI)</th>
<th>Anticipated absolute effects (95% CI)</th>
<th>Quality</th>
<th>What happens</th>
</tr>
</thead>
<tbody>
<tr>
<td>Hearing Loss</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>assessed with: Fail audiometry sweep at 25dB HL; fail on more than two out of five frequencies in both ears follow up: 9 months No of participants: 141 (1 RCT)</td>
<td></td>
<td>RR 1.17 (0.87 to 1.58)</td>
<td>50.7% 59.4% (44.1 to 80.2)</td>
<td>8.6% more (NS) (6.6 fewer to 29.4 more)</td>
<td>⬤⬤⬤ ○◯ LOW</td>
</tr>
<tr>
<td>Resolution OME - short term assessed with: pneumo-otoscopy +/- tympanometry follow up: range 3 weeks to 4 weeks No of participants: 238 (2 RCTs)</td>
<td></td>
<td>RR 0.85 (0.63 to 1.15)</td>
<td>46.3% 39.3% (29.2 to 53.2)</td>
<td>6.9% fewer (NS) (17.1 fewer to 6.9 more)</td>
<td>⬤⬤⬤ ◯ ◯ MODERATE</td>
</tr>
<tr>
<td>Resolution OME - medium term assessed with: pneumo-otoscopy +/- tympanometry follow up: range 3 to 6 months No of participants: 234 (2 RCTs)</td>
<td></td>
<td>RR 1.42 (0.85 to 2.37)</td>
<td>51.7% 73.4% (43.9 to 100.0)</td>
<td>21.7% more (NS) (7.8 fewer to 70.8 more)</td>
<td>⬤⬤⬤ ◯ ◯ LOW slight</td>
</tr>
<tr>
<td>Resolution OME - long term assessed with: pneumo-otoscopy +/- tympanometry follow up: median 9 months No of participants: 144 (1 RCT)</td>
<td></td>
<td>RR 0.85 (0.65 to 1.11)</td>
<td>65.3% 55.5% (42.4 to 72.5)</td>
<td>9.8% fewer (NS) (22.8 fewer to 7.2 more)</td>
<td>⬤⬤⬤ ◯ ◯ LOW slight</td>
</tr>
</tbody>
</table>
**Summary of findings:**

### 16. Topical / intranasal steroids compared to placebo for otitis media with effusion

**Patient or population:** Children aged 2 to 12 years with otitis media with effusion.

**Setting:** Primary health care.

**Intervention:** Topical / Intranasal steroids (Studies used: Aerosolised dexamethasone 1 spray each nostril, 3 times a day and mometasone furoate 50 - 200mcg once daily) Duration was for 3 to 16 weeks.

**Comparison:** Placebo.

<table>
<thead>
<tr>
<th>Outcome</th>
<th>Relative effect (95% CI)</th>
<th>Anticipated absolute effects (95% CI)</th>
<th>Quality</th>
<th>What happens</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td></td>
<td>Without Topical / Intranasal steroids</td>
<td>With Topical / Intranasal steroids</td>
<td>Difference</td>
</tr>
<tr>
<td>Adverse effects (No major adverse effects reported. Minor adverse effects during treatment includes: cough, dry throat, epistaxis, nasal stinging) assessed with: parental report follow up: range 2 weeks to 6 months</td>
<td>RR 1.21 (0.78 to 1.89)</td>
<td>22.0%</td>
<td>26.7% (17.2 to 41.6)</td>
<td>4.6% more (NS) (4.8 fewer to 19.6 more)</td>
</tr>
<tr>
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<td></td>
</tr>
<tr>
<td>Quality of life score assessed with: Glasgow Children Benefit Inventory follow up: mean 24 weeks</td>
<td>RR 1.21 (0.78 to 1.89)</td>
<td>22.0%</td>
<td>26.7% (17.2 to 41.6)</td>
<td>4.6% more (NS) (4.8 fewer to 19.6 more)</td>
</tr>
<tr>
<td></td>
<td>Glasgow Children Benefit Inventory showed statistically significant improvement in QOL with score of 37.11 +/- 25.5 (topical steroids) vs 11.02 +/- 19.8 (placebo) (p value 0.0001).</td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

*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

**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**

b. Risk of Bias: Attrition bias
c. Imprecision: Broad estimate of effect. Confidence interval covers significant benefit and harm. Single, small study.
e. Inconsistency: Different measures for OME resolution between studies, however low heterogeneity between studies on statistical analysis.
f. Studies taken from: Cochrane Review, Simpson 2011 (Williamson 2009) and Bhargava 2014

g. Inconsistency: High heterogeneity - rate of OME clearance very different between studies which may be due to inclusion criteria. Bhargava recruited via tertiary ENT service with adenoid hypertrophy, whilst Williamson recruited via primary care with 3 months of OME.

h. Imprecision: Optimal information size not met.

i. Indirectness: Not specifically evaluated for children with hearing loss due to OME

References


17. Oral steroids compared to placebo for otitis media with effusion

Patient or population: Children aged 6 months to 14 years with otitis media with effusion

Setting: Primary health care.

Intervention: Oral steroids [Prednisolone (0.5-1.5 mg/kg daily (max 30 mg) in divided dose tapering over 7 or 14 days), Dexamethasone (0.15 mg/kg daily in divided dose tapering over 14 days) and Betamethasone (5mg as single dose)]

Comparison: Placebo

<table>
<thead>
<tr>
<th>Outcome</th>
<th>Relative effect (95% CI)</th>
<th>Anticipated absolute effects (95% CI)</th>
<th>Quality</th>
<th>What happens</th>
</tr>
</thead>
<tbody>
<tr>
<td>Hearing loss</td>
<td>RR 1.09 (0.80 to 1.49)</td>
<td>Without Oral steroids: 73.9% (59.1 to 100.0)</td>
<td>6.7% more(NS) (14.8 fewer to 36.2 more)</td>
<td>LOW b,c,d</td>
</tr>
<tr>
<td>OME resolution (two weeks) assessed with: pneumo-otoscopy &amp; tympanometry</td>
<td>RR 3.80 (0.93 to 15.52)</td>
<td>Without Oral steroids: 5.8% (5.4 to 89.5)</td>
<td>16.2% more(NS) (0.4 fewer to 83.8 more)</td>
<td>MODERATE c</td>
</tr>
<tr>
<td>OME resolution assessed with: pneumo-otoscopy &amp; tympanometry follow up: range 4 to 6 weeks</td>
<td>RR 1.54 (0.76 to 3.14)</td>
<td>Without Oral steroids: 17.6% (13.4 to 55.4)</td>
<td>9.5% more(NS) (4.2 fewer to 37.8 more)</td>
<td>LOW c,d</td>
</tr>
</tbody>
</table>

*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

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
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- **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

b. Risk of bias: Study terminated early due to concern that steroid was impairing resolution. Likely to result in lack of power rather than bias.
c. Imprecision: Small numbers / optimal information size not reached
d. Imprecision: single study
f. Inconsistency: Different treatments and regimens between studies, however low heterogeneity of pooled data.
g. Risk of Bias: Attrition bias (Niederman 1984), some imbalance in baseline characteristics (Niederman 1984), allocation concealment / selection bias not described across all studies.

References
Summary of findings:

18 Oral steroids compared to placebo for otitis media with effusion (antibiotics in both arms of studies)

**Patient or population:** Children aged 6 months to 15 years with otitis media with effusion

**Setting:** Primary health care and Hospital

**Intervention:** Oral steroids (Prednisolone (0.5-1.5 mg/kg daily) (max 30 mg) in divided dose tapering over 7 or 14 days), Dexamethasone (0.15 mg/kg daily in divided dose tapering over 14 days) and Betamethasone (5mg as single dose)) and Antibiotics (Amoxicillin (0.5 mg/kg twice daily on days 1 through 10 (total daily dose 1 mg/kg, maximum 30 mg/d), then days 11 through 14 given once daily (total daily dose 0.5 mg/kg, maximum 15 mg/d); then 40 mg/kgid in 3 divided doses from days 15 through 28), Trimethoprim/sulfamethoxazole (5mg/kg/dose twice daily 30 days or 50 mg/kg/day twice daily for 7 days) and Cefixime for 10 days used across studies).

**Comparison:** Placebo and Antibiotics (Amoxicillin, Trimethoprim/sulfamethoxazole and Cefixime used across studies)

<table>
<thead>
<tr>
<th>Outcome</th>
<th>Ne of participants (studies)</th>
<th>Relative effect (95% CI)</th>
<th>Anticipated absolute effects (95% CI)</th>
<th>Quality</th>
<th>What happens</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td></td>
<td></td>
<td>Without Oral steroids</td>
<td>With Oral steroids</td>
<td>Difference</td>
</tr>
<tr>
<td>OME resolution (short term follow-up) assessed with: otoscopy, pneumatic otoscope, tympanometry +/- audiometry. follow up: range 7 to 28 days Ne of participants: 409 (5 RCTs)</td>
<td>RR 1.99 (1.14 to 3.49)</td>
<td>23.1%</td>
<td>46.0% (26.4 to 80.7)</td>
<td>22.9% more (3.2 more to 57.6 more)</td>
<td>🟢🟢🟢 LOW</td>
</tr>
<tr>
<td>Adverse effects - mild to moderate. Assessed with: parental report follow up: range 2 weeks to 6 months Ne of participants: 255 (2 RCTs)</td>
<td>RR 1.34 (0.84 to 2.14)</td>
<td>18.1%</td>
<td>24.3% (15.2 to 38.8)</td>
<td>6.2% more (NS) (2.9 fewer to 20.6 more)</td>
<td>🟢🟢🟢 MDERATE</td>
</tr>
</tbody>
</table>

*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

**GRADE Working Group grades of evidence**

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- **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**

b. Imprecision: Small numbers / optimal information size not reached
c. Risk of bias: attrition bias (Berman 1990). Poor reporting with unclear risk of bias on many aspects of several studies. Not rated down.
d. Inconsistency: High heterogeneity likely due to different medications and regimens used in pooled studies.
e. Adverse effects included: dermatological, gastrointestinal, hyperactivity and irritability. No serious adverse effects reported. In Mandel 2002 treatments were administered in two phases (four-arm study analysed as two-arm) and adverse effects reported separately for both phases; data from end of first phase (completion of two-week steroid treatment) used in meta-analysis. No patients withdrew medications due to steroids. In Hemlin 1997 follow-up was until 6 months however treatment failures at visit 2 were not followed up beyond that time frame.
g. Risk of bias: Study terminated early due to concern that steroid was impairing resolution. Likely to result in lack of power rather than bias.
h. Inconsistency: Different treatments and regimens between studies, however low heterogeneity of pooled data.

**References**

Summary of findings:

19 Antihistamines and/or decongestants compared to placebo for otitis media with effusion

Patient or population: Children aged 5 months to 15 years with otitis media with effusion

Setting: Primary health care

Intervention: Antihistamines and/or decongestants (Studies used: chlorpheniramine & pseudoephedrine, ebastine, cinnarizine, oxymetazoline, phenylpropanolamine, phenylpropanolamine & brompheniramine, tripolidine & pseudoephedrine, phenylephrine, diphenhydramine & pseudoephedrine)

Comparison: Placebo

<table>
<thead>
<tr>
<th>Outcome</th>
<th>Relative effect (95% CI)</th>
<th>Anticipated absolute effects (95% CI)</th>
<th>Quality</th>
<th>What happens</th>
</tr>
</thead>
<tbody>
<tr>
<td>Hearing assessed with: &lt;20dB hearing improvement or no improvement follow up: median 1 month</td>
<td>RR 1.08 (0.93 to 1.27)</td>
<td>60.2%</td>
<td>65.0% (56.0 to 76.5)</td>
<td>4.8% more (NS) (4.2 fewer to 16.3 more)</td>
</tr>
<tr>
<td>Hearing assessed with: &lt;20dB hearing improvement or no improvement follow up: median 1 year</td>
<td>RR 1.50 (0.63 to 3.56)</td>
<td>25.0%</td>
<td>37.5% (15.8 to 89.0)</td>
<td>12.5% more (NS) (9.3 fewer to 64 more)</td>
</tr>
<tr>
<td>Persistent OME assessed with: tympanometry and otoscopy follow up: median 1 month</td>
<td>RR 0.99 (0.92 to 1.05)</td>
<td>74.9%</td>
<td>74.1% (68.9 to 78.6)</td>
<td>0.7% fewer (NS) (6 fewer to 3.7 more)</td>
</tr>
<tr>
<td>Persistent OME assessed with: tympanometry and otoscopy follow up: range 1 to 3 months</td>
<td>RR 1.06 (0.92 to 1.22)</td>
<td>55.0%</td>
<td>58.3% (50.6 to 67.1)</td>
<td>3.3% more (NS) (4.4 fewer to 12.1 more)</td>
</tr>
</tbody>
</table>
Summary of findings:

19 Antihistamines and/or decongestants compared to placebo for otitis media with effusion

Patient or population: Children aged 5 months to 15 years with otitis media with effusion

Setting: Primary health care

Intervention: Antihistamines and/or decongestants (Studies used: chlorpheniramine & pseudoephedrine, ebastine, cinnarizine, oxymetazoline, phenylpropanolamine, phenylpropanolamine & brompheniramine, tripolidine & pseudoephedrine, phenylephrine, diphenhydramine & pseudoephedrine)

Comparison: Placebo

<table>
<thead>
<tr>
<th>Outcome</th>
<th>Relative effect (95% CI)</th>
<th>Anticipated absolute effects (95% CI)</th>
<th>Quality</th>
<th>What happens</th>
</tr>
</thead>
<tbody>
<tr>
<td>Persistent OME assessed with: tympanometry and otoscopy follow up: range 3 to 12 months Nr of participants: 119 (2 RCTs)</td>
<td>RR 1.24 (0.72 to 2.13)</td>
<td>27.3% 33.8% (19.6 to 58.1)</td>
<td>6.5% more (NS) (7.6 fewer to 30.8 more)</td>
<td>In children with OME treated with antihistamines and/or decongestants compared to placebo there is possibly no difference of OME after 3-12 months. NNT Not applicable</td>
</tr>
<tr>
<td>Adverse effects (most commonly irritability, sedation and gastrointestinal upset) assessed with: parental report follow up: median 1 months Nr of participants: 1144 (6 RCTs)</td>
<td>RR 2.70 (1.87 to 3.88)</td>
<td>6.4% 17.4% (12.0 to 25.0)</td>
<td>10.9% more (5.6 more to 18.5 more)</td>
<td>In children with OME treated with antihistamines and/or decongestants compared to placebo there are probably more adverse events. NNH ~10</td>
</tr>
<tr>
<td>Surgery required (tympanostomy, myringotomy) follow up: range 1 to 3 months Nr of participants: 295 (4 RCTs)</td>
<td>RR 1.07 (0.81 to 1.41)</td>
<td>40.3% 43.2% (32.7 to 56.9)</td>
<td>2.8% more (NS) (7.7 fewer to 16.5 more)</td>
<td>In children with OME treated with antihistamines and/or decongestants compared to placebo there is possibly no difference in need for surgical interventions. NNT Not Applicable</td>
</tr>
</tbody>
</table>

*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
Summary of findings:

19 Antihistamines and/or decongestants compared to placebo for otitis media with effusion

**Patient or population:** Children aged 5 months to 15 years with otitis media with effusion

**Setting:** Primary health care

**Intervention:** Antihistamines and/or decongestants (Studies used: chlorpheniramine & pseudoephedrine, ebastine, cinnarizine, oxymetazoline, phenylpropanolamine, phenylephrine, diphenhydramine & pseudoephedrine)

**Comparison:** Placebo

<table>
<thead>
<tr>
<th>Outcome</th>
<th>Relative effect (95% CI)</th>
<th>Anticipated absolute effects (95% CI)</th>
<th>Quality</th>
<th>What happens</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td></td>
<td>Without Antihistamines and/or decongestants</td>
<td>With Antihistamines and/or decongestants</td>
<td>Difference</td>
</tr>
<tr>
<td>№ of participants (studies)</td>
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</tr>
</tbody>
</table>

**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**

b. Inconsistency: Different treatment regimens used between studies.
c. Imprecision: Small studies, Optimal informational size not reached
f. Risk of bias: risk selection bias (not clear in several studies), attrition bias (Saunte 1978, Hayden 1984) - however removal of these studies does not influence the outcome - not rated down.
i. Indirectness: Noted to have wide range of time points for outcome, data converted from outcome measure of ears in meta-analysis. Not rated down.
k. Imprecision: Optimal information size not reached, but significant difference noted. Not rated down.

**References**

Summary of findings:

20. Oral analgesia compared to placebo for pain relief in acute otitis media

Patient or population: Children aged 1 to 6.75 years with acute otitis media and pain

Setting: Primary health care

Intervention: Oral analgesia (Paracetamol 10mg/kg/dose three times daily and NSAID - ibuprofen 10mg/kg/dose three times daily)

Comparison: Placebo

<table>
<thead>
<tr>
<th>Outcome</th>
<th>Relative effect (95% CI)</th>
<th>Anticipated absolute effects (95% CI)</th>
<th>Quality</th>
<th>What happens</th>
</tr>
</thead>
<tbody>
<tr>
<td>Pain - Paracetamol compared to placebo assessed with: parental report follow up: median 48 hours</td>
<td>RR 0.38 (0.17 to 0.85)</td>
<td>25.3% 9.6% (4.3 to 21.5)</td>
<td>15.7% fewer (21 fewer to 3.8 fewer)</td>
<td>LOW b,c</td>
</tr>
<tr>
<td>Pain - NSAID compared to placebo assessed with: parental report follow up: median 48 hours</td>
<td>RR 0.28 (0.11 to 0.70)</td>
<td>25.3% 7.1% (2.8 to 17.7)</td>
<td>18.2% fewer (22.5 fewer to 7.6 fewer)</td>
<td>LOW b,c</td>
</tr>
<tr>
<td>Adverse events (nausea, vomiting, abdominal pain &amp; cutaneous rash) - Paracetamol compared to placebo assessed with: parental report follow up: median 48 hours</td>
<td>RR 1.03 (0.21 to 4.93)</td>
<td>4.0% 4.1% (0.8 to 19.7)</td>
<td>0.1% more (NS) (3.2 fewer to 15.7 more)</td>
<td>VERY LOW b,c,d</td>
</tr>
</tbody>
</table>
Summary of findings:

20. Oral analgesia compared to placebo for pain relief in acute otitis media

Patient or population: Children aged 1 to 6.75 years with acute otitis media and pain

Setting: Primary health care

Intervention: Oral analgesia (Paracetamol 10mg/kg/dose three times daily and NSAID - ibuprofen 10mg/kg/dose three times daily)

Comparison: Placebo

<table>
<thead>
<tr>
<th>Outcome</th>
<th>Relative effect (95% CI)</th>
<th>Anticipated absolute effects (95% CI)</th>
<th>Quality</th>
<th>What happens</th>
</tr>
</thead>
<tbody>
<tr>
<td>Adverse events (nausea, vomiting, abdominal pain &amp; cutaneous rash) - NSAID compared to placebo assessed with: parental report follow up: median 48 hours</td>
<td>RR 1.76 (0.44 to 7.10)</td>
<td>Placebo: 4.0% (1.8 to 28.4) With paracetamol / NSAID: 7.0% (2.2 fewer to 24.4 more)</td>
<td>VERY LOW</td>
<td>In children with AOM treated with NSAIDs compared to placebo there is insufficient evidence to report on adverse events. NNH Not Applicable</td>
</tr>
</tbody>
</table>

*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

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

b. Indirectness: Antibiotics given to patient concurrently with analgesia during study
c. Imprecision: Optimal information size not met.
d. Imprecision: Broad estimate of effect.

References

Summary of findings:

21. NSAIDs +/- Paracetamol compared to paracetamol for pain relief in acute otitis media

Patient or population: Children aged 6 months to 18 years with acute otitis media and pain

Setting: Primary health care

Intervention: NSAID (ibuprofen) 10mg/kg/dose 6-8 hourly (maximum 3 doses in 24 hours) +/- Paracetamol 10-15mg/kg/dose 4-6 hourly (maximum 3-4 doses in 24 hours)

Comparison: Paracetamol 10-15mg/kg/dose 4-6 hourly (maximum 3-4 doses in 24 hours) alone

<table>
<thead>
<tr>
<th>Outcome</th>
<th>Nr of participants (studies)</th>
<th>Relative effect (95% CI)</th>
<th>Anticipated absolute effects (95% CI)</th>
<th>Quality</th>
<th>What happens</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td></td>
<td></td>
<td>Paracetamol</td>
<td>NSAID +/- Paracetamol</td>
<td>Difference</td>
</tr>
<tr>
<td>Pain</td>
<td></td>
<td>RR 0.83</td>
<td>77.8%</td>
<td>64.6%</td>
<td>13.2% fewer</td>
</tr>
<tr>
<td></td>
<td></td>
<td>(0.59 to 1.18)</td>
<td>(45.9 to 91.8)</td>
<td>95% CI</td>
<td>(NS) (31.9 fewer to 14 more)</td>
</tr>
<tr>
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<td></td>
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<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td>RR 1.07</td>
<td>70.6%</td>
<td>75.5%</td>
<td>4.9% more</td>
</tr>
<tr>
<td></td>
<td></td>
<td>(0.78 to 1.47)</td>
<td>(55.1 to 100.0)</td>
<td></td>
<td>(NS) (15.5 fewer to 33.2 more)</td>
</tr>
<tr>
<td>Adverse events</td>
<td></td>
<td>RR 1.71</td>
<td>3.0%</td>
<td>5.1%</td>
<td>2.1% more</td>
</tr>
<tr>
<td></td>
<td></td>
<td>(0.43 to 6.90)</td>
<td>(1.3 to 20.7)</td>
<td></td>
<td>(NS) (1.7 fewer to 17.7 more)</td>
</tr>
</tbody>
</table>
### Summary of findings:

**21. NSAIDs +/- Paracetamol compared to paracetamol for pain relief in acute otitis media**

**Patient or population:** Children aged 6 months to 18 years with acute otitis media and pain

**Setting:** Primary health care

**Intervention:** NSAID (ibuprofen) 10mg/kg/dose 6-8 hourly (maximum 3 doses in 24 hours) +/- Paracetamol 10-15mg/kg/dose 4-6 hourly (maximum 3-4 doses in 24 hours)

**Comparison:** Paracetamol 10-15mg/kg/dose 4-6 hourly (maximum 3-4 doses in 24 hours) alone

<table>
<thead>
<tr>
<th>Outcome</th>
<th>Nr of participants (studies)</th>
<th>Relative effect (95% CI)</th>
<th>Anticipated absolute effects (95% CI)</th>
<th>Quality</th>
<th>What happens</th>
</tr>
</thead>
<tbody>
<tr>
<td>Adverse events (gastrointestinal, cutaneous and wheeze - NSAID + Paracetamol vs Paracetamol assessed with: patient/parental report follow up: 2 weeks Nr of participants: 56 (1 RCT)</td>
<td>not estimable</td>
<td></td>
<td>Paracetamol</td>
<td>NSAID +/- Paracetamol</td>
<td>Difference</td>
</tr>
</tbody>
</table>

Note: 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

**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. Imprecision: Optimal information size not met.
- c. Risk of Bias: Performance bias (lack of blinding) (Little 2013)
- d. Imprecision: Broad estimate of effect.
- f. Studies taken from: Cochrane Review, Sjoukes 2016 (Little 2013)

**References**
### Summary of findings:

**22. Topical analgesia as an adjunct to simple oral analgesia compared to placebo ear drops for immediate pain relief in acute otitis media**

**Patient or population:** Children aged 3 to 19 years with acute otitis media and pain.

**Setting:** Emergency departments

**Intervention:** Topical analgesic ear drops as an adjunct to simple oral analgesia (Studies used: 2% aqueous lignocaine or antipyrine benzocaine glycerine. Both studies offered paracetamol 15mg/kg/dose single dose). Single dose of ear drops given on presentation to emergency department.

**Comparison:** Placebo ear drops (Studies used: Normal saline or olive oil. Both studies offered paracetamol 15mg/kg/dose single dose)

<table>
<thead>
<tr>
<th>Outcome</th>
<th>Relative effect (95% CI)</th>
<th>Anticipated absolute effects (95% CI)</th>
<th>Quality</th>
<th>What happens</th>
</tr>
</thead>
<tbody>
<tr>
<td>50% reduction in ear pain assessed: two visual analogue scales follow up: median 10 minutes</td>
<td>RR 2.13 (1.19 to 3.80)</td>
<td>Without Topical analgesia as an adjunct to simple oral analgesia</td>
<td>20.3% (24.2 to 77.3)</td>
<td>23.0% more (3.9 more to 56.9 more)</td>
</tr>
<tr>
<td></td>
<td>RR 1.24 (0.88 to 1.74)</td>
<td>With Topical analgesia as an adjunct to simple oral analgesia</td>
<td>43.3% (41.8 to 82.6)</td>
<td></td>
</tr>
<tr>
<td></td>
<td>RR 1.43 (1.12 to 1.81)</td>
<td>Difference</td>
<td>23.0% more (3.9 more to 56.9 more)</td>
<td></td>
</tr>
<tr>
<td>50% reduction in ear pain assessed: two visual analogue scales follow up: median 20 minutes</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>50% reduction in ear pain assessed: two visual analogue scales follow up: median 30 minutes</td>
<td></td>
<td></td>
<td></td>
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<td></td>
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</tr>
</tbody>
</table>

*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; AOMwoP: Acute otitis media without perforation
Summary of findings:

22. Topical analgesia as an adjunct to simple oral analgesia compared to placebo ear drops for immediate pain relief in acute otitis media

Patient or population: Children aged 3 to 19 years with acute otitis media and pain.

Setting: Emergency departments

Intervention: Topical analgesic ear drops as an adjunct to simple oral analgesia (Studies used: 2% aqueous lignocaine or antipyrine benzocaine glycerine. Both studies offered paracetamol 15mg/kg/dose single dose). Single dose of ear drops given on presentation to emergency department.

Comparison: Placebo ear drops (Studies used: Normal saline or olive oil. Both studies offered paracetamol 15mg/kg/dose single dose)

<table>
<thead>
<tr>
<th>Outcome</th>
<th>Relative effect (95% CI)</th>
<th>Anticipated absolute effects (95% CI)</th>
<th>Quality</th>
<th>What happens</th>
</tr>
</thead>
<tbody>
<tr>
<td>Nr of participants (studies)</td>
<td></td>
<td>Without Topical analgesia as an adjunct to simple oral analgesia</td>
<td>With Topical analgesia as an adjunct to simple oral analgesia</td>
<td>Difference</td>
</tr>
</tbody>
</table>

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
b. Indirectness: Studies of children 3-18 years of age. Peak incidence AOM is 6-15 months of age.
c. Imprecision: Small studies

References
Summary of findings:

### 23. Antibiotics compared to placebo for acute otitis media - short term outcomes

**Patient or population:** Children aged 2 months to 12 years with acute otitis media

**Setting:** Primary health care

**Intervention:** Antibiotics (Studies used: amoxicillin 40-90mg/kg/day three times daily, amoxicillin with clavulinate 40-90 / 5.7-6.4mg/kg/day twice daily, ampicillin 100 mg/kg/day four times daily, phenoxymethyl penicillin 50 mg/kg/day twice daily and penicillin 500-1500mg/day four times daily with dose adjusted with age. Duration was from 5-14 days.)

**Comparison:** Placebo

<table>
<thead>
<tr>
<th>Outcome</th>
<th>Relative effect (95% CI)</th>
<th>Anticipated absolute effects (95% CI)</th>
<th>Quality</th>
<th>What happens</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td></td>
<td>Without Antibiotics</td>
<td>With Antibiotics</td>
<td>Difference</td>
</tr>
<tr>
<td>Pain assessed with: parental report +/- clinical assessment follow up: median 24 hours</td>
<td></td>
<td>42.6%</td>
<td>37.9%</td>
<td>4.7% fewer (NS) (9.4 fewer to 0.4 more)</td>
</tr>
<tr>
<td>Pain assessed with: parental report +/- clinical assessment follow up: range 2 to 3 days</td>
<td></td>
<td>15.9%</td>
<td>11.1%</td>
<td>4.8% fewer (6.8 fewer to 2.2 fewer)</td>
</tr>
<tr>
<td>Pain assessed with: parental report +/- clinical assessment follow up: range 4 to 7 days</td>
<td></td>
<td>24.1%</td>
<td>18.3%</td>
<td>5.8% fewer (8.9 fewer to 2.2 fewer)</td>
</tr>
<tr>
<td>Pain assessed with: parental report +/- clinical assessment follow up: range 10 to 12 days</td>
<td></td>
<td>21.6%</td>
<td>7.1%</td>
<td>14.5% fewer (17.9 fewer to 7.3 fewer)</td>
</tr>
</tbody>
</table>
Summary of findings:

23. Antibiotics compared to placebo for acute otitis media - short term outcomes

**Patient or population:** Children aged 2 months to 12 years with acute otitis media

**Setting:** Primary health care

**Intervention:** Antibiotics (Studies used: amoxycillin 40-90mg/kg/day three times daily, amoxycillin with clavulanate 40-90 / 5.7-6.4mg/kg/day twice daily, ampicillin 100 mg/kg/day four times daily, phenoxymethyl penicillin 50 mg/kg/day twice daily and penicillin 500-1500mg/day four times daily with dose adjusted with age. Duration was from 5-14 days.)

**Comparison:** Placebo

<table>
<thead>
<tr>
<th>Outcome</th>
<th>Relative effect (95% CI)</th>
<th>Anticipated absolute effects (95% CI)</th>
<th>Quality</th>
<th>What happens</th>
</tr>
</thead>
<tbody>
<tr>
<td>Adverse events (vomiting, diarrhoea or rash) assessed with: parental report follow up: range 7 days to 4 weeks</td>
<td>RR 1.38 (1.19 to 1.59)</td>
<td>19.6%</td>
<td>27.0% (23.3 to 31.1)</td>
<td>7.4% more (3.7 more to 11.5 more)</td>
</tr>
<tr>
<td>Tympanic membrane perforation assessed with: otoscopy follow up: range 7 days to 4 weeks</td>
<td>RR 0.37 (0.18 to 0.76)</td>
<td>4.8%</td>
<td>1.8% (0.9 to 3.6)</td>
<td>3.0% fewer (3.9 fewer to 1.2 fewer)</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Treatment failure (lack of substantial improvement, worsening of otoscopic signs, worsening clinical condition at any time)</th>
<th>Proportion of children &gt; 2 years of age with unilateral AOM (N of participants: 611; 6 RCTs)</th>
<th>Proportion of children &lt;2 years (N of participants: 567; 6 RCTs)</th>
</tr>
</thead>
<tbody>
<tr>
<td>RR 0.92 (0.85 to 1.01)</td>
<td>26.2% â†’ 24.1% (22.3 to 26.5)</td>
<td>2.1% fewer (NS) (3.9 fewer to 0.3 more)</td>
</tr>
</tbody>
</table>

Assessed with: parental report +/- clinical
### Explanations

#### Proportion of children with bilateral AOM at diagnosis (N of participants: 456; 6 RCTs)\(^{1,2}\)

<table>
<thead>
<tr>
<th>RR (95% CI)</th>
<th>Proportion</th>
<th>Risk Effect</th>
<th>GRADE</th>
<th>Evidence Quality</th>
</tr>
</thead>
<tbody>
<tr>
<td>0.77 (0.68 to 0.89)</td>
<td>47.6% (\pm)</td>
<td>10.9% fewer (15.2 fewer to 5.2 fewer)</td>
<td>![MD_MODERATE]</td>
<td>Low</td>
</tr>
</tbody>
</table>

In children <2 years treated with antibiotics compared to placebo there is probably fewer treatment failures during 3-5 days follow-up. NNT ~10

#### Proportion of children with otorrhea through TM perforations at diagnosis (N of participants: 116; 6 RCTs)\(^{2,4}\)

<table>
<thead>
<tr>
<th>RR (95% CI)</th>
<th>Proportion</th>
<th>Risk Effect</th>
<th>GRADE</th>
<th>Evidence Quality</th>
</tr>
</thead>
<tbody>
<tr>
<td>0.72 (0.62 to 0.84)</td>
<td>47.5% (\pm)</td>
<td>13.3% fewer (18 fewer to 7.6 fewer)</td>
<td>![MD_MODERATE]</td>
<td>Low</td>
</tr>
</tbody>
</table>

In children <2 years treated with antibiotics compared to placebo there is probably fewer treatment failures during 3-5 days follow-up. NNT ~8

#### Proportion of children >2 years of age with treatment failure assessed with: pain, fever or both follow up: range 3 to 7 days N of participants: 1076 (6 RCTs)\(^{2,3}\)

<table>
<thead>
<tr>
<th>RR (95% CI)</th>
<th>Proportion</th>
<th>Risk Effect</th>
<th>GRADE</th>
<th>Evidence Quality</th>
</tr>
</thead>
<tbody>
<tr>
<td>0.52 (0.37 to 0.73)</td>
<td>60.0% (\pm)</td>
<td>28.8% fewer (37.8 fewer to 16.2 fewer)</td>
<td>![MD_MODERATE]</td>
<td>Low</td>
</tr>
</tbody>
</table>

In children >2 years of age with AOM and otorrhea treated with antibiotics compared to placebo there is probably fewer treatment failures at 3-5 days follow-up. NNT ~4

<table>
<thead>
<tr>
<th>RR (95% CI)</th>
<th>Proportion</th>
<th>Risk Effect</th>
<th>GRADE</th>
<th>Evidence Quality</th>
</tr>
</thead>
<tbody>
<tr>
<td>0.86 (0.60 to 0.93)</td>
<td>30.9%</td>
<td>4.3% fewer (6.2 fewer to 2.2 fewer)</td>
<td>![MD_MODERATE]</td>
<td>Low</td>
</tr>
</tbody>
</table>

In children >2 years of AOM treated with antibiotics compared to placebo there is probably fewer treatment failures at 3-7 days follow-up. NNT ~24

---

*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

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**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
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- **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

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**Explanations**

a. Studies include amoxicillin alone, amoxicillin with clavulanate, and penicillin
b. Proportion of children with any pain at timepoint - various instruments across studies
e. Imprecision: Optimal information size not reached
g. Studies taken from: Cochrane Review, Venekamp 2015 (Hoberman 2011)
h. Indirectness: Timepoint not specified a priori as an outcome of interest
k. Treatment failure - composite outcome of persisting pain and or fever, worsening of otoscopic signs, and/or deterioration of patient's overall condition
m. Some data estimated from published data
n. Note: Hoberman 2011, Tahtinen 2011 - <2 year old children, strict diagnostic criteria

References
### Summary of findings:

#### 24. Antibiotics compared to placebo for acute otitis media – long term outcomes

**Patient or population:** Children aged 6 months to 15 years with acute otitis media

**Setting:** Primary health care.

**Intervention:** Antibiotics (Studies used: amoxicillin 40-90mg/kg/day three times daily, amoxicillin with clavulanate 40-90 / 5.7-6.4mg/kg/day twice daily, ampicillin 100 mg/kg/day four times daily, phenoxymethyl penicillin 50 mg/kg/day twice daily and penicillin 500-1500mg/day four times daily with dose adjusted with age. Duration was from 5-14 days.)

**Comparison:** Placebo

<table>
<thead>
<tr>
<th>Outcome</th>
<th>Relative effect (95% CI)</th>
<th>Anticipated absolute effects (95% CI)</th>
<th>Quality</th>
<th>What happens</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td></td>
<td>Without Antibiotics</td>
<td>With Antibiotics</td>
<td>Difference</td>
</tr>
<tr>
<td>Abnormal tympanometry assessed by: tympanometry follow up: median 3 months</td>
<td>RR 0.97 (0.76 to 1.24)</td>
<td>24.1%</td>
<td>23.4% (18.3 to 29.9)</td>
<td>0.7% fewer (NS) (5.8 fewer to 5.8 more)</td>
</tr>
<tr>
<td>Contralateral AOM (in unilateral cases) assessed by: otoscopy follow up: range 1 to 12 months</td>
<td>RR 0.49 (0.25 to 0.95)</td>
<td>18.8%</td>
<td>9.2% (4.7 to 17.8)</td>
<td>9.6% fewer (14.1 fewer to 0.9 fewer)</td>
</tr>
<tr>
<td>Late AOM recurrence assessed by: otoscopy +/- parental report follow up: range 15 days to 6 months</td>
<td>RR 0.93 (0.78 to 1.10)</td>
<td>20.1%</td>
<td>18.7% (15.6 to 22.1)</td>
<td>1.4% fewer (NS) (4.4 fewer to 2 more)</td>
</tr>
</tbody>
</table>

*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

**GRADE Working Group grades of evidence**

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- **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. Imprecision: Optimal information size not reached

b. Inconsistency: High heterogeneity

c. Time point chosen since persistent effusion for 3 months post AOM warrants a diagnosis of persistent OME and specific management strategies.

References
Summary of findings:

### 25. Twice daily compared to three daily doses of Amoxicillin (+/- clavulanate) for acute otitis media

**Patient or population:** Children aged 2 months to 12 years with acute otitis media

**Setting:** Primary health care.

**Intervention:** Amoxicillin (+/- clavulanate) twice daily (Studies used: amoxicillin 40-60mg/kg/day, amoxicillin/clavulanate 40-70/10 mg/kg/day). Duration was 7 to 10 days.

**Comparison:** Amoxicillin (+/- clavulanate) three times daily (Studies used: amoxicillin 40-60mg/kg/day, amoxicillin/clavulanate 45-60 / 6.4-15 mg/kg/ day). Duration was 7 to 10 days.

<table>
<thead>
<tr>
<th>Outcome</th>
<th>Nr of participants (studies)</th>
<th>Relative effect (95% CI)</th>
<th>Anticipated absolute effects (95% CI)</th>
<th>Quality</th>
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</tr>
</thead>
<tbody>
<tr>
<td></td>
<td></td>
<td></td>
<td>With Three daily doses</td>
<td>With Twice daily</td>
<td>Difference</td>
</tr>
<tr>
<td>Clinical cure rate at the end of therapy assessed by: clinical, otoscopy +/- tympanometry follow up: range 7 to 10 days</td>
<td>1601 (5 RCTs) (^1)</td>
<td>RR 1.03 (0.99 to 1.07)</td>
<td>86.4%</td>
<td>89.0% (85.6 to 92.5)</td>
<td>2.6% more (NS) (0.9 fewer to 6.1 more)</td>
</tr>
<tr>
<td>Adverse reactions to medication (gastrointestinal and cutaneous) assessed by: parental report follow up: range 28 to 42 days</td>
<td>878 (2 RCTs) (^1)</td>
<td>RR 0.92 (0.52 to 1.63)</td>
<td>29.9%</td>
<td>27.5% (15.6 to 48.8)</td>
<td>2.4% fewer (14.4 fewer to 18.8 more)</td>
</tr>
<tr>
<td>AOM complications: Recurrent AOM after completion of therapy assessed by: clinical, otoscopy +/- tympanometry follow up: range 42 to 90 days</td>
<td>1029 (3 RCTs) (^1)</td>
<td>RR 1.21 (0.52 to 2.81)</td>
<td>9.2%</td>
<td>11.1% (4.8 to 25.7)</td>
<td>1.9% more (4.4 fewer to 16.6 more)</td>
</tr>
<tr>
<td>Compliance rate assessed by: parental report follow up: range 7 to 14 days</td>
<td>1520 (4 RCTs) (^1)</td>
<td>RR 1.04 (0.98 to 1.10)</td>
<td>81.8%</td>
<td>85.1% (80.2 to 90.0)</td>
<td>3.3% more (1.6 fewer to 8.2 more)</td>
</tr>
</tbody>
</table>
Summary of findings:

25. Twice daily compared to three daily doses of Amoxicillin (+/- clavulanate) for acute otitis media

**Patient or population:** Children aged 2 months to 12 years with acute otitis media

**Setting:** Primary health care.

**Intervention:** Amoxicillin (+/- clavulanate) twice daily (Studies used: amoxicillin 40-60mg/kg/day, amoxicillin/clavulanate 40-70/10 mg/kg/day). Duration was 7 to 10 days.

**Comparison:** Amoxicillin (+/- clavulanate) three times daily (Studies used: amoxicillin 40-60mg/kg/day, amoxicillin/clavulanate 45-60 / 6.4-15 mg/kg/ day). Duration was 7 to 10 days.

<table>
<thead>
<tr>
<th>Outcome</th>
<th>Nr of participants (studies)</th>
<th>Relative effect (95% CI)</th>
<th>Anticipated absolute effects (95% CI)</th>
<th>Quality</th>
<th>What happens</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td></td>
<td></td>
<td>With Three daily doses</td>
<td>With Twice daily</td>
<td>Difference</td>
</tr>
</tbody>
</table>

*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).

**GRADE Working Group grades of evidence**

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- **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**

- b. Risk of Bias: Attrition bias (Behre & Damrikarnlert), selective reporting (Murph 1993)
- d. Imprecision: High heterogeneity
- e. Imprecision: Optimal information size not met, noted and not rated down.
- g. Inconsistency: Borderline high heterogeneity noted but not rated down.
- h. Imprecision: Low event rate, optimal information size not reached

**References**

### Summary of findings:

#### 26. Short course (3-5 days) compared to longer course (7-10 days) antibiotics for acute otitis media

**Patient or population:** Children aged 1 month to 14.3 years with acute otitis media

**Setting:** Primary health care.

**Intervention:** Short course (3-5 days) antibiotics (Studies used: Amoxicillin/clavulanate 80-90mg / 6.4-10mg/kg/day, Cefixime 8mg/kg/day, Cefpodoxime 8mg/kg/day, Ceflucor 40mg/kg/day, Cefuroxime 30mg/kg/day, Cefprozil 30mg/kg/day, Penicillin V 25mg/kg/day).

**Comparison:** longer course (7-10 days) antibiotics (Studies used: Amoxicillin/clavulanate 80-90mg / 6.4-10mg/kg/day, Cefixime 8mg/kg/day, Cefpodoxime 8mg/kg/day, Ceflucor 40mg/kg/day, Cefuroxime 30mg/kg/day, Cefprozil 30mg/kg/day, Penicillin V 25mg/kg/day).

<table>
<thead>
<tr>
<th>Outcome</th>
<th>Relative effect (95% CI)</th>
<th>Anticipated absolute effects (95% CI)</th>
<th>Quality</th>
<th>What happens</th>
</tr>
</thead>
<tbody>
<tr>
<td>Treatment failure - Sensitivity Analysis: same antibiotic in treatment arms assessed by: clinical assessment and otoscopy follow up: median 1 months</td>
<td>RR 1.57 (1.36 to 1.82)</td>
<td>14.3% (19.4 to 25.9)</td>
<td>8.1% more (5.1 more to 11.7 more)</td>
<td>MODERATE</td>
</tr>
<tr>
<td>Treatment failure - Amoxicillin-clavulanate - 5 versus 10 days assessed by: clinical assessment and otoscopy follow up: median 1 months</td>
<td>RR 1.82 (1.49 to 2.23)</td>
<td>16.6% (24.7 to 36.9)</td>
<td>13.6% more (8.1 more to 20.4 more)</td>
<td>LOW</td>
</tr>
<tr>
<td>Adverse effects (gastrointestinal) assessed by: parental report follow up: median 1 month</td>
<td>RR 0.79 (0.69 to 0.91)</td>
<td>15.1% (10.4 to 13.8)</td>
<td>3.2% fewer (4.7 fewer to 1.4 fewer)</td>
<td>LOW</td>
</tr>
</tbody>
</table>

*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;
26. Short course (3-5 days) compared to longer course (7-10 days) antibiotics for acute otitis media

**Patient or population:** Children aged 1 month to 14.3 years with acute otitis media

**Setting:** Primary health care.

**Intervention:** Short course (3-5 days) antibiotics (Studies used: Amoxicillin/clavulanate 80-90mg / 6.4-10mg/kg/day, Cefixime 8mg/kg/day, Cefpodoxime 8mg/kg/day, Ceflacr 40mg/kg/day, Cefuroxime 30mg/kg/day, Cefprozil 30mg/kg/day, Penicillin V 25mg/kg/day).

**Comparison:** longer course (7-10 days) antibiotics (Studies used: Amoxicillin/clavulanate 80-90mg / 6.4-10mg/kg/day, Cefixime 8mg/kg/day, Cefpodoxime 8mg/kg/day, Ceflacr 40mg/kg/day, Cefuroxime 30mg/kg/day, Cefprozil 30mg/kg/day, Penicillin V 25mg/kg/day).

---

### Outcome

<table>
<thead>
<tr>
<th>Outcome</th>
<th>Relative effect (95% CI)</th>
<th>Anticipated absolute effects (95% CI)</th>
<th>Quality</th>
<th>What happens</th>
</tr>
</thead>
<tbody>
<tr>
<td>N of participants (studies)</td>
<td>Without Short course (3-5 days)</td>
<td>With Short course (3-5 days)</td>
<td>Difference</td>
<td></td>
</tr>
</tbody>
</table>

**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**

- b. Risk of bias: Selection bias (many studies), reporting bias, attrition bias
- d. Risk of bias: Reporting bias (Cohen, Hoberman), industry funding (Hoberman 1997)
- e. Imprecision: Optimal information size not met
- g. Inconsistency: High heterogeneity

---

**References**

Summary of findings:

### 27. Azithromycin compared to Amoxicillin with or without clavulanate for acute otitis media

**Patient or population:** Children aged 3 months to 15 years old with acute otitis media.

**Setting:** Primary health care.

**Intervention:** Azithromycin (Studies used: 30-60mg/kg (60mg/kg extended release tablet)) Duration was a single stat dose or daily for 3-6 days.

**Comparison:** Amoxicillin with or without clavulanate (Studies used: 40-90mg/kg/day two to three divided doses daily.) Duration was for 7-10 days.

<table>
<thead>
<tr>
<th>Outcome</th>
<th>Relative effect (95% CI)</th>
<th>Anticipated absolute effects (95% CI)</th>
<th>Quality</th>
<th>What happens</th>
</tr>
</thead>
<tbody>
<tr>
<td>Treatment failure assessed by: clinical and otoscopic assessment. follow up: ≤1 months Ne of participants: 5150 (19 RCTs)</td>
<td>RR 0.99 (0.89 to 1.11)</td>
<td>22.0% 21.8% (19.6 to 24.4)</td>
<td><img src="https://example.com/mild.png" alt="MODERATE" /></td>
<td>In children with AOM treated with Azithromycin compared to Amoxicillin+/- clavulanate there is probably no reduction in treatment failure during 1 month follow-up. NNT Not Applicable</td>
</tr>
<tr>
<td>Treatment failure assessed by: clinical and otoscopic assessment. follow up: range 8 to 19 days Ne of participants: 5274 (19 RCTs)</td>
<td>RR 1.18 (0.98 to 1.43)</td>
<td>12.5% 14.8% (12.3 to 17.9)</td>
<td><img src="https://example.com/moderate.png" alt="MODERATE" /></td>
<td>In children with AOM treated with Azithromycin compared to Amoxicillin+/- clavulanate there is probably no reduction in treatment failure during 8-19 days follow-up. NNT Not Applicable</td>
</tr>
<tr>
<td>Treatment failure (Single dose Azithromycin compared to longer course Amoxicillin+/- clavulanate) assessed by: clinical and otoscopic assessment. follow up: ≤1 months Ne of participants: 1320 (4 RCTs)</td>
<td>RR 0.95 (0.80 to 1.12)</td>
<td>26.9% 25.6% (21.5 to 30.2)</td>
<td><img src="https://example.com/moderate.png" alt="MODERATE" /></td>
<td>In children with AOM treated with single dose Azithromycin compared to Amoxicillin+/- clavulanate there is probably no reduction in treatment failure during 1 month follow-up. NNT Not Applicable</td>
</tr>
<tr>
<td>Treatment failure by end of therapy in remote Aboriginal children assessed by: video pneumatic otoscopy, tympanometry follow up: range 6 to 11 days Ne of participants: 320 (1 RCT)</td>
<td>RR 0.93 (0.75 to 1.15)</td>
<td>53.5% 49.8% (40.2 to 61.6)</td>
<td><img src="https://example.com/moderate.png" alt="MODERATE" /></td>
<td>In remote Australian Aboriginal Children with AOM treated with single dose Azithromycin compared to Amoxicillin there is probably no reduction in treatment failure at 6-11 days follow-up. NNT Not Applicable</td>
</tr>
</tbody>
</table>
Summary of findings:

27. Azithromycin compared to Amoxicillin with or without clavulanate for acute otitis media

Patient or population: Children aged 3 months to 15 years old with acute otitis media.

Setting: Primary health care.

Intervention: Azithromycin (Studies used: 30-60mg/kg (60mg/kg extended release tablet)) Duration was a single stat dose or daily for 3-6 days.

Comparison: Amoxicillin with or without clavulanate (Studies used: 40-80mg/kg/day two to three divided doses daily.) Duration was for 7-10 days.

<table>
<thead>
<tr>
<th>Outcome</th>
<th>Relative effect (95% CI)</th>
<th>Anticipated absolute effects (95% CI)</th>
<th>Quality</th>
<th>What happens</th>
</tr>
</thead>
<tbody>
<tr>
<td>Adverse effects (gastrointestinal) assessed by: parental report follow up: median 1 months</td>
<td>RR 0.59 (0.52 to 0.68)</td>
<td>17.9% Without Azithromycin 10.5% (9.3 to 12.1) With Azithromycin Difference 7.3% fewer (8.6 fewer to 5.7 fewer)</td>
<td>LOW b b</td>
<td>In children with AOM treated with Azithromycin compared to Amoxicillin +/- clavulanate there are possibly fewer gastrointestinal adverse effects during 1 month follow-up. NNT ~14</td>
</tr>
</tbody>
</table>

*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

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- **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 the effect

Explanations


b. Risk of bias: selection and performance bias (several studies)


d. Risk of Bias: Interin analysis (selective reporting bias) (Arguedas 2005)

e. Study: Morris 2010

f. Imprecision: Small study, not powered to detect equivalence


h. Inconsistency: High heterogeneity

References


Summary of findings:

### 28. Immediate antibiotics compared to watchful waiting for acute otitis media

**Patient or population:** Children aged 6 months to 16 years with acute otitis media

**Setting:** Primary health care

**Intervention:** Immediate antibiotics (Studies used: Amoxicillin 90mg/kg/day twice daily for 7 to 10 days and Phenoxymethylpenicillin 50mg/kg/day twice daily for 5 days)

**Comparison:** Watchful waiting

<table>
<thead>
<tr>
<th>Outcome</th>
<th>Relative effect (95% CI)</th>
<th>Anticipated absolute effects (95% CI)</th>
<th>Quality</th>
<th>What happens</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td></td>
<td>Without Immediate antibiotics</td>
<td>With Immediate antibiotics</td>
<td>Difference</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td>8.9% fewer (NS) (17.8 fewer to 4.3 more)</td>
</tr>
<tr>
<td>Pain assessed: parental report follow up: range 3 to 7 days Ne of participants: 959 (4 RCTs)</td>
<td>RR 0.75 (0.50 to 1.12)</td>
<td>35.6%</td>
<td>26.7% (17.8 to 39.8)</td>
<td>MODERATE</td>
</tr>
<tr>
<td>Pain assessed: parental report follow up: range 11 to 14 days Ne of participants: 247 (1 RCT)</td>
<td>RR 0.91 (0.75 to 1.10)</td>
<td>66.9%</td>
<td>60.9% (50.2 to 73.6)</td>
<td>LOW</td>
</tr>
<tr>
<td>Adverse effects (vomiting, diarrhoea or rash) assessed: parental report follow up: range 7 to 40 days Ne of participants: 550 (2 RCTs)</td>
<td>RR 1.71 (1.24 to 2.36)</td>
<td>16.7%</td>
<td>28.5% (20.7 to 39.3)</td>
<td>MODERATE</td>
</tr>
<tr>
<td>Abnormal tympanometry assessed: tympanometry follow up: median 4 weeks Ne of participants: 207 (1 RCT)</td>
<td>RR 1.03 (0.78 to 1.35)</td>
<td>49.5%</td>
<td>51.0% (38.6 to 66.8)</td>
<td>LOW</td>
</tr>
</tbody>
</table>
Summary of findings:

### 28. Immediate antibiotics compared to watchful waiting for acute otitis media

**Patient or population**: Children aged 6 months to 16 years with acute otitis media

**Setting**: Primary health care

**Intervention**: Immediate antibiotics (Studies used: Amoxicillin 90mg/kg/day twice daily for 7 to 10 days and Phenoxymethylpenicillin 50mg/kg/day twice daily for 5 days)

**Comparison**: Watchful waiting

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<th>Quality</th>
<th>What happens</th>
</tr>
</thead>
<tbody>
<tr>
<td>Tympanic membrane perforation assessed: otoscopy follow up: median 3 months Ne of participants: 179 (1 RCT) ² ³</td>
<td>not estimable</td>
<td>0.0% 0.0% (0.0 to 0.0)</td>
<td>☀ ☀ ☀</td>
<td>In children with AOM treated with immediate antibiotics compared to watchful waiting there is probably no difference to report on TM perforation as sequelae of AOM.</td>
</tr>
<tr>
<td>AOM recurrences assessed: acute ear symptoms / abnormal tympanic membrane / AOM severity score higher than that at enrolment follow up: range 13 to 30 days Ne of participants: 209 (1 RCT) ³ ⁵ ⁶</td>
<td>RR 1.41 (0.74 to 2.69) ⁷</td>
<td>13.0% 18.3% (9.6 to 35.0)</td>
<td>☀ ☀ ☀</td>
<td>In children with AOM treated with immediate antibiotics compared to watchful waiting there is probably no difference to report on AOM recurrences. NNT Not Applicable.</td>
</tr>
<tr>
<td>Outpatient antibiotic prescriptions Ne of participants: 313932 (1 observational study) ² ² ⁸</td>
<td>Large Israeli observational study. Guidelines introduced in 2004 which recommended watchful waiting. Pre-guideline prescription rates for first episode AOM in children &gt;24 months was 56%. From 2004 to 2007, rate decreased to 47%.</td>
<td>☀ ☀ ☀ ☀ VERY LOW ⁹</td>
<td>☀ ☀ ☀ ☀ VERY LOW ⁹</td>
<td>In children with AOM treated with immediate antibiotics compared to watchful waiting there is possibly a reduction of antibiotic prescriptions.</td>
</tr>
</tbody>
</table>

*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).

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Explanations
b. Imprecision: Confidence interval for estimate of effect covers both benefit and harm.
d. Risk of bias: Attrition bias
e. Imprecision: Optimal information size not reached
g. Studies taken from: Cochrane Review, Venekamp 2015 (McCormick 2005)
h. Studies taken from: Cochrane Review, Venekamp 2015 (Neumark 2007)
i. Imprecision: Low event rate
j. Grossman 2010
k. Script rates are a surrogate for overall antibiotic consumption, itself only important insofar as it promotes resistance, which was not measured here

References
### Summary of findings:

#### 29 Prophylactic antibiotics compared to placebo / no treatment for prevention of recurrent acute otitis media

**Patient or population:** Prevention of recurrent acute otitis media in children aged 0 to 14 years.

**Setting:** Primary health care.

**Intervention:** Prophylactic antibiotics (Studies used Amoxycillin 20-50mg/kg daily, Ampicillin 125-250mg/day (dose age dependant), Trimethoprim/sulfamethoxazole 4-8/12-40 mg/kg/day twice daily, Sulfisoxazole 75 mg/kg/day or 500-1000mg (dose age dependant) twice daily and Phenoxymethyl penicillin V 25 mg/kg/day). Duration was 6.5 weeks to 2 years.

**Comparison:** Placebo / no treatment

<table>
<thead>
<tr>
<th>Outcome</th>
<th>Relative effect (95% CI)</th>
<th>Anticipated absolute effects (95% CI)</th>
<th>Quality</th>
<th>What happens</th>
</tr>
</thead>
<tbody>
<tr>
<td>Prevention - any AOM or CSOM during treatment assessed by: clinical assessment, pneumatic otoscope / otoscope +/- tympanostomy. follow up: range 10 weeks to 24 months</td>
<td>RR 0.65 (0.53 to 0.79)</td>
<td>55.7%</td>
<td>36.2% (29.5 to 44.0)</td>
<td>19.5% fewer (26.2 fewer to 11.7 fewer)</td>
</tr>
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</table>

| Prevention - episodes of AOM or CSOM during treatment assessed by: clinical assessment, pneumatic otoscope / otoscope +/- tympanostomy. follow up: range 10 weeks to 24 months | Incidence Rate Ratio 0.51 (0.39 to 0.66) | | | | MODERATE b |
| | | | | | In children with rAOM treated with prophylactic antibiotics compared to placebo/no treatment there are probably fewer episodes of AOM during Rx. Prevents ~1.5 episodes per year of treatment, per child. |

| Adverse effects (any clinical side effects during intervention) assessed by: parental report follow up: range 10 weeks to 24 months | RR 1.99 (0.25 to 15.89) | 0.8% | 1.7% (0.2 to 13.2) | 0.8% more (NS) (0.6 fewer to 12.4 more) | VERY LOW i,e |
| | | | | | In children with rAOM treated with prophylactic antibiotics compared to placebo/no treatment there is possibly no difference to report on adverse effects during 24 months follow-up. NNH Not Applicable |
Summary of findings:

29 Prophylactic antibiotics compared to placebo / no treatment for prevention of recurrent acute otitis media

Patient or population: Prevention of recurrent acute otitis media in children aged 0 to 14 years.

Setting: Primary health care.

Intervention: Prophylactic antibiotics (Studies used Amoxycillin 20-50mg/kg daily, Ampicillin 125-250mg/day (dose age dependant), Trimethoprim/sulfamethoxazole 4-8/12-40 mg/kg/day twice daily, Sulfisoxazole 75 mg/kg/day or 500-1000mg (dose age dependant) twice daily and Phenoxyethyl penicillin V 25 mg/kg/day). Duration was 6.5 weeks to 2 years.

Comparison: Placebo / no treatment

<table>
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<tr>
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<th>Quality</th>
<th>What happens</th>
</tr>
</thead>
<tbody>
<tr>
<td>Antibiotic resistance during intervention assessed by: nasopharyngeal swabs follow up: range 12 to 24 months</td>
<td>RR 1.37 (0.83 to 2.26)</td>
<td>Without Prophylactic antibiotics (22.5%)</td>
<td>LOW</td>
<td>In children with rAOM treated with prophylactic antibiotics compared to placebo there is possibly no difference to report on antibiotic resistance. NNT Not applicable.</td>
</tr>
<tr>
<td>Number of participants (studies)</td>
<td></td>
<td>With Prophylactic antibiotics (30.8%)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Number of participants: 181 (2 RCTs)</td>
<td></td>
<td>Difference (8.3% more (NS))</td>
<td></td>
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</tbody>
</table>

*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).

Ct: Confidence interval; RR: Risk ratio; NS: Not significant; NNT: Number needed to treat; NNH: Number needed to harm

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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

b. Inconsistency: High heterogeneity
e. Imprecision: Low event rate. Optimal information size not reached. Confidence interval covers benefit and harm.
g. Indirectness: Nasopharyngeal carriage of only a small number of specific bacteria reported. Surrogate marker for clinically important resistant disease.
h. Imprecision: Optimal information size not reached

References

### 30. Tympanostomy tubes compared to no surgery for recurrent acute otitis media

**Patient or population:** Children aged 0 to 3 years with recurrent acute otitis media (rAOM).

**Setting:** Hospital.

**Intervention:** Tympanostomy tubes (TTs)

**Comparison:** No surgery.

<table>
<thead>
<tr>
<th>Outcome</th>
<th>Relative effect (95% CI)</th>
<th>Anticipated absolute effects (95% CI)</th>
<th>Quality</th>
<th>What happens</th>
</tr>
</thead>
</table>
| **Hearing loss**<br>- Difference in mean decibel hearing. Ears with TTs compared to contralateral ears used as controls assessed with: Pure tone audiometry follow up: median 2 years | Without Tympanostomy tubes: At 6 months post TT insertion a small but significant difference is found between TT and non-TT ears, better hearing in TT ears (-3.7dB [-7 to 0 dB]).<br>At 12 months post insertion there is no significant difference (-0.8dB [-4.0 to +2.0 dB]).<br>At 24 months, a small but significant difference is found; better hearing in non-TT ears (1.7dB [0 to +4.0dB]). | With Tympanostomy tubes | | LOW b,c<sup>1</sup>
In children with rAOM receiving TTs compared to no surgery there is possibly an improvement in hearing at 6 months, which is not sustained at 12 months follow-up. | NNT not evaluable |
| **Incident rate of AOM episodes/child/year**<br>- assessed with: parental report + pneumatic otoscopy +/- tympanometry +/- otomicroscopy +/- otorrhea.<br>follow up: range 6 to 12 months | The mean incident rate of AOM episodes/child/year was 1.29 episodes/patient/year<sup>1</sup> | - | rate ratio 0.8 episodes/patient/year fewer (0.45 more to 1.43 more) | VERY LOW b,f,g<sup>2</sup> | In children with rAOM receiving TTs compared to no surgery there are possibly fewer AOM episodes/child/year. |
| **Proportion of children otitis free**<br>- follow up: range 6 months to 2 years | RR 1.81<br>(1.44 to 2.27) | 28.6% | 51.8% | 23.2% more<br>(12.6 more to 36.4 more) | LOW b,g<sup>2</sup> | Children with rAOM receiving TTs compared to no surgery are possibly more likely to remain free of otitis media at 6-24 months follow-up. | NNT ~4 |
Summary of findings:

### 30. Tympanostomy tubes compared to no surgery for recurrent acute otitis media

**Patient or population:** Children aged 0 to 3 years with recurrent acute otitis media (rAOM).

**Setting:** Hospital.

**Intervention:** Tympanostomy tubes (TTs)

**Comparison:** No surgery.

<table>
<thead>
<tr>
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<th>Quality</th>
<th>What happens</th>
</tr>
</thead>
<tbody>
<tr>
<td>Change in Quality of Life from baseline assessed with: QOL-OM-6 tool follow up: range 4 to 12 months</td>
<td>-</td>
<td>Without Tympanostomy tubes, With Tympanostomy tubes</td>
<td>LOW (≠)</td>
<td>In children with rAOM treated with TTs compared to no surgery there is possibly no difference in QOL scores at 4-12 months follow-up.</td>
</tr>
<tr>
<td>Ne of participants (studies)</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>12</td>
<td>45</td>
<td>35</td>
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</table>

*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).*

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

**GRADE Working Group grades of evidence**

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### Explanations

- a. Study: Le 1991
- b. Risk of Bias: Selection and performance bias
- c. Imprecision: Estimate of effect covers harm and benefit at different time points
- e. Mean incident rate calculated with an unweighted mean.
- f. Inconsistency: High heterogeneity
- g. Imprecision: Optimal information size not reached / small study
- i. Study: Kujala 2014
- j. Risk of Bias: Attrition bias, raw QOL data not available

### References

<table>
<thead>
<tr>
<th></th>
<th>Reference</th>
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</table>
Summary of findings:

31. Adenoidectomy +/- tympanostomy tubes compared to no surgery / tympanostomy tubes alone for recurrent acute otitis media

Patient or population: Children aged 10 months to 18 years with recurrent acute otitis media.

Setting: Hospital

Intervention: Adenoidectomy +/- Tymanostomy tubes

Comparison: No surgery / Tymanostomy tubes alone

<table>
<thead>
<tr>
<th>Outcome</th>
<th>No of participants (studies)</th>
<th>Relative effect (95% CI)</th>
<th>Anticipated absolute effects (95% CI)</th>
<th>Quality</th>
<th>What happens</th>
</tr>
</thead>
<tbody>
<tr>
<td>Treatment failure (classified as: ≥4 episodes AOM per year, presence effusion for &gt;50% of time (&gt;6 months), need for additional surgery, hearing improvement &lt;10dB) follow up: 12 months</td>
<td></td>
<td>RR 0.58 (0.36 to 0.94)</td>
<td>28.2%</td>
<td>16.4% (10.1 to 26.5)</td>
<td>11.8% fewer (18 fewer to 1.7 fewer)</td>
</tr>
</tbody>
</table>

| Subgroup analysis - Patients <2 years old: Treatment failure (classified as: ≥4 episodes AOM per year, presence effusion for >50% of time (>6 months), need for additional surgery, hearing improvement <10dB) follow up: 12 months | | RR 0.57 (0.42 to 0.78) | 27.4% | 15.6% (11.5 to 21.4) | 11.8% fewer (15.9 fewer to 6 fewer) | LOW b,c | In children <2 years old with rAOM undergoing adenoidectomy +/- TTs compared to no surgery/TTs alone, there are possibly fewer treatment failures at 12 months follow-up. NNT ~9 |
Summary of findings:

31. Adenoidectomy +/- tympanostomy tubes compared to no surgery / tympanostomy tubes alone for recurrent acute otitis media

**Patient or population:** Children aged 10 months to 18 years with recurrent acute otitis media.

**Setting:** Hospital

**Intervention:** Adenoidectomy +/- Tympanostomy tubes

**Comparison:** No surgery / Tympanostomy tubes alone

<table>
<thead>
<tr>
<th>Outcome</th>
<th>N of participants (studies)</th>
<th>Relative effect (95% CI)</th>
<th>Anticipated absolute effects (95% CI)</th>
<th>Quality</th>
<th>What happens</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td></td>
<td></td>
<td>Without Adenoidectomy +/- tympanostomy tubes</td>
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<td></td>
<td></td>
<td></td>
<td>With Adenoidectomy +/- tympanostomy tubes</td>
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<td>Difference</td>
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</tr>
<tr>
<td>Subgroup analysis - Patients &gt;2 years old: Treatment failure (classified as: ≥4 episodes AOM per year, presence effusion for &gt;50% of time (&gt;6 months), need for additional surgery, hearing improvement &lt;10dB) follow up: 12 months N of participants: 84 (5 RCTs)</td>
<td>RR 7.27 (95 to 55.60)</td>
<td>2.5%</td>
<td>18.2% (2.4 to 100.0)</td>
<td>15.7% more (NS) (0.1 fewer to 136.5 more)</td>
<td>☝️☐☐ LOW b,c,e</td>
</tr>
</tbody>
</table>

*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

**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**

b. Risk of Bias: Attrition bias, selection bias (Mattila 2003)
c. Imprecision: Optimal information size not reached
e. Imprecision: Broad estimate of effect

**References**

Summary of findings:

### 32. Adenoidectomy compared to no adenoidectomy as an adjunct to tympanostomy tube placement for recurrent acute otitis media

**Patient or population:** Children aged Recurrent acute otitis media in children aged

**Setting:** Hospital

**Intervention:** Adenoidectomy and tympanostomy tubes.

**Comparison:** No adenoidectomy / Tympanostomy tubes alone.

<table>
<thead>
<tr>
<th>Outcome</th>
<th>Relative effect (95% CI)</th>
<th>Anticipated absolute effects (95% CI)</th>
<th>Quality</th>
<th>What happens</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td></td>
<td>Without Adenoidectomy / TT alone</td>
<td>With Adenoidectomy + TT</td>
<td>Difference</td>
</tr>
<tr>
<td>Treatment failure (classified as: ≥4 episodes of AOM per year, presence effusion for &gt;50% of time (&gt;6 months), need for additional surgery, hearing improvement &lt;10dB) follow up: 12 months</td>
<td></td>
<td>RR 0.81 (0.27 to 2.40)</td>
<td>12.3%</td>
<td>9.9% (3.3 to 29.5)</td>
</tr>
</tbody>
</table>

NNT Not applicable

| Subgroup analysis - Patients >2 years old: Treatment failure (classified as: ≥4 episodes of AOM per year, presence effusion for >50% of time (>6 months), need for additional surgery, hearing improvement <10dB) follow up: 12 months |                          | RR 7.09 (0.93 to 54.20) | 2.6% | 18.2% (2.4 to 100.0) | 15.6% more (NS) (0.2 fewer to 136.4 more) | ☢☢  LOW b,d,e | In children >2 years old with rAOM undergoing TTs placement and adjunct adenoidectomy compared to no adenoidectomy, there is possibly no reduction in treatment failures at 12 months follow-up. |

NNT Not Applicable
Summary of findings:

32. Adenoidectomy compared to no adenoidectomy as an adjunct to tympanostomy tube placement for recurrent acute otitis media

Patient or population: Children aged Recurrent acute otitis media in children aged

Setting: Hospital

Intervention: Adenoidectomy and tympanostomy tubes.

Comparison: No adenoidectomy / Tympanostomy tubes alone.

<table>
<thead>
<tr>
<th>Outcome</th>
<th>Relative effect (95% CI)</th>
<th>Anticipated absolute effects (95% CI)</th>
<th>Quality</th>
<th>What happens</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td></td>
<td>Without Adenoidectomy / TT alone</td>
<td>With Adenoidectomy + TT</td>
<td>Difference</td>
</tr>
<tr>
<td>Subgroup analysis - Patients &lt;2 years old: Treatment failure (classified as: ≥4 episodes of AOM per year, presence effusion for &gt;50% of time (&gt;6 months), need for additional surgery, hearing improvement &lt;10dB) follow up: 12 months</td>
<td>RR 0.66 (0.41 to 1.06)</td>
<td>16.5%</td>
<td>10.9% (6.8 to 17.5)</td>
<td>5.6% fewer (NS) (9.7 fewer to 1 more)</td>
</tr>
</tbody>
</table>

*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).

Ct: Confidence interval; RR: Risk ratio; NS: Not significant; NNT: Number needed to treat; NNH: Number needed to harm

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
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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

b. Risk of Bias: Attrition bias, selection bias (Mattila 2003)
c. Inconsistency: noted to have borderline heterogeneity. Not rated down.
d. Imprecision: Optimal information size not reached
e. Imprecision: Wide confidence interval
f. Strong association however only rated up one level given small numbers and low event rates.

References

Summary of findings:

33. Topical antibiotics compared to ear toilet alone for chronic suppurative otitis media

**Patient or population:** Children and adults with chronic suppurative otitis media

**Setting:** Primary health care

**Intervention:** Topical antibiotics (Studies used: Oxfloxacin single dose and Ciprofloxacin three times daily for 7 days.)

**Comparison:** Ear toilet alone

<table>
<thead>
<tr>
<th>Outcome</th>
<th>Relative effect (95% CI)</th>
<th>Anticipated absolute effects (95% CI)</th>
<th>Quality</th>
<th>What happens</th>
</tr>
</thead>
<tbody>
<tr>
<td>Persistent discharge assessed with: otoscopy follow up: 1 week No of participants: 197 (2 RCTs)</td>
<td>RR 0.45 (0.34 to 0.59)</td>
<td>Without Topical antibiotics: 80.8% With Topical antibiotics: 36.4% (27.5 to 47.7)</td>
<td>44.4% fewer (53.3 fewer to 33.1 fewer)</td>
<td>LOW b,c,d</td>
</tr>
</tbody>
</table>

*C 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).

**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
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- **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**

- b. Risk of Bias: Attrition bias noted (Kasemsuwan) but not rated down
- c. Inconsistency: High heterogeneity
- d. Imprecision: Small studies / optimal information size not reached.

**References**

Summary of findings:

34. Topical quinolone antibiotic compared to topical antiseptic for chronic suppurative otitis media

**Patient or population:** Children and adults with chronic suppurative otitis media.

**Setting:** Primary health care

**Intervention:** Topical quinolone antibiotic (Studies used: Ofloxacin 3 drops, three times daily and Ciprofloxacin 3-6 drops twice to three times daily.) Duration varied from 10 days to 4 weeks.

**Comparison:** Topical antiseptic (Studies used: 1 to 5% Povidone iodine, 2% Acetic acid, 2% Boric acid and 1% Aluminium acetate). Duration varied from 10 days to 4 weeks

<table>
<thead>
<tr>
<th>Outcome</th>
<th>Ne of participants (studies)</th>
<th>Relative effect (95% CI)</th>
<th>Anticipated absolute effects (95% CI)</th>
<th>Quality</th>
<th>What happens</th>
</tr>
</thead>
<tbody>
<tr>
<td>Persistent discharge assessed with: otoscopy follow up: range 2 to 4 weeks Ne of participants: 702 (5 RCTs)</td>
<td>RR 0.56 (0.46 to 0.67)</td>
<td>57.0% (26.2 to 38.2)</td>
<td>25.1% fewer (30.8 fewer to 18.8 fewer)</td>
<td>+ + +</td>
<td>Moderate</td>
</tr>
<tr>
<td>Healing of the tympanic membrane assessed with: otoscopy follow up: median 4 weeks Ne of participants: 399 (1 RCT)</td>
<td>RR 1.54 (0.91 to 2.61)</td>
<td>10.1% (9.1 to 26.2)</td>
<td>5.4% more (NS) (0.9 fewer to 16.2 more)</td>
<td>+ + + +</td>
<td>Low</td>
</tr>
</tbody>
</table>

*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).*

Ct: Confidence interval; RR: Risk ratio; NS: Not significant; NNT: Number needed to treat; NNH: Number needed to harm

**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

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**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**

b. Risk of Bias: Attrition bias (van Hasselt 1997) noted however only small number in meta-analysis and removal does not affect overall result of data. Not rated down.
c. Indirectness: various antiseptic solutions used
e. Imprecision: Small studies / optimal information size not reached
f. Imprecision: Single study
References


### Summary of findings:

#### 35. Topical quinolone compared to topical non-quinolone antibiotic for chronic suppurative otitis media

**Patient or population:** Children and adults with chronic suppurative otitis media.

**Setting:** Primary health care.

**Intervention:** Topical quinolone antibiotic. (Studies used: Ciprofloxacin 0.3% 2-5 drops, three times daily, Ofloxacin 0.3% 3 - 6 drops, twice to three times daily or 6 drops once weekly.) Duration varied from 8 days to 3 weeks

**Comparison:** Topical non-quinolone antibiotic (Studies used: Tobramycin 0.3% 2-5 drops, three times daily, Gentamicin 0.3% 5 drops, three times daily, 0.5% Neomycin, 0.1% polymyxin B 3-6 drops, twice to three times daily or 6 drops weekly.) Duration varied from 8 days to 3 weeks

<table>
<thead>
<tr>
<th>Outcome</th>
<th>Relative effect (95% CI)</th>
<th>Anticipated absolute effects (95% CI)</th>
<th>Quality</th>
<th>What happens</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td></td>
<td>Without Topical quinolone</td>
<td>With Topical quinolone</td>
<td>Difference</td>
</tr>
<tr>
<td>Persistent discharge assessed with: otoscopy follow up: 2 weeks</td>
<td>RR 0.65 (0.46 to 0.92)</td>
<td>37.4%</td>
<td>24.3% (17.2 to 34.4)</td>
<td>13.1% fewer (20.2 fewer to 3 fewer)</td>
</tr>
<tr>
<td>Persistent discharge assessed with: otoscopy follow up: range 2 to 3 weeks</td>
<td>RR 0.76 (0.55 to 1.04)</td>
<td>36.4%</td>
<td>27.6% (20.0 to 37.8)</td>
<td>8.7% fewer (NS) (16.4 fewer to 1.5 more)</td>
</tr>
<tr>
<td>Persistent discharge - Topical quinolone vs topical non-quinolone with steroid assessed with: otoscopy follow up: median 14 days</td>
<td>RR 0.97 (0.57 to 1.64)</td>
<td>70.5%</td>
<td>68.4% (40.2 to 100.0)</td>
<td>2.1% fewer (NS) (30.3 fewer to 45.1 more)</td>
</tr>
</tbody>
</table>
### Summary of findings:

#### 35. Topical quinolone compared to topical non-quinolone antibiotic for chronic suppurative otitis media

**Patient or population:** Children and adults with chronic suppurative otitis media.

**Setting:** Primary health care.

**Intervention:** Topical quinolone antibiotic. (Studies used: Ciprofloxacin 0.3% 2-5 drops, three times daily, Ofloxacin 0.3% 3 - 6 drops, twice to three times daily or 6 drops once weekly.) Duration varied from 8 days to 3 weeks.

**Comparison:** Topical non-quinolone antibiotic (Studies used: Tobramycin 0.3% 2-5 drops, three times daily, Gentamicin 0.3% 5 drops, three times daily, 0. 5% Neomycin, 0.1% polymyxin B 3-6 drops, twice to three times daily or 6 drops weekly.) Duration varied from 8 days to 3 weeks.

---

<table>
<thead>
<tr>
<th>Outcome</th>
<th>No of participants (studies)</th>
<th>Relative effect (95% CI)</th>
<th>Anticipated absolute effects (95% CI)</th>
<th>Quality</th>
<th>What happens</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td></td>
<td></td>
<td>Without Topical quinolone</td>
<td>With Topical quinolone</td>
<td>Difference</td>
</tr>
<tr>
<td>Persistent discharge - Topical quinolone vs topical non-quinolone with steroid. Remote Aboriginal children. assessed with: otoscopy follow up: range 6 to 8 weeks</td>
<td>97 (1 RCT)</td>
<td>RR 0.97 (0.75 to 1.25)</td>
<td>72.3%</td>
<td>70.2% (54.3 to 90.4)</td>
<td>2.2% fewer (NS) (18.1 fewer to 18.1 more)</td>
</tr>
</tbody>
</table>

*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

---

**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

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**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**

b. Inconsistency: High heterogeneity
c. Imprecision: Small studies / optimal information size not reached
f. Risk of Bias: Performance bias (no blinding - Miro 2000), early termination of study noted (Couzos 2003) due to poor recruitment.
g. Study taken from: Leach 2008

---

**References**

Summary of findings:

36. Systemic antibiotic compared to topical antibiotic for chronic suppurative otitis media

**Patient or population:** Children and adults with chronic suppurative otitis media.

**Setting:** Primary health care.

**Intervention:** Systemic antibiotic [oral amoxicillin-clavulanic acid (375mg) three times daily, for 7 days; Ciprofloxacin (500mg) twice daily for 10 days; intramuscular Gentamicin sulfate (80mg) twice daily for 5-10 days].

**Comparison:** Topical quinolone antibiotic [Studies used: Ofloxacin eardrops 0.3% three times daily, for 7 days; Ciprofloxacin eardrops (250 microgram/mL) twice daily for 5-10 days].

<table>
<thead>
<tr>
<th>Outcome</th>
<th>Relative effect (95% CI)</th>
<th>Anticipated absolute effects (95% CI)</th>
<th>Quality</th>
<th>What happens</th>
</tr>
</thead>
<tbody>
<tr>
<td>Treatment failure - Systemic non-quinolone vs topical quinolone assessed with: persistent discharge on otoscopy follow up: range 1 to 2 weeks</td>
<td>RR 3.21 (1.98 to 5.49)</td>
<td>20.3% - 65.3% (38.2 to 100.0)</td>
<td>44.9% more (17.9 more to 91.3 more)</td>
<td>MODERATE</td>
</tr>
<tr>
<td>Treatment failure - Systemic quinolone vs topical quinolone assessed with: persistent discharge on otoscopy follow up: range 1 to 2 weeks</td>
<td>RR 3.18 (1.87 to 5.43)</td>
<td>15.0% - 47.7% (28.1 to 81.4)</td>
<td>32.7% more (13.1 more to 66.5 more)</td>
<td>MODERATE</td>
</tr>
</tbody>
</table>

*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

GRADE Working Group grades of evidence

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**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

b. Risk of Bias: Performance bias (blinding not described and not likely - Esposito 1992).
c. Imprecision: Optimal information size not reached.
e. Study taken from: Browning 1983

References
### Summary of findings:

**37 Oral Trimethoprim/Sulfamethoxazole compared to placebo for adjunct treatment (with topical quinolones) for chronic suppurative otitis media.**

**Patient or population:** Children aged 1 to 12 years with chronic suppurative otitis media (TMP).

**Setting:** Primary health care.

**Intervention:** Oral Trimethoprim/Sulfamethoxazole (8 mg/kg/day - trimethoprim component - in two divided doses) adjunct treatment (with topical quinolones) for 6 to 12 weeks.

**Comparison:** Placebo adjunct treatment (with topical quinolones)

<table>
<thead>
<tr>
<th>Outcome (and its 95% confidence interval)</th>
<th>NNT or NNH (95% CI)</th>
<th>Relative effect (95% CI)</th>
<th>Anticipated absolute effects (95% CI)</th>
<th>Quality</th>
<th>What happens</th>
</tr>
</thead>
<tbody>
<tr>
<td>Persistent otorhoea assessed with: otoscopy follow up: mean 6 weeks</td>
<td>RR 0.52 (0.31 to 0.80)</td>
<td>52.9%</td>
<td>27.5% (16.4 to 47.1)</td>
<td>⬠ Acrobat ⬠ Acrobat ⬠ Acrobat</td>
<td>MODERATE ⬠ ⬠ ⬠</td>
</tr>
<tr>
<td>Persistent otorhoea assessed with: otoscopy follow up: mean 12 weeks</td>
<td>RR 0.68 (0.41 to 1.14)</td>
<td>46.9%</td>
<td>31.9% (19.2 to 53.5)</td>
<td>⬠ Acrobat ⬠ Acrobat ⬠ Acrobat</td>
<td>MODERATE ⬠ ⬠ ⬠</td>
</tr>
<tr>
<td>Persistent otorhoea assessed with: otoscopy follow up: mean 1 year</td>
<td>RR 1.28 (0.59 to 2.76)</td>
<td>19.6%</td>
<td>25.0% (11.5 to 54.4)</td>
<td>LOW ⬠ Acrobat ⬠ Acrobat ⬠ Acrobat</td>
<td>LOW ⬠ Acrobat ⬠ Acrobat ⬠ Acrobat</td>
</tr>
<tr>
<td>Adverse events (diarrhoea or vomiting) assessed with: parental report follow up: mean 6 weeks</td>
<td>RR 4.34 (0.50 to 37.46)</td>
<td>2.0%</td>
<td>8.5% (1.0 to 73.5)</td>
<td>⬠ Acrobat ⬠ Acrobat ⬠ Acrobat</td>
<td>MODERATE ⬠ ⬠ ⬠</td>
</tr>
</tbody>
</table>

*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
### Summary of findings:

37 Oral Trimethoprim/Sulfamethoxazole compared to placebo for adjunct treatment (with topical quinolones) for chronic suppurative otitis media.

**Patient or population:** Children aged 1 to 12 years with chronic suppurative otitis media (TMP).

**Setting:** Primary health care.

**Intervention:** Oral Trimethoprim/Sulfamethoxazole (8 mg/kg/day - trimethoprim component - in two divided doses) adjunct treatment (with topical quinolones) for 6 to 12 weeks.

**Comparison:** Placebo adjunct treatment (with topical quinolones)

<table>
<thead>
<tr>
<th>Outcome</th>
<th>Relative effect (95% CI)</th>
<th>Anticipated absolute effects (95% CI)</th>
<th>Quality</th>
<th>What happens</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Without Oral Trimethoprim/ Sulfamethoxazole</td>
<td>With Oral Trimethoprim/ Sulfamethoxazole</td>
<td>Difference</td>
<td></td>
</tr>
</tbody>
</table>

**GRADE Working Group grades of evidence**

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- **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. Study taken from: van der Veen 2007
b. Imprecision: Small study
c. After 12 weeks study medication discontinued and patients referred back to care provider. Treatment recommendation in case otorrhea was: trimethoprim/sulfamethoxazole (18 mg/kg, 2 times per day, for 6–12 weeks) for the placebo group and azithromycin (5 mg/kg, once per day, for 6–12 weeks) for the trimethoprim/sulfamethoxazole group, however this was up to discretion of doctor and other treatment could be offered.
d. Risk of Bias: Performance bias (lack blinding)

### References

Summary of findings:

38. Topical quinolone with steroids compared to topical quinolone without steroids for chronic suppurative otitis media

**Patient or population:** Adults (>18 years) with chronic suppurative otitis media

**Setting:** Primary health care.

**Intervention:** Topical quinolone with steroids (Ofloxacin 0.3% and dexamethasone 0.1% combination, 12 drops, twice daily for 10 days).

**Comparison:** Topical quinolone without steroids (Ofloxacin 0.3%, 12 drops twice daily for 10 days).

<table>
<thead>
<tr>
<th>Outcome</th>
<th>Relative effect (95% CI)</th>
<th>Anticipated absolute effects (95% CI)</th>
<th>Quality</th>
<th>What happens</th>
</tr>
</thead>
<tbody>
<tr>
<td>Clinical cure assessed with: otoscopy follow up: mean 15 days</td>
<td>RR 0.88 (0.67 to 1.15)</td>
<td>71.2% 62.6% (47.7 to 81.8)</td>
<td>8.5% fewer (NS) (23.5 fewer to 10.7 more)</td>
<td>LOW b</td>
</tr>
</tbody>
</table>

*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

**GRADE Working Group grades of evidence**

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- **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. Study: Panchasara 2015
b. Imprecision: Small, single study. Rated down by two.

References

Summary of findings:

39 Swimming in a chlorinated pool compared to no swimming for treatment chronic suppurative otitis media

Patient or population: Remote Australian Aboriginal children aged 5 to 12 years with chronic suppurative otitis media

Setting: Primary care - remote Australian Aboriginal community.

Intervention: Swimming in a chlorinated pool daily for 4 weeks

Comparison: No swimming.

<table>
<thead>
<tr>
<th>Outcome</th>
<th>Relative effect</th>
<th>Anticipated absolute effects (95% CI)</th>
<th>Quality</th>
<th>What happens</th>
</tr>
</thead>
<tbody>
<tr>
<td>Ear discharge / CSOM assessed with: tympanometry, pneumatic &amp; video otoscope follow up: 4 weeks</td>
<td>RR 0.88 (0.63 to 1.22)</td>
<td>Without swimming in a chlorinated pool: 66.7% (42.0 to 81.3)</td>
<td>LOW</td>
<td>In remote Australian Aboriginal children with CSOM who swim daily compared to no swimming there is possibly no difference in ear discharge at 4 weeks follow-up. NNT Not Applicable</td>
</tr>
<tr>
<td></td>
<td>With swimming in a chlorinated pool: 58.7% (24.7 fewer to 14.7 more)</td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

*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

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. Study taken from: Stephen 2013. Note: this data conflicts with observational studies showing significant benefit. Methodology is higher in this study.
b. Indirectness: Unique setting, data cannot be generalised to all children
c. Imprecision: Small study

References

### Summary of findings:

#### 40. Antiseptic irrigation of middle ear at time of surgery compared to no treatment for the prevention of post-operative tympanostomy tube otorrhoea

**Patient or population:** Children < 12 years with rAOM or OME undergoing tympanostomy tube (TTs) insertion.

**Setting:** Hospital.

**Intervention:** Single application of triple irrigation of the ear canal with 50% solution of povidone-iodine topical antiseptic (Betadine) and saline for one minute before insertion TTs.

**Comparison:** No treatment.

<table>
<thead>
<tr>
<th>Outcome</th>
<th>Relative effect (95% CI)</th>
<th>Anticipated absolute effects (95% CI)</th>
<th>Difference</th>
<th>Quality</th>
<th>What happens</th>
</tr>
</thead>
<tbody>
<tr>
<td>Post-operative TTO (by child) follow up: 1 weeks</td>
<td>RR 1.25 (0.36 to 4.38)</td>
<td>8.0% Without antiseptic irrigation of middle ear at time of surgery</td>
<td>10.0% (2.9 to 35.0) With antiseptic irrigation of middle ear at time of surgery</td>
<td>2.0% more (NS) (5.1 fewer to 27 more)</td>
<td>VERY LOW</td>
</tr>
</tbody>
</table>

*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; TTs: Tympanostomy tubes; TTO: Tympanostomy tube otorrhoea

---

**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**

- b. Risk of Bias: Selection bias, participants and outcome assessor not blinded.

**References**

Summary of findings:

41. Saline irrigation at time of surgery compared to topical antibiotics for the prevention of post-operative tympanostomy tube otorrhoea

**Patient or population:** Children 3-11 years with AOM or OME undergoing tympanostomy tube (TTs) insertion.

**Setting:** Hospital

**Intervention:** Saline irrigation of middle ear at time of surgery.

**Comparison:** Ofloxacin for 5 days post-operatively.

<table>
<thead>
<tr>
<th>Outcome</th>
<th>Relative effect (95% CI)</th>
<th>Anticipated absolute effects (95% CI)</th>
<th>Quality</th>
<th>What happens</th>
</tr>
</thead>
<tbody>
<tr>
<td>N number of participants (studies)</td>
<td>5-day post-operative Ofloxacin</td>
<td>With Saline irrigation of middle ear at time of surgery</td>
<td>Difference</td>
<td></td>
</tr>
<tr>
<td>Post-operative TTO follow up: 2 weeks</td>
<td>RR 1.83 (0.72 to 4.68)</td>
<td>8.6%</td>
<td>15.7% (6.2 to 40.1)</td>
<td>7.1% more (NS) (2.4 fewer to 31.5 more)</td>
</tr>
<tr>
<td>N number of participants: 140 (1 RCT)</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

In children undergoing TTs surgery, saline irrigation at time of surgery compared to 5-days post-surgery treatment with topical Ofloxacin there is possibly no difference in TTO at 2 weeks follow-up.

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; TTs: Tympanostomy tubes; TTO: Tympanostomy tube otorrhoea

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


b. Risk of Bias: Participants not blinded, however outcome assessor blinded. Not rated down.

c. Imprecision: Single, small study

References

Summary of findings:

42. Single dose Ciprofloxacin compared to prolonged application Ciprofloxacin for the prevention of post-operative tympanostomy tube otorrhea

Patient or population: Children 3-14 years with rAOM or OME undergoing tympanostomy tube (TTs) insertion.

Setting: Hospital.


Comparison: Prolonged application Ciprofloxacin for 5 days.

<table>
<thead>
<tr>
<th>Outcome</th>
<th>Relative effect (95% CI)</th>
<th>Anticipated absolute effects (95% CI)</th>
<th>Quality</th>
<th>What happens</th>
</tr>
</thead>
<tbody>
<tr>
<td>Post-operative TTO follow up: 2 weeks</td>
<td>RR 0.71 (0.13 to 3.72)</td>
<td>16.7% 11.8% (2.2 to 62.0)</td>
<td>⬤ ○ ○ ○ VERY LOW b,c</td>
<td>In children with TTs treated with single dose Ciprofloxacin compared to Ciprofloxacin for 5 days post-surgery there is no difference in TTO at 2 weeks follow-up. NNT Not Applicable</td>
</tr>
</tbody>
</table>

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; TTs: tympanostomy tubes; TTO: Tympanostomy tube otorrhea

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


b. Risk of Bias: Participants not blinded and unclear if outcome assessor blinded.


References

43. Topical antibiotic ear-drops (with or without a corticosteroid) compared to no treatment for tympanostomy tube otorrhoea

**Patient or population:** Children aged 1 to 10 years with tympanostomy tube otorrhoea.

**Setting:** Primary health care.

**Intervention:** Antibiotic ear-drops (Study used: hydrocortisone–bacitracin–colistin ear-drops, five drops, three times daily, in the discharging ear or ears for 7 days).

**Comparison:** No treatment

<table>
<thead>
<tr>
<th>Outcome</th>
<th>Relative effect (95% CI)</th>
<th>Anticipated absolute effects (95% CI)</th>
<th>Quality</th>
<th>What happens</th>
</tr>
</thead>
<tbody>
<tr>
<td>Resolution of ear discharge assessed with: otoscopy follow up: 2 weeks</td>
<td>RR 2.09 (1.62 to 2.69)</td>
<td>45.3% (73.4 to 100.0)</td>
<td>49.4% more (28.1 more to 76.6 more)</td>
<td>☯◯◯◯ MODERATE</td>
</tr>
<tr>
<td>Resolution of ear discharge assessed with: otoscopy follow up: &gt;4 weeks</td>
<td>RR 0.08 (0.01 to 0.62)</td>
<td>16.4% (0.2 to 10.2)</td>
<td>15.1% fewer (16.3 fewer to 6.2 fewer)</td>
<td>☯◯◯◯ MODERATE</td>
</tr>
</tbody>
</table>

*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

**GRADE Working Group grades of evidence**

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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**


b. Risk of Bias: Open label trial

c. Imprecision: Small study, however trial stopped early due to recommendation by committee given results of interim analysis.

**References**

### Summary of findings:

**44. Antibiotic eardrops (without a corticosteroid) compared to saline rinsing of the ear canal for children with tympanostomy tube otorrhoea**

**Patient or population:** Children aged 7 months to 9 years with tympanostomy tube otorrhoea.

**Setting:** Primary health care.

**Intervention:** Antibiotic eardrops (Study used: Ciprofloxacin 3 mg/mL otic drops, four drops, twice daily for 1 week. This was accompanied by massage of the tragus).

**Comparison:** Saline rinsing of the ear canal (Study used: 10 mL saline through a syringe, by the parents, three times daily for 1 week).

<table>
<thead>
<tr>
<th>Outcome</th>
<th>No of participants (studies)</th>
<th>Relative effect (95% CI)</th>
<th>Anticipated absolute effects (95% CI)</th>
<th>Quality</th>
<th>What happens</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td></td>
<td>RR 1.87 (1.04 to 2.69)</td>
<td>46.2%</td>
<td>++</td>
<td>In children with TTO treated with topical Ciprofloxacin compared to saline rinsing there is probably more resolution of ear discharge at 1 week follow-up. NNT ~4</td>
</tr>
<tr>
<td>Resolution of ear discharge assessed with: otoscopy follow up: 1 weeks</td>
<td>46.2%</td>
<td>77.1% (48.0 to 100.0)</td>
<td>30.9% more (1.8 more to 78 more)</td>
<td>++</td>
<td></td>
</tr>
<tr>
<td>Tube blockage assessed with: otoscopy follow up: 1 weeks</td>
<td>7.7%</td>
<td>13.6% (2.5 to 74.4)</td>
<td>5.9% more (NS) (5.2 fewer to 66.7 more)</td>
<td>++</td>
<td></td>
</tr>
</tbody>
</table>

*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

**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 (Heslop 2010)


c. Imperception: Small study

d. Imperception: Low event rate

### References

Summary of findings:

45. Antibiotic(s) + corticosteroid eardrops compared to antibiotic ear-drops for children with tympanostomy tube otorrhoea

Patient or population: Children aged 6 months to 12 years with tympanostomy tube otorrhoea (TTO)

Setting: Primary health care.

Intervention: Antibiotic(s) + corticosteroid ear-drops (Studies used: Ciprofloxacin 0.3% & fluocinolone acetonide 0.025% twice daily, Ciprofloxacin (0.3%) & dexamethasone (0.1%) 3-4 drops, twice daily.) Duration was for 7 days.

Comparison: Antibiotic ear-drops (Studies used: Ofloxacin 5 drops twice daily, Ciprofloxacin 3 drops twice daily) Duration was 7-10 days.

<table>
<thead>
<tr>
<th>Outcome</th>
<th>No of participants (studies)</th>
<th>Relative effect (95% CI)</th>
<th>Anticipated absolute effects (95% CI)</th>
<th>Quality</th>
<th>What happens</th>
</tr>
</thead>
<tbody>
<tr>
<td>Resolution of ear discharge assessed with: physician assessment / parental report follow up: &lt;2 weeks No of participants: 590 (2 RCTs)</td>
<td>RR 1.76 (1.33 to 2.31)</td>
<td>19.9%</td>
<td>35.1% (26.5 to 46.0)</td>
<td>15.1% more (6.6 more to 26.1 more)</td>
<td>LOW</td>
</tr>
<tr>
<td>Adverse events assessed with: parental report follow up: &lt;4 weeks No of participants: 1023 (3 RCTs)</td>
<td>RR 0.86 (0.55 to 1.32)</td>
<td>7.8%</td>
<td>6.7% (4.3 to 10.3)</td>
<td>1.1% fewer (NS) (3.5 fewer to 2.5 more)</td>
<td>LOW</td>
</tr>
<tr>
<td>Resolution of ear discharge assessed with: physician assessment / parental report follow up: range 2 to 4 weeks No of participants: 590 (2 RCTs)</td>
<td>RR 1.09 (0.90 to 1.31)</td>
<td>76.0%</td>
<td>82.9% (68.4 to 99.6)</td>
<td>6.8% more (NS) (7.5 fewer to 23.6 more)</td>
<td>LOW</td>
</tr>
</tbody>
</table>

*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

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:

c. Imprecision: Optimal information size not reached. Not rated down
d. Risk publication bias: 2 studies not published and not included in meta-analysis.
References

Summary of findings:

46. Ear plugs compared to no ear plugs when swimming or bathing for prevention of tympanostomy tube otorrhoea

**Patient or population:** Children aged 6 months to 6 years with tympanostomy tubes (TT).

**Setting:** Community.

**Intervention:** Ear plugs (Soft, plastic, prefabricated ear plug (Doc’s Proplugs) or mouldable silicone ear plug (Insta-Putty, Insta-Mold Products) when swimming or bathing. Duration was 1 year.

**Comparison:** No ear plugs when swimming or bathing.

<table>
<thead>
<tr>
<th>Outcome</th>
<th>Nr of participants (studies)</th>
<th>Relative effect (95% CI)</th>
<th>Anticipated absolute effects (95% CI)</th>
<th>Quality</th>
<th>What happens</th>
</tr>
</thead>
</table>
| Rate of otorrhoea (annual) assessed with: physician diagnosed by otoscopy follow up: 1 years | 172 (1 RCT) | - | - | MD 0.36 lower (0.45 lower to 0.27 lower) | Low | In children with TTO who wear ear plugs compared to no ear plugs when swimming or bathing there are possibly fewer episodes of otorrhoea at 1 year follow-up.

*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

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, Moualed 2016 (Goldstein 2005)
b. Risk of Bias: Performance bias and attrition bias
c. Imprecision: Small study

References
### Summary of findings:

#### 47. No swimming or head submersion during bathing compared to unrestricted swimming or head submersion during bathing for prevention of tympanostomy tube otorrhoea

**Patient or population:** Children aged 3 months to 12 years with tympanostomy tubes (TTs).

**Setting:** Community.

**Intervention:** No swimming or head submersion during bathing. Duration was for 1 year.

**Comparison:** Unrestricted swimming or head submersion during bathing.

<table>
<thead>
<tr>
<th>Outcome</th>
<th>Relative effect (95% CI)</th>
<th>Anticipated absolute effects (95% CI)</th>
<th>Quality</th>
<th>What happens</th>
</tr>
</thead>
<tbody>
<tr>
<td>Rate of otorrhoea (annual) assessed with: review of medical record and parental report follow up: 1 year</td>
<td>-</td>
<td>The mean rate of otorrhoea (annual) was 1.17 episodes otorrhoea / year</td>
<td>-</td>
<td>MD 0 episodes otorrhoea / year (0.14 lower to 0.14 higher)</td>
</tr>
</tbody>
</table>

*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

**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. Study taken from: Cochrane Review, Moualed 2016 (Parker 1994)

b. Some caution must be taken with interpretation of the 95% confidence interval in this case as it was not possible to calculate standard deviations for the study data and Goldstein 2005 values have been used.

c. Risk of Bias: Performance bias, selection bias, attrition bias

d. Imprecision: Small study

### References

Summary of findings:

48. Oral antibiotics compared to placebo or no treatment for children with tympanostomy tube otorrhoea

**Patient or population:** Children aged 6 months to 10 years with tympanostomy tube otorrhoea (TTO).

**Setting:** Primary health care.

**Intervention:** Oral antibiotics (Studies used: Amoxicillin+clavulanate 45 mg/kg/day divided into 2 doses or 30/7.5 mg/kg per day divided into 3 doses.) Duration was for 7 days.

**Comparison:** Placebo or no treatment.

<table>
<thead>
<tr>
<th>Outcome</th>
<th>Relative effect (95% CI)</th>
<th>Anticipated absolute effects (95% CI)</th>
<th>Quality</th>
<th>What happens</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td></td>
<td>Without Oral antibiotics</td>
<td>With Oral antibiotics</td>
<td>Difference</td>
</tr>
<tr>
<td>Resolution of ear discharge assessed with: physician assessment by otoscopy and suction. follow up: &lt;2 weeks</td>
<td>RR 2.21 (1.36 to 3.60)</td>
<td>32.5%</td>
<td>71.8% (44.2 to 100.0)</td>
<td>39.3% more (11.7 more to 84.5 more)</td>
</tr>
<tr>
<td>Resolution of ear discharge assessed with: physician assessment by otoscopy follow up: 2 weeks</td>
<td>RR 1.23 (0.90 to 1.69)</td>
<td>45.3%</td>
<td>55.8% (40.8 to 76.6)</td>
<td>10.4% more(NS) (4.5 fewer to 31.3 more)</td>
</tr>
<tr>
<td>Adverse events (contralateral acute otitis media with perforation of the tympanic membrane, extrusion of tympanostomy tube, granulation, gastrointestinal and cutaneous) assessed with: parental report follow up: &lt;2 weeks</td>
<td>RR 1.71 (0.69 to 4.25)</td>
<td>15.0%</td>
<td>25.7% (10.3 to 63.7)</td>
<td>10.7% more(NS) (4.7 fewer to 46.8 more)</td>
</tr>
<tr>
<td>Chronic ear discharge (&gt;4 weeks) assessed with: parental report follow up: 6 months</td>
<td>RR 0.41 (0.15 to 1.11)</td>
<td>16.4%</td>
<td>6.7% (2.5 to 18.2)</td>
<td>9.7% fewer (NS) (14 fewer to 1.8 more)</td>
</tr>
</tbody>
</table>
Summary of findings:

48. Oral antibiotics compared to placebo or no treatment for children with tympanostomy tube otorrhoea

**Patient or population:** Children aged 6 months to 10 years with tympanostomy tube otorrhoea (TTO).

**Setting:** Primary health care.

**Intervention:** Oral antibiotics (Studies used: Amoxicillin+clavulanate 45 mg/kg/day divided into 2 doses or 30/7.5 mg/kg per day divided into 3 doses.) Duration was for 7 days.

**Comparison:** Placebo or no treatment.

<table>
<thead>
<tr>
<th>Outcome</th>
<th>Relative effect (95% CI)</th>
<th>Anticipated absolute effects (95% CI)</th>
<th>Quality</th>
<th>What happens</th>
</tr>
</thead>
<tbody>
<tr>
<td>Tube extrusion assessed with: physician assessment and otoscopy follow up: &lt;2 weeks</td>
<td>RR 0.51 (0.05 to 5.43)</td>
<td>5.0%</td>
<td>2.6% (0.3 to 27.2)</td>
<td>2.5% fewer (NS) (4.8 fewer to 22.1 more)</td>
</tr>
</tbody>
</table>

*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).

**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**

- b. Risk of Bias: Attrition bias noted but not rated down (Ruohola 2003)
- c. Imprecision: Small study
- e. Risk of bias: Open label study
- f. Imprecision: Low event rate
- g. Imprecision: Broad estimate of effect; confidence interval includes significant both significant benefit and harm.

**References**

Summary of findings:

49. Oral antibiotics compared to saline rinsing of the ear canal for children with tympanostomy tube otorrhoea

**Patient or population:** Children aged 7 months to 9 years with tympanostomy tube otorrhoea (TTO).

**Setting:** Primary health care.

**Intervention:** Oral antibiotics (Study used: Amoxicillin 25-50 mg/kg/day divided into three daily doses for one week. In case of penicillin allergy, erythromycin, 40 mg/kg/day divided into three doses daily for a week was chosen).

**Comparison:** Saline rinsing of the ear canal (Study used: 10 mL saline through a syringe, by the parents, three times daily for 1 week).

<table>
<thead>
<tr>
<th>Outcome</th>
<th>No of participants (studies)</th>
<th>Relative effect (95% CI)</th>
<th>Anticipated absolute effects (95% CI)</th>
<th>Quality</th>
<th>What happens</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td></td>
<td></td>
<td>Without Oral antibiotics</td>
<td>With Oral antibiotics</td>
<td>Difference</td>
</tr>
<tr>
<td>Resolution of ear discharge assessed with: otoscopy follow up: 1 weeks</td>
<td>RR 0.65 (0.30 to 1.43)</td>
<td>46.2%</td>
<td>30.0% (13.8 to 66.0)</td>
<td>16.2% fewer (NS) (32.3 fewer to 19.8 more)</td>
<td>✗✗◯◯ LOW b</td>
</tr>
<tr>
<td>Proportion of patients with tube blockage assessed with: otoscopy follow up: 1 weeks</td>
<td>RR 1.95 (0.36 to 10.58)</td>
<td>7.7%</td>
<td>15.0% (2.8 to 81.4)</td>
<td>7.3% more (NS) (4.9 fewer to 73.7 more)</td>
<td>✗✗◯◯ LOW b</td>
</tr>
</tbody>
</table>

*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).

**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
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- **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**

- b. Imprecision: Small study
- c. Imprecision: Low event rate

**References**

Summary of findings:

50. Antibiotic eardrops (with or without a corticosteroid) compared to Oral antibiotics for children with tympanostomy tube otorrhea

**Patient or population:** Children aged 6 months to 12 years with tympanostomy tube otorrhea (TTO).

**Setting:** Primary health care.

**Intervention:** Antibiotic ear-drops with or without a corticosteroid (Studies used: Ciprofloxacin 4 drops twice daily, Ofloxacin 0.25 ml twice daily, Ciprofloxacin + Hydrocortisone 4 drops twice daily, Hydrocortisone–Bacitracin–Colistin 5 drops three times daily). Duration was for 7-10 days.

**Comparison:** Oral antibiotics (Studies used: Amoxicillin+clavulanate 25-80 / 7.5 mg/kg per day divided into 2 to 3 doses.) Duration was for 7-10 days. In case of penicillin allergy, erythromycin, 40 mg/kg/day divided into 3 doses daily for 7 days was chosen.

<table>
<thead>
<tr>
<th>Outcome</th>
<th>Relative effect (95% CI)</th>
<th>Anticipated absolute effects (95% CI)</th>
<th>Certainty</th>
<th>What happens</th>
</tr>
</thead>
<tbody>
<tr>
<td>Resolution of ear discharge follow up: 1 weeks</td>
<td>RR 2.58 (1.27 to 5.22)</td>
<td>30.0% 77.4% (38.1 to 100.0)</td>
<td>47.4% more (8.1 more to 126.6 more)</td>
<td>MODERATE 2,6</td>
</tr>
<tr>
<td>Resolution of ear discharge - Antibiotic-corticosteroid eardrops versus oral antibiotics follow up: range 2 to 4 weeks</td>
<td>RR 1.59 (1.35 to 1.88)</td>
<td>57.3% 91.1% (77.3 to 100.0)</td>
<td>33.8% more (20 more to 50.4 more)</td>
<td>LOW 6</td>
</tr>
<tr>
<td>Resolution of ear discharge - Antibiotic-corticosteroid eardrops versus oral antibiotics (Sensitivity analysis) follow up: median 2 weeks</td>
<td>RR 1.70 (1.38 to 2.08)</td>
<td>55.6% 94.9% (77.1 to 100.0)</td>
<td>39.1% more (21.2 more to 60.3 more)</td>
<td>MODERATE 6</td>
</tr>
<tr>
<td>Resolution of ear discharge - Antibiotic-only eardrops versus oral antibiotics follow up: range 2 to 4 weeks</td>
<td>RR 1.00 (0.91 to 1.09)</td>
<td>89.4% 89.4% (81.3 to 97.4)</td>
<td>0.0% fewer (NS) (8 fewer to 8 more)</td>
<td>LOW 6</td>
</tr>
</tbody>
</table>
Summary of findings:

50. Antibiotic eardrops (with or without a corticosteroid) compared to Oral antibiotics for children with tympanostomy tube otorrhoea

Patient or population: Children aged 6 months to 12 years with tympanostomy tube otorrhoea (TTO).

Setting: Primary health care.

Intervention: Antibiotic ear-drops with or without a corticosteroid (Studies used: Ciprofloxacin 4 drops twice daily, Ofloxacin 0.25 ml twice daily, Ciprofloxacin + Hydrocortisone 4 drops twice daily, Hydrocortisone–Bacitracin–Colistin 5 drops three times daily). Duration was for 7-10 days.

Comparison: Oral antibiotics (Studies used: Amoxicillin+/-clavulanate 25-50 / 7.5 mg/kg per day divided into 2 to 3 doses.) Duration was for 7-10 days. In case of penicillin allergy, erythromycin, 40 mg/kg/day divided into 3 doses daily for 7 days was chosen.

<table>
<thead>
<tr>
<th>Outcome</th>
<th>Relative effect (95% CI)</th>
<th>Anticipated absolute effects (95% CI)</th>
<th>Certainty</th>
<th>What happens</th>
</tr>
</thead>
<tbody>
<tr>
<td>Adverse events (ear pain, gastrointestinal)</td>
<td>RR 0.37 (0.12 to 1.09)</td>
<td>31.7% (3.8 to 34.5)</td>
<td>LOW</td>
<td>In children with TTO treated with antibiotic+/-steroid eardrops compared to oral antibiotics there is possibly no difference to report on adverse effects at 2-3 weeks follow-up. NNT Not Applicable</td>
</tr>
<tr>
<td>Proportion of patients with chronic ear discharge (&gt;4 weeks) followed up: 6 months</td>
<td>RR 0.20 (0.02 to 1.67)</td>
<td>6.8% (0.1 to 11.3)</td>
<td>LOW</td>
<td>In children with TTO treated with hydrocortisone–bacitracin–colistin eardrops compared to amoxicillin+calvulanate there is possibly no difference to report on chronic ear discharge at 6 months follow-up. NNT Not Applicable</td>
</tr>
<tr>
<td>Proportion of patients with tube blockage followed up: range 1 to 3 weeks</td>
<td>RR 1.20 (0.33 to 4.45)</td>
<td>5.0% (1.7 to 22.3)</td>
<td>VERY LOW</td>
<td>In children with TTO treated with antibiotic+/-steroid ear drops compared to oral antibiotics there is possibly no difference to report on tube blockage. NNT Not Applicable</td>
</tr>
<tr>
<td>QOL scores - measured with otitis media-6 questionnaire assessed with: parental report followed up: 2 weeks</td>
<td>RR 1.00 (0.90 to 1.11)</td>
<td>1.0% (0.3 to 2.2)</td>
<td>LOW</td>
<td>In children with TTO treated with hydrocortisone–bacitracin–colistin eardrops compared to amoxicillin+calvulanate there are possibly better QOL scores at 2 weeks follow-up.</td>
</tr>
</tbody>
</table>

*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

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 (Heslop 2010)
b. Risk of bias: Lack of participant blinding however not rated down (outcome assessors blinded and adequate allocation concealment)

c. Imprecision: Small study / optimal information size not reahed


e. Risk of bias: Open label trial, stopped early due to recommendation by committee given results of interim analysis - not rated down for this (van Dongen); attrition bias (Goldblatt); performance bias (Goldblatt and Dohar)


g. Studies taken from: Cochrane Review, Venekamp 2016 (Goldblatt 1998)


i. Inconsistency: High heterogeneity explained by excluding van Dongen. Not rated down.


References

Summary of findings:

51. Oral corticosteroids compared to placebo for children with tympanostomy tube otorrhoea

**Patient or population:** Children aged 6 months to 12 years with tympanostomy tube otorrhoea (TTO).

**Setting:** Primary health care.

**Intervention:** Oral corticosteroids (Studies used: Prednisolone 2 mg/kg/day divided into 3 equal doses for 3 days).

**Comparison:** Placebo.

<table>
<thead>
<tr>
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<th>Anticipated absolute effects (95% CI)</th>
<th>Quality</th>
<th>What happens</th>
</tr>
</thead>
<tbody>
<tr>
<td>Resolution of ear discharge assessed with: physician assessment (when discharge could no longer be suctioned from ear canal) follow up: 2 weeks</td>
<td>RR 1.08 (0.92 to 1.26)</td>
<td>88.9%</td>
<td>96.0% (81.8 to 100.0)</td>
<td>7.1% more (NS) (7.1 fewer to 23.1 more)</td>
</tr>
<tr>
<td>Adverse events (gastrointestinal) assessed with: parental report follow up: 7 days</td>
<td>RR 0.23 (0.01 to 4.63)</td>
<td>7.4%</td>
<td>1.7% (0.1 to 34.3)</td>
<td>5.7% fewer (NS) (7.3 fewer to 26.9 more)</td>
</tr>
</tbody>
</table>

*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

**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**

b. Risk of bias: Attrition bias
c. Imprecision: Small study

**References**