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.

Outcome № of participants (studies)	Relative effect (95% CI)	Anticipated absolute effects (95% CI)			Quality	What happens
		Without probiotics	**With probiotics**	**Difference**		
Incidence of AOM during treatment with probiotics (Lactobacillus rhamnosus GG) assessed with: physician diagnosed AOM follow up: range 3 to 12 months № of participants: 1805 (4 RCTs) [1,a]	**RR 0.76** (0.64 to 0.91)	24.4%	**18.5%** (15.6 to 22.2)	**5.9% fewer** (8.8 fewer to 2.2 fewer)	⨁⨁◯◯ LOW [b,c]	In children receiving probiotics (LGG) compared to placebo there is possibly fewer episodes of AOM at 3-12 months follow-up. NNT ~17
≥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 years № of participants: 224 (1 RCT) [2,d,e]	**RR 1.0** (0.8 to 1.2)	71.4%	**71.4%** (57.1 to 85.7)	0.0% fewer (NS) (14.3 fewer to 14.3 more)	⨁⨁◯◯ LOW [f]	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
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 № of participants: 69 (1 RCT) [3,g]	**RR 1.54** (0.62 to 3.87)	17.1%	**26.4%** (10.6 to 66.3)	9.3% more (NS) (6.5 fewer to 49.2 more)	⨁◯◯◯ VERY LOW [h,i]	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

Summary of findings:

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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.

Outcome № of participants (studies)	Relative effect (95% CI)	Anticipated absolute effects (95% CI)			Quality	What happens
		Without probiotics	**With probiotics**	**Difference**		
Adverse events (gastrointestinal and dermatological) follow up: range 3 to 12 months № of participants: 586 (3 RCTs) [2,4,5,j,k]	**RR 0.88** (0.52 to 1.47)	24.2%	**21.3%** (12.6 to 35.6)	2.9% fewer (NS) (11.6 fewer to 11.4 more)	⨁⨁◯◯ LOW [c]	In children receiving probiotics compared to placebo there is possibly no difference in adverse events during 3-12 months follow-up. NNH Not Applicable.

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

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

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: Liu Meta-analysis 2013 (Hatakka 2001, Hojsak 2010, Kukkonen 2008, Rautava 2009)
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
f. Imprecision: Broad estimate of effect. Small study.
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.
k. Studies: Meta-analysis of Cohen 2013, Hojsak 2010, Rautava 2009.

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