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. [a]

Outcome № of participants (studies)	Relative effect (95% CI)	Anticipated absolute effects (95% CI)			Quality	What happens
		Without xylitol (administered as syrup, gum or lozenge)	**With xylitol (administered as syrup, gum or lozenge)**	**Difference**		
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 № of participants: 1826 (3 RCTs) [1,b]	**RR 0.75** (0.65 to 0.88)	29.9%	**22.4%** (19.4 to 26.3)	**7.5% fewer** (10.5 fewer to 3.6 fewer)	⨁⨁⨁◯ MODERATE [c,d,e]	In children receiving xylitol compared to placebo there is probably a reduction in AOM episodes during treatment. NNT ~14
Final diagnosis of at least one episode of AOM - during respiratory infection assessed with: tympanometry + pneumatic otoscopy follow up: median 3 weeks № of participants: 1253 (1 RCT) [1,f]	**RR 1.13** (0.83 to 1.53)	11.5%	**13.0%** (9.5 to 17.6)	1.5% more (NS) (2 fewer to 6.1 more)	⨁⨁⨁◯ MODERATE [c,g,h]	In children receiving xylitol compared to placebo during respiratory infection there is probably no reduction in AOM episodes during 3 weeks follow-up. NNT Not applicable
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 № of participants: 326 (1 RCT) [1,i]	**RR 0.90** (0.67 to 1.21)	36.7%	**33.1%** (24.6 to 44.5)	3.7% fewer (NS) (12.1 fewer to 7.7 more)	⨁⨁◯◯ LOW [h,j,k]	In otitis prone children receiving xylitol compared to placebo there is possibly no reduction in AOM episodes at ~3 months follow-up. NNT Not Applicable.

Summary of findings:

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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. [a]

Outcome № of participants (studies)	Relative effect (95% CI)	Anticipated absolute effects (95% CI)			Quality	What happens
		Without xylitol (administered as syrup, gum or lozenge)	**With xylitol (administered as syrup, gum or lozenge)**	**Difference**		
Adverse events (gastrointestinal related) assessed with: parental report follow up: range 2 to 3 months № of participants: 1826 (3 RCTs) [1,b]	**RR 1.43** (0.74 to 2.75)	1.7%	**2.4%** (1.3 to 4.7)	0.7% more (NS) (0.4 fewer to 3 more)	⨁⨁⨁◯ MODERATE [l]	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).

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. Placebo was sucrose alternative (Uhari 1996), sorbitol (Vernacchio 2014) or low dose xylitol 0.5g (Uhari 1998, Hautalahti 2007, Tapiainen 2002)
b. Studies taken from: Cochrane Review, Azarpazhooh 2016 (Uhari 1996, 1998, Hautalahti 2007).
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.
f. Studies taken from: Cochrane Review, Azarpazhooh 2016 (Tapiainen 2002)
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

1. Azarpazhooh A, Lawrence HP, Shah PS. Xylitol for preventing acute otitis media in children up to 12 years of age. The Cochrane database of systematic reviews. 2016(8):Cd007095. Epub 2016/08/04. doi: 10.1002/14651858.CD007095.pub3. PubMed PMID: 27486835.