

Summary of findings:





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.

Outcome No. of participants (studies)	Relative effect (95% CI)	Anticipated absolute effects (95% CI)			Quality	What happens
		Without seasonal influenza vaccine	With seasonal influenza vaccine	Difference		
At least one episode of AOM assessed with: otoscopy +/- tympanometry follow up: range 6 to 18 months No of participants: 4736 (5 RCTs) ^{1,a}	RR 0.80 (0.67 to 0.96)	26.4%	21.1% (17.7 to 25.3)	5.3% fewer (8.7 fewer to 1.1 fewer)	 MODERATE ^{b,c,d}	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
AOM by season (respiratory and influenza season) assessed with: otoscopy +/- tympanometry follow up: median 6 months No of participants: 899 (2 RCTs) ^{1,e}	not pooled	42.9%	not pooled	not pooled	 LOW ^{b,f,g}	In children receiving seasonal influenza vaccine compared to placebo / no treatment there is insufficient evidence for or against vaccination during respiratory and influenza season. NNV Not Applicable
Adverse events - Fever follow up: range 11 days to 8 months No of participants: 10199 (6 RCTs) ^{1,h}	RR 1.15 (1.06 to 1.24)	17.4%	20.0% (18.4 to 21.5)	2.6% more (1 more to 4.2 more)	 MODERATE ⁱ	In children receiving seasonal influenza vaccine compared to placebo / no treatment there are probably more adverse events of fever. NNH ~39
Courses of antibiotics assessed with: number antibiotic prescriptions. follow up: range 6 to 12 months No of participants: 1223 (2 RCTs) ^{1,j}	RR 0.70 (0.59 to 0.83)	36.2%	25.4% (21.4 to 30.1)	10.9% fewer (14.9 fewer to 6.2 fewer)	 MODERATE ^k	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

*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

- a. Studies taken from: Cochrane Review, Norhayati 2015 (Belshe 2000, Clements 1995, Hoberman 2003, Lum 2010, Vesikari 2006)
- 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.
- e. Studies taken from: Cochrane Review, Norhayati 2015 (Clements 1995, Hoberman 2003). Not pooled due to substantial heterogeneity.
- f. Inconsistency: Two trials with effect estimates in opposite directions. High heterogeneity precluded meta-analysis.
- g. Imprecision: Optimal information size not reached.
- h. Studies taken from: Cochrane Review, Norhayati 2015 (Bracco 2009, Gruber 1996, Lum 2010, Swierkosz 1994, Tam 2007, Vesikari 2006)
- i. Risk of Bias: Attrition bias in 2 studies (Swierkosz 1994, Bracco 2009)
- j. Studies taken from: Cochrane Review, Norhayati 2015 (Marchisio 2002, Vesikari 2006)
- k. Risk of bias: Single blinded study (participants not blinded - risk of under-reporting symptoms) Marchisio.

References

1. Norhayati MN, Ho JJ, Azman MY. Influenza vaccines for preventing acute otitis media in infants and children. The Cochrane database of systematic reviews. 2015(3):Cd010089. Epub 2015/03/25. doi: 10.1002/14651858.CD010089.pub2. PubMed PMID: 25803008.