Influenza vaccine in healthy children: a meta-analysis

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CRD summary

This review assessed the efficacy of influenza vaccination in healthy children. The authors concluded that the influenza vaccine prevents laboratory-confirmed and clinical influenza, and that inactivated and live-attenuated vaccines have similar overall efficacy. It is difficult to assess the reliability of the authors' conclusions given the limited search for studies, the lack of reporting of review methods, and inadequate assessment of study quality.

Authors' objectives

To assess the efficacy of the influenza vaccine in healthy children.

Searching

MEDLINE, EMBASE and the Cochrane Library were searched for studies published in English between 1990 and 2003. The authors reported using one search term: 'influenza vaccine'. The reference lists of retrieved papers were checked.

Study selection

Study designs of evaluations included in the review

Randomised controlled trials (RCTs) with at least 30 patients per treatment arm were eligible for inclusion.

Specific interventions included in the review

Studies that compared live or inactivated influenza vaccine with no influenza A vaccine were eligible for inclusion. The included studies used inactivated and live attenuated vaccines and often included more than one viral strain; some studies used more than one vaccine type and lasted more than one year. Most of the studies were conducted in the USA or Russia; other studies were set in Kazakhstan, Cuba and Italy.

Participants included in the review

Studies in which more than 75% of the patients were healthy children aged 18 years or younger were eligible for inclusion. The included studies were conducted in children aged 6 months to 18 years.

Outcomes assessed in the review

Studies that assessed culture- or serologically-confirmed influenza or clinical influenza-like illness during the influenza season following vaccination were eligible for inclusion. Studies that only assessed otitis media were excluded.

How were decisions on the relevance of primary studies made?

The authors did not state how the studies were selected for the review, or how many reviewers performed the selection.

Assessment of study quality

The authors did not state that they assessed validity.

Data extraction

The authors did not state how the data were extracted for the review, or how many reviewers performed the data extraction. When several clinical outcomes were reported, the outcome closest to influenza-like illness was chosen. For each study, the numbers of patients with events of interest were extracted and risk ratios (RRs) and odds ratios (ORs) were calculated.

Methods of synthesis

How were the studies combined?

The studies were grouped by outcome (culture-confirmed, serologically-confirmed and clinical influenza-like illness) and pooled ORs and RRs, with corresponding 95% confidence intervals (CIs), were calculated using fixed-effect and random-effects meta-analyses. Where more than one active treatment was compared with the same control, the entire control group was used for each comparison in the meta-analyses. Publication bias was assessed using Begg and Mazumdar's test and Egger's test. Vaccine efficacy was calculated as 100 multiplied by (1 - RR).

How were differences between studies investigated?

Statistical heterogeneity was assessed using the chi-squared test. Separate meta-analyses were conducted for inactivated and live-attenuated vaccines. Meta-analyses were repeated, splitting the data from the control groups from the studies with more than one treatment arm into subgroups of similar size and influenza rate. This meant that the data from the participants in the control groups were included only once.

Results of the review

Thirteen RCTs with 31 comparisons were included (n at least 139,973; the total number was unclear because of the potential double-counting of patients in the control groups).

The results reported below were obtained from random-effects models.

Culture-confirmed influenza (5 RCTs with 12 comparisons, n=6,668): all 5 studies were set in the USA. The influenza vaccine significantly reduced culture-confirmed influenza (OR 0.21, 95% CI: 0.13, 0.34). Significant heterogeneity was found (P<0.0001). The one study showing a different direction of treatment effect had the lowest influenza attack rate amongst controls.

The OR for the inactivated vaccine was 0.28 (95% CI: 0.17, 0.47; no significant heterogeneity found, P=0.14) and the OR for the live-attenuated vaccine was 0.16 (95% CI: 0.08, 0.34; significant heterogeneity found, P=0.0002). There was significant heterogeneity between vaccines (P=0.01).

Serologically-confirmed influenza (4 RCTs with 11 comparisons, n=3,581): 2 studies were set in Russia and two in the USA. The influenza vaccine significantly reduced serologically-confirmed influenza (OR 0.30, 95% CI: 0.20, 0.45). Significant heterogeneity was found (P=0.0003).

The OR for the inactivated vaccine was 0.26 (95% CI: 0.18, 0.38; no significant heterogeneity found, P=0.20) and the OR for the live-attenuated vaccine was 0.36 (95% CI: 0.18, 0.74; significant heterogeneity found, P=0.0001). There was no significant heterogeneity between vaccines (P=0.17).

Clinical influenza-like illness (6 RCTs with 16 comparisons, n=161,390): the studies were conducted in five different countries. The influenza vaccine significantly reduced clinical influenza-like illness (OR 0.54, 95% CI: 0.50, 0.59). Significant heterogeneity was found (P<0.0001).

The OR for the inactivated vaccine was 0.51 (95% CI: 0.40, 0.64; significant heterogeneity found, P=0.0009) and the OR for the live-attenuated vaccine was 0.54 (95% CI: 0.49, 0.59; significant heterogeneity found, P<0.0001). The P-value for difference between vaccines was 0.06.

Estimated efficacy was 74% for culture-confirmed influenza, 59% for serologically-confirmed influenza and 33% for clinical influenza-like illness.

There was no evidence of publication bias (P-values for Begg and Muzumdar and Egger's tests ranged from 0.08 to 0.94 across outcomes).

The results were similar when data from the control groups were used only once.

Authors' conclusions

Influenza vaccine prevents laboratory-confirmed and clinical influenza in healthy children. Inactivated and live-attenuated vaccines have similar efficacy overall.

CRD commentary

The review addressed a clear question that was defined in terms of the participants, intervention, outcomes and study design. Three relevant sources were searched but, since only one search term was used, not all relevant studies might have been identified. It was unclear how extensive the search for unpublished studies was. However, appropriate methods were used to assess the possibility of publication bias and no evidence of it was found. Limiting the included studies to publications in English meant that some relevant studies might have been missed, and also raises the possibility of language bias. Only RCTs were included but validity, other than blinding, was not assessed.

The studies were combined in meta-analyses and some data contributed to the same analyses more than once. For most meta-analyses there was significant heterogeneity, although the direction of treatment effect was consistent. The influence of vaccine type on outcomes was explored, but even within these subgroups significant heterogeneity was common. This means that estimates of reduction in risks of influenza may not be reliable. It was difficult to assess the robustness of the authors' conclusions given the lack of reporting of review methods, inadequate assessment of study quality, limited search and heterogeneity between the studies.

Implications of the review for practice and research

Practice: The authors stated that influenza vaccination prevents laboratory-confirmed and clinical influenza in healthy children. However, no assessment of infants or younger children could be made.

Research: The authors stated that evaluating the safety of different types of vaccines in different ages of children is important to assess the costs and benefits of influenza vaccination in children.

Bibliographic details

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This is a critical abstract of a systematic review that meets the criteria for inclusion on DARE. Each critical abstract

contains a brief summary of the review methods, results and conclusions followed by a detailed critical assessment on the reliability of the review and the conclusions drawn.