The efficacy of influenza vaccine in elderly persons: a meta-analysis and review of the literature

Gross P A, Hermogenes A W, Sacks H S, Lau J, Levandowski R A

Authors' objectives
To review the protective efficacy of influenza vaccination in elderly people.

Searching
MEDLINE was searched (search dates are unclear) using the terms 'influenza vaccine', 'vaccine efficacy', 'elderly', 'mortality', 'hospitalised' and 'pneumonia', and appropriate references in the retrieved literature were identified.

Study selection
Study designs of evaluations included in the review
Eleven retrospective cohort trials, 9 prospective cohort trials, 3 case-control trials and 1 randomised controlled trial (RCT). Only cohort trials were used for the meta-analysis (n=20).

Specific interventions included in the review
Influenza vaccine.

Participants included in the review
Institutionalised elderly people, both male and female over the age of 65, who were not artificially exposed to the influenza virus.

Outcomes assessed in the review
Upper respiratory illness, pneumonia, hospitalisation, mortality, match or mismatch of epidemic strain and vaccine.

How were decisions on the relevance of primary studies made?
Of the retrieved literature studies describing only upper respiratory illness scores, those that made no effort to account for a developing epidemic while vaccination was in progress, or contained no descriptions of epidemic or vaccine strains, were excluded. By whom, and how, these criteria were determined are not stated.

Assessment of study quality
No formal quality weighting was given to the primary studies, although differences in quality were discussed narratively. The number of participants in each study varied from 17 to more than 1000, but generally it was greater than 100. Sex distribution was only reported in 6 of the studies and the majority of these individuals were female. Definitions of respiratory illness and criteria for diagnosing pneumonia varied between studies, as did the authors' definition of 'high-risk' patients.

Data extraction
The authors do not state how the data were extracted for the review, or how many of the authors performed the data extraction.

Methods of synthesis
How were the studies combined?
The studies were combined in a meta-analysis using the random-effects model of DerSimonian and Laird (see Other Publications of Related Interest no 1), which gives an absolute percentage reduction between the control and treatment groups. The Yusuf-Peto modification of the Mantel-Haenszel test, which produces an estimate of the odds ratio (OR),
was used to confirm the results.

How were differences between studies investigated?
The model of DerSimonian and Laird used in the initial analysis adjusts for the amount of heterogeneity in the studies. Small sample size or numerators of 3 or less were identified as reasons for extreme outliers in the 95% confidence intervals (CIs). Tau-squared was used to express the degree of heterogeneity. No heterogeneity was found for hospitalisation (tau-squared=0.0000) or mortality (tau-squared=0.0000), while heterogeneity was found for pneumonia (tau-squared=0.0770) and for respiratory illness (tau-squared=0.4039). Subgroup analysis was used to investigate the effect of vaccine type and virus strain on efficacy.

Results of the review
Eighteen cohort studies examined the effect of influenza vaccination on respiratory illness (4,368 vaccinated and 4,944 unvaccinated patients).

Nine cohort studies examined the effect of influenza vaccination on the occurrence of pneumonia (5,938 vaccinated and 18,836 unvaccinated patients).

Six cohort studies examined the effect of influenza vaccination on hospitalisation (5,476 vaccinated and 18,848 unvaccinated patients).

Twenty cohort studies examined the effect of influenza vaccination on mortality (8,302 vaccinated and 21,726 unvaccinated patients).

Eighteen cohort studies examined vaccine efficacy when the epidemic strain was the same or a drift variant (4,357 vaccinated and 5,119 unvaccinated).

The pooled estimates of vaccine efficacy (OR 1) based on the 20 cohort studies are:

56% (CI: 39%, 68%) for preventing respiratory illness,
53% (CI: 35%, 66%) for preventing pneumonia,
48% (CI: 28%, 65%) for preventing hospitalisation, and
68% (CI: 56%, 76%) for preventing mortality.

Vaccine efficacy in relation to the epidemic strain were expressed as ORs. Respiratory illness: same strain 0.51 (CI: 0.36, 0.73); drift strain 0.34 (CI: 0.20, 0.58).

Pneumonia: same strain 0.41 (CI: 0.26, 0.65); drift strain 0.32 (CI: 0.12, 0.83).

Hospitalisation: same strain 0.44 (CI: 0.28, 0.68); drift strain 0.30 (CI: 0.08, 1.07).

Mortality: same strain 0.31 (CI: 0.21, 0.46); drift strain 0.21 (CI: 0.10, 0.43).

Results from the case-control studies and the randomised double-blind placebo-controlled trial were not statistically combined; the authors simply stated the results of each study. In the case-control studies, vaccine efficacy ranged from:

32% to 45% for preventing hospitalisation for pneumonia,
31% to 65% for preventing mortality from pneumonia and influenza,
43% to 50% for preventing hospital deaths from all respiratory illnesses, and
27% to 30% for preventing deaths from all causes.
In the randomised double-blind placebo-controlled trial the vaccine was found to have a 50% or greater reduction in influenza-related illness.

**Cost information**
The authors considered two cost-effectiveness studies published in 1994. In the first of these studies, vaccination for influenza resulted in reductions in hospitalisation of 48 to 57% for patients with pneumonia and influenza, and 27 to 39% for those with acute/chronic respiratory conditions. It was calculated that this represented a mean direct saving (combined cost of influenza vaccine and hospitalisation of a vaccinated person minus the cost of hospitalisation for an unvaccinated person) of $117 per person per year. In the second study, the vaccine reduced influenza hospitalisations by 30% for high-risk elderly and 40% for non-high-risk elderly, representing an overall net saving of $1.10 per person. The net saving was calculated using the following cost: prevention of hospitalisation, outpatients contracts, vaccination, promotion, delivery and waste, and adverse reactions.

**Authors' conclusions**
Although there is a lack of randomised trials, there are now many studies which affirm that influenza vaccination reduces the risk of hospitalisation, pneumonia and mortality in the elderly during an influenza epidemic, assuming that the vaccine and epidemic strain are identical or similar. The authors propose that annual vaccination of elderly persons over the age of 65 is an indispensable part of their care.

**CRD commentary**
This is probably the most influential systematic review available in this field, to date. The authors provide an informative and well-reasoned appraisal of the literature. Conclusions are correctly determined from the evidence.

The authors recognise the inherent bias in all of the primary studies caused by non-standardised definitions for influenza-like illness, influenza related pneumonia, hospitalisation and death. Without precise deterrents and routine testing of hospitalised patients suspected of contracting influenza, attribution of morbidity and mortality may be imprecise. Similarly, vaccine efficacy is probably on the conservative side since other respiratory agents may cause hospitalisation and mortality, which is frequently ascribed to influenza.

The included studies evaluate the effect of the vaccine in the community and as such determine effectiveness rather than efficacy as suggested by the title.

The lack of RCTs in this research field reflects the ethical difficulties in withholding vaccine from elderly people.

**Implications of the review for practice and research**
All people over the age of 65 should be considered for influenza vaccination in the UK.

**Funding**
Part funded by the Center for Biologics Evaluation and Research, Food and Drug Administration, contract 223-90-1102.

**Bibliographic details**

**PubMedID**
7661497

**Original Paper URL**
Other publications of related interest

Indexing Status
Subject indexing assigned by NLM

MeSH
Age Factors; Aged; Chronic Disease; Cost-Benefit Analysis; Female; Hospital Mortality; Humans; Influenza Vaccines /economics; Influenza, Human /prevention & control; Male; Odds Ratio; Pneumonia, Viral /mortality /prevention & control; Severity of Illness Index; Sex Factors

AccessionNumber
11995002722

Date bibliographic record published
31/01/1997

Date abstract record published
31/01/1997

Record Status
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.