Influenza as a trigger for acute myocardial infarction or death from cardiovascular disease: a systematic review

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CRD summary
This review investigated whether influenza vaccines provided protection against cardiac events and concluded that there was some evidence that influenza vaccines were effective at reducing the risk of cardiac events in patients with established cardiovascular disease. Potential for error and bias, unclear study quality and possible inappropriate pooling of studies suggested that these conclusions should be viewed with caution.

Authors' objectives
To examine the effectiveness of influenza vaccines at protecting against cardiac events and to review the evidence that influenza triggers acute myocardial infarction or cardiovascular death. Only the review of vaccine effectiveness has been abstracted.

Searching
PubMed (to February 2009) and EMBASE (1980 to February 2009) were searched without language restrictions. Search terms were reported. References of relevant articles were searched for additional studies.

Study selection
Ecological, case-control, cohort, case-only and randomised controlled trials (RCTs) that evaluated the effects of influenza vaccination on the outcomes myocardial infarction or death from cardiovascular disease (or more specific causes) were eligible for inclusion. Studies with insufficient description of study methods were excluded.

The review of effectiveness of influenza vaccines on cardiac outcomes included RCTs of patients with acute myocardial infarction, patients that received elective percutaneous coronary intervention (with a history of acute myocardial infarction, unstable angina, coronary artery bypass graft or percutaneous coronary intervention) and patients with angiographically-confirmed coronary artery disease. Studies compared influenza vaccine with control.

The authors stated neither how studies were selected for the review nor how many reviewers performed the selection.

Assessment of study quality
Methodological quality was assessed using criteria described in the STROBE statement. The authors did not state how many reviewers assessed study quality.

Data extraction
The number of events in the treatment and control groups and hazard ratios (HRs) and corresponding 95% confidence intervals (CIs) were extracted. The authors did not state how many reviewers extracted the data.

Methods of synthesis
Numbers of events in the treatment and control groups were pooled in a weighted Mantel-Haenszel fixed-effect model and a DerSimonian and Laird random-effects model to calculate relative risks (RRs) and 95% CIs. Statistical heterogeneity was assessed using the I² statistic.

Results of the review
Two RCTs were included in the meta-analysis (n=959). Allocation concealment and randomisation methods were unclear in one RCT.

Influenza vaccination was associated with a significant reduction in the risk of cardiovascular death in the vaccinated group using the fixed-effect model (RR 0.39, 95% CI 0.20 to 0.77; n=959) and was associated with significant heterogeneity (I²=61.1%, p=0.077). There was no significant effect for vaccine versus control when the random-effects
model was used. Influenza vaccination was not associated with any effect on the risk of acute myocardial infarction when either model was used. No heterogeneity was detected for this outcome.

Authors’ conclusions
There was some evidence that influenza vaccines were effective at reducing the risk of cardiac events in patients with established cardiovascular disease.

CRD commentary
The research question was supported by inclusion criteria for study design, outcomes and intervention, but not for participants. Two databases were searched for studies in any language, which reduced the possibility of language bias. Unpublished studies were not sought, so publication bias was a possibility. Study quality was assessed, but the way in which the criteria were used to assess quality was not well described. The tool used was designed for observational studies; criteria designed to evaluate RCTs may have been more appropriate. The review process was not described, so it was not known whether steps were taken to reduce reviewer error and bias (such as by performing processes in duplicate). Little patient data were reported, so it was not known whether pooling in meta-analysis was appropriate. Statistical heterogeneity was measured, but possible sources of heterogeneity were not investigated. The authors stated that the findings may not have been generalisable to patients without established cardiovascular disease. The potential for error and bias, unclear study quality and possible inappropriate pooling of studies suggested that the authors’ conclusions should be viewed with caution.

Implications of the review for practice and research

Practice: The authors stated that there was a need to encourage influenza vaccine uptake where ever indicated, especially in people with diabetes and existing cardiovascular disease.

Research: The authors stated that further evidence was needed on the effectiveness of influenza vaccines to reduce the risk of cardiac events in people without established vascular disease.

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