Clinical effectiveness of pneumococcal vaccine: meta-analysis

Authors' objectives
To determine the effectiveness of pneumococcal vaccine.

Searching
MEDLINE was searched from January 1966 to November 1966 and Index Medicus back to 1938 (manual search). EMBASE and SciSearch were also searched, and reference lists of all retrieved articles were examined. Additional published and unpublished data were identified by contacting all first authors of clinical studies of pneumococcal vaccine effectiveness and all organisations producing immunisation guidelines.

Study selection
Study designs of evaluations included in the review
Randomised controlled trials (RCTs), prospective cohorts, or case-controlled studies were eligible. Only randomised or quasi-randomised controlled trials were reported in the review.

Specific interventions included in the review
Pneumococcal (Streptococcus pneumoniae) vaccinations were eligible. The vaccines that were included contained from 2 to 17 pneumococcal serotypes.

Participants included in the review
Adult patients were eligible. Participants included elderly people, chronically-ill people, and institutionalised people.

Outcomes assessed in the review
Only studies reporting any clinical outcome were eligible. The following outcomes were assessed: vaccine-type systematic pneumococcal infection; systematic pneumococcal infection (positive culture of blood or any normally sterile body fluid); vaccine-type pneumococcal pneumonia; pneumococcal pneumonia (diagnosed either clinically or radiologically); and non-vaccine-type pneumococcal pneumonia.

How were decisions on the relevance of primary studies made?
Two reviewers selected the studies. It was unclear whether there was independent duplication or checking of the two selections.

Assessment of study quality
Validity was assessed using the following criteria: allocation (random or quasi-random); follow-up (active, passive, cannot tell); completeness of follow-up (90% or greater, 80% or greater and less than 90%, less than 80%, cannot tell); outcome assessment (blinded or all-cause mortality; death or illness with isolation of S. pneumoniae from normally sterile tissues or body fluids without blinding, or radiologically-confirmed pneumoniae without blinding; hospitalisation with respiratory illness or clinical illness with isolation of S. pneumoniae without blinding; clinical illness with no blinding); and blinding of providers and patients (placebo-controlled with blinding of providers and patients, blinding of patients or providers only, no blinding, cannot tell). Three investigators independently assessed validity with any disagreements resolved by consensus.

Data extraction
Two investigators independently extracted the following data: characteristics of study population, type of vaccine, and raw data for incidence of clinical outcomes. For studies where outcomes were not reported as proportions, rates were calculated.
Methods of synthesis
How were the studies combined?
Pooled odds ratios (OR) and 95% confidence intervals (CIs) were estimated for each outcome using exact methods.

How were differences between studies investigated?
Statistical heterogeneity was assessed. When significant heterogeneity was found (p<0.05), logistic regression was used to test for possible sources of variability. Possible explanatory variables were dichotomised and the following factors were considered: whether the study was a RCT; whether the vaccine was at least 12 valent; and whether patients were exclusively elderly, chronically ill, or institutionalised. Interactions with vaccination status were assessed.

Sensitivity analysis was conducted in which 3 unblinded trials were excluded.

Results of the review
Eleven RCTs and 2 quasi-RCTs were included (65,007 patients).

For more than half the included studies it could not be ascertained how complete the follow-up had been, or whether patients had been routinely followed-up or investigators had relied on routinely-collected data.

Systematic pneumococcal disease. Vaccine-type systematic pneumococcal infection (4 studies): OR 0.17 (95% CI: 0.09, 0.31), risk reduction 83%. No evidence of heterogeneity was found (p=0.25).

Systematic pneumococcal infection due to any type of pneumococcus (6 studies): pooled OR 0.27 (95% CI: 0.13, 0.49), risk reduction 73%. No evidence of heterogeneity was found (p=0.08).

Pneumococcal pneumonia.

Vaccine-type pneumococcal pneumonia (9 RCTs): significant heterogeneity was found (p<0.0001). Results were inconsistent. Six RCTs reported a significant reduction in vaccine-type pneumonia with ORs ranging from 0.08 to 0.85, 2 RCTs showed a non significant reduction, and 1 RCT did not report a reduction.

Pneumococcal pneumonia with any type of pneumococcus (7 RCTs): significant heterogeneity was found (p<0.0001). Results were inconsistent. Three RCTs reported a significant reduction in vaccine type pneumonia with ORs ranging from 0.24 to 0.69.

Non-vaccine-type pneumococcal pneumonia (5 RCTs): significant heterogeneity was found (p=0.036). Results were inconsistent with 4 RCTs reporting no significant effect of the vaccine, and 1 RCT reporting a statistically-significant reduction.

Special populations.

1. Elderly (studies were substantially or exclusively elderly).

For vaccine-type pneumococcal pneumonia (4 studies) and pneumococcal pneumonia (6 studies), there was no significant interaction between vaccination and the presence or absence of exclusively elderly or near-elderly study populations.

2. Chronically-ill people (studies were substantially or exclusively of chronically-ill people).

For vaccine-type systemic pneumococcal (1 study) or systemic pneumococcal infection (4 studies), no significant effect of vaccine was found in any of the studies.

For pneumococcal pneumonia (4 studies), there was no significant interaction between vaccination and the presence or absence of exclusively elderly or near-elderly study populations.
3. Institutionalised people. Vaccine-type systemic pneumococcal infection (1 RCT): there was a significant reduction in risk with pneumococcal vaccine, compared to control; pooled OR 0.07 (95% CI: 0.00, 0.50).

Systemic pneumococcal infection (2 RCTs): results were inconsistent with only 1 RCT reporting a significant reduction.

Vaccine-type pneumococcal pneumonia (3 RCTs) and pneumococcal pneumonia (3 RCTs): in all three studies, both outcomes were less frequent, but not significantly less frequent, among those who had been vaccinated.

Sensitivity analysis.

Exclusion of 3 unblinded RCTs (which were also the studies with quasi-randomisation) had little effect on pooled OR for vaccine-type systemic pneumococcal infection; OR 0.19 (95% CI: 0.09, 0.36). For systemic pneumococcal infection, the pooled OR increased and was no longer statistically significant; OR 0.53 (95% CI: 0.14, 1.78). After exclusion of the non-blinded studies, pooled OR for non-vaccine-type pneumococcal pneumonia was 1.14 (95% CI: 0.61, 2.15), and statistical heterogeneity was eliminated (p=1.00).

Authors’ conclusions
Vaccination with pneumococcal polysaccharide vaccine can be expected to reduce the risk of systematic infection due to pneumococcal types included in the vaccine by 83%, and systematic infection due to all pneumococci by 73%. The authors found no evidence that the vaccine was less efficacious for the elderly, institutionalised people, or those with chronic disease.

CRD commentary
The aims were stated and inclusion criteria defined in terms of study design, intervention, and outcome. Several relevant databases were searched but details of the keywords used were not reported. Attempts were made to locate unpublished material, and methods used to select studies were described. Validity was assessed and scored using defined criteria, and methods used were reported. Methods used to extract data were described, and relevant details of the included studies were presented in tabular format. Studies were pooled appropriately with results presented as a forest plot. Statistical heterogeneity was assessed, and sensitivity analysis conducted to explore the influence of patient characteristics and blinding on results. The discussion includes consideration of potential sources of heterogeneity, such as the influence of the unreliability and variability of outcome measurement. No mention was made of the incidence of adverse reactions to the vaccine.

The evidence as presented in this review appears to support the authors’ conclusions.

Implications of the review for practice and research
Practice: The authors state that antipneumococcal vaccine is effective in preventing vaccine-type pneumonia and systemic pneumococcal infections; that the vaccine can be expected to protect institutionalised and elderly patients; and that for people older than 65 years (where the incidence of pneumococcal pneumonia is about 50 cases per 100,000 people), 250 people will need to be vaccinated to prevent one case of bacterial pneumonia per year.

Research: The authors did not state any implications for further research.

Bibliographic details

PubMedID
10540698
This additional published commentary may also be of interest. Are pneumococcal vaccines effective? Bandolier 2000;72:5-7.

Indexing Status
Subject indexing assigned by NLM

MeSH
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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.