The contribution of the case-control approach to vaccine evaluation: Pneumococcal and Haemophilus influenzae type B PRP vaccines

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Authors' objectives
To assess the efficacy of pneumococcal polysaccharide and Haemophilus influenzae type B polyribosylribitol phosphate (Hib-PRP) vaccines.

Searching
MEDLINE and the Science Citation Index were searched for English language articles, and the references cited in the retrieved articles were examined. No keywords or other restrictions are stated.

Study selection
Study designs of evaluations included in the review
The review includes RCTs and case-control studies. Inclusion criteria for the RCTs were randomisation, placebo control and a measure of vaccine efficacy. For case-control studies the inclusion criteria were English language articles, as well as adult patients for pneumococcal vaccine.

Specific interventions included in the review
Pneumococcal polysaccharide and Hib-PRP vaccines.

Participants included in the review
Participants in the review of pneumococcal polysaccharide varied in age (young to over 55 years), setting (South African and New Guinea gold mines to Veterans Administration clinics and hospitals in USA) and level of risk as defined by medical condition (high, medium and low). In the review of Hib-PRP vaccine, participants differed in age (18 to 72 months) and setting (day care facilities in USA to children in Finland).

Outcomes assessed in the review
The review focuses on the efficacy of the vaccines in preventing pneumococcal pneumonia and Haemophilus influenzae type B. As such, the randomised controlled trials (RCTs) assess the number of vaccine and placebo patients infected with the disease, whilst the case-control studies the number of cases and controls retrospectively exposed to the vaccine.

How were decisions on the relevance of primary studies made?
The authors do not state how the papers were selected for the review, or how many of the authors performed the selection.

Assessment of study quality
The authors do not report the criteria used to assess validity, or how the validity assessment was performed.

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 through the calculation of a weight-adjusted odds ratio (OR), using the inverse of the
variance in the log domain, with 95% confidence intervals (CIs).

How were differences between studies investigated?
No test for heterogeneity was reported although the review undertook sensitivity analyses which excluded studies with outlying results.

**Results of the review**
Seven studies (14,179 patients) of pneumococcal vaccine and 9 studies (77,634 patients) of Haemophilus influenzae type B vaccine.

For the pneumococcal polysaccharide vaccine, the RCTs provide a pooled OR of 0.73 and the case-control studies a pooled OR of 0.56 (95% CI: 0.44, 0.66). Sensitivity analysis, excluding an RCT and a case-control study with older patients that had negative efficacies, provided ORs of 0.79 (95% CI: 0.69, 0.86) for the RCTs and 0.59 (95% CI: 0.47, 0.68) for the case-control studies. The pooled efficacy for Haemophilus influenzae type B vaccine was 0.80 (95% CI: 0.66, 0.97) for the RCT and 0.38 (95% CI: 0.15, 0.55) for the case-control studies.

**Authors’ conclusions**
The totality of the evidence firmly supports the efficacy of the pneumococcal polysaccharide and Hib-PRP vaccines.

**CRD commentary**
The objective, interventions, participants, outcomes, study designs, study details and methods of pooling the results are clearly stated within the review. The search strategy lists sources but it fails to provide any keywords or date restrictions, thus limiting an assessment of the coverage of the literature. Heterogeneity was evident within the studies, the effect of which was assessed through sensitivity analysis. Unfortunately the review does not provide any information on the criteria for assessing the validity and relevance of the primary studies, or on the process by which these decisions and the extraction of data were undertaken. No cost information was reported. The conclusions appear justified although the limitations evident within the review affect the strength of the evidence.

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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.