Do childhood vaccines have non-specific effects on mortality?

Cooper W O, Boyce T G, Wright P F, Griffin M R

CRD summary
This review investigated the reduction in mortality in children receiving childhood vaccines. The authors concluded that the measles vaccine reduces mortality, but there is insufficient evidence to suggest a mortality benefit above that caused by its effect on measles disease and its resulting complications. Limitations in methodological quality, and the potential for publication and language bias, should be considered when interpreting the results of this review.

Authors’ objectives
The authors appear to have studied the reduction in mortality in children receiving childhood vaccines.

Searching
MEDLINE (from 1966 to March 2001), EMBASE (from 1980 to March 2001) and Current Contents (March 2001) were searched; the search terms were reported. Only studies in English were included in the review. The reference lists of retrieved studies were also checked.

Study selection
Study designs of evaluations included in the review
There were no specific inclusion criteria relating to the study design. All of the included studies were observational studies that compared differences in mortality between vaccinated and unvaccinated children. Study details were not reported for most studies. Where reported, the studies were either case-control studies (+/- matched), nested case-control studies, or cohort studies (retrospective or prospective).

Specific interventions included in the review
Studies of childhood vaccinations were eligible for inclusion. The included studies evaluated the measles vaccine, diphtheria-tetanus-pertussis vaccine (DTP), oral poliovirus vaccine (OPV) or the bacille Calmette-Guerin vaccine (BCG).

Participants included in the review
Studies of infants and children were eligible for inclusion. Fifty per cent of the studies did not report population details. Where reported, the age of the participants ranged from 0 to 120 months.

Outcomes assessed in the review
Studies reporting mortality were eligible for inclusion. The included studies reported all-cause mortality, mortality due to the disease being vaccinated against, or death due to sudden infant death syndrome (SIDS).

How were decisions on the relevance of primary studies made?
One author selected studies to be retrieved for detailed assessment. Two authors independently assessed the full articles.

Assessment of study quality
Study quality was assessed in relation to verification of death, adequacy of follow-up, comparison at baseline, and cointerventions. Two reviewers assessed study quality.

Data extraction
The authors did not state how the data were extracted for the review, or how many reviewers performed the data extraction. The number and proportion of events in each vaccine group and the reduction in mortality (with 95% confidence intervals) were calculated.
**Methods of synthesis**

How were the studies combined?
The studies were combined in a narrative, grouped by vaccine.

How were differences between studies investigated?
Differences between the studies were discussed in the text.

**Results of the review**

Twenty-four studies (reported in 35 articles) were included in the review (number of participants not reported). The study designs included prospective and retrospective cohorts, case controls, nested case controls and matched case controls, although details were not given for all studies included in the review.

The results of the quality assessment were only presented for 16 of the 24 included studies. Of these, all had death verified, 15 had no cointerventions, 14 had an adequate period of follow-up, 7 considered sociodemographics, and 2 had populations comparable at baseline.

Measles vaccine: vaccinated children experienced a 62 to 86% relative reduction in death following measles (3 studies). The 2 highest quality studies reported 31% and 46% relative reductions in all-cause mortality in vaccinated children. The lower quality studies (7 studies) reported greater relative decreases in all-cause mortality (35 to 85%) than the higher quality studies.

DTP vaccine: vaccinated children had a relative reduction in SIDS of 30 to 80% (4 studies), with these reductions being statistically significant in 2 studies.

Other vaccines: mortality was higher in children receiving a single dose of DTP and of OPV than in unvaccinated children (2 studies). The estimated reduction in mortality of children receiving the BCG vaccine, compared with unvaccinated children, was 38%.

**Authors' conclusions**
The measles vaccine reduced mortality, but there was insufficient evidence to suggest a mortality benefit above that caused by its effect on measles disease and its resulting complications.

**CRD commentary**
The review question was clear in terms of the populations, intervention and outcome. Three relevant databases were searched but only English language articles were included, leaving a potential for language bias. The authors did not investigate the potential for publication bias. The second stage of the study selection process and the quality assessment were carried out in duplicate. However, a single reviewer conducted the initial stage of the study selection process, there was no information as to how any disagreements were resolved, and the method used to extract the data was not reported. Thus, there is potential for the introduction of error or bias into the review process.

Insufficient details of the studies and populations were provided. Limited information for some studies was supplied on the journal's website. See Web Address at end of abstract. The decision to combine the studies in a narrative was appropriate. The poor quality of the studies included in the review, the absence of comparable study groups, and the potential for publication and language bias, should be kept in mind when considering the reliability of the authors' conclusions.

**Implications of the review for practice and research**

Practice: The authors did not state any implications for practice.

Research: The authors suggested that clinical trials of vaccines should incorporate safety and mortality assessments; observational studies should identify and control for differences between vaccinated and unvaccinated populations; post-
marketing surveillance in developed and developing countries should be conducted. They went on to say that time-series designs may be possible in large studies measuring mortality that have a well-defined intervention point, and where a new vaccine is introduced, large randomised controlled trials would allow a comparison of mortality between vaccinated and unvaccinated children.

Bibliographic details

PubMedID
14758409

Original Paper URL

Indexing Status
Subject indexing assigned by NLM

MeSH
Cause of Death; Child, Preschool; Diphtheria-Tetanus-Pertussis Vaccine /therapeutic use; Humans; Infant; Infant Mortality; Measles /mortality /prevention & control; Measles Vaccine /adverse effects /therapeutic use; Sudden Infant Death /epidemiology /prevention & control; Treatment Outcome; Vaccines /adverse effects /therapeutic use

AccessionNumber
12004008111

Date bibliographic record published
31/12/2005

Date abstract record published
31/12/2005

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.