Metaanalysis of vaccine effectiveness in varicella outbreaks
Bayer O, Heininger U, Heiligensetzer C, von Kries R

CRD summary
This review estimated vaccine effectiveness for one dose of immunisation with the live-attenuated OKA-strain of varicella vaccine and assessed the time course of waning immunity. The authors found limited vaccine effectiveness for one dose of this vaccine in varicella (chicken-pox) outbreaks. Due to methodological and reporting weaknesses, the authors' conclusions may not be reliable.

Authors' objectives
To estimate vaccine effectiveness for one dose of immunisation with the live-attenuated OKA-strain of varicella virus and to assess the time course of waning immunity.

Searching
PubMed and EMBASE were searched from 1995 to December 2006 for English or German language articles. Search terms were reported.

Study selection
Reports of outbreaks of varicella in populations that were at least partially vaccinated and that reported vaccine effectiveness and measures of its variance (or data that would enable calculation of this), were eligible for inclusion in the review. Outbreaks of varicella in restricted subgroups were excluded.

The median age of the included participants, where reported, ranged from four to eight years and the percentage population vaccinated ranged from 30 to 96%. The authors reported that all outbreaks included in the analysis were in children in day-care centres or elementary school. In most studies, the cases were defined as having developed an acute maculo-papulo-vesicular rash in the outbreak period, with only a few being microbiologically confirmed. Outcomes that were confirmed by laboratory diagnosis, parental or physician diagnosis within the outbreak setting were also eligible for inclusion.

Studies were selected independently by two reviewers.

Assessment of study quality
The authors did not state that they assessed validity.

Data extraction
Attack rates, vaccine effectiveness and, if available, subgroup analysis on vaccine effectiveness in relation to time since immunisation, were extracted. Also, relative risk estimates in vaccinated children, categorised by time since immunisation accepting any cut-point applied, were considered for extraction. The absolute numbers were extracted for the risk analysis (which was limited to children without a history of varicella in the vaccinated and non-vaccinated groups). Relative risks and corresponding 95% confidence intervals were calculated.

The authors did not state how the data were extracted for the review, or how many reviewers performed the data extraction.

Methods of synthesis
Pooled relative risks with 95% confidence intervals were calculated using a Mantel-Haenszel meta-analysis and transformed to vaccine effectiveness. Children vaccinated before 12 months of age, and those with a prior history of varicella, were excluded from the risk analysis. Correlation between vaccine effectiveness, percentage of immunised cases and immunisation coverage was quantified using Pearson's r. Publication bias was investigated using a funnel plot.

Results of the review
Fourteen studies were included in the analysis (n=3,157 participants). Study designs were not reported. Publication bias was not indicated by the funnel plot.

The proportion of vaccinated children among those with varicella was positively correlated with increasing vaccine coverage, while vaccine effectiveness remained constant (r=0.3, p=0.28). The pooled vaccine effectiveness of one dose of varicella vaccine was 72.5% (95% confidence interval: 68.5 to 76.0). Time since immunisation was associated with a decrease in vaccine effectiveness in four studies but was not found to be a risk factor for breakthrough varicella in two studies (assessment of this was not described in these two studies).

**Authors’ conclusions**
There was limited vaccine effectiveness for one dose of OKA-strain varicella vaccine. Waning immunity may be an important causal factor.

**CRD commentary**
The review question was well defined, with inclusion criteria for participants, outcomes and intervention. However, there were no inclusion criteria specified for study design, which may have led to subjective decisions when selecting studies. The authors only included studies published in English and German and did not report any attempts to identify unpublished studies, increasing the possibility of language and publication bias. The authors did attempt to assess the risk of publication bias but this assessment is unlikely to be reliable given the relatively low number of included studies. Though study selection was reported and steps taken to minimise bias and error in this process this was not reported for data extraction, so it is not known whether similar steps were taken. Validity of the primary studies was not assessed, so it is not known whether the results of these studies and their synthesis are reliable. Also, few details of the study populations were reported, so it was not possible to assess whether it was clinically appropriate to pool the primary studies. Due to the methodological and reporting weaknesses in this review, the authors' conclusions may not be reliable.

**Implications of the review for practice and research**
- **Practice**: The authors stated that there is a need for sustained surveillance, even after the introduction of a two dose immunisation schedule.
- **Research**: The authors did not state any implications for research.

**Funding**
One author is supported by a LMUinnovativ research priority project MCHealth (sub-project II) grant.

**Bibliographic details**

PubMedID
17706845

DOI
10.1016/j.vaccine.2007.07.010

**Additional Data URL**
http://www.mrw.interscience.wiley.com/cochrane/clsysrev/articles/CD001833/frame.html

**Other publications of related interest**
Indexing Status
Subject indexing assigned by NLM

MeSH
Chickenpox /epidemiology /immunology /prevention & control; Chickenpox Vaccine /immunology; Disease Outbreaks /prevention & control; Humans; Infant; Time Factors; Treatment Outcome

AccessionNumber
12007003222

Date bibliographic record published
30/09/2008

Date abstract record published
05/08/2009

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.