Authors' objectives
To estimate the rate of clinical measles after vaccine-induced seroconversion of measles vaccines using a meta-analysis.

Searching
The computerised National Library of Congress listing of medical publications (including books and MEDLINE) was searched using BRS Colleague, from 1966 to 1995 for English language studies; the search terms are given in the authors' text. Additional material was located by examining the bibliographies of retrieved literature, and searching back two generations, and by checking the authors' personal files.

Study selection
Study designs of evaluations included in the review
Cohort studies were included.

Specific interventions included in the review
Measles vaccine containing either live or killed virus.

Participants included in the review
Healthy individuals receiving a measles-containing vaccine over the age of 12 months were included.

Outcomes assessed in the review
Secondary failures of vaccination. Primary failures are failures of the vaccine to produce measurable specific antibodies after immunisation. Secondary failures are the manifestation of the disease in an individual previously shown to have measurable specific antibodies after vaccination.

How were decisions on the relevance of primary studies made?
Two reviewers independently assessed each study according to defined inclusion criteria and sought consensus where disagreements occurred.

Assessment of study quality
Each study was assigned a quality score using the following criteria: a community-based study; the active follow-up of a cohort; an accounting of drop-outs; the documentation of disease by specified clinical criteria; the documentation of disease by acute and convalescent sera; and the documentation of vaccination from medical records. Two reviewers independently scored each study and sought consensus where disagreements occurred.

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 classified into 3 homogeneous groups and the pooled failure rate calculated.

Group A used vaccines that contained killed virus.

Group B used live virus vaccines. The study data were difficult to interpret with respect to the lack of verification of
vaccination, immunisation before 12 months, a non-North American study site, and vaccine manufacture.

Group C used live virus vaccines. The participants were US citizens that were older than 12 months at vaccination, and received a US-manufactured vaccine that was documented in a medical record.

How were differences between studies investigated?
Fisher's exact test for homogeneity was used to identify those studies that appeared to be outliers. When all studies were combined a P-value of <0.00005 was reported, identifying significant heterogeneity and suggesting that the studies represented different populations. Standard meta-analytic pooling was inappropriate. Hence, the grouping of studies into the three categories was deemed necessary.

Results of the review
Ten studies were included.

The figures given below relate to the number of studies, the pooled failure rate of those cases exposed (%), and the pooled 95% confidence intervals (CIs) for secondary failure rate.

Group A: 1 study; failure rate 3 out of 13 (23.1%), 95% CI: 5.05, 53.81
Group B: 3 studies; 32 out of 572 (5.59%), 95% CI: 3.86, 7.81
Group C: 6 studies; 0 out of 2,061 (0.0%), 95% CI: 0, 0.15

The grouping of studies appeared robust as the transfer of one study to another group resulted in significant heterogeneity within that group. The reasons for heterogeneity between the studies is analysed by a narrative discussion in the authors' text.

Authors' conclusions
Reports of secondary failure from measles vaccination exist, and in those studies that allow pooling the rate of secondary failure appears to be less than 0.2%. This low rate may infer that continuing outbreaks of measles in the US result from other factors than secondary failure, i.e. failure to vaccinate children.

CRD commentary
A well-structured and documented review. The authors decision to avoid pooling of inappropriate studies is to be commended, as is their investigation for the variables responsible for heterogeneity. It may have been useful to the reader if the details on the included studies were expanded, particularly with reference to the characteristics of the included participants and the sample size of each trial. The literature search did not include non-English trials and had a heavy US bias. This may affect the robustness of the analysis and it would only take one study with a few cases to overturn the authors' conclusion.

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