Meta-analysis of trials of streptococcal throat treatment programs to prevent rheumatic fever

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CRD summary
The authors concluded that penicillin used in a school or community-based programme resulted in approximately 60% reduction in rheumatic fever cases. Given the unclear quality of the included diverse studies and weaknesses in the analysis, the authors’ conclusions should be treated with caution.

Authors’ objectives
To assess the effectiveness of streptococcal pharyngitis school or community based treatment programmes in preventing rheumatic fever.

Searching
MEDLINE, DARE, Cochrane Central Register of Controlled Trials (CENTRAL), NHS EED, NICE, NRMC and Clinical Evidence databases and CDC (Centers for Disease Control and Prevention) website were searched for articles in English. Where possible, titles and abstracts of non-English articles were checked. Search terms were reported. The personal filing system of one reviewer was checked. Researchers in the field were contacted for unpublished studies.

Study selection
Randomised controlled trials (RCT) or before/after studies that investigated the impact of sore throat treatment in a school or community setting on incidence of rheumatic fever were eligible for inclusion. Studies with no events of rheumatic fever in either group were excluded.

Most included studies were of children or adolescents in a school setting. Sore throats were swabbed and if the children were group A Streptococcus (GAS) positive they were administered treatment or referred elsewhere for further treatment. In one study, the treatment was reported to be penicillin; other studies did not report details of the antibiotic treatment. Most studies were set in schools; one study was set in a primary care inner city clinic. Three studies had a high proportion of indigenous people as participants. Outcomes reported were rheumatic fever diagnosed using the 1965 Jones Criteria, cardiologist diagnosis, past medical record search according to International Classification of Diseases (ICD) criteria or echocardiography. Studies were conducted in USA, a province of Cuba and New Zealand.

Two reviewers independently selected the studies for review. Disagreements were resolved by discussion.

Assessment of study quality
The authors did not assess validity.

Data extraction
The number of events in each group was extracted and used to calculated relative risks (RR) with corresponding 95% confidence intervals (CI).

Two reviewers independently extracted the data. Disagreements were resolved by consensus.

Methods of synthesis
Pooled relative risks with 95% CIs were calculated. Statistical heterogeneity was assessed using $\chi^2$ and $I^2$ statistics. The authors stated that a random-effects model was used due to significant heterogeneity.

Results of the review
Six studies were included for review (n=1,087,874 in forest plot); one RCT (n=24,000 in table and 63,785 in forest plot after adjustment to allow for unit of randomisation); two observational studies (n=680,683); and three before/after
studies (n=343,406). Quality of included studies was not assessed, but the authors reported that the quality of many included studies was poor.

Community interventions for sore throat reduced the risk of rheumatic fever by 60% (RR 0.41, 95% CI 0.23 to 0.70). There was evidence of significant statistical heterogeneity ($I^2=70.5\%$).

**Authors' conclusions**
Penicillin used in a school or community-based programme resulted in approximately a 60% reduction in rheumatic fever cases.

**CRD commentary**
The review addressed a clear question. Inclusion criteria were clearly stated for study design and outcomes, but broad for intervention and participants. Several relevant databases were searched. Some attempts were made to minimise the risk of publication and language biases. Appropriate steps were taken at the study selection and data extraction stages to minimise the risk of reviewer error or bias. No validity assessment was performed, so it was not possible to determine the quality of included studies. However, most studies were of weaker design. There was insufficient information on all included studies to determine the exact nature of the intervention. The authors’ conclusions referred to penicillin, but only one of the included studies reported using this treatment. Pooling data from different study designs is not recommended. As the incidence of rheumatic fever may have decreased over time in the absence of any intervention, the findings from before and after studies may be influenced by factors other than the intervention. Given the unclear quality of the included diverse studies and weaknesses in the analysis, the authors' conclusions should be treated with caution.

**Implications of the review for practice and research**
**Practice:** The authors stated that school or community-based programmes for the prevention of rheumatic fever should be considered in communities with a rate of rheumatic fever greater than 50 per 100,000 children per year.

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

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