CRD summary
This review concluded that chemonucleolysis with chymopapain was superior to placebo and as effective as collagenase, but heterogeneity between studies in the comparison with surgery made interpretation of the summary measure difficult. Given the small number of studies included, the potential for missed studies and the apparent publication bias, the conclusions of the review should be interpreted with some caution.

Authors' objectives
To evaluate the efficacy of chemonucleolysis in the treatment of lumbar disc herniation.

Searching
MEDLINE, EMBASE and Cochrane Central Register of Controlled Trials were searched from 1966 to June 2003 for studies published in any language; search terms were reported. Reference lists of retrieved articles and the contents lists of relevant journals were searched.

Study selection
Randomised and non-randomised clinical trials (RCTs and non-RCTs) of chemonucleolysis with chymopapain or collagenase compared to placebo or surgery in patients with symptomatic lumbar disc herniation with sciatic pain who had undergone computerised tomography (CT), magnetic resonance imaging (MRI) or myelography were eligible for inclusion. Follow-up ranged from three months to two years. Patients ranged in age from 16 to 77 years. Most studies administered 4,000 IU chymopapain; the rest used between 2,000 IU and 4,000 IU. The outcome of interest was pain relief.

The authors stated neither how studies were selected for the review nor how many reviewers performed the study selection.

Assessment of study quality
Study quality was assessed by two independent reviewers in terms of randomisation, blinding, time from intervention to outcome, loss to follow-up and use of a standardised outcome measure using the Jadad and Cochrane Collaborative Group scales. Disagreements were resolved by consensus.

Data extraction
The number or proportion of patients who achieved pain relief were extracted from each study and a risk ratio (RR) and 95% confidence intervals (CI) calculated. Data were extracted by two independent reviewers; disagreements were resolved by consensus.

Methods of synthesis
Pooled RR and 95% CI were calculated using a fixed-effect meta-analysis (FE) using inverse-variance weighting, unless significant heterogeneity was observed (p<0.1) in which case a random effects model (RE) was used; the method used to assess heterogeneity was not reported. Sensitivity analyses were undertaken for comparisons where statistically significant heterogeneity was observed. Publication bias was assessed using a funnel plot.

Results of the review
Twenty one trials met the inclusion criteria and provided sufficient data for inclusion in the review (n=2,485, range 29 to 358). Fifteen studies reported randomisation, three reported participation choice and two reported consecutive cases; one study did not report on allocation. Jadad scores were reported as ranging from 1 to 9 (the top score is usually 5); only two studies achieved a score greater than 3. Only one study achieved a Cochrane score of A and the rest achieved C. Chemonucleolysis with chymopapain significantly improved pain relief compared to placebo (FE: RR 1.51, 95% CI 1.27 to 1.80; five studies), but not compared to collagenase (FE: RR 1.07, 95% CI 0.95 to 1.20; four studies) or
surgery (RE: RR 0.9, 95% CI 0.8 to 1.0; 12 studies). The funnel plot indicated that publication bias may have been present.

**Authors' conclusions**
Chemonucleolysis with chymopapain was superior to placebo and as effective as collagenase, but heterogeneity between studies in the comparison with surgery made interpretation of the summary measure difficult.

**CRD commentary**
The authors addressed a clearly defined question. Relevant sources were searched, but there was no specific attempt to locate unpublished studies and publication bias was evident. Data extraction and validity assessment were conducted in duplicate, which reduced the potential for error and bias; it was unclear whether the same measure was taken during study selection. Study quality was assessed using appropriate criteria and the results reported for each study. More information on how the Jadad and Cochrane scores were determined would have been useful, especially as the authors reported a Jadad score of 9 when it is usual to have a maximum Jadad score of 5. Clinical heterogeneity between studies, particularly those that compared chemonucleolysis with surgery where statistical heterogeneity was also observed, made the reliability of the pooled results uncertain. Given the small number of studies included, the potential for missed studies and the apparent publication bias, the conclusions of the review should be interpreted with some caution.

**Implications of the review for practice and research**
The authors did not state implications for practice or research.

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