Adhesive capsulitis is a common, painful, and disabling condition that has been managed with corticosteroid injections for over 50 years. There is debate over the use of single or multiple injections, but no systematic review has investigated the effects of administering multiple injections.

**Aim**
To assess the efficacy of treating adhesive capsulitis of the shoulder with multiple corticosteroid injections.

**Design of study**
Systematic review.

**Method**
An English language search for randomised controlled trials was conducted from: MEDLINE®, EMBASE, CINAHL, PEDro, SIGLE, National Technical Information Service, British National Bibliography, Index of Scientific and Technical Proceedings® databases, and the Cochrane Library. Randomised controlled trials were identified from reference lists of review and eligible articles. The studies were assessed using a recognised rating system of methodological trial quality. The conclusions and results of the identified studies, based on their main outcome measures, were then summarised.

**Results**
Nine randomised controlled trials were identified and four studies were rated as high quality. Three high quality studies showed a beneficial effect for the use of multiple corticosteroid injections with outcome measures of pain reduction, improved function, and increased range of shoulder movement.

**Conclusion**
The evidence suggested that multiple injections were beneficial until 16 weeks from the date of the first injection. Up to three injections were beneficial, with limited evidence that four to six injections were beneficial. No evidence was found to support giving more than six injections.

**Keywords**
adhesive capsulitis; injections; randomised clinical trials; review, systematic; shoulder; steroids.

**INTRODUCTION**
Adhesive capsulitis of the shoulder is a common affliction, affecting 2–5% of the general adult population and up to 20% of patients with diabetes. An average general practice list of 6250 patients in England would expect to see 15 to 16 new cases each year.

Painful stiffening of the shoulder was given the term ‘adhesive capsulitis’ by Neviaser in 1945. Codman used the term ‘frozen shoulder’ to describe a painful shoulder condition of insidious onset with stiffness and difficulty sleeping on the affected side. However, it was Duplay in 1872 who originally described the condition as ‘periarthrite scapulo–humérale’. These terms are now used synonymously.

Adhesive capsulitis is a clinical diagnosis made from a history of the gradual onset of severe shoulder pain with the progressive limitation of active and passive glenohumeral movements. The most significant loss of movement is in the external rotation of the joint.

The condition is widely reported as a disease of middle age and is characterised by three phases. A painful phase, lasting between 3 and 8 months is followed by a phase of progressive stiffness or ‘adhesive phase’, typically lasting 4–6 months. The final resolution phase of gradual return of motion usually lasts 5–24 months.

Many treatments have been advocated to treat the condition: rest, analgesia, active and passive mobilization, physiotherapy, oral and injected corticosteroids, capsular distension, manipulation under anaesthetic, and arthroscopic capsular release. Currently there is no consensus as to which...
is most effective. Some authors recommend a course of injections, with the number varying from one to 10. Others question the benefits of corticosteroid injections.

The management of shoulder disorders and shoulder pain with corticosteroid injections has been the subject of several systematic reviews. No review has specifically examined the results of trials that gave multiple injections of corticosteroids for adhesive capsulitis.

METHOD
The process of this review followed the guidelines of the QUOROM statement. The Cochrane Library, MEDLINE®, EMBASE, CINAHL, and PEDro databases were searched from their inception up to June 2006. Searching the "grey literature" to retrieve less accessible studies was undertaken using SIGLE, the National Technical Information Service, the British National Bibliography, and the Index of Scientific and Technical Proceedings.

Searching was limited to reports in English due to lack of resources. The reference lists of publications retrieved were also reviewed to identify further studies for consideration in this review. The review strategy was to include all randomised controlled trials as they are widely viewed as the most appropriate research design for studying the effectiveness of an intervention or treatment.

Key descriptors were identified from previous systematic reviews and are shown in Box 1.

The inclusion criterion was a randomised controlled trial in adults with adhesive capsulitis having multiple steroid injections. Exclusion criteria were non-randomised controlled trials, shoulder conditions other than adhesive capsulitis, one or no corticosteroid injection, and patients aged <18 years, as the condition is rare in children.

A validity assessment of the methodological quality of the studies was made using the criteria scale advocated by Van der Heijden et al in their systematic review of steroid injections for shoulder disorders. This scale gave an overall single quality score by combining individual items from a quality assessment tool. This scale has been used by other similar systematic reviews and it mirrored similar items to the Delphi consensus and the CONSORT quality statement for the publication of randomised controlled trials. The identified studies were assessed independently for inclusion and quality and mean scores were used to grade them.

The scale had four main categories (study population, interventions, measurements of effects, and data presentation), which were divided into a total of 15 sections and each score points. The maximum total score was 100 with a high methodology achieving a score of more than 50. This point was chosen because the value had been used by other studies as a determination of quality (Supplementary Table 1).

Data abstraction was carried out independently. Data were analysed for the reported effect measures of reductions in pain, disability, and increase in external rotation of the shoulder joint.

RESULTS
The search process identified 23 potentially relevant citations that met the search criteria. Six trials failed to meet the search criteria after reading the abstracts, as they were either not randomised or did not involve multiple injections. Full copies of the remaining 17 trials were obtained. After analysis a further eight were excluded as they did not meet the inclusion criteria. The remaining nine studies were included in the review.

Population characteristics
The total number of patients included in all the studies was 476. The largest trial involved 114 patients, the smallest included 22 patients, and one trial did not provide any data on the number involved. Most of the studies were of small size with only two having more than 100 participants.

Two studies made a power calculation, but only one of these achieved the necessary group sizes of

How this fits in
There are no systematic reviews on the use of multiple corticosteroid injections for adhesive capsulitis of the shoulder. There is debate over whether to give single or multiple injections. This systematic review of randomised controlled trials suggests that multiple injections were beneficial up to 16 weeks from the date of the first injection. The evidence also suggests that up to three injections were beneficial; there was limited evidence that giving up to six injections was beneficial.
their calculation. The mean age of participants showed little variation between the nine studies, with a maximum of 56 years and a minimum of 47 years of age. The sex distribution showed a considerable range between the studies (38–67% females).

**Settings**

None of the studies were conducted in general practice in the UK. Four were conducted in UK outpatients and two in general practice in Holland. The remaining three studies were in outpatients in Holland, Denmark, and the US.

**Inclusion and exclusion criteria**

All studies used similar inclusion criteria, with the four highest-ranking studies having very similar inclusion criteria (significant loss of passive external rotation, and severe shoulder pain). However, there was not enough information reported by the studies to determine if these signs and symptoms were comparable.

The exclusion criteria of the studies showed considerable variation: bilateral symptoms, diabetes, previous treatment, and neurological symptoms.

**Timescale**

There was variation between the studies with a reported duration of the symptoms at baseline, ranging from a mean of 8 to 32 weeks.

**Treatment completion**

Loss to follow-up was low apart from the study of Winters et al who lost 59% of their manipulation group and 51% of their physiotherapy group by the end of the 11 weeks of their study.

**Comparison groups**

Physiotherapy was the only intervention to be compared more than once. The nature of the physiotherapy itself was not directly comparable in terms of the type of treatment given, number of sessions, and the total duration of treatment.

**Outcome measures**

All the studies assessed the participants pain and range of movement at the glenohumeral joint, some studies measured disability using differing scales, and one used a questionnaire.

Pain was measured using a 10-centimetre visual analogue scale (VAS) in four studies, and differing scales in three studies. Two studies did not state how pain was assessed.

Range of shoulder movement was assessed by clinical observation using different methods in four studies, and by the use of differing goniometers in four studies. The remaining study did not state how range of movement was assessed. Functional ability was assessed in three studies by differing methods. One study used a questionnaire and two used different scales. Shoulder dynamometry was assessed by a blinded observer by one study.

The lowest scoring study failed to give any details of its methods of outcome assessment. There were no other common assessment methods used by the studies. Statistical comparisons were not possible between the studies because of differences in outcome assessment, duration of follow up, assessment points, and lack of data. Table 1 shows the main features of the identified studies.

**Co-interventions**

Only one study avoided co-interventions completely. The other eight studies all differed in the co-interventions used, which reduced their external validity.

**Treatment period**

This ranged from 2 weeks to a maximum of 12 weeks.

**Single versus multiple injections**

No trial compared single versus multiple corticosteroid injections. Multiple injections were compared against saline, local anaesthetic, and no treatment: one study compared a high dose of steroid against a low dose. The type, dosage, site (intra-articular, subacromial or acromioclavicular joint), volume of injection (1–20 ml), addition of local anaesthetic to the injection solution,
Systematic Reviews

Table 1. Identified studies.

<table>
<thead>
<tr>
<th>Study</th>
<th>Score</th>
<th>Setting and numbers</th>
<th>Comparison groups (n)</th>
<th>Steroid [mg] volume used (ml)</th>
<th>Treatment period, weeks</th>
<th>Maximum number of injections</th>
<th>Assessment period, weeks</th>
<th>Changed outcome measures</th>
<th>Reviewers’ conclusion</th>
</tr>
</thead>
<tbody>
<tr>
<td>Van de Windt</td>
<td>70.5</td>
<td>Dutch GP 109</td>
<td>IA (53) vs physio (56)</td>
<td>TA [40] (1)</td>
<td>6</td>
<td>3</td>
<td>52</td>
<td>Symptom, pain, disability 13 weeks only</td>
<td>Significantly more effective at 7 and</td>
</tr>
<tr>
<td>De Jong</td>
<td>59.5</td>
<td>Dutch OP 57</td>
<td>High dose IA (25) vs low dose IA (32)</td>
<td>TA [40] [10] (1)</td>
<td>3</td>
<td>3</td>
<td>6</td>
<td>Pain, sleep, function, ROM low dose</td>
<td>High dose significantly more effective than</td>
</tr>
<tr>
<td>Jacobs</td>
<td>55</td>
<td>UK OP 50</td>
<td>IA (16) vs distension with steroid (16) or air (18)</td>
<td>TA [40] (1/5/10)</td>
<td>12</td>
<td>3</td>
<td>16</td>
<td>ROM, function, pain, analgesic use</td>
<td>Significant improvement in pain and ROM only</td>
</tr>
<tr>
<td>Garm</td>
<td>54.5</td>
<td>Denmark OP 20</td>
<td>IA 8 vs distension with steroid (12)</td>
<td>TH [20] (1/20)</td>
<td>6</td>
<td>6</td>
<td>12</td>
<td>Symptoms, pain, ROM, analgesic use</td>
<td>Significant improvement with distension in all criteria</td>
</tr>
<tr>
<td>Winters</td>
<td>49.5</td>
<td>Dutch GP 124</td>
<td>IA SA AC (47) vs physio (35) vs manipulation (42)</td>
<td>TA [40] (10)</td>
<td>3</td>
<td>3</td>
<td>11</td>
<td>Pain, ROM</td>
<td>Significant improvement</td>
</tr>
<tr>
<td>Richardson</td>
<td>46.5</td>
<td>UK OP 101</td>
<td>IA (54) vs placebo (47)</td>
<td>P [50] (2)</td>
<td>2</td>
<td>2</td>
<td>6</td>
<td>Pain, ROM</td>
<td>No significant improvement</td>
</tr>
<tr>
<td>Bulgen</td>
<td>42</td>
<td>UK OP 42</td>
<td>IA and SA (11) vs mobilization (11) vs ice therapy (12) vs no treatment (8)</td>
<td>MP [20] (1)</td>
<td>3</td>
<td>3</td>
<td>26</td>
<td>Pain, ROM</td>
<td>No significant improvement</td>
</tr>
<tr>
<td>Rizk</td>
<td>34</td>
<td>US OP 48</td>
<td>IA (16) or SA (16) vs LA IA (8) or SA (8)</td>
<td>MP [40] (3)</td>
<td>3</td>
<td>3</td>
<td>26</td>
<td>Pain, ROM</td>
<td>No significant improvement</td>
</tr>
<tr>
<td>Williams</td>
<td>15</td>
<td>UK OP No data</td>
<td>IA vs stellate ganglion block</td>
<td>H [50] No data</td>
<td>3</td>
<td>3</td>
<td>12</td>
<td>Pain, ROM, analgesic use</td>
<td>Equally effective</td>
</tr>
</tbody>
</table>

AC = acromoclavicular, GP = general practice, H = hydrocortisone acetate, IA = intra-articular injection, LA = local anaesthetic (lidocaine), MP = methyl prednisolone acetate, OP = outpatients, physio = physiotherapy, P = prednisolone acetate, ROM = range of movement, SA = subacromial injection, TA = triamcinolone acetonide, TH= triamcinolone hexacetonide, vs = versus.

and frequency of injection also varied with the studies, as did the type of local anaesthetic when used. Only two studies attempted to confirm the site of injection27,34 which was reported as ‘inconsistent’ by the study of Richardson.27

Duration of follow up
The final outcome assessment point of the studies showed considerable variation from 6 weeks after baseline30 to 52 weeks.33

Adverse reactions
Adverse reactions to corticosteroid injections were reported by four studies.30,33–35 These were increased pain after injection (10–44%), facial flushing (12.5–20%), rash (4%), and irregular menstrual bleeding (10.5%). Nineteen per cent of the side effects reported in one study30 were fever, skin irritation, sweating, fatigue, dry mouth, dizziness, and headache. No other side effects were reported.

Conclusions of the studies
The authors of the four high-methodology scoring trials concluded that steroid injections had a positive effect in their studies.30,33–35 The five highest scoring trials found that multiple injections reduced pain and/or improved movement (external rotation) from 4–16 weeks.30,33–35

DISCUSSION
Summary of main findings
The evidence suggests that multiple corticosteroid injections improve pain and range of motion in the short term (6–16 weeks) from first injection.30,33–35 This is of clinical value as pain and limitation of movement can often be severe. From the change in outcome measures in the studies of high methodology30,33–35 there was evidence that up to three corticosteroid injections was beneficial,30,33,35 limited evidence that up to six injections was beneficial,34 but no evidence for giving more than six injections to treat adhesive capsulitis.

In terms of conservative management there was limited evidence that multiple injections were of
equivalent benefit to physiotherapy in the long term of 6–12 months.36

**Strengths and limitations of the study**

The limitations of the review include publication bias, which may have occurred as limited resources meant that translation facilities were not available. Some trials may have been missed because they used keywords other than those identified by the search strategy, which was chosen for convenience from strategies used by reviews for answering similar, but not identical questions.15–17 The strategies used to identify the ‘grey literature’ of non-indexed and unpublished studies may not have identified all possible studies. Trials that are unpublished generally tend to have negative results, so it is important to identify this to avoid overestimation of the beneficial effects of corticosteroid injections.27 The two reviewers were not blinded, which may have caused bias in the results of the methodology scores,34 although some studies have found large discrepancies between multiple reviewers.38 A comparative quantitative presentation of the results was not possible due to differences in measurement of effects and missing or incompatible data, so the precision of the results could not be estimated.

Five different corticosteroids were used by the studies identified. Triamcinolone acetonide was the most popular.29,30,32,35 Five studies had treatment groups that combined the corticosteroid with local anaesthetic. Lidocaine was used in four studies, in volumes of 1, 3, 110, and 20 mL.34 One study used bupivacaine in 10 mL.30 All nine studies gave the injections intra-articularly. Three studies also injected the subacromial bursa,30,31,32 and one involved injection of the acromoclavicular joint.35

Only two of the studies were based in general practice and neither of these was in the UK.30,32 Caution should be placed on generalising the findings of this review to UK general practice as the location of studies can be a source of bias in systematic reviews30 and the management of shoulder pain across Europe has been reported to vary.31

No cost-effectiveness analyses were calculated by the studies. It has been reported by others that injections are cheaper and as equally effective as physiotherapy for unilateral shoulder pain in primary care.31,42

This review used a detailed assessment tool to grade the quality of the studies. However, the score or weighting of each methodological criterion remains rather arbitrary.25,41 This is important when considering weaknesses of a study that could influence its internal validity such as:

- Small study size (n<40). This can exaggerate treatment effects by up to 33%.44
- Duration of symptoms before treatment. Since adhesive capsulitis has three phases the studies may have been treated at differing stages of the condition.19–21
- High drop-out rate.
- The use of co-interventions.
- Significance of adverse events. This may have not been fully assessed as most of the studies were of small size and short duration so not suitable to detect rare adverse events.45

Heterogeneity of the studies and the reasons for it have been analysed. As a result of this the evidence for the use of multiple injections would be suggested as a guide with need for further, more detailed, high quality studies.

**Comparison with existing literature**

The use of corticosteroid injections for shoulder disorders and shoulder pain has been the subject of five systematic reviews.15–17 Three of these reviews looked at shoulder disorders and shoulder pain as a whole.15–17 Partly as a consequence of their broad research questions, these reviews did not interpret their results on the basis of a specific diagnosis. The other reviews combined the results of trials that used single and multiple injections in their treatment of adhesive capsulitis and rotator cuff disease.14,16 None of these reviews specifically examined the results of trials that gave multiple injections of corticosteroids for adhesive capsulitis or the number of injections to be given and their frequency.

**Implications for clinical practice and future research**

This review assessed four randomised controlled trials as high quality, which justified giving multiple corticosteroid injections for adhesive capsulitis. The small sample sizes and heterogeneity of the studies meant that overall there was limited evidence to guide treatment decisions in adhesive capsulitis. There is a need for further randomised controlled trials of high methodological quality, to look at the optimum number, frequency, dose, volume, type of corticosteroid, and the importance of the anatomical site of needle placement. Better outcome to steroid injection has been reported from accurately placed injections in patients with shoulder symptoms.46,47

The adoption of a uniform definition and staging of the condition combined with a standard set of outcome measures would greatly enhance the value and generalisability of this future research.

The authors’ own practice has been modified following the above evidence to inject 40 mg of triamcinolone acetonide (high dose more effective than low dose)31 with 10 mL 1% lidocaine (distension with or
without corticosteroid seems beneficial,\textsuperscript{40} 10,13,24 intra-articularly at intervals, increasing by 7 days each time until the patient is pain free.\textsuperscript{4} The normal volume of the glenohumeral joint is usually reduced to less than 10 ml in adhesive capsulitis.\textsuperscript{44} Using this method a maximum of three injections have been needed.\textsuperscript{46} Mobilizations (active and passive) can then be introduced.

**Supplementary information**

Additional information accompanies this article at http://www.ncbi.nlm.nih.gov/pmc/articles/PMC3579623/

**Competing interests**

The authors have stated that there are none

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