Interventions for management of primary frozen shoulder: a systematic review

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1. Introduction

1.1. Rationale

In 2012, a NIHR HTA programme funded systematic review concluded that there was limited clinical evidence on the effectiveness of different treatment options in the management of a primary frozen shoulder, including intensive or invasive interventions: arthrographic distension (hydrodilatation), manipulation under anaesthesia (MUA), and arthroscopic capsular release.[1] The review findings informed the design and funding of the multi-centre randomised, parallel group, superiority study called United Kingdom Frozen Shoulder Trial (UK FROST).[2] UK FROST compared the clinical and cost-effectiveness of early structured physiotherapy versus manipulation under anaesthesia (MUA) versus arthroscopic capsular release in secondary care for patients with primary frozen shoulder. The purpose of the current review is to put the findings of UK FROST in the context of the studies identified in the original review and any studies undertaken since then. This has involved a focused update of the original review.

The 2012 review had a broad remit to provide an overview of all NHS relevant treatments, including the comparison of individual physiotherapy modalities and steroid injection as a stand-alone treatment. However, the current review focuses on the interventions evaluated in UK FROST in order to place the results of the trial in the context of existing evidence. Since a survey of United Kingdom health professionals was published in 2012, which found that only 5% used hydrodilatation in the treatment of primary frozen shoulder,[3] there is anecdotal evidence that this treatment option has increased in popularity. Moreover, in qualitative interviews with health care professionals, undertaken as a nested study within UK FROST, some surgeons and physiotherapists commented that hydrodilatation could have been a treatment option in the trial. This update, therefore, includes hydrodilatation.

The aim of the 2012 review was to provide a comprehensive overview of the evidence, quasi-experimental study designs and case series (for surgical interventions) were included. This focused update of the evidence includes randomised controlled trials (RCTs) only. The protocol was reported in alignment with the PRISMA-P checklist and the findings are reported in line with the PRISMA reporting guidance.[4]

1.2. Objective

The objective was to undertake a systematic review to assess the effectiveness of MUA, arthroscopic capsular release, hydrodilatation and physiotherapy with steroid injection in the management of patients with a primary frozen shoulder. This is to place the findings of UK FROST in the context of existing evidence for these treatments.

2. Methods

2.1. Protocol and registration

We selected the studies for this review based on prospectively developed and registered protocol. PROSPERO registration number: CRD42019122999.

2.2. Eligibility criteria

2.2.1. Study design

RCT was the only study design that was included.

2.2.2. Participants

Participants aged 18 years or older with idiopathic (primary) frozen shoulder (adhesive capsulitis), with or without diabetes were included. Studies that included participants with general shoulder

conditions were only included if: a) outcome data was reported separately for participants with frozen shoulder; or b) over 90% of participants had primary frozen shoulder.

2.2.3. Interventions

The following interventions were eligible for inclusion:

- MUA, in which the shoulder was freed by rotation while the patient was under a short general anaesthesia, with or without a steroid injection;
- Arthroscopic capsular release, a surgical procedure conducted under general or regional anaesthesia during which the contracted tissue was released, with or without an MUA. This did not include 'open' capsular release;
- Physiotherapy and a steroid injection. The physiotherapy delivered in UK FROST was a multicomponent intervention that was developed using recommendations from national guidelines[5] and a Delphi study. Whilst components of physiotherapy were 'disallowed' in the trial intervention (i.e. provision of a brace, craniosacral therapy, deep tendon friction, laser therapy, shockwave therapy, interferential therapy) these did not apply to assessing the eligibility of studies for this review;
- Hydrodilatation (arthrographic distension), which involved controlled dilatation of the joint capsule with or without guidance by radiological imaging. Any combination of fluids to distend the joint capsule were permitted.

When steroid injections were administered for these interventions the inclusion of studies was not limited to whether imaging guidance was used or not.[6] MUA, arthroscopic capsular release and hydrodilatation were included with or without follow-up physiotherapy.

2.2.4. Comparators

- Any of the above treatment interventions
- No treatment
- Supportive care e.g. leaflets, home exercises, watchful waiting, pain killers

2.2.5. Outcomes

The primary outcome of interest was patient self-reported function and disability (e.g. Oxford Shoulder Score, Shoulder Disability Questionnaire). Other included outcomes were: quality of life (using standardised outcome measures), pain (e.g. visual analogue pain scores), time to recovery, return to work and recreation, complications and adverse events (number and type).

2.2.6. Timing

The primary end-point was 12 month follow-up.

2.2.7. Setting

There was no restriction on the setting in which a study was undertaken.

2.2.8. Language

No language restrictions were applied.

2.3. Information sources

The following databases were searched: Medline, EMBASE, PEDro, Science Citation Index and Clinicaltrials.gov search date were searched on 7th December 2018; Central was searched on 5th December 2018; and WHO International Clinical Trials Registry was searched on 11th December 2018.

The reference lists of eligible studies were reviewed for further studies. The RCTs identified from the original review were re-assessed for inclusion in this review.

2.4. Search strategy

The search strategy used in the original review[1] was adapted to search for RCTs of the interventions of interest by an information specialist with expertise in systematic review searching (see Appendix 1). The searches for the original systematic review were undertaken in March 2010; therefore, the start date of January 2010 was used for the updated search, the overlapping to allow for any delays in articles being added to the bibliographic databases. The data bases were searched up to 11 December 2018.

2.4.1. Screening and study selection

Literature search results were uploaded to EndNote referencing software that facilitates collaboration among reviewers during the study selection process. This software and Covidence was also used to remove duplicate publications.[7]

Two researchers independently screened all titles and abstracts identified from the searches to identify potentially relevant studies. Full manuscripts of potentially relevant studies were independently assessed by two researchers against the eligibility criteria. Disagreements over eligibility were resolved by recourse to a third researcher. This was carried out in Covidence.[7]

2.5. Data collection process

A data extraction form was developed in Microsoft Excel, piloted on a small selection of studies and adjusted as necessary. Data extraction was performed by one researcher and checked by a second researcher. Any discrepancies were resolved through discussion or by recourse to a third researcher.

Data items extracted include details of the study design, number randomised, loss to follow-up, country, setting, patient characteristics (including average age, gender, presence of diabetes, stage of condition), description of the interventions (and comparators), concomitant treatments and outcome measures used.

For continuous outcomes the post-intervention mean (standard deviation, SD and number of participants) for each group was extracted, where available. Otherwise the mean change from baseline for each group was extracted or the effect estimate and standard error (SE). Authors were contacted where clarification of data was required for any of the primary outcomes (e.g. where data is presented in graph format only) but this was not required. Unadjusted and adjusted data were extracted, and the latter used where possible. Standard data imputation methods were used, where necessary, to calculate SDs or SEs.[8] Where this information was not available, the SD was imputed based on the average SD across all interventions for that outcome or from online resources. When the number of participants in an analysis was unclear, the number randomised minus the number of dropouts was used. Where only median and ranges are reported, these were extracted. For binary outcomes the number of participants with the event of interest (and number of participants) in each group were extracted. Otherwise effect estimates and standard errors were extracted. For the time to recovery outcome, estimates of the log hazard ratio and its standard error were calculated using statistics computed during log-rank analysis (values of O-E and V for each study) or from hazard ratios and SEs.

2.5.1. Outcomes and prioritisation

The primary outcome was patient self-reported shoulder function and disability at 12 month follow-up. Where studies did not report the same length of follow-up, outcomes were grouped by short-, medium- and long-term follow-up. For short-term follow-up the data point from each study at 3 months' follow-up or the closest data point before 3 months' follow-up was used. For medium-term follow-up, the data point at 6 months or the closest data point between 3 and 6 months was used.

For long-term follow-up, the data point at 12 months or the closest data point between 6 and 12 months was used. The primary end-point was at 12 months.

2.6. Risk of bias in individual studies

The Cochrane Risk of Bias Tool was used to assess the risk of bias in included RCTs.[8] Quality assessment was undertaken by one researcher and checked by a second; disagreements were adjudicated by a third researcher. Baseline heterogeneity was assessed by carrying out a meta-analysis of baseline age by treatment group.

2.7. Synthesis of results

A narrative and tabular summary of key study characteristics, results and quality assessment are provided. This includes baseline population characteristics; a description of intervention and comparator; study methods (e.g. study design, how outcomes were measured and defined, length of follow-up); and risk of bias. An assessment was made about the clinical and methodological similarity of included RCTs to establish whether a quantitative synthesis was appropriate to be undertaken. When this was not feasible, a narrative synthesis was undertaken and the results tabulated. Studies were grouped by intervention and comparator.

2.8. Meta-analysis

Given the multiple interventions being included, a mixed treatment comparison (MTC) would have been an appropriate approach to the evidence synthesis. The plan was to undertake an MTC in order to explore the relative effectiveness of the interventions with respect to each other if sufficient data were available and RCTs were sufficiently homogenous to be combined.[9] However this was not possible. Where appropriate, we undertook pair-wise meta-analyses depending on clinical and statistical heterogeneity, the necessary data being available and using methods that allow for studies with multiple intervention groups.[8,10] A random effects model was used to calculate the pooled effect and 95% confidence interval. Depending on the outcome measure, a weighted mean difference or standardised mean difference (if different measurements scales are used) were calculated for continuous outcomes and a risk ratio for dichotomous data. Where estimates and SEs were extracted we used a generic inverse variance approach. For the time to event outcome, depending on the type of data extracted, we used either a fixed effect Peto method or a random effect generic inverse variance method. Statistical heterogeneity was assessed using the chi-squared test and quantified using the I-squared statistic.

2.9. Risk of bias across studies

We planned to explore the effect of risk of bias on the effect estimate in a sensitivity analysis, if there were sufficient studies, by omitting studies that were judged to be of high risk of bias. We planned to explore the potential for reporting bias using funnel plots if sufficient studies were available.

2.10. Additional analysis

Having undertaken the main analyses on the primary outcome, if there were sufficient studies we planned to stratify analysis on the characteristics of patients (e.g. with or without diabetes), interventions (e.g. whether imaging was used or not) and whether the interventions are consistent with the UK FROST trial (e.g. whether arthroscopic capsular release included MUA or not).

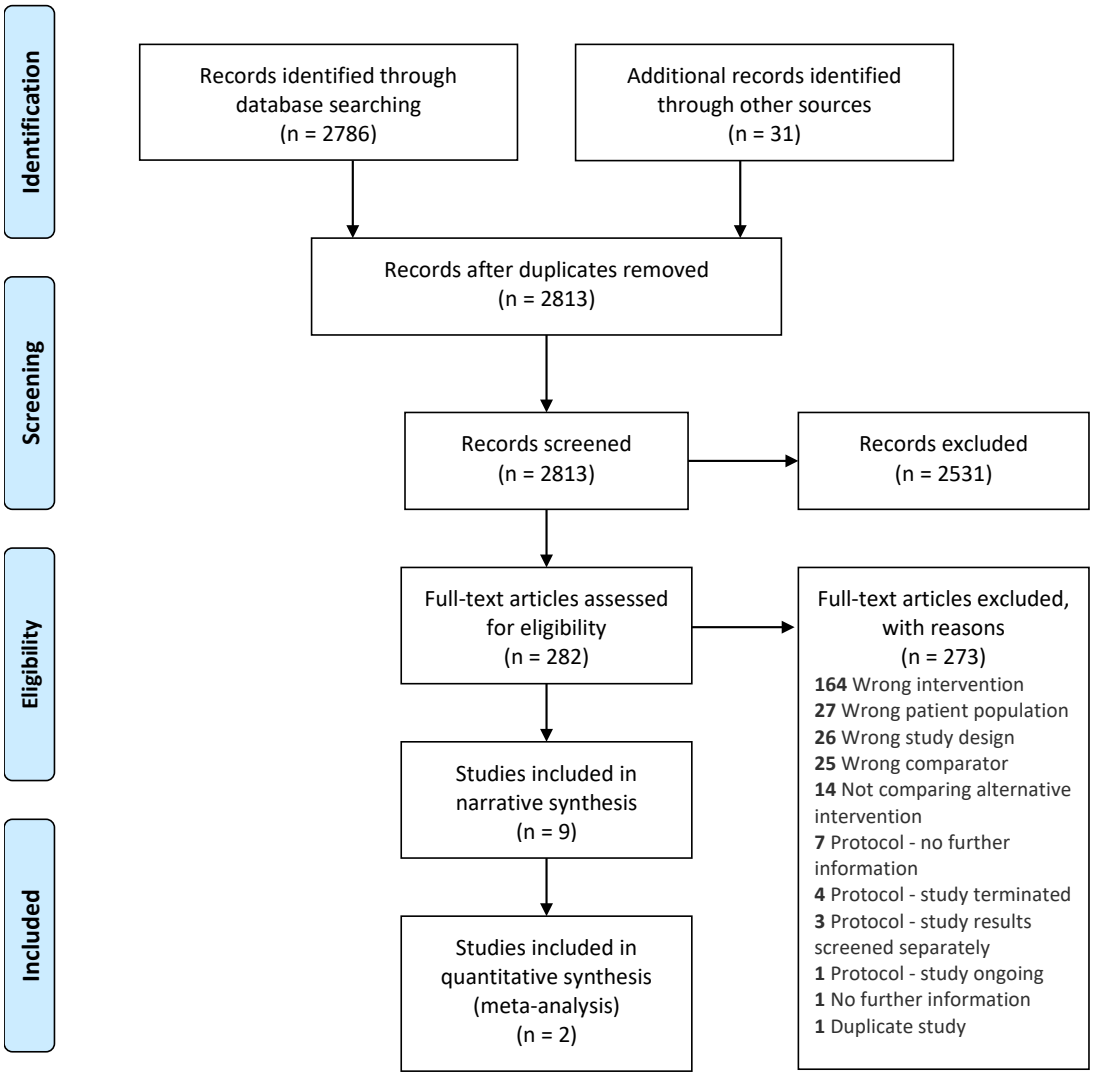
3. Results

3.1. Study selection

Figure 1 summarises the study selection process. Following deduplication there were 2813 studies in total transferred to Covidence for screening. A further four studies were found to be duplicates so

were removed. 2531 studies were excluded during the title and abstract screening stage. 282 full-text studies were assessed. 273 studies were excluded due to studies not meeting our eligibility criteria or when we were not able to get enough information. Nine studies (including UK FROST) were eligible for inclusion for this review. Summary information of these included studies can be found in Tables 1 and 2.

Figure 1: Flow Diagram



3.2. Study characteristics

In addition to UK FROST there were eight studies published between 2007 and 2018. Four of the included studies were published since the 2012 HTA review. As detailed in Table 1, UK FROST is the only study that compared MUA with Steroid + Physio and ACR with MUA. UK FROST, De Carli et al.[11] and Mukherjee et al.[12] compared ACR with Steroid + Physio. Jacobs et al.[13] and Quraishi et al.[14] compared MUA with Hydrodilatation. Kivimaki et al.[15] compared MUA with Supportive care. Gallacher et al. [16] is the only study that compared ACR with Hydrodilatation. Smitherman et al.[17] compared ACR with Supportive care. Mun et al.[18] compared Hydrodilatation with Steroid + Physio.

Table 2 summarises participant characteristics in the included studies. Most of the studies described their population as having stage 2 Adhesive Capsulitis. Three of the selected studies were

undertaken in the UK. The final follow-up for most studies was 12 months but it ranged from 20 weeks to 24 months. The total number of randomised participants ranged from 26 to 503. The drop-out rate ranged from 4.35% to 36.8%; average dropout rate was 15.45%. The mean age of the population included in study ranged from 50.4 to 56.75 years. There were more female participants than male in all the studies that reported this information. Seven out of nine included studies recruited diabetic patients; one did not include diabetic patients and another did not report this information. Overall the percentage of diabetic patients ranged from 13% to 30% (average 20%). The overall duration of symptoms ranged from 4.4 to 10.9 months and average duration was 7.4 months.

Table 1: Summary of study characteristics

Description		UK FROST	De Carli et al., 2012	Gallacher et al., 2018	Jacobs et al., 2009	Kivimaki et al., 2007	Mukherjee et al., 2017	Mun et al., 2016	Quraishi et al., 2007	Smitherman et al., 2015
Interventions tested	MUA	✓			✓	✓			✓	
	ACR	✓	✓	✓			✓			✓
	Steroid + Physio	✓	✓				✓	✓		
	Hydrodilatation			✓	✓			✓	✓	
	Supportive Care					✓				✓
Country		UK	Italy	UK	UK	Finland	India	Korea	UK	USA
Follow-up time-points* (excludes baseline)	2 weeks				✓			✓		✓
	3 weeks		✓							
	4 weeks						✓			
	2 months								✓	
	6 weeks		✓	✓	✓	✓		✓		✓
	8 weeks						✓			
	12 weeks / 3 months	✓	✓	✓	✓	✓	✓	✓		✓
	16 weeks				✓†		✓			
	20 weeks						✓			
	24 weeks							✓		
	6 months	✓	✓	✓‡	✓	✓			✓	
	48 weeks							✓		
	12 months	✓‡	✓		✓	✓				✓
	18 months				✓					
	24 months				✓					
Number randomised	MUA	201			28	65			17	

Description		UK FROST	De Carli et al., 2012	Gallacher et al., 2018	Jacobs et al., 2009	Kivimaki et al., 2007	Mukherjee et al., 2017	Mun et al., 2016	Quraishi et al., 2007	Smitherman et al., 2015
	ACR	203	25	25			30			13
	Steroid and Physio	99	21				30	69		
	Hydrodilatation			25	25			67	19	
	Supportive Care					60				13
Number dropped out N (%)	MUA	18 (8.96%)			9 (32.14%)	28 (43.08%)			2 (11.76%)	
	ACR	28 (13.79%)	2 (8%)	6 (24%)			2 (6.67%)			3 (23.08%)
	Steroid and Physio	11 (11.11%)	0 (0%)				2 (6.67%)	8 (11.59%)		
	Hydrodilatation			5 (20%)	1 (4%)			7 (10.45%)	1 (5.26%)	
	Supportive Care					18 (30%)				6 (46.15%)

* De Carli et al. follow-up time points were from the date of intervention (not baseline)

† Jacobs et al. reported results for 16 weeks but it was unclear whether data was collected at an unscheduled follow-up or whether this was an analytic adjustment.

‡ Primary end-point

Table 2: Summary of participant characteristics

Description		UK FROST	De Carli et al., 2012	Gallacher et al., 2018	Jacobs et al., 2009	Kivimaki et al., 2007	Mukherjee et al., 2017	Mun et al., 2016	Quraishi et al., 2007	Smitherman et al., 2015
Age in years Mean (SD)	MUA	54.5 (7.7)			56.5	53 (8.4)			54.5	
	ACR	53.9 (7.7)	57	52.6 (8.1)			48.1 (9.6)			51.5 (11.1)
	Steroid and Physio	54.5 (7.8)	54				52.6 (7.9)	53.9 (5.9)		
	Hydrodilatation			55.2 (9.8)	57			52.1 (6.4)	55.2	
	Supportive Care					53 (8.6)				52 (6.8)
Females %	MUA	64.18%			53.57%	71%				
	ACR	62.07%	56.00%	85.00%						
	Steroid and Physio	64.65%	52.38%					67.21%		
	Hydrodilatation			57.00%	80.00%			58.33%		
	Supportive Care					65.00%				
	Overall	63.42%	54.35%	70.00%	66.04%	68.00%	58.93%	62.81%	58.33%	
Inc. diabetic patients?	Yes	✓	✓	✓		✓	✓		✓	✓
	No				✓					
	Unknown							✓		
Diabetic patients %	MUA	60 (29.85%)							3 (17.65%)	
	ACR	60 (29.56%)	4 (16%)	3 (12%)						
	Steroid and Physio	30 (30.3%)	2 (9.52%)							
	Hydrodilatation			5 (20%)					3 (15.79%)	
	Supportive Care									

	Overall %	150 (29.82%)	6 (13.04%)	8 (16%)	0	18 (14.4%)	16 (28.57%)		6 (16.67%)	
Duration of symptoms (in months)	MUA	10.5			4.75	7.4			9.16	
	ACR	11.3								
	Steroid and Physio	10.8						6.3		
	Hydrodilatation				4			6.7	8.61	
	Supportive Care					7				
	Overall	10.9			4.4	7.2	6.3	6.5	8.9	

Table 3: Baseline pain and functioning

Study	Outcome*	Outcome description	MUA	ACR	Steroid + Physio.	Hydro.	Supportive care
UK FROST *Mean (SD)*	**Pain NRS**	Range: 0 to 10 Lower is better	6.8 (2.23)	7 (1.89)	6.9 (2.37)		
	OSS	Range: 0 – 60 Higher is better	20.5 (8.88)	19.1 (7.72)	20.3 (7.97)		
De Carli et al. *Mean*	**SST**	Range: 0 to 100 Higher is better		15.6	30.1		
Gallacher et al. *Mean (SD)*	**OSS**	Range: 0 to 60 Higher is better		17.3 (7.2)		16.2 (5.2)	
Kivimaki et al. *Mean (SD)*	**SDQ**	Range: 0 to 28 Lower is better	22.7 (4.9)				21.7 (4.6)
Mukherjee et al. *Mean (SD)*	**Pain VAS**	Range: 0 to 10 Lower is better		7.1 (1.8)	7.1 (1.8)		
Quraishi et al. *Mean (range)*	**Pain VAS**	Range: 0 to 10 Lower is better	5.7 (3 to 8.5)			6.1 (4 to 10)	
Smitherman et al. *Mean (SD)*	**SPADI**	Range: 0 to 100 Lower is better		70 (11)			82 (12)

*****NRS – Numeric Rating Scale; OSS – Oxford Shoulder Score; SST – Simple Shoulder Test; SDQ – Shoulder Disability Questionnaire; VAS – Visual Analogue Scale; SPADI – Shoulder Pain and Disability Index

Table 3 provides an overview of baseline pain and functioning. The different measures used limits any comparison between studies, though two studies show evidence of baseline imbalance between the two groups.[11, 17]

The interventions evaluated varied a lot between studies, for example ACR was performed with MUA for two studies and without for three studies. The eligibility criteria were fairly consistent across studies.

Table 4: Treatment description and eligibility criteria

Study details	Trial treatments	Eligibility criteria
UK FROST Three arm RCT n = 503 ACR: n=203 MUA: n=201 Steroid + Physio: n=99	**ACR with MUA:** - Arthroscopic release under GA of contracted rotator interval and anterior capsule followed by MUA. Postoperatvie analgesia including nerve blocks allowed - A programme of physiotherapy of up to 12 weeks - Information leaflet about advice on pain management and home exercise programme - Steroid injection avoided during physiotherapy - Pain meds allowed	**Inclusion criteria:** - Aged 18 years or older - Present with a clinical diagnosis of frozen shoulder characterised by restriction of passive external rotation in the affected shoulder to less than 50% of the contralateral shoulder

Study details	Trial treatments	Eligibility criteria
	MUA: - Shoulder manipulated to stretch and tear the tight capsule and to improve range of movement. intra-articular corticosteroid injection to the glenohumeral joint unless contraindicated. Postoperatvie analgesia including nerve blocks allowed. - A programme of physiotherapy of up to 12 weeks. - Information leaflet about advice on pain management and home exercise programme - Steroid injection avoided during physiotherapy - Pain meds allowed **Steroid + Physio:** - Up to 12 sessions of structured physiotherapy over 12 weeks comprised of essential 'focussed physiotherapy' and optional 'supplementary physiotherapy'. - 'Focussed physiotherapy' include an information leaflet containing education, advice on pain management and function; an intra-articular steroid injection and 'hands-on' mobilisation techniques and instruction on a graduated home exercise programme .- Pain meds allowed	- Have radiographs that exclude glenohumeral arthritis and other pathology **Exclusion criteria:** - Have a bilateral concurrent frozen shoulder - Have a frozen shoulder secondary to trauma - Have a frozen shoulder secondary to other causes - Trial treatments are contraindicated - Not resident in a catchment area of a trial site - Lack mental capacity to understand the trial or instructions for treatment
De Carli et al. 2012 Two arm RCT n=46 ACR: n=25 Steroid + Physio: n=21	**ACR with MUA:** - Included shoulder manipulation - Glenohumeral circumfrential capsular release - Passive exercises from first postoperative day - Active strengthening from fifth post-operative week **Steroid and Physio:** - Peri-capsular injection of local anaesthetic (2–3 cc of 2% lidocaine) followed by Glenohumeral Steroid injection (4 cc of 2% lidocaine and 1 cc of methylprednisolone acetate (Depo-medrol) under ultrasound guidance - A cycle of three steroid infiltrations-one each for 3 weeks - Intensive physical therapy protocol started day after first injection - Included manual schedule led by physiotherapist along with self-exercises	**Inclusion criteria:** - A clinical history of pain and restriction of passive and active ROM of the shoulder for at least three months, - A diagnosis of stage II adhesive capsulitis according to Reeves et al. - Unsatisfactory outcome after conservative protocol (e.g. physical therapy, oral non steroidal anti-inflammatory medications). **Exclusion criteria:** - Presence of calcific tendonitis or severe glenohumeral arthritis on X-ray
Gallacher et al. 2018 Two-arm RCT	**ACR:** - Under interscalene blockade and light GA - Included anterior release, superior and posterio-superior capsular release -posterior release for patients with poor internal rotation	**Inclusion criteria:** - Aged 18 years and older - Diagnosis of idiopathic frozen shoulder and with

Study details	Trial treatments	Eligibility criteria
n=50 ACR: n=25 Hydro: n=25	- Performed using radiofrequency - Included gentle shoulder manipulation to effect the inferior release and steroid injection (80 mg of methylprednisolone, and 10 mL of 0.5% bupivacaine) - Instructed on Codman exercises along with a standardised physiotherapy regimen **Hydrodilatation:** - Performed by consultant musculoskeletal radiologist under fluoroscopic guidance - A mixture of 1 mL of triamcinone (80 mg), 4 mL of local anaesthetic (2% lidocaine), and 40 mL of normal saline was injected into the GH joint slowly and with pressure. Same volume used for all patients - Injection was continued until the capsule ruptured. - Instructed on Codman exercises along with a standardised physiotherapy regimen	normal anteroposterior and axillary radiographs - Had at least 3 months duration of symptoms - Course of physiotherapy had failed. **Exclusion criteria:** - Medical contraindication to surgery - Perioperatively determined secondary cause of frozen shoulder - Rotator cuff tears found at the time of surgery or hydrodilatation - Evidence that the patient would be unable to adhere to trial procedures or complete questionnaires.
Jacobs et al. 2009 Two arm RCT n=53 MUA: n=28 Hydro: n=25	**MUA:** - Patient's arm was manipulated into full adduction and forward flexion, full external rotation, full internal rotation, and finally, full abduction. - Exercises shown by a physiotherapist - Home exercises **Hydrodilataion:** - Received 3 GH injection treatments with a steroid and distension at 6 week intervals - Local anaesthetic (40 mg of triamcinolone (in 1 mL), 5 mL of 2% lignocaine, 10 mL of 0.25% bupivacaine) and 5 mL of air (to check capsular rupture) used. Same volume for all patients - Instruction leaflet detailing the same exercises as MUA - Home exercises	**Inclusion criteria:** - Aged 40 to 75 years - Have primary frozen shoulder - Every patient was assessed by the senior author **Exclusion criteria:** - Additional or alternative pathologies - Patients with medical conditions such as diabetes type 1 or 2 - have received a steroid injection into the affected shoulder previously
Kivimaki et al. 2007 Two arm RCT n=125 MUA: n=65 Supportive care: n=60	**MUA:** - The upper arm manipulated in flexion and abduction while supporting the scapula against the thoracic cage - The shoulder stretched into flexion, then elbow flexed to a right angle, and the upper arm gently rotated into internal and external rotation. - Physiotherapy advice in 2 sessions - Written instructions (included pendulum exercises and stretching techniques) - Home exercises **Supportive care:** - Physiotherapy advice in 2 sessions	**Inclusion criteria:** - Adult patients with gradually increasing shoulder pain and stiffness were included in the study. - Shoulder mobility of no more than 140° in elevation and 30° in external rotation was allowed. **Exclusion criteria:** - Arthritis, osteoarthritis, or traumatic bone or tendon changes in the affected shoulder.

Study details	Trial treatments	Eligibility criteria
	- Written instructions (included pendulum exercises and stretching techniques) - Home exercises	- A rotator cuff rupture
Mukherjee et al. 2017 Two arm RCT n=60 ACR: n=30 Steroid + Physio: n=30	**ACR:** - 360 degree ACR under GA involving excising the tissues in the rotator interval up to the coracoids process, division of the superior, middle and inferior glenohumeral ligaments and release of the anterior, posterior, superior and inferior capsule - Subacromial bursa was not viewed. - Physio with active and passive range of motion exercises - Pain killers (NSAID with tramadol) **Steroid and Physio:** - Single dose of steroid injection (40 mg methylprednisolone acetate) along with local anesthetic (3 mL of 2% lignocaine) injected into the affected shoulder without image guidance through the posterior approach. - physio with active and passive range of motion exercises - Pain killers (NSAID with tramadol)	**Inclusion criteria:** - Idiopathic stiffness of the shoulder with global restriction of movements for min six months - Normal findings on plain radiograph - Global restrictions would imply decrease in active and passive movements in all directions. **Exclusion criteria:** - Prior history of trauma - Surgery or injections to the shoulder - Received treatment to the affected shoulder other than physiotherapy
Mun et al. 2016 Two arm RCT n=136 Hydro: n=67 Steroid + Physio: n=69	**Hydrodilatation:** - By interventional radiologist following ultrasound-guided interscalene block (20 mL of 1% lidocaine) - A mixture of steroid (1 mL triamcinolone (40 mg)), local anaesthetic (10 mL 1% lidocaine), and 30 mL saline solution was injected GHJ to expand the capsule. - Outflow of injection solution to the subscapular bursa confirmed on US - Pain killers (Oral NSAIDs) for 2 weeks - Rehabilitation exercise guided by a professional physical therapist twice a week for a month - Home exercises based on self exercise program booklet **Steroid and Physio:** - GH joint injection under ultrasonographic guidance by orthopaedic specialist - A mixture of steroid (1 mL triamcinolone (40 mg)) and local anaesthetic (5 mL 1% lidocaine) used - Pain killers (Oral NSAIDs) for 2 weeks - Rehabilitation exercise guided by a professional physical therapist twice a week for a month after 2 weeks of injection - Home exercises based on self-exercise program booklet	**Inclusion criteria:** - Continuous pain in the shoulder joint not responding to medication and physical therapy - Limitation of shoulder motion in at least 2 directions; forward flexion limited to 120° or less; <50% range of external rotation and internal rotation compared to opp. shoulder - No abnormal findings on radiologic examination and ultrasonography - Symptom duration minimum 3 months - Availability for follow-up for a minimum of 1 year. **Exclusion criteria:** - Patients with abnormal findings on radiologic examination - Secondary frozen shoulder - History of surgery for rotator cuff tears, shoulder dislocations, or fractures

Study details	Trial treatments	Eligibility criteria
Quraishi et al. 2007 Two arm RCT n=36 MUA: n=17 Hydro: n=19	**MUA:** - MUA consisted of restoration of shoulder movement following a specific protocol to ensure safe breakage of adhesions by using a short lever arm - A mixture of local anaesthetic (2 ml of 2% lignocaine) and steroid (30 mg (0.75 ml) of triamcinolone acetonide) injected anteriorly into GH joint - Permitted to resume normal activities with self-exercise programme. **Hydrodilatation:** - Performed by consultant radiologist through an anterior approach into GH joint. - Saline solution injected until the capsule ruptured (between 10 ml and 55 ml used, usually 30 ml to 40 ml to cause rupture) - Position checked by image intensifier - Permitted to resume normal activities as soon as possible with self-exercise programme	**Inclusion criteria:** - Aged over 18 years - Stage II primary adhesive capsulitis - Global loss of shoulder movement; restriction of external rotation to less than 50% of normal - Normal anteroposterior and axillary lateral radiographs of the glenohumeral joint. **Exclusion criteria:** - Post-traumatic or other extrinsic cause; - Suspected osteoporosis - Unfit for general anaesthesia.
Smitherman et al. 2015 Two arm RCT n=26 ACR: n=13 Supportive care: n=13	**ACR:** - Included release of the rotator interval, anterior capsule, inferior capsule and posterior capsule with radiofrequency and under regional nerve block - Gentle shoulder manipulation performed after rotator interval release, release of anterior and inferior capsule - Home based stretching program immediately after surgery for 3 months - Compliance monitored using a personal diary **Supportive care:** - Home based stretching program immediately after surgery for 3 months - Compliance monitored using a personal diary	**Inclusion criteria:** - Diagnosis of adhesive capsulitis - Progressive loss of 40 degree ER of GH joint with arm at side or with ER difference of 40 degree or more compared with contralateral shoulder **Exclusion criteria:** - Patients with fractures - Previous ipsilateral shoulder surgery - Degenerative arthritis of the shoulder or neurologic injury.

3.3. Risk of Bias

Figure 2 and 3 illustrate risk of bias in the included studies. Most of the studies reported how the allocation sequence was generated and were considered as low risk but two studies did not provide enough information to make a judgement; hence were marked as 'Unclear'.[11, 13] Allocation concealment was mostly well reported; but one study failed to provide enough details about measures taken to ensure allocation concealment, hence was marked as 'Unclear' risk of selection bias.[17]

Due to the nature of the interventions, participants were not blinded to their treatment group. Since the outcomes of interest for this review were all patient reported, all studies were marked as high risk of bias for 'blinding of participants and personnel' and 'blinding of outcome assessment'.

Studies with high attrition rate (i.e. over 30% in any single arm) were marked as high risk of bias for 'Incomplete outcome data'.[13, 15, 17] Two studies reported pain score for only one follow-up time point so were marked as high risk of bias for selective reporting.[11, 13]

Three studies did not provide clear reasons for non-consent and drop outs;[11, 15, 16] one study only followed-up patients for 20 weeks;[12] one was from a single institution.[18] These studies were marked as 'Unclear' for other risk of bias.

One study had all MUA treatments performed by a single surgeon and hydrodilatation by another doctor potentially introducing treatment bias[14] and another reported treatment efficacy based on a very low sample size.[17] These studies were considered as 'high' other risk of bias.

All the studies were marked as high risk of bias for blinding of participants and personal and blinding of outcome assessment; three studies for incomplete outcome reporting; two studies for selective reporting; and two for other biases.

Figure 2: Risk of Bias Summary (% of studies)

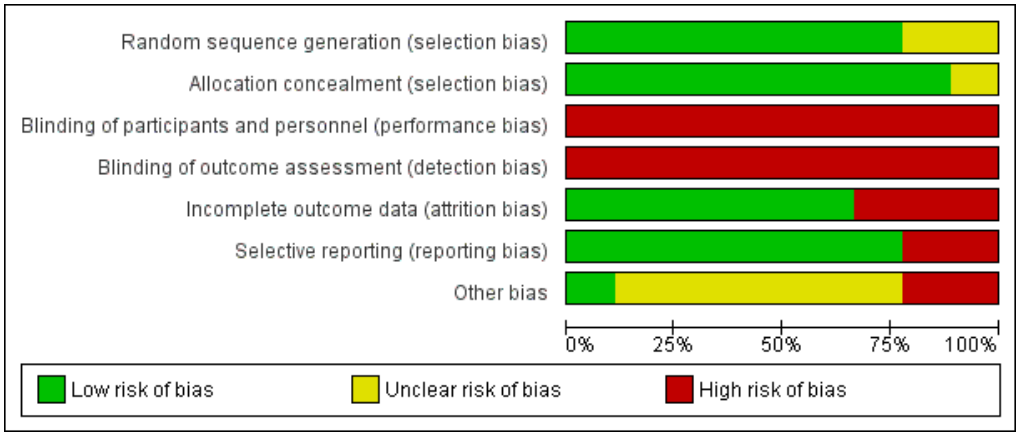
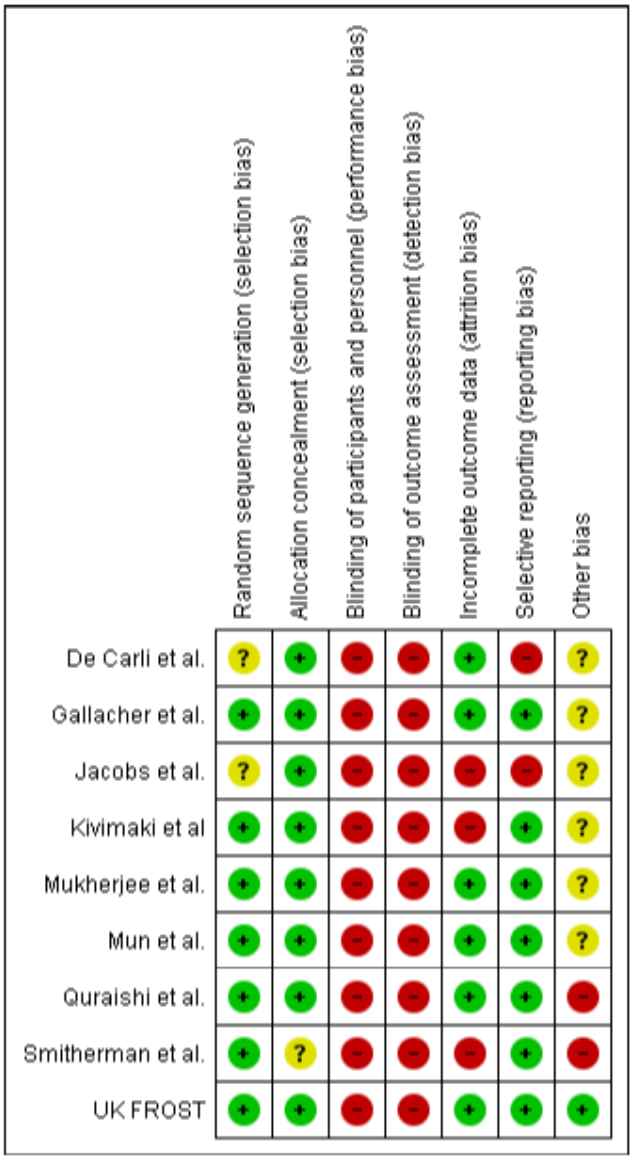


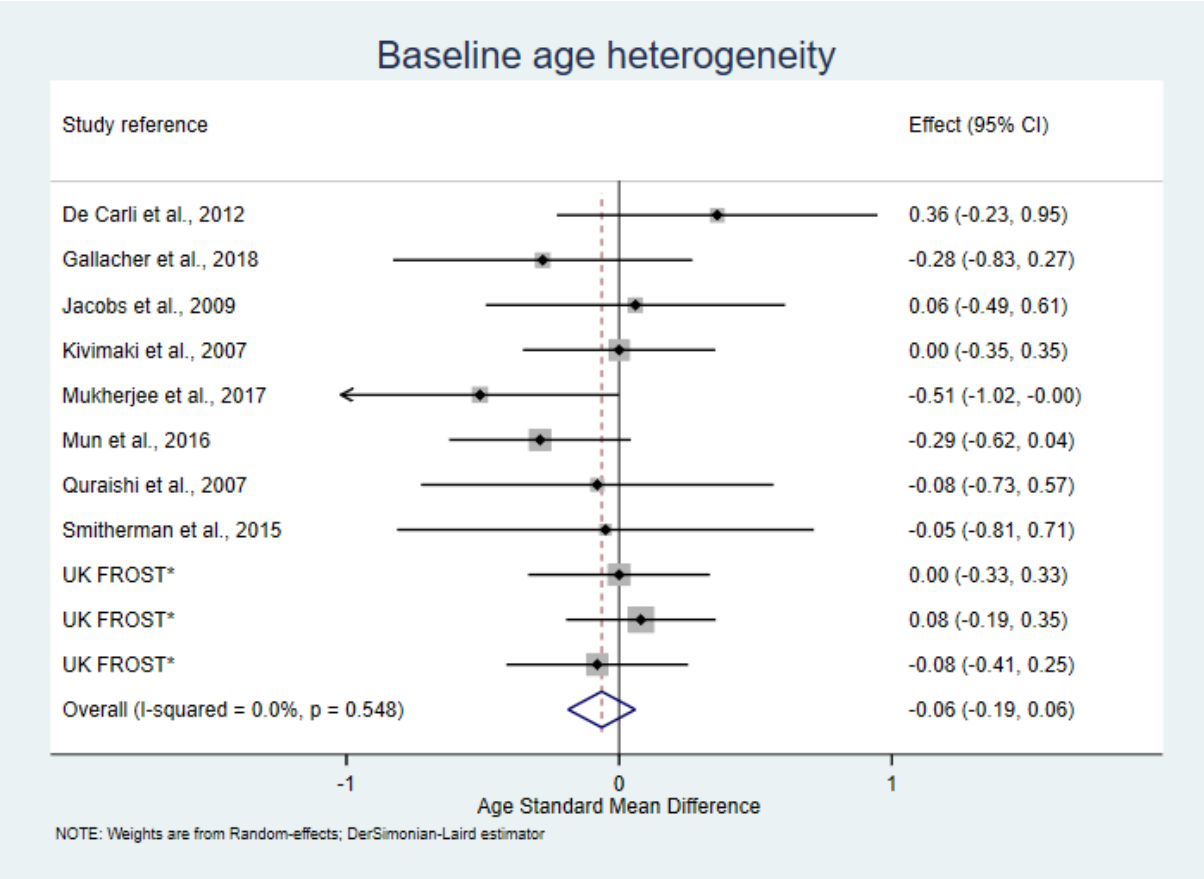
Figure 3: Risk of Bias by Study



3.4. Baseline heterogeneity

Figure 4 shows that baseline heterogeneity was assessed by using baseline age supplied for different treatment groups. For UK FROST, total number of patients in each group were divided by two, to account for multiple comparisons. Overall I^2 measure of heterogeneity was 0% suggesting that there is not enough evidence of large baseline heterogeneity. Only one study[12] resulted in a upper confidence interval that was not positive (i.e. zero). Other baseline variables were not included for this assessment, as they were not fully reported.

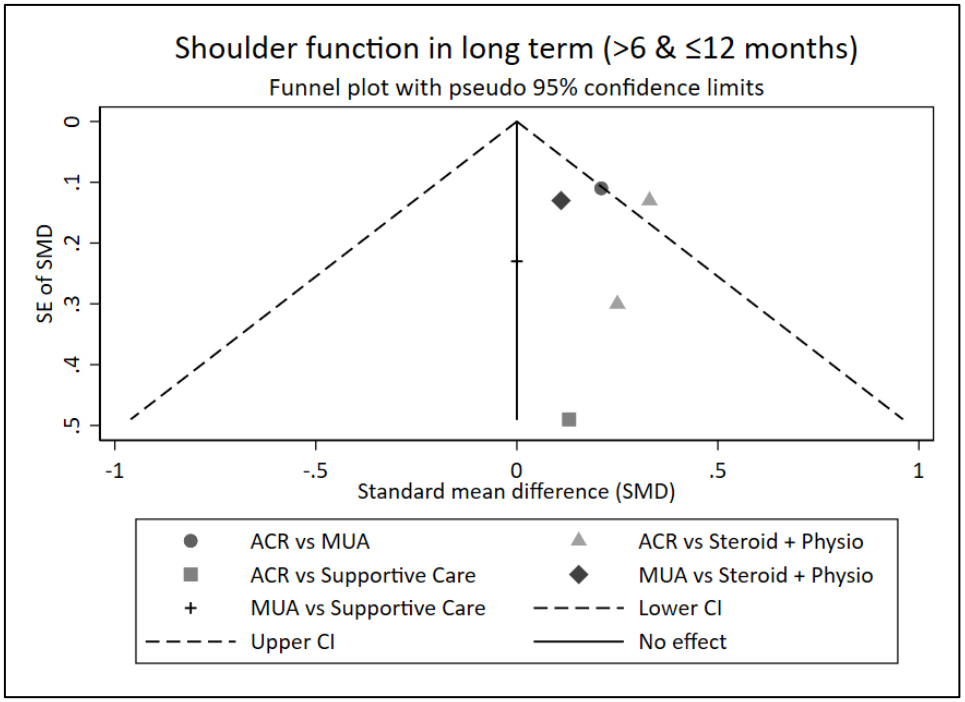
Figure 4: Baseline age heterogeneity



3.5. Publication bias assessments

Potential publication bias was assessed using a funnel plot as shown in Figure 5. Standard Mean Difference of shoulder function in the long term was plotted. All the studies that compared ACR with other treatments found ACR to be more effective.

Figure 5: Shoulder function scores* in long term (> 6 & ≤ 12 months)



*Shoulder Disability Questionnaire and Shoulder Pain Disability Index Scores were reversed so that positive result implies better outcome. This was done to be consistent with other shoulder scores (e.g. OSS and SST).

3.6. Study results

Due to the variability in measures used in the included studies, the standardised mean difference (SMD) in addition to mean difference (MD) are reported in Table 5 to allow comparison between studies.

Table 5: Systematic review summary results

Study	Scale	Short term (≤ 3 months)	Medium term (> 3 and ≤ 6 months)	Long term (>6 and ≤ 12 months)
ACR vs Hydrodilatation				
Oxford Shoulder Score (Higher is better)				
Gallacher et al., 2018	MD		5.3 (1.16 to 9.44)	
	SMD		0.77 (0.12 to 1.42)	
ACR vs MUA				
Oxford Shoulder Score (Higher is better)				
UK FROST	MD	-3.36 (-5.27 to -1.45)	-1.17 (-3.02 to 0.67)	2.01 (0.1 to 3.91)
	SMD	-0.35 (-0.56 to -0.14)	-0.13 (-0.34 to 0.08)	0.21 (0.00 to 0.42)
Numerical Rating Scale - Pain (Lower is better)				
UK FROST	MD	0.59 (0.1 to 1.07)	0.05 (-0.43 to 0.52)	-0.73 (-1.2 to -0.25)
	SMD	0.24 (0.03 to 0.44)	0.00 (-0.21 to 0.21)	-0.32 (-0.53 to -0.11)
ACR vs Supportive care				
Shoulder Pain and Disability Index (Lower score is better)				
Smitherman et al., 2015	MD	-5 (-29.16 to 19.16)		-2 (-15.39 to 11.39)
	SMD	-0.20 (-1.17 to 0.77)		-0.13 (-1.10 to 0.83)
ACR vs Steroid + Physio				
Oxford Shoulder Score (Higher is better)				
UK FROST	MD	-4.72 (-7.06 to -2.39)	0.98 (-1.31 to 3.26)	3.06 (0.71 to 5.41)
	SMD	-0.50 (-0.76 to -0.24)	0.11 (-0.15 to 0.38)	0.33 (0.07 to 0.59)
Simple Shoulder Test (SST) (Higher is better)				
De Carli et al., 2012	MD	1.44 (0.08 to 2.8)	1.18 (-0.18 to 2.54)	0.59 (-0.77 to 1.95)
	SMD	0.61 (0.01 to 1.22)	0.50 (-0.10 to 1.11)	0.25 (-0.34 to 0.85)
Note: SST score was reported as a percentage so was converted to original scale. Standard deviation (SD) was not provided so was imputed by taking the average SD reported by Yoon et al.[19].				
Numerical Rating Scale - Pain (Lower is better)				
UK FROST	MD	1.02 (0.42 to 1.61)	-0.14 (-0.74 to 0.45)	-0.81 (-1.39 to -0.23)

Study	Scale	Short term (≤ 3 months)	Medium term (> 3 and ≤ 6 months)	Long term (>6 and ≤ 12 months)
	SMD	0.38 (0.13 to 0.64)	-0.09 (-0.36 to 0.18)	-0.38 (-0.64 to -0.12)
Visual Analogue Scale – Pain (Lower is better)				
Mukherjee et al., 2017	MD	-1.2 (-2.04 to -0.36)	-1.2 (-2.04 to -0.36)	
	SMD	-0.74 (-1.28 to -0.20)	-0.74 (-1.28 to -0.20)	
Hydrodilatation vs Steroid + Physiotherapy				
Visual Analogue Scale – Pain (Lower is better)				
Mun et al., 2016	MD	-0.9 (-1.16 to -0.64)		-0.1 (-0.39 to 0.19)
	SMD	-1.23 (-1.62 to -0.84)		-0.12 (-0.48 to 0.23)
MUA vs Hydrodilatation				
Visual Analogue Scale – Pain (Lower is better)				
Jacobs et al., 2009	MD	-0.02 (-1.15 to 1.11)		
	SMD	-0.01 (-0.61 to 0.59)		
Quraishi et al., 2007	MD	2.3 (1.51 to 3.09)	1 (0.21 to 1.79)	
	SMD	1.90 (1.08 to 2.73)	0.83 (0.12 to 1.53)	
Note: VAS Pain SD was not reported by Quraishi et al., 2007. This value was imputed by taking the average SD reported from other VAS scores reported.				
MUA vs Supportive care				
Shoulder Disability Questionnaire Score (Lower score is better)				
Kivimaki et al., 2007	MD	0.3 (-2.69 to 2.75)	-1.7 (-5.3 to 1.9)	0 (-3.2 to 3.2)
	SMD	0.04 (-0.35 to 0.43)	-0.2 (-0.63 to 0.23)	0 (-0.44 to 0.44)
MUA vs Steroid + Physio				
Oxford Shoulder Score (Higher is better)				
UK FROST	MD	-1.36 (-3.7 to 0.98)	2.15 (-0.12 to 4.42)	1.05 (-1.28 to 3.39)
	SMD	-0.15 (-0.4 to 0.10)	0.24 (-0.02 to 0.51)	0.12 (-0.14 to 0.37)
Numerical Rating Scale - Pain (Lower is better)				
UK FROST	MD	0.43 (-0.17 to 1.03)	-0.19 (-0.78 to 0.4)	-0.08 (-0.66 to 0.5)
	SMD	0.17 (-0.09 to 0.42)	-0.09 (-0.35 to 0.18)	-0.04 (-0.30 to 0.21)

3.6.1. ACR vs Hydrodilatation

Gallacher et al.[16] compared ACR with Hydrodilatation. At their final follow-up at 6 months follow-up, the OSS was significantly higher (better) in the ACR group than in the Hydrodilatation group (43.8, 95% CI, 42.2 to 45.2 vs. 38.5, 95% CI, 34.6 to 42.4, P = 0.023). This study was marked as high risk of bias on two categories. This was a single centre study.

3.6.2. ACR vs MUA

UK FROST compared ACR with MUA. At their primary end point at 12 months, participants randomised to ACR were shown to have significantly higher (better) OSS scores than MUA (2.01 points, 95% CI 0.10 to 3.91) after adjusting for baseline OSS, age, gender and diabetes in a mixed covariance pattern model. This study was marked as high risk of bias on two categories. This was a multi-centre study.

3.6.3. ACR vs Supportive care

Smitherman et al.[17] compared ACR with supportive care. At their final follow up at 12 months, participants to ACR had slightly lower (better) SPADI scores than the Supportive group (-2, 95% CI -15.39 to 11.39) but this difference was not statistically significant. This study was marked as high risk of bias on four categories. This study was conducted from two institutes.

3.6.4. ACR vs Steroid + Physiotherapy

Three studies compared ACR to Steroid + Physiotherapy,[2, 11, 12] two of which reported function and disability at 12 months. Two studies were marked as high risk of bias on two categories and one on three categories.

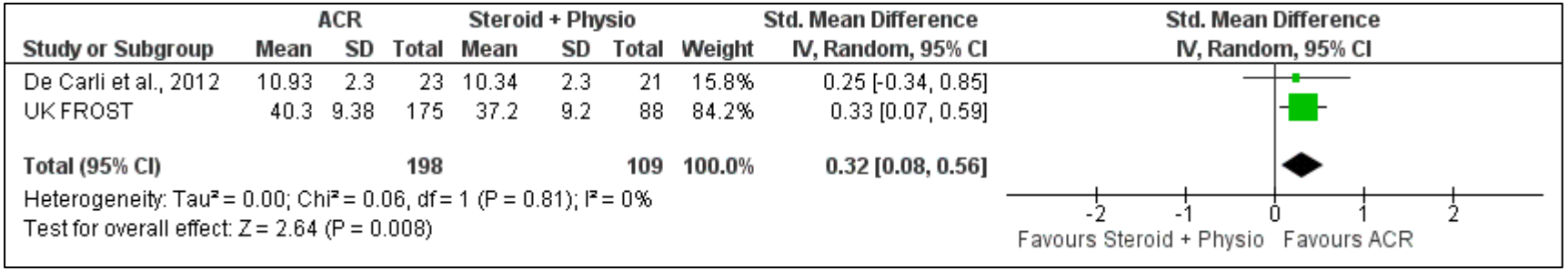
De Carli et al[11] and UK FROST, reported primary outcome at 12 months and were similar enough to pool the data (I^2 = 0%). De Carli is a single centre study, whilst UK FROST is multi-centre.

Pooled standardised mean difference based on shoulder function scores shows that ACR was statistically higher (better) than Steroid + Physiotherapy (SMD: 0.32 points, 95% CI 0.08 to 0.56).

Due to heterogeneity (I^2 ranging from 27% to 100%), for the other follow-up points pooled estimates are not reported.

Mukherjee et al.[12] at their final follow-up at 20 weeks, found participants in ACR group had statistically significant lower (better) pain than the Steroid + Physiotherapy group (-1.2 points difference, 95% CI -2.04 to -0.36). This study appeared to be from a single centre.

Figure 6: Shoulder function in long term (>6 & ≤ 12 months): ACR vs Steroid + Physiotherapy



3.6.5. Hydrodilatation vs Steroid + Physiotherapy

Mun et al. [18] compared Hydrodilatation with Steroid + Physiotherapy. At their final follow-up at 12 months, they did not find a statistically significant difference between groups on VAS pain scores (-0.1 points, 95% CI -0.39 to 0.19). This study was marked as high risk of bias on two categories. This is a single centre study.

3.6.6. MUA vs Hydrodilatation

Two studies compared MUA with Hydrodilatation but the results were not pooled due to evidence of heterogeneity (I^2 = 93%).

Jacobs et al.[13] reported results only for the first 16 weeks. VAS mean difference reported at this time-point was not statistically significant (-0.02 points, 95% CI -1.15 to 1.11). This study was marked as high risk of bias on four categories. This was a single centre study.

Quraishi et al.[14] at six months follow-up found that, VAS pain in the MUA group was significantly higher (worse) than in the Hydrodilatation group over (1 point, 95% CI 0.21 to 1.79). This study was marked as high risk of bias on three categories. This study appeared to be from a single centre.

3.6.7. MUA vs Supportive care

Kivimaki et al.[15] compared MUA with Supportive care, at their final follow up at 12 months, they did not find any statistically significant difference between treatment groups based on SDQ score (0 point, 95% CI -3.2 to 3.2). This study was marked as high risk of bias on three categories. This study was conducted from three regional hospitals.

3.6.8. MUA vs Steroid + Physiotherapy

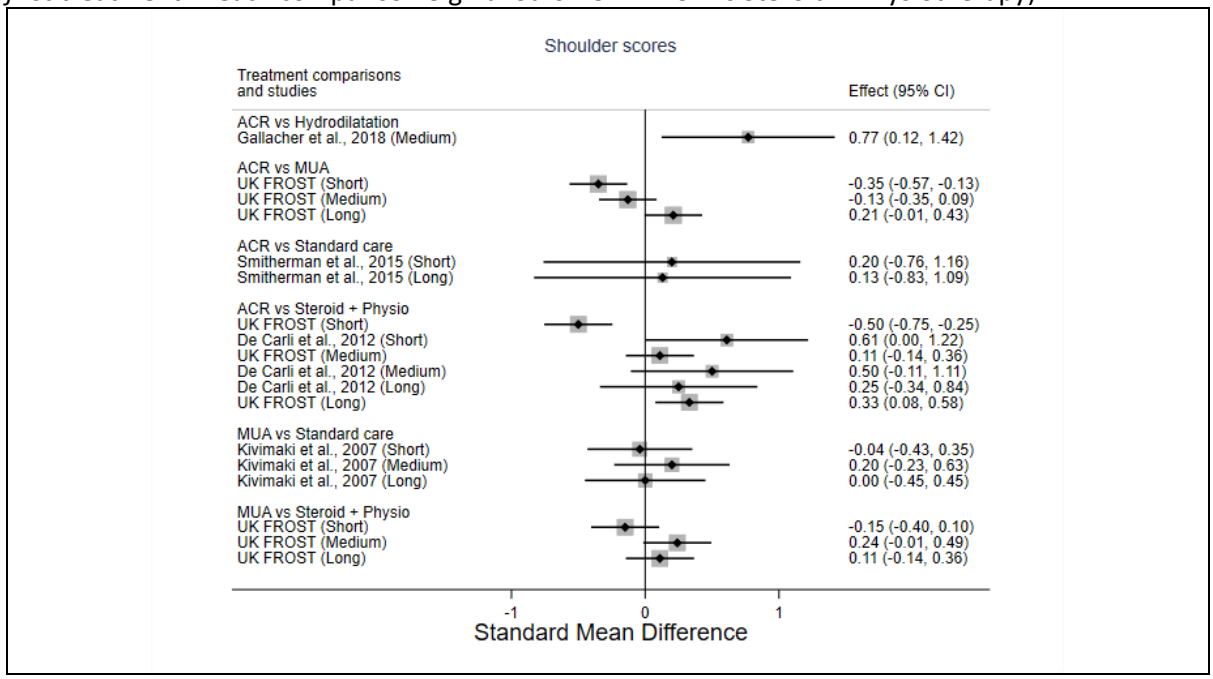
UK FROST compared MUA with Steroid + Physiotherapy. At the primary end-point of 12 months, they did not find a statistically significant difference between groups (0.78 point, 95% CI -1.56 to 3.11). This study was marked as high risk of bias on two categories.

3.6.9. Study results summary

The standardised mean effect of the shoulder function and pain scores reported for short, medium and long term follow-up time points are illustrated using forest plots (Figures 7 and 8).

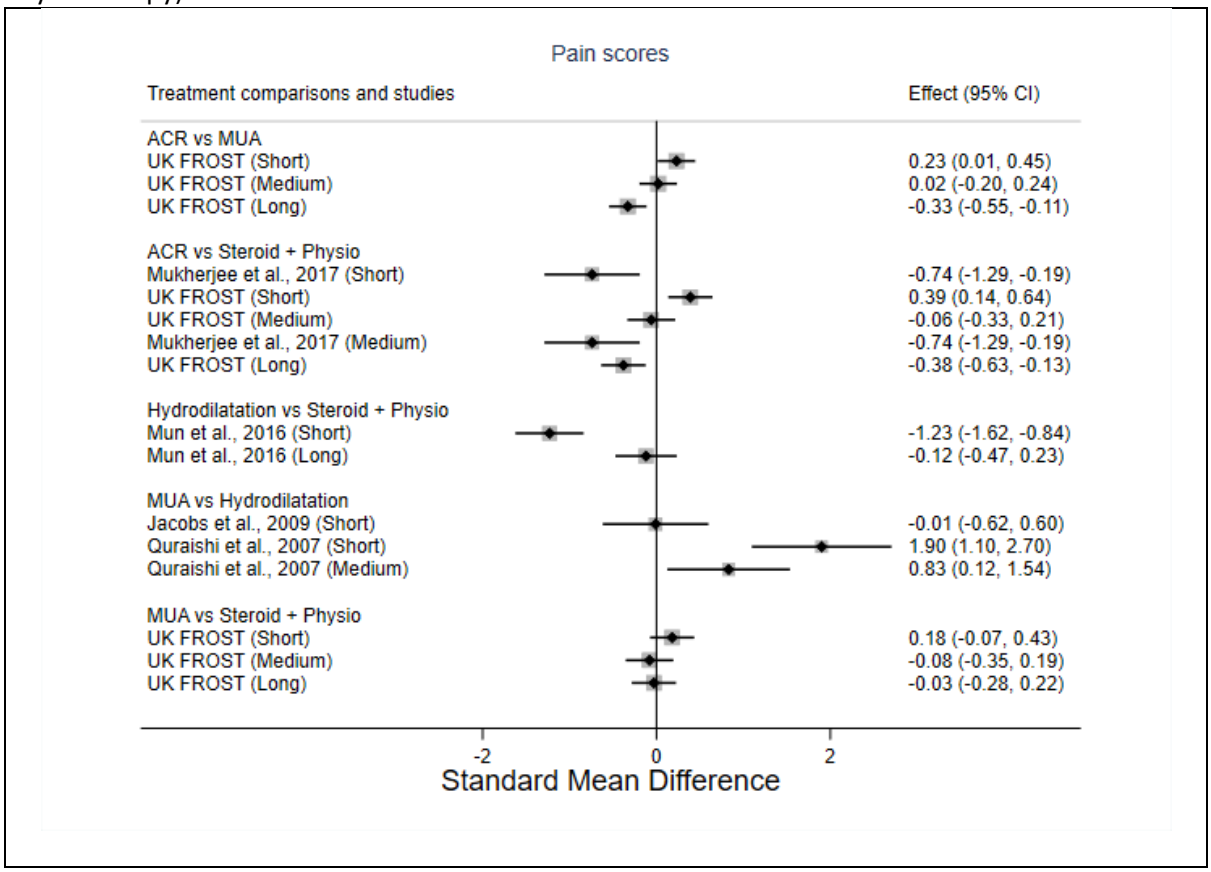
Network meta-analysis was not undertaken due to the limited number of studies included in this review.

Figure 7: Shoulder function scores* (a positive SMD indicates a more favourable outcome for the *first* treatment in each comparison e.g. favours ACR in ACR vs Steroid + Physiotherapy)



*Shoulder Disability Questionnaire and Shoulder Pain Disability Index Scores were reversed so that positive result implies better outcome. This was done to be consistent with other shoulder scores (e.g. OSS and SST).

Figure 8: Pain scores across different studies (a positive SMD indicates a more favourable outcome for the *second* treatment in each comparison e.g. favours Steroid + Physiotherapy in ACR vs Steroid + Physiotherapy)



3.7. Complications reported

Of the nine RCTs included in the systematic review, five reported that there were no complications in any of the treatment groups.[11, 13, 16-18] One RCT did not report whether there were any complications at all, therefore it is unclear whether these were assessed.[14] Kivimaki et al.[15] reported that there were no major complications in the MUA group but small injuries of the joint were possible, as were verified on arthroscopy. No complications were reported on for the supportive care group. Mukherjee et al.[12] reported that there was one case of articular cartilage scuffing of glenoid and one case of the humeral head in the ACR group. Complications were not reported on at all in the Steroid + Physiotherapy group.

4. Discussion

4.1. Summary of evidence

Out of 2817 studies screened, only eight met our selection criteria. All studies were of much smaller scale compared with UK FROST. Including UK FROST, there were nine studies included that incorporated eight different treatment combinations. Due to the limited number of studies for many of the comparisons, and evidence of heterogeneity for some comparisons, it was mostly a narrative synthesis.

Summary of average treatment effect estimates:

- ACR vs Hydrodilatation: In a single study medium term shoulder function results showed that ACR was favoured.[16]
- ACR vs MUA: In UK FROST, short and medium term shoulder function and pain score results favoured MUA, but ACR did better long term.
- ACR vs Standard care: The short and long term results both favoured ACR.[17]
- ACR vs Steroid + Physio: Short term shoulder function results for UK FROST favoured Steroid + Physiotherapy, however De Carli et al.[11] favoured ACR. Medium term follow-up for both these studies favoured ACR. Short term pain results for UK FROST favoured Steroid + Physiotherapy. Mukherjee et al.[12] favoured ACR, and medium term pain results for both these studies favoured ACR. Long term shoulder function results from both studies favoured ACR; and long term pain score for UK FROST favoured ACR.
- Hydrodilatation vs Steroid + Physio: Short and long term pain results favoured Hydrodilatation.[18]
- MUA vs Hydrodilatation: Jacobs et al.[13] found similar short term pain scores for both groups, but Quraishi et al.[14] found that patients in Hydrodilatation arm did better. Medium term pain scores for Quraishi et al.[14] also favoured Hydrodilatation.
- MUA vs Standard care: Short and long term shoulder function results were similar for both groups, but medium term results favoured MUA.[15]
- MUA vs Steroid + Physio: In UK FROST, shoulder function and pain results favoured MUA in the short term, but Steroid + Physiotherapy in the medium and long term.

In summary, differences in short and medium term pain and shoulder function varied considerably between studies, whereas long term outcomes tended to favour more invasive treatment, such as ACR.

4.2. Strengths and Limitations

We undertook systematic searches to put the findings from UK FROST in the context of current evidence. Standard methods were used to reduce error and bias such as using two researchers to screen studies and check data extraction and assess for risk of bias. We used a core set of electronic sources that had successfully identified the studies in the 2012 review. However, our searches were

not exhaustive and there is a potential risk that relevant studies were missed. Only nine studies comparing five interventions met our selection criteria. Meaningful inference could not be made from the pooled treatment effects, based on the large variation in the number of patients included in the selected studies (number randomised to an individual study arm ranged from 13 to 203 trial participants). Three of the selected studies were at high risk for bias for incomplete outcome reporting and two for selective reporting which could have an effect on the results.

4.3. Conclusions

The volume of evidence on invasive interventions for frozen shoulder remains limited and there is considerable variability in the interventions used, the outcomes assessed and when follow-up is assessed. Most of the comparisons between treatments are informed by single studies at single sites. The strongest evidence comes from UK FROST.

UK FROST did not include Hydrodilatation as a treatment option but this treatment was investigated in four studies. Two of these studies showed a positive effect for Hydrodilatation compared to the other treatments they compared.

5. References

1. Maund E, Craig D, Suekarran S, Neilson A, Wright K, Brealey S*, et al.* Management of frozen shoulder: a systematic review and cost-effectiveness analysis. *Health Technol Assess* 2012;**16**:1-264. http://dx.doi.org/10.3310/hta16110
2. Brealey S, Armstrong AL, Brooksbank A, Carr AJ, Charalambous CP, Cooper C*, et al.* United Kingdom Frozen Shoulder Trial (UK FROST), multi-centre, randomised, 12 month, parallel group, superiority study to compare the clinical and cost-effectiveness of Early Structured Physiotherapy versus manipulation under anaesthesia versus arthroscopic capsular release for patients referred to secondary care with a primary frozen shoulder: study protocol for a randomised controlled trial. *Trials* 2017;**18**:614. http://dx.doi.org/10.1186/s13063-017-2352-2
3. Dennis L, Brealey S, Rangan A, Rookmoneea M, Watson J. Managing Idiopathic Frozen Shoulder: A Survey of Health Professionals' Current Practice and Research Priorities. *Shoulder & Elbow* 2010;**2**:294-300. http://dx.doi.org/10.1111/j.1758-5740.2010.00073.x
4. Shamseer L, Moher D, Clarke M, Ghersi D, Liberati A, Petticrew M*, et al.* Preferred reporting items for systematic review and meta-analysis protocols (PRISMA-P) 2015: elaboration and explanation. *BMJ : British Medical Journal* 2015;**349**:g7647. http://dx.doi.org/10.1136/bmj.g7647
5. Hanchard NC, Goodchild L, Thompson J, O'Brien T, Davison D, Richardson C. Evidence-based clinical guidelines for the diagnosis, assessment and physiotherapy management of contracted (frozen) shoulder: quick reference summary. *Physiotherapy* 2012;**98**:117-20. http://dx.doi.org/10.1016/j.physio.2012.01.001
6. Bloom JE, Rischin A, Johnston RV, Buchbinder R. Image-guided versus blind glucocorticoid injection for shoulder pain. *Cochrane Database Syst Rev* 2012; 10.1002/14651858.CD009147.pub2:Cd009147. http://dx.doi.org/10.1002/14651858.CD009147.pub2
7. *Covidence (systematic review management)*. Accessed 2019. URL: https://www.covidence.org/ (Accessed).
8. Higgins JPT, Green S. Cochrane Handbook for Systematic Reviews of Interventions Version 5.1.0 [updated March 2011]. In: The Cochrane Collaboration; 2011.
9. Ades AE. A chain of evidence with mixed comparisons: models for multi-parameter synthesis and consistency of evidence. *Statistics in Medicine* 2003;**22**:2995-3016.
10. CRD. Systematic reviews: CRD's guidance for undertaking reviews in healthcare. *University of York* 2009.

11. De Carli A, Vadala A, Perugia D, Frate L, Iorio C, Fabbri M*, et al.* Shoulder adhesive capsulitis: manipulation and arthroscopic arthrolysis or intra-articular steroid injections? 2012;**36**:101-6. http://dx.doi.org/https://dx.doi.org/10.1007/s00264-011-1330-7
12. Mukherjee RN, Pandey RM, Nag HL, Mittal R. Frozen shoulder - A prospective randomized clinical trial. 2017;**8**:394-9. http://dx.doi.org/https://dx.doi.org/10.5312/wjo.v8.i5.394
13. Jacobs LG, Smith MG, Khan SA, Smith K, Joshi M. Manipulation or intra-articular steroids in the management of adhesive capsulitis of the shoulder? A prospective randomized trial. *J Shoulder Elbow Surg* 2009;**18**:348-53. http://dx.doi.org/10.1016/j.jse.2009.02.002
14. Quraishi NA, Johnston P, Bayer J, Crowe M, Chakrabarti AJ. Thawing the frozen shoulder. A randomised trial comparing manipulation under anaesthesia with hydrodilatation. *J Bone Joint Surg Br* 2007;**89**:1197-200. http://dx.doi.org/10.1302/0301-620x.89b9.18863
15. Kivimaki J, Pohjolainen T, Malmivaara A, Kannisto M, Guillaume J, Seitsalo S*, et al.* Manipulation under anesthesia with home exercises versus home exercises alone in the treatment of frozen shoulder: a randomized, controlled trial with 125 patients. *J Shoulder Elbow Surg* 2007;**16**:722-6. http://dx.doi.org/10.1016/j.jse.2007.02.125
16. Gallacher S, Beazley JC, Evans J, Anaspure R, Silver D, Redfern A*, et al.* A randomized controlled trial of arthroscopic capsular release versus hydrodilatation in the treatment of primary frozen shoulder. 2018;**27**:1401-6. http://dx.doi.org/https://dx.doi.org/10.1016/j.jse.2018.04.002
17. Smitherman JA, Struk AM, Cricchio M, McFadden G, Dell RB, Horodyski M*, et al.* Arthroscopy and manipulation versus home therapy program in treatment of adhesive capsulitis of the shoulder: a prospective randomized study. 2015;**24**:69-74.
18. Mun SW, Baek CH. Clinical efficacy of hydrodistention with joint manipulation under interscalene block compared with intra-articular corticosteroid injection for frozen shoulder: a prospective randomized controlled study. 2016;**25**:1937-43. http://dx.doi.org/https://dx.doi.org/10.1016/j.jse.2016.09.021
19. Yoon JP, Chung SW, Kim JE, Kim HS, Lee HJ, Jeong WJ*, et al.* Intra-articular injection, subacromial injection, and hydrodilatation for primary frozen shoulder: a randomized clinical trial. *J Shoulder Elbow Surg* 2016;**25**:376-83. http://dx.doi.org/10.1016/j.jse.2015.11.009

6. Appendix 1

MEDLINE
Via OVID
Search date=7th December 2018
Records identified=1080

Database: Ovid MEDLINE(R) and Epub Ahead of Print, In-Process & Other Non-Indexed Citations and Daily <1946 to December 06, 2018>

1 (frozen adj6 shoulder$).ti,ab,kw. (1203)
2 (stiff$ adj6 shoulder$).ti,ab,kw. (830)
3 (adhesive adj (capsulitis or capsulitides)).ti,ab,kw. (780)
4 ((bursitis or bursitides) adj6 shoulder$).ti,ab,kw. (173)
5 ((capsulitis or capsulitides) adj6 shoulder$).ti,ab,kw. (416)
6 ((periarthritis or peri-arthritis or periarthritides or peri-arthritides or peri-capsulitis or pericapsulitis) adj6 shoulder$).ti,ab,kw. (447)
7 exp bursitis/ (4529)
8 shoulder pain/ (4317)
9 (shoulder$ adj3 (pain or pains or painful or complain$)).ti,ab,kw. (8818)
10 Shoulder Impingement Syndrome/ (1643)
11 (shoulder$ adj6 impinge$).ti,ab,kw. (978)
12 subacromial impingement syndrome.ti,ab,kw. (371)

13 1 or 2 or 3 or 4 or 5 or 6 or 7 or 8 or 9 or 10 or 11 or 12 (17237)
14 Arthrography/ (4898)
15 (arthrograph$ adj6 (distension$ or distention$)).ti,ab,kw. (57)
16 (arthrogram$ adj6 (distension$ or distention$)).ti,ab,kw. (4)
17 (glenohumeral adj6 (distension$ or distention$)).ti,ab,kw. (14)
18 Dilatation/ (10665)
19 (dilatation or hydrodilat$).ti,ab,kw. (49989)
20 or/14-19 (62074)
21 13 and 20 (303)
22 Arthroscopy/ (21349)
23 (arthroscop$ adj6 (releas$ or decompress$ or capsulotom$)).ti,ab,kw. (1212)
24 ((capsular adj2 releas$) or interventional microadhesiolysis or capsulotomy).ti,ab,kw. (3135)
25 or/22-24 (24614)
26 exp Musculoskeletal Manipulation/ (15513)
27 (manipulat$ adj3 (anesthesia or anaesthesia or anesthetic$ or anaesthetic$)).ti,ab,kw. (691)
28 MUA.ti,ab,kw. (3296)
29 26 or 27 or 28 (19196)
30 25 or 29 (43602)
31 13 and 30 (1871)
32 Injections, Intra-Articular/ (7136)
33 injections/ (40831)
34 ((bursa$ or intrabursa$ or intra bursa$ or periartic$ or peri artic$ or intraartic$ or intra artic$) adj3 inject$).ti,ab,kw. (6140)
35 ((subacromial or acromioclavicular or glenohumeral) adj3 inject$).ti,ab,kw. (390)
36 ((extra articular or extraarticular) adj3 inject$).ti,ab,kw. (32)
37 (IA inject$ or RI inject$ or SA inject$).ti,ab,kw. (602)
38 32 or 33 or 34 or 35 or 36 or 37 (51397)
39 13 and 38 (860)
40 exp Physical Therapy Modalities/ (139739)
41 (physiotherapy or physiotherapies or physical therap$ or manual therap$).ti,ab,kw. (39931)
42 (passive adj (motion or movement)).ti,ab,kw. (2256)
43 CPM.ti,ab,kw. (5575)
44 muscle stretching exercises/ (1458)
45 (stretching or stretches).ti,ab,kw. (32430)
46 (mobilisation or mobilization).ti,ab,kw. (53016)
47 (exercise$ adj2 (program$ or strength$ or intervention$ or training or prescription$ or prescrib$)).ti,ab,kw. (36905)
48 (exercise$ adj2 (therap$ or therapeutic)).ti,ab,kw. (6101)
49 ((home or supervis$) adj2 exercis$).ti,ab,kw. (4512)
50 ((pendular or pendulum) adj exercis$).ti,ab,kw. (29)
51 ((isokinetic or resist$) adj2 exercise$).ti,ab,kw. (6663)
52 or/40-51 (276161)
53 13 and 52 (2746)
54 21 or 31 or 39 or 53 (4712)
55 randomized controlled trial.pt. (472057)
56 controlled clinical trial.pt. (92771)
57 randomized.ab. (428436)
58 placebo.ab. (193714)
59 clinical trials as topic.sh. (185394)
60 randomly.ab. (301468)
61 trial.ti. (190979)

62 55 or 56 or 57 or 58 or 59 or 60 or 61 (1185601)
63 exp animals/ not humans.sh. (4519948)
64 62 not 63 (1090663)
65 54 and 64 (1080)

CENTRAL
Via John Wiley's The Cochrane Library
Search date=5th December 2018
Records identified= 1634

#1 (frozen NEAR/6 shoulder*):ti,ab,kw (Word variations have been searched)
#2 (stiff* NEAR/6 shoulder*):ti,ab,kw (Word variations have been searched)
#3 (adhesive NEAR/6 (capsulitis or capsulitides)):ti,ab,kw (Word variations have been searched)
#4 ((bursitis or bursitides) NEAR/6 shoulder*):ti,ab,kw (Word variations have been searched)
#5 ((capsulitis or capsulitides) NEAR/6 shoulder*):ti,ab,kw (Word variations have been searched)
#6 ((periarthritis or peri-arthritis or periarthritides or peri-arthritides or peri-capsulitis or pericapsulitis) NEAR/6 shoulder*):ti,ab,kw (Word variations have been searched)
#7 MeSH descriptor: [Bursitis] explode all trees
#8 MeSH descriptor: [Shoulder Pain] explode all trees
#9 (shoulder* NEAR/3 (pain or pains or painful or complain*)):ti,ab,kw (Word variations have been searched)
#10 MeSH descriptor: [Shoulder Impingement Syndrome] explode all trees
#11 (shoulder* NEAR/6 impinge*):ti,ab,kw (Word variations have been searched)
#12 ("subacromial impingement syndrome"):ti,ab,kw (Word variations have been searched)
#13 #1 OR #2 OR #3 OR #4 OR #5 OR #6 OR #7 OR #8 OR #9 OR #10 OR #11 OR #12
#14 MeSH descriptor: [Arthrography] explode all trees
#15 (arthrograph* NEAR/6 (distension* or distention*)):ti,ab,kw (Word variations have been searched)
#16 (arthrogram* NEAR/6 (distension* or distention*)):ti,ab,kw (Word variations have been searched)
#17 (glenohumeral NEAR/6 (distension* or distention*)):ti,ab,kw (Word variations have been searched)
#18 MeSH descriptor: [Dilatation] explode all trees
#19 ((dilatation or hydrodilat*)):ti,ab,kw (Word variations have been searched)
#20 #14 OR #15 OR #16 OR #17 OR #18 OR #19
#21 #13 AND #20
#22 MeSH descriptor: [Arthroscopy] explode all trees
#23 (arthroscop* NEAR/6 (releas* or decompress* or capsulotom*)):ti,ab,kw (Word variations have been searched)
#24 ((capsular NEAR/2 releas*) or "interventional microadhesiolysis" or capsulotomy):ti,ab,kw (Word variations have been searched)
#25 MeSH descriptor: [Musculoskeletal Manipulations] explode all trees
#26 (manipulat* NEAR/3 (anesthesia or anaesthesia or anesthetic* or anaesthetic*)):ti,ab,kw OR (MUA):ti,ab,kw (Word variations have been searched)
#27 #22 OR #23 OR #24 OR #25 OR #26
#28 #13 AND #27
#29 MeSH descriptor: [Injections, Intra-Articular] explode all trees
#30 MeSH descriptor: [Injections] explode all trees

#31 ((bursa* or intrabursa* or intra bursa* or periartic* or peri artic* or intraartic* or intra artic*) NEAR/3 inject*):ti,ab,kw (Word variations have been searched)
#32 ((subacromial or acromioclavicular or glenohumeral) NEAR/3 inject*):ti,ab,kw (Word variations have been searched)
#33 ((extra articular or extraarticular) NEAR/3 inject*):ti,ab,kw (Word variations have been searched)
#34 (("IA inject*" or "RI inject*" or "SA inject*")):ti,ab,kw (Word variations have been searched)
#35 #29 OR #30 OR #31 OR #32 OR #33 OR #34
#36 #13 AND #35
#37 MeSH descriptor: [Physical Therapy Modalities] explode all trees
#38 (physiotherapy or physiotherapies or "physical therap*" or "manual therap*"):ti,ab,kw (Word variations have been searched)
#39 (passive NEAR/2 (motion or movement)):ti,ab,kw (Word variations have been searched)
#40 (CPM):ti,ab,kw (Word variations have been searched)
#41 MeSH descriptor: [Muscle Stretching Exercises] explode all trees
#42 ((stretching or stretches)):ti,ab,kw (Word variations have been searched)
#43 ((mobilisation or mobilization)):ti,ab,kw (Word variations have been searched)
#44 (exercise* NEAR/2 (program* or strength* or intervention* or training or prescription* or prescrib*)):ti,ab,kw (Word variations have been searched)
#45 (exercise* NEAR/2 (therap* or therapeutic)):ti,ab,kw (Word variations have been searched)
#46 ((home or supervis*) NEAR/2 exercis*):ti,ab,kw (Word variations have been searched)
#47 ((pendular or pendulum) NEAR/ exercis*):ti,ab,kw (Word variations have been searched)
#48 ((isokinetic or resist*) NEAR/2 exercise*):ti,ab,kw (Word variations have been searched)
#49 #37 OR #38 OR #39 OR #40 OR #41 OR #42 OR #43 OR #44 OR #45 OR #46 OR #47 OR #48
#50 #13 AND #49
#51 #21 OR #28 OR #36 OR #50

EMBASE
Via OVID
Search date=7th December 2018
Records identified=1986
Database: Embase <1974 to 2018 Week 49>

1 (frozen adj6 shoulder$).ti,ab,kw. (1476)
2 (stiff$ adj6 shoulder$).ti,ab,kw. (1164)
3 (adhesive adj (capsulitis or capsulitides)).ti,ab,kw. (1089)
4 ((bursitis or bursitides) adj6 shoulder$).ti,ab,kw. (170)
5 ((capsulitis or capsulitides) adj6 shoulder$).ti,ab,kw. (587)
6 ((periarthritis or peri-arthritis or periarthritides or peri-arthritides or peri-capsulitis or pericapsulitis) adj6 shoulder$).ti,ab,kw. (307)
7 exp bursitis/ (4361)
8 shoulder pain/ (14558)
9 (shoulder$ adj3 (pain or pains or painful or complain$)).ti,ab,kw. (11841)
10 Shoulder Impingement Syndrome/ (2544)
11 (shoulder$ adj6 impinge$).ti,ab,kw. (1359)
12 subacromial impingement syndrome.ti,ab,kw. (489)
13 1 or 2 or 3 or 4 or 5 or 6 or 7 or 8 or 9 or 10 or 11 or 12 (27058)
14 Arthrography/ (5871)
15 (arthrograph$ adj6 (distension$ or distention$)).ti,ab,kw. (58)
16 (arthrogram$ adj6 (distension$ or distention$)).ti,ab,kw. (7)
17 (glenohumeral adj6 (distension$ or distention$)).ti,ab,kw. (17)

18 Dilatation/ (16639)
19 (dilatation or hydrodilat$).ti,ab,kw. (72836)
20 or/14-19 (79870)
21 13 and 20 (780)
22 Shoulder arthroscopy/ (1771)
23 (arthroscop$ adj6 (releas$ or decompress$ or capsulotom$)).ti,ab,kw. (1394)
24 ((capsular adj2 releas$) or interventional microadhesiolysis or capsulotomy).ti,ab,kw. (3750)
25 or/22-24 (6524)
26 exp Musculoskeletal Manipulation/ (2815)
27 (manipulat$ adj3 (anesthesia or anaesthesia or anesthetic$ or anaesthetic$)).ti,ab,kw. (832)
28 MUA.ti,ab,kw. (7069)
29 26 or 27 or 28 (10472)
30 25 or 29 (16919)
31 13 and 30 (1187)
32 Intraarticular Drug Administration/ (6097)
33 Injections/ (115219)
34 ((bursa$ or intrabursa$ or intra bursa$ or periartic$ or peri artic$ or intraartic$ or intra artic$) adj3 inject$).ti,ab,kw. (8868)
35 ((subacromial or acromioclavicular or glenohumeral) adj3 inject$).ti,ab,kw. (475)
36 ((extra articular or extraarticular) adj3 inject$).ti,ab,kw. (49)
37 (IA inject$ or RI inject$ or SA inject$).ti,ab,kw. (952)
38 32 or 33 or 34 or 35 or 36 or 37 (126307)
39 13 and 38 (1280)
40 Physiotherapy/ (75119)
41 Home Physiotherapy/ (272)
42 Muscle Stretching/ (5114)
43 Stretching Exercise/ (2602)
44 Joint mobilization/ (1080)
45 Isokinetic exercise/ (2247)
46 (physiotherapy or physiotherapies or physical therap$ or manual therap$).ti,ab,kw. (60613)
47 (passive adj (motion or movement)).ti,ab,kw. (2813)
48 CPM.ti,ab,kw. (7488)
49 muscle stretching exercises/ (2337)
50 (stretching or stretches).ti,ab,kw. (32638)
51 (mobilisation or mobilization).ti,ab,kw. (69668)
52 (exercise$ adj2 (program$ or strength$ or intervention$ or training or prescription$ or prescrib$)).ti,ab,kw. (51672)
53 (exercise$ adj2 (therap$ or therapeutic)).ti,ab,kw. (9177)
54 ((home or supervis$) adj2 exercis$).ti,ab,kw. (6926)
55 ((pendular or pendulum) adj exercis$).ti,ab,kw. (34)
56 ((isokinetic or resist$) adj2 exercise$).ti,ab,kw. (8262)
57 or/40-56 (267428)
58 13 and 57 (4164)
59 21 or 31 or 39 or 58 (6314)
60 randomized controlled trial/ (525863)
61 Controlled clinical study/ (459630)
62 random$.ti,ab. (1356792)
63 randomization/ (80264)
64 intermethod comparison/ (242546)
65 placebo.ti,ab. (279891)
66 (compare or compared or comparison).ti. (466002)

67 ((evaluated or evaluate or evaluating or assessed or assess) and (compare or compared or comparing or comparison)).ab. (1832417)
68 (open adj label).ti,ab. (67434)
69 ((double or single or doubly or singly) adj (blind or blinded or blindly)).ti,ab. (212868)
70 double blind procedure/ (155888)
71 parallel group$1.ti,ab. (22585)
72 (crossover or cross over).ti,ab. (95303)
73 ((assign$ or match or matched or allocation) adj5 (alternate or group$1 or intervention$1 or patient$1 or subject$1 or participant$1)).ti,ab. (293234)
74 (assigned or allocated).ti,ab. (344449)
75 (controlled adj7 (study or design or trial)).ti,ab. (306257)
76 (volunteer or volunteers).ti,ab. (228780)
77 human experiment/ (427572)
78 trial.ti. (257503)
79 60 or 61 or 62 or 63 or 64 or 65 or 66 or 67 or 68 or 69 or 70 or 71 or 72 or 73 or 74 or 75 or 76 or 77 or 78 (4444632)
80 (animal/ or animal experiment/ or animal model/ or animal tissue/ or nonhuman/) not exp human/ (5612936)
81 editorial.pt. or case report.ti. (850343)
82 79 not (80 or 81) (3900081)
83 59 and 82 (1986)

PEDro
Via https://www.pedro.org.au/
Search date=7th December 2018
Records identified=52

Three separate searches were conducted, the results were downloaded and combined in one Endnote library to give 52 unique records
The first search:
"adhesive capsulitis" and clinical trials and 2009 onwards. This identified 41 records
The second search:
"frozen shoulder" and clinical trials and 2009 onwards. This identified 30 records
The third search:
"stiff shoulder" and clinical trials and 2009 onwards. This identified 1 record

Science Citation Index
Via Web of Science
Search date=7th December 2018
Records identified=1420

22 1,420
#20 OR #16 OR #14 OR #12
Refined by: PUBLICATION YEARS: (2018 OR 2017 OR 2016 OR 2015 OR 2014 OR 2013 OR 2012 OR 2011 OR 2010)
Indexes=SCI-EXPANDED Timespan=All years

21 2,358
#20 OR #16 OR #14 OR #12
Indexes=SCI-EXPANDED Timespan=All years

20 1,831
#19 AND #10
Indexes=SCI-EXPANDED Timespan=All years

19 296,861
#18 OR #17
Indexes=SCI-EXPANDED Timespan=All years

18 271,166
TOPIC: (passive NEAR/2 (motion or movement)) OR TOPIC: (CPM) OR TOPIC: (stretching or stretches) OR TOPIC: (mobilisation or mobilization) OR TOPIC: (exercise* NEAR/2 (program* or strength* or intervention* or training or prescription* or prescrib*)) OR TOPIC: (exercise* NEAR/2 (therap* or therapeutic)) OR TOPIC: ((home or supervis*) NEAR/2 exercis*) OR TOPIC: ((pendular or pendulum) NEAR/2 exercis*) OR TOPIC: ((isokinetic or resist*) NEAR/2 exercise*)
Indexes=SCI-EXPANDED Timespan=All years

17 31,720
TOPIC: (physiotherapy or physiotherapies or "physical therap*" or "manual therap*")
Indexes=SCI-EXPANDED Timespan=All years

16 389
#15 AND #10
Indexes=SCI-EXPANDED Timespan=All years

15 6,535
TOPIC: ((bursa* or intrabursa* or "intra bursa*" or periartic* or "peri artic*" or intraartic* or "intra artic*") NEAR/3 inject*) OR TOPIC: ((subacromial or acromioclavicular or glenohumeral) NEAR/3 inject*) OR TOPIC: (extraarticular NEAR/3 inject) OR TOPIC: ("extra articular" NEAR/3 inject*) OR TOPIC: ("IA inject*" or "RI inject*" or "SA inject*")
Indexes=SCI-EXPANDED Timespan=All years

14 452
#13 AND #10
Indexes=SCI-EXPANDED Timespan=All years

13 7,632
TOPIC: (arthroscop* NEAR/6 (releas* or decompress* or capsulotom*)) OR TOPIC: (capsular NEAR/2 releas*) OR TOPIC: ("Musculoskeletal Manipulat*") OR TOPIC: (manipulat* NEAR/3 (anesthesia or

anaesthesia or anesthetic* or anaesthetic*)) OR TOPIC: (MUA) OR TOPIC: ("interventional microadhesiolysis") OR TOPIC: (capsulotomy)
Indexes=SCI-EXPANDED Timespan=All years

12 68
#11 AND #10
Indexes=SCI-EXPANDED Timespan=All years

11 45,556
TOPIC: (arthrograph* NEAR/6 (distension* or distention*)) OR TOPIC: (arthrogram* NEAR/6 (distension* or distention*)) OR TOPIC: (glenohumeral NEAR/6 (distension* or distention*)) OR TOPIC: (dilatation or hydrodilat*)
Indexes=SCI-EXPANDED Timespan=All years

10 11,243
#9 OR #8 OR #7 OR #6 OR #5 OR #4 OR #3 OR #2 OR #1
Indexes=SCI-EXPANDED Timespan=All years

9 536
TOPIC: ("subacromial impingement syndrome")
Indexes=SCI-EXPANDED Timespan=All years

8 1,226
TOPIC: (shoulder* NEAR/6 impinge*)
Indexes=SCI-EXPANDED Timespan=All years

7 8,484
TOPIC: (shoulder* NEAR/3 (pain or pains or painful or complain*))
Indexes=SCI-EXPANDED Timespan=All years

6 114
TOPIC: ((periarthritis or peri-arthritis or periarthritides or peri-arthritides or peri-capsulitis or pericapsulitis) NEAR/6 shoulder*)
Indexes=SCI-EXPANDED Timespan=All years

5 325
TOPIC: ((capsulitis or capsulitides) NEAR/6 shoulder*)
Indexes=SCI-EXPANDED Timespan=All years

4 104
TOPIC: ((bursitis or bursitides) NEAR/6 shoulder*)
Indexes=SCI-EXPANDED Timespan=All years

3 928
TOPIC: (adhesive NEAR/6 (capsulitis or capsulitides))
Indexes=SCI-EXPANDED Timespan=All years

2 666
TOPIC: (stiff* NEAR/6 shoulder*)
Indexes=SCI-EXPANDED Timespan=All years

1 1,415
TOPIC: (frozen NEAR/6 shoulder*)
Indexes=SCI-EXPANDED Timespan=All years

Clinicaltrials.gov
Search date=7th December 2018
Records retrieved = 67

Three separate searches were conducted, the results were downloaded and combined in one Endnote library to give 67 unique records
The first search "adhesive capsulitis" identified 50 records
The second search "frozen shoulder" identified 47 records
The third search "stiff shoulder" identified 9 records

WHO International Clinical Trials Registry Platform
Search date=11th December 2018
Records retrieved = 54

Three separate searches were conducted, the results were downloaded and combined in one Endnote library to give 54 unique records
The first search "adhesive capsulitis" identified 37 records
The second search "frozen shoulder" identified 27 records
The third search "stiff shoulder" identified 4 records