Management of adults with primary frozen shoulder in secondary care (UK FROST): a multicentre, pragmatic, three-arm, superiority randomised clinical trial

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Summary

Background Manipulation under anaesthesia and arthroscopic capsular release are costly and invasive treatments for frozen shoulder, but their effectiveness remains uncertain. We compared these two surgical interventions with early structured physiotherapy plus steroid injection.

Methods In this multicentre, pragmatic, three-arm, superiority randomised trial, patients referred to secondary care for treatment of primary frozen shoulder were recruited from 35 hospital sites in the UK. Participants were adults (≥18 years) with unilateral frozen shoulder, characterised by restriction of passive external rotation (≥50%) in the affected shoulder. Participants were randomly assigned (2:2:1) to receive manipulation under anaesthesia, arthroscopic capsular release, or early structured physiotherapy. In manipulation under anaesthesia, the surgeon manipulated the affected shoulder to stretch and tear the tight capsule while the participant was under general anaesthesia, supplemented by a steroid injection. Arthroscopic capsular release, also done under general anaesthesia, involved surgically dividing the contracted anterior capsule in the rotator interval, followed by manipulation, with optional steroid injection. Both forms of surgery were followed by postprocedural physiotherapy. Early structured physiotherapy involved mobilisation techniques and a graduated home exercise programme supplemented by a steroid injection. Both early structured physiotherapy and postprocedural physiotherapy involved 12 sessions during up to 12 weeks. The primary outcome was the Oxford Shoulder Score (OSS; 0–48) at 12 months after randomisation, analysed by initial randomisation group. We sought a target difference of 5 OSS points between physiotherapy and either form of surgery, or 4 points between manipulation and capsular release. The trial registration is ISRCTN48804508.

Findings Between April 1, 2015, and Dec 31, 2017, we screened 914 patients, of whom 503 (55%) were randomly assigned. At 12 months, OSS data were available for 189 (94%) of 201 participants assigned to manipulation (mean estimate 38·3 points, 95% CI 36·9 to 39·7), 191 (94%) of 203 participants assigned to capsular release (40·3 points, 38·9 to 41·7), and 93 (94%) of 99 participants assigned to physiotherapy (37·2 points, 35·3 to 39·2). The mean group differences were 2·01 points (0·10 to 3·91) between the capsular release and manipulation groups, 3·06 points (0·71 to 5·41) between capsular release and physiotherapy, and 1·05 points (–1·28 to 3·39) between manipulation and physiotherapy. Eight serious adverse events were reported with capsular release and two with manipulation. At a willingness-to-pay threshold of £20 000 per quality-adjusted life-year, manipulation under anaesthesia had the highest probability of being cost-effective (0·8632, compared with 0·1366 for physiotherapy and 0·0002 for capsular release).

Interpretation All mean differences on the assessment of shoulder pain and function (OSS) at the primary endpoint of 12 months were less than the target differences. Therefore, none of the three interventions were clinically superior. Arthoscopic capsular release carried higher risks, and manipulation under anaesthesia was the most cost-effective.

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Introduction

Frozen shoulder, also known as adhesive capsulitis, is a painful condition that most commonly affects people in the sixth decade of life.[1,2] The capsule of the shoulder joint becomes inflamed, then scarred and contracted, causing pain, stiffness, and loss of function.[3] People with frozen shoulder can struggle with basic daily activities and have sleep disturbance due to shoulder pain.[4] The cumulative incidence of frozen shoulder has been estimated at 2·4 per 1000 population per year in the Netherlands,[1] affecting 8·2% of men and 10·1% of women of working age.[2] The exact cause remains unknown, which is why it is often labelled as idiopathic or primary frozen shoulder. Recognised associations include diabetes, cardiovascular

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Research in context

Evidence before this study

Frozen shoulder is a common and painful condition in which movements in the shoulder become restricted. Although it is often a self-limiting condition, there can be slow and incomplete resolution, during which people can struggle with basic daily activities and work, and have disturbed sleep from the pain. Generally, conservative treatments are provided in a primary care setting in the UK. More invasive, surgical treatments, such as manipulation under anaesthesia or arthroscopic capsular release, are used in hospital. In 2012, we published a systematic review, which concluded that there was inadequate evidence for the clinical effectiveness and cost-effectiveness of different treatment options in the management of a primary frozen shoulder, including intensive or invasive interventions. We updated that review by searching MEDLINE (from 1946 to Dec 6, 2018), Central (from inception to Dec 5, 2018), Embase (from 1974 to Dec 7, 2018), PEDro (from 2009 to Dec 7, 2018), WHO International Clinical Trials Registry Platform (from inception to Dec 11, 2018), and Science Citation Index and ClinicalTrials.gov (from inception to Dec 7, 2018), using the search terms "adhesive capsulitis", "frozen shoulder", "stiff shoulder", "bursitis", and "periarthritis", with no language restriction, to assess the effectiveness of interventions. We included hydrodilatation because of its increasing popularity despite a paucity of evidence. Nine trials (including UK FROST) were included, with the number of participants in other trials ranging from 26 to 136. The quality of the trials was variable, and considerable heterogeneity of the interventions made it difficult to combine studies or draw conclusions. Only two trials were pooled in a meta-analysis that compared long-term functioning between arthroscopic capsular release and physiotherapy plus steroid injection. The pooled effect favoured capsular release (standardised mean difference 0·32 SDs, 95% CI 0·08–0·56), but was smaller in magnitude than the clinical threshold of the standard effect size used in UK FROST. The evidence of the effectiveness of hydrodilatation from four trials was inconclusive.

Following a 2010 national survey of 303 health-care professionals in the UK, we determined that physiotherapy, manipulation under anaesthesia, and arthroscopic capsular release were the more frequently used interventions in a secondary care setting. Only 6% of respondents at the time suggested hydrodilatation as a comparator. We therefore aimed to evaluate the clinical (pain and function) effectiveness and cost-effectiveness of physiotherapy compared with the two forms of surgery for treating frozen shoulder.

Added value of this study

To our knowledge, UK FROST is the largest randomised trial to compare early structured physiotherapy, manipulation under anaesthesia, and arthroscopic capsular release. Early structured physiotherapy was a multicomponent secondary care physiotherapy intervention, including steroid injection, that we developed using recommendations from national guidelines and a Delphi study of shoulder specialist physiotherapists. The two surgical interventions did not have better clinically important outcomes for shoulder pain and function compared with physiotherapy at 12 months. Arthroscopic capsular release carried higher risks. Physiotherapy was a low-cost option that could be accessed more quickly but was not clinically superior. The health economic comparison found manipulation to be the most cost-effective intervention within the UK health-care setting. Our embedded qualitative study identified that early medical help and quicker access to National Health Service (NHS) care pathways was important to patients.

Implications of all the available evidence

UK FROST provides robust evidence that none of the three trial treatments were superior on patient-reported outcomes for shoulder pain and function at 12 months. However, a marginal clinically important benefit of capsular release over physiotherapy might exist in the wider population. Our specifically designed early structured physiotherapy pathway was accessed more quickly than were the surgical options, and was lower in cost; therefore, its implementation in clinical practice should be carefully considered. Importantly, manipulation under anaesthesia was the most cost-effective option. Manipulation under anaesthesia is an existing pathway in the NHS and requires less theatre time than arthroscopic capsular release. Capsular release carries higher risks and costs compared with manipulation and physiotherapy, but fewer participants in this group required further treatment. Our evidence suggests that arthroscopic capsular release should be used more selectively when less costly and less invasive interventions fail.

disease, trauma, stroke, neurosurgery, and thyroid disease. Association with diabetes is considered to make frozen shoulder more resistant to treatment.[5]

Diagnosis of frozen shoulder is based on clinical features of an insidious onset of deep-seated pain in the shoulder and upper arm with increasing stiffness, and clinical findings of limited active and passive external rotation in the absence of crepitus.[6] X-rays are not routinely required,[7] but can be done to exclude shoulder arthritis or posterior dislocation, which could present with similar clinical signs.

Frozen shoulder can spontaneously resolve, but recovery might be slow or incomplete. Around 40% of patients report persistent symptoms even 4 years after onset.[8] Primarily, the severity of pain and disability arising from the restriction of movement drives patients to seek treatment.[4] A range of treatment options with increasing degrees of invasiveness are available, but there is uncertainty about when these should be offered and their clinical effectiveness or cost-effectiveness.[9] A survey of specialist health professionals that we conducted in the UK identified three interventions as

most commonly used: physiotherapy, manipulation under anaesthesia, and arthroscopic capsular release.[10] The UK national physiotherapy guidelines for frozen shoulder, based on a systematic review, recommend exercise and manual therapy either in isolation or to supplement intra-articular injection of glucocorticoid (steroid), manipulation, or capsular release.[11] We further developed and standardised the non-surgical care pathway for this trial to include intra-articular steroid injection followed by structured physiotherapy, using the best available evidence and consensus from expert shoulder physiotherapists. We called this early structured physiotherapy because it is more quickly accessible within secondary care than are the surgical interventions.[12] It is not known whether early structured physiotherapy or either of the surgical interventions followed by physiotherapy is more effective.[13] Systematic reviews have identified large gaps in evidence and a need for high quality primary research.[13,14] With the intention of facilitating quicker recovery, manipulation and capsular release are increasingly used despite the dearth of good evidence.[13,15]

We designed the UK Frozen Shoulder Trial (UK FROST) to assess the effectiveness and cost-effectiveness of three care pathways to treat adults with a frozen shoulder: two commonly used surgical interventions within the UK National Health Service (NHS) hospitals (manipulation and capsular release), and our specifically designed non-surgical physiotherapy pathway.

Methods

Study design

This multicentre, pragmatic, superiority randomised trial compared three parallel groups for patients referred to secondary care for treatment of primary frozen shoulder, who were recruited from 35 hospital sites in the UK. The trial interventions were delivered by 90 surgeons and 285 physiotherapists who were experienced in using these treatments. Two additional hospitals screened patients but did not recruit to the trial.

Ethics approval was obtained from the National Research Ethics Service (NRES Committee North East, 14/NE/1176), and local site-specific NHS research and development approvals were obtained from each participating site. The study was adopted to the UK Clinical Research Network portfolio (17719). Our detailed study protocol has been published elsewhere.[16]

Participants

Patients referred to participating NHS hospitals were eligible if they were 18 years or older and presented with a clinical diagnosis of unilateral frozen shoulder, characterised by the restriction of passive external rotation in the affected shoulder to less than 50% of the opposite shoulder,[17] for which there was evidence of good inter-rater agreement.[18] Plain radiographs (anteroposterior and axillary view) of the affected shoulder were obtained to exclude other pathology. Detailed exclusion criteria are in the protocol and included bilateral concurrent frozen shoulder, having frozen shoulder secondary to trauma that required hospital care or secondary to other causes, except diabetes (eg, recent breast surgery), not having sufficient mental capacity to understand the instructions or treatment, not being a resident in a catchment area of a trial site, and if any of the trial treatments were contraindicated (eg, if patients were unfit for anaesthesia or corticosteroid injection). Patients with diabetes were included, because this is significantly associated with impaired shoulder mobility in this patient population.[19] Informed written consent was obtained from all trial participants by suitably qualified local study personnel at each participating site.

Randomisation and masking

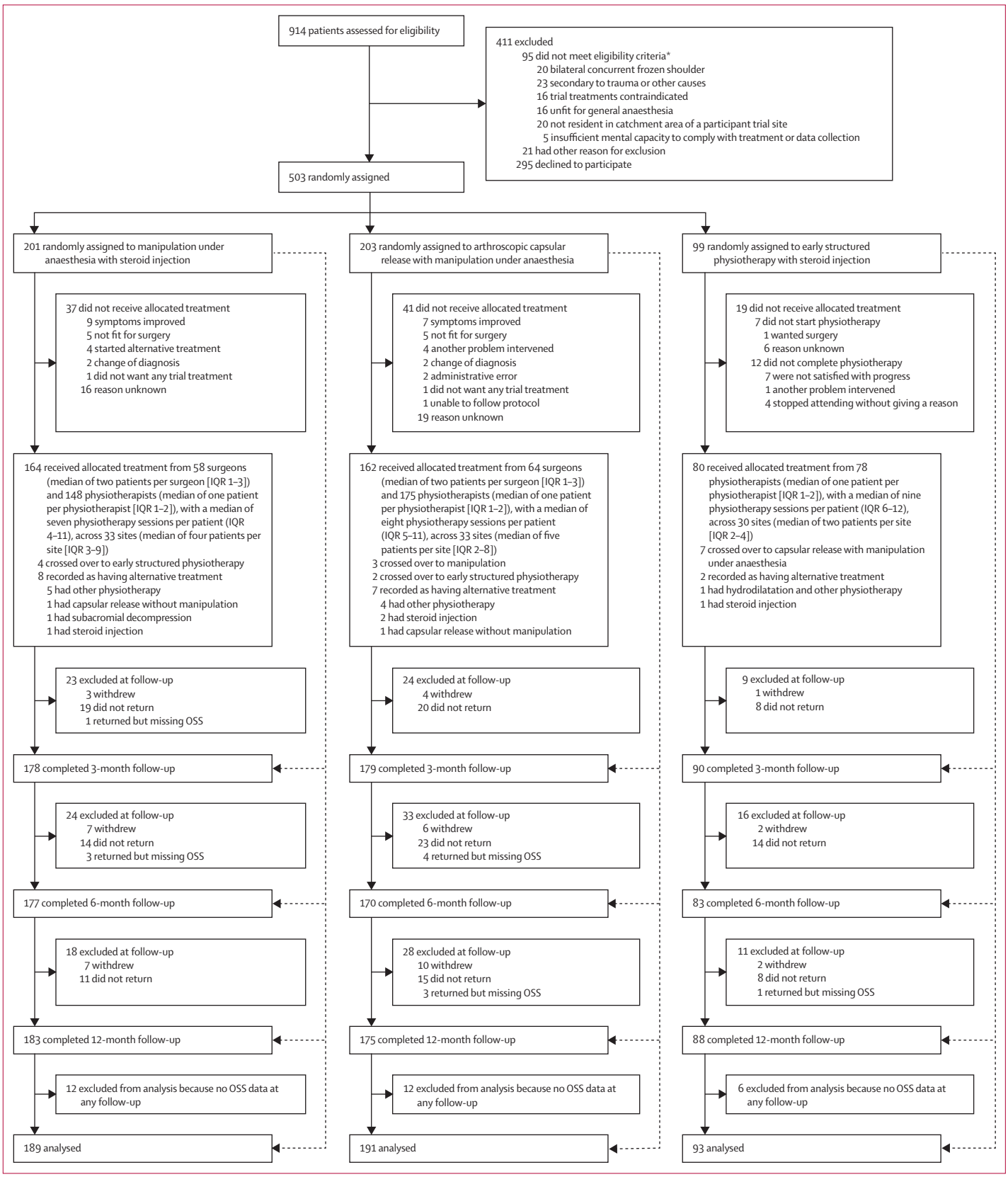
After surgeons or physiotherapists confirmed eligibility and baseline data was collected for eligible and consenting patients, the research nurse accessed a secure remote randomisation service via telephone or internet, provided by a registered clinical trials unit at the University of York. Individual participants were randomly assigned with unequal allocation (2:2:1) to arthroscopic capsular release, manipulation under anaesthesia, or early structured physiotherapy, to allow for different effect sizes between groups. Allocation was based on a computer-generated randomisation algorithm that used random block sizes of 10 and 15 and stratified patients by presence of diabetes. Concealment was ensured by registering participants before the remote computer-generated randomisation with randomly varying block sizes.

Blinding of participants and clinicians to treatment allocation was not possible or desirable in this pragmatic trial. Therefore, participants and clinicians were informed about treatment allocation immediately after randomisation.

Procedures

Participants underwent standardised physiotherapy programmes in all three groups. The early structured physiotherapy and postprocedural physiotherapy programmes were standardised using evidence from a systematic review,[13] UK guidelines, and previous surveys of UK physiotherapists and Delphi consensus methodology.[20] The full standard course of early structured physiotherapy and postprocedural physiotherapy was 12 sessions during up to 12 weeks. If the physiotherapist and participant were satisfied with their progress, not all 12 sessions were necessary; otherwise, participants were encouraged to attend the full standard course.

In the early structured physiotherapy intervention, at the earliest opportunity before starting physiotherapy, an intra-articular steroid (glucocorticoid) injection was administered with or without imaging guidance, depending on usual practice of the hospital site, because


914 patients assessed for eligibility
411 excluded
95 did not meet eligibility criteria*
20 bilateral concurrent frozen shoulder
23 secondary to trauma or other causes
16 trial treatments contraindicated
16 unfit for general anaesthesia
20 not resident in catchment area of a participant trial site
5 insufficient mental capacity to comply with treatment or data collection
21 had other reason for exclusion
295 declined to participate
503 randomly assigned
201 randomly assigned to manipulation under anaesthesia with steroid injection
203 randomly assigned to arthroscopic capsular release with manipulation under anaesthesia
99 randomly assigned to early structured physiotherapy with steroid injection
37 did not receive allocated treatment
9 symptoms improved
5 not fit for surgery
4 started alternative treatment
2 change of diagnosis
1 did not want any trial treatment
16 reason unknown
41 did not receive allocated treatment
7 symptoms improved
5 not fit for surgery
4 another problem intervened
2 change of diagnosis
2 administrative error
1 did not want any trial treatment
1 unable to follow protocol
19 reason unknown
19 did not receive allocated treatment
7 did not start physiotherapy
1 wanted surgery
6 reason unknown
12 did not complete physiotherapy
7 were not satisfied with progress
1 another problem intervened
4 stopped attending without giving a reason
164 received allocated treatment from 58 surgeons (median of two patients per surgeon [IQR 1–3]) and 148 physiotherapists (median of one patient per physiotherapist [IQR 1–2]), with a median of seven physiotherapy sessions per patient (IQR 4–11), across 33 sites (median of four patients per site [IQR 3–9])
4 crossed over to early structured physiotherapy
8 recorded as having alternative treatment
5 had other physiotherapy
1 had capsular release without manipulation
1 had subacromial decompression
1 had steroid injection
162 received allocated treatment from 64 surgeons (median of two patients per surgeon [IQR 1–3]) and 175 physiotherapists (median of one patient per physiotherapist [IQR 1–2]), with a median of eight physiotherapy sessions per patient (IQR 5–11), across 33 sites (median of five patients per site [IQR 2–8])
3 crossed over to manipulation
2 crossed over to early structured physiotherapy
7 recorded as having alternative treatment
4 had other physiotherapy
2 had steroid injection
1 had capsular release without manipulation
80 received allocated treatment from 78 physiotherapists (median of one patient per physiotherapist [IQR 1–2]), with a median of nine physiotherapy sessions per patient (IQR 6–12), across 30 sites (median of two patients per site [IQR 2–4])
7 crossed over to capsular release with manipulation under anaesthesia
2 recorded as having alternative treatment
1 had hydrodilatation and other physiotherapy
1 had steroid injection
23 excluded at follow-up
3 withdrew
19 did not return
1 returned but missing OSS
24 excluded at follow-up
4 withdrew
20 did not return
9 excluded at follow-up
1 withdrew
8 did not return
178 completed 3-month follow-up
179 completed 3-month follow-up
90 completed 3-month follow-up
24 excluded at follow-up
7 withdrew
14 did not return
3 returned but missing OSS
33 excluded at follow-up
6 withdrew
23 did not return
4 returned but missing OSS
16 excluded at follow-up
2 withdrew
14 did not return
177 completed 6-month follow-up
170 completed 6-month follow-up
83 completed 6-month follow-up
18 excluded at follow-up
7 withdrew
11 did not return
28 excluded at follow-up
10 withdrew
15 did not return
3 returned but missing OSS
11 excluded at follow-up
2 withdrew
8 did not return
1 returned but missing OSS
183 completed 12-month follow-up
175 completed 12-month follow-up
88 completed 12-month follow-up
12 excluded from analysis because no OSS data at any follow-up
12 excluded from analysis because no OSS data at any follow-up
6 excluded from analysis because no OSS data at any follow-up
189 analysed
191 analysed
93 analysed

current evidence did not support the superiority of either approach.[21] Full details about the physiotherapy programmes are given elsewhere,[12,16] and included information on pain management, mobilisation techniques (increasingly stretching into the stiff part of the range of movement), and a graduated home exercise programme that progressed from gentle pendular exercises to firm stretching exercises according to the stage of frozen shoulder, as is accepted good practice.[11,20]

Manipulation under anaesthesia and arthroscopic capsular release were done as day case surgical procedures within 18 weeks of randomisation. In manipulation under anaesthesia, the surgeon manipulated the affected shoulder in a controlled way to stretch and tear the tight capsule while the participant was under general anaesthesia, supplemented by an intra-articular steroid injection during surgery. If the manipulation was judged to be incomplete, the surgeon did not cross over intraoperatively to capsular release, to allow assessment of outcome of the manipulation.

Arthroscopic capsular release was done under general anaesthesia by a surgeon to surgically divide the contracted anterior capsule in the rotator interval, followed by manipulation under anaesthesia to complete and confirm optimal capsular release. Additional procedures, such as posterior capsular release and subacromial decompression, were permitted at the discretion of the operating surgeon, and were recorded. Supplementary steroid injections were used at the surgeon's discretion. Both manipulation and capsular release were followed by postprocedural physiotherapy, normally beginning within 24 h, in which all participants were provided with information on pain management and instructions on a graduated home exercise programme, as described earlier, with the optional addition of mobilisation techniques.

All interventions were delivered by participating surgeons who were familiar with the surgical procedures (as judged by the Principal Investigator at each site) and by qualified physiotherapists (ie, not students or assistants). There was no minimum number of surgical procedures that the surgeon had to have done, and no grades of surgeon were excluded. No additional training was required for either programme of physiotherapy.

Outcomes

The primary outcome was the Oxford Shoulder Score (OSS), a 12-item patient-reported outcome measure of shoulder pain and function with five response categories and an overall scale ranging from 0 (worst) to 48 (best).[22] The primary endpoint was 12 months after randomisation.

Figure 1: **Trial profile**
OSS=Oxford Shoulder Score. *Some patients did not meet multiple eligibility criteria.

Secondary patient-reported outcome measures were the Quick Disabilities of the Arm, Shoulder, and Hand (QuickDASH)[23] score, as a further region-specific measure of response to treatment;[24] health-related quality of life using the 5-level version of the EuroQOL 5-Dimension questionnaire;[25] the Numeric Rating Scale for pain;[26] and the perceived extent of recovery measured by a single visual analogue scale (VAS) ranging from 0 (no need to seek further treatment) to 100 (definite need). The VAS for treatment recovery was purposefully designed for the study with input from patients and clinicians. All outcome measures were collected at baseline, 3 months, 6 months, and 12 months after randomisation. In addition, OSS was collected at the start of treatment and 6 months after that point. Any complications and adverse events were recorded. Following completion of the allocated intervention, any further treatments for the frozen shoulder were recorded.

Statistical analysis

A full description of the sample size calculation and statistical analysis plan is in the published protocol.[16] The sample size was based on the primary outcome measure at 12 months after randomisation and was calculated using a minimum clinically important difference of 5 points in OSS when comparing early structured physiotherapy with either surgical treatment, or a difference of 4 points when comparing the two surgical treatments. The larger difference when comparing early structured physiotherapy with a surgical treatment was required to justify the greater costs and potential risks associated with surgery.[22] To observe the above differences with 90% power and two-sided 5% significance, adjusting for a conservative estimate (r=0·4) of the correlation between OSS during 12 months and allowing for 20% loss to follow-up, a total sample size of 500 patients was required. No adjustment was made for multiple comparisons, owing to the a priori specified sequence of treatment comparisons (manipulation *vs* physiotherapy, capsular release *vs* physiotherapy, and manipulation *vs* capsular release; results were interpreted as if from three independent trials, with inference for one comparison independent of the outcome of another).[27]

The analysis of primary and secondary outcomes followed intention-to-treat principles, such that comparisons were according to the randomised group, irrespective of compliance, without imputation for minimal missing data, excluding participants for whom no OSS data were available. We used a linear mixed model incorporating all timepoints and using an unstructured covariance pattern. The model adjusted for age (in years), gender (male or female), diabetes status (diabetic or non-diabetic), and OSS at baseline as fixed effects, and recruitment site (35 sites) as a random effect. A single model was used for the analysis, and treatment group differences at each timepoint were presented as three separate two-way comparisons. The OSS at 12 months, QuickDASH, pain

	As randomised (n=503)			As analysed (n=473)		
	Manipulation under anaesthesia (n=201)	Arthroscopic capsular release (n=203)	Early structured physiotherapy (n=99)	Manipulation under anaesthesia (n=189)	Arthroscopic capsular release (n=191)	Early structured physiotherapy (n=93)
Gender						
Male	72 (36%)	77 (38%)	35 (35%)	68 (36%)	74 (39%)	31 (33%)
Female	129 (64%)	126 (62%)	64 (65%)	121 (64%)	117 (61%)	62 (67%)
Age (years)						
Mean (SD)	54·5 (7·7)	53·9 (7·7)	54·5 (7·8)	54·4 (7·3)	54·4 (7·6)	54·8 (7·8)
Median (IQR)	54 (54–60)	54 (54–59)	53 (53–60)	54 (54–60)	55 (55–59)	53 (53–60)
Diabetes						
No	141 (70%)	143 (70%)	69 (70%)	131 (69%)	135 (71%)	66 (71%)
Type 1	12 (6%)	12 (6%)	5 (5%)	12 (6%)	11 (6%)	5 (5%)
Type 2	48 (24%)	48 (24%)	25 (25%)	46 (24%)	45 (24%)	22 (24%)
Affected shoulder						
Left	127 (63%)	121 (60%)	56 (57%)	119 (63%)	114 (60%)	54 (58%)
Right	73 (36%)	80 (39%)	43 (43%)	69 (37%)	75 (39%)	39 (42%)
Data missing	1 (<0·5%)	2 (1%)	0	1 (1%)	2 (1%)	0
Dominant arm affected						
Yes	81 (40%)	82 (40%)	39 (39%)	77 (41%)	76 (40%)	36 (39%)
No	115 (57%)	120 (59%)	59 (60%)	107 (57%)	114 (60%)	56 (60%)
Ambidextrous	0	1 (<1%)	0	0 (0%)	1 (1%)	0
Data missing	5 (2%)	0	1 (1%)	5 (3%)	0	1 (1%)
Duration of symptoms (months)						
Patients with data	n=196	n=201	n=98	n=185	n=190	n=92
Mean (SD)	10·5 (8·6)	11·3 (10·0)	10·8 (8·8)	10·7 (8·7)	11·3 (10·1)	11·0 (9·0)
Median (IQR)	8 (6–12)	9 (6–12)	8 (6–12)	8 (6–12)	9 (6–12)	8 (6–12)
Range	2–60	0–96	2–72	2–60	2–96	2–72
Duration of symptoms						
<9 months	103 (51%)	95 (47%)	51 (52%)	96 (51%)	90 (47%)	48 (52%)
≥9 months	93 (46%)	106 (52%)	47 (47%)	89 (47%)	100 (52%)	44 (47%)
Data missing	5 (2%)	2 (1%)	1 (1%)	4 (2%)	1 (1%)	1 (1%)
X-rays						
Anteroposterior view	200 (100%)	201 (99%)	99 (100%)	188 (99%)	190 (99%)	93 (100%)
Axillary view	174 (87%)	179 (88%)	86 (87%)	163 (86%)	169 (88%)	80 (86%)
Modified axillary	29 (14%)	24 (12%)	14 (14%)	27 (14%)	24 (13%)	14 (15%)
Employment status summary						
In paid work	129 (64%)	118 (58%)	53 (54%)	124 (66%)	111 (58%)	50 (54%)
Not in paid work	69 (34%)	82 (40%)	46 (46%)	62 (33%)	78 (41%)	43 (46%)
Data missing	3 (1%)	3 (1%)	0	3 (2%)	2 (1%)	0 (0%)
Type of employment						
Unskilled manual	17 (8%)	15 (7%)	8 (8%)	16 (8%)	13 (7%)	7 (8%)
Skilled manual	21 (10%)	18 (9%)	18 (18%)	19 (10%)	16 (8%)	17 (18%)
Unskilled non-manual	19 (9%)	17 (8%)	4 (4%)	19 (10%)	17 (9%)	4 (4%)
Skilled non-manual	41 (20%)	37 (18%)	13 (13%)	40 (21%)	37 (19%)	12 (13%)
Professional	13 (6%)	19 (9%)	10 (10%)	13 (7%)	18 (9%)	10 (11%)
Other	20 (10%)	17 (8%)	10 (10%)	18 (10%)	15 (8%)	10 (11%)
Currently taking steroids for affected shoulder						
Yes	2 (1%)	7 (3%)	0	2 (1%)	7 (4%)	0
No	196 (98%)	195 (96%)	99 (100%)	184 (97%)	183 (96%)	93 (100%)
Data missing	3 (1%)	1 (<0·5%)	0	3 (2%)	1 (1%)	0

(Table 1 continues on next page)

	As randomised (n=503)			As analysed (n=473)		
	Manipulation under anaesthesia (n=201)	Arthroscopic capsular release (n=203)	Early structured physiotherapy (n=99)	Manipulation under anaesthesia (n=189)	Arthroscopic capsular release (n=191)	Early structured physiotherapy (n=93)
(Continued from previous page)						
Had steroid injection for affected shoulder						
Yes	97 (48%)	117 (58%)	55 (56%)	93 (49%)	112 (59%)	53 (57%)
No	102 (51%)	86 (42%)	44 (44%)	94 (50%)	79 (41%)	40 (43%)
Data missing	2 (1%)	0	0	2 (1%)	0	0
Previous physiotherapy for affected shoulder						
Yes	125 (62%)	124 (61%)	59 (60%)	117 (62%)	117 (61%)	58 (62%)
No	76 (38%)	77 (38%)	39 (39%)	72 (38%)	73 (38%)	35 (38%)
Data missing	0	2 (1%)	1 (1%)	0	1 (1%)	0
Number of weeks had shoulder problem (median [IQR])	32 (24–52)	35 (24–52)	32 (24–48)	34 (24–52)	36 (24–52)	32 (24–48)
Similar shoulder problem on the opposite side						
Yes	62 (31%)	53 (26%)	13 (13%)	59 (31%)	51 (27%)	12 (13%)
No	132 (66%)	146 (72%)	85 (86%)	124 (66%)	136 (71%)	80 (86%)
Data missing	7 (3%)	4 (2%)	1 (1%)	6 (3%)	4 (2%)	1 (1%)
Oxford Shoulder Score (0–48)*						
Mean (SD)	20·4 (8·9)	19·2 (7·7)	20·3 (8·0)	20·6 (8·9)	19·2 (7·5)	20·3 (8·1)
Median (IQR)	20 (14–27)	19 (13–25)	20 (15–26)	20 (14–27)	19 (14–25)	20 (15–26)
QuickDASH score (0–100)						
Patients with data	n=192	n=197	n=96	n=181	n=187	n=90
Mean (SD)	57·0 (21·0)	61·7 (18·5)	59·4 (19·7)	56·8 (21·1)	61·3 (18·5)	59·1 (20·0)
Median (IQR)	59 (42–75)	64 (52–75)	60 (46–73)	59 (43–73)	64 (50–73)	59·5 (46–73)
Pain Numeric Rating Scale (0–10)						
Patients with data	n=199	n=201	n=99	n=187	n=190	n=93
Mean (SD)	6·8 (2·2)	7·0 (1·9)	6·9 (2·4)	6·7 (2·3)	7·0 (1·9)	6·8 (2·4)
Median (IQR)	7 (5–8)	7 (6–8)	7 (5–8)	7 (5–8)	7 (6–8)	7 (5–8)
Symptom severity (0–100)						
Patients with data	198	201	99	186	189	93
Mean (SD)	83·8 (21·8)	86·2 (20·1)	89·2 (15·4)	83·9 (22·1)	86·0 (20·4)	89·0 (15·5)
Median (IQR)	90 (75–100)	95 (80–100)	100 (80–100)	90 (80–100)	95 (80–100)	100 (80–100)

Data are n (%) or median (IQR) unless otherwise specified. QuickDASH=Quick Disabilities of the Arm, Shoulder, and Hand. *Includes two imputed missing baseline scores (one for manipulation and one for capsular release).

Table 1: **Baseline characteristics**

Numeric Rating Scale, and extent of recovery VAS were analysed in a similar way.

To address the effect of delays in receiving the allocated treatment, we used a separate, secondary, intention-to-treat, linear mixed model, which incorporated time as a continuous variable. This model included data from all available timepoints for each participant (additionally including the OSS score before treatment and 6 months after treatment) and adjusted for the same covariates as the primary analysis model. Treatment effect estimates were extracted at 3 months, 6 months, and 12 months after randomisation.

Complier Average Causal Effect (CACE) analysis investigated the effect of adherence with early structured physiotherapy on the OSS at 12 months using instrumental variable regression. Further sensitivity analyses included additional adjustment for predictors of missing data, exclusion of response data received beyond 6 weeks of each intended follow-up, and adjustment for observed baseline differences in employment status. Subgroup analyses explored whether the treatment response was influenced by presence of diabetes, previous physiotherapy treatment, and participant treatment preference at baseline by including treatment by subgroup interactions in the model. Adverse events and complications were listed by allocated group and compared by the χ^2 test.

All statistical testing was done at the two-sided 5% significance level and estimates given with 95% CIs using Stata 15. The statistical analysis plan was approved by an independent data monitoring committee and the trial steering committee. The trial is registered with the International Standard Randomised Controlled Trial Register (ISRCTN48804508).

Health economic analyses were conducted in accordance with the National Institute for Health and Care Excellence (NICE) reference case standards.[28] The base-case analysis was conducted on an intention-to-treat basis with multiple imputation for missing data, which was assumed missing at random. The analysis was conducted from an NHS and Personal Social Services perspective and included the cost of the initial intervention, hospital stays and outpatient appointments after initial intervention, and visits to primary and community health-care professionals during one year. Costs were calculated using national UK unit costs expressed in British Pound Sterling (GBP) at the 2018 price. Outcomes were measured in terms of quality-adjusted life-years (QALYs) during one year. We used a mapping function to derive utilities[29,30] and the area under the curve method to estimate QALYs.

We used differences in mean costs and mean QALYs at 12 months to derive the incremental cost-effectiveness ratios, which represent the greater benefit per GBP spent. This ratio was estimated by comparing mean differences in expected costs and QALYs between treatment groups. The mean estimates and their 95% CIs were generated using seemingly unrelated regression. Decisions about whether a treatment is efficient (ie, value for money) are determined according to whether the cost per QALY gained (ie, the incremental cost-effectiveness ratio) is below some threshold value. The threshold represents the opportunity cost of delivering an intervention (ie, the health forgone from providing this intervention). At present, the NICE threshold ranges between £20 000 and £30 000 per QALY. According to the current established decision rules, if the estimated cost per QALY is below the £20 000 threshold, the intervention would be considered cost-effective in terms of QALYs gained.

To compute the probability of each intervention being cost-effective, we did the seemingly unrelated regression within a bootstrapping approach on five imputed data sets to generate 100 000 replicates of incremental costs and benefits. The probability that each intervention is cost-effective was reported at the cost-effectiveness threshold applied by NICE (£20 000 to £30 000 per QALY) and at a further recommended threshold of £13 000 per QALY.[31,32]

	Manipulation under anaesthesia (n=164)	Arthroscopic capsular release (n=162)	Early structured physiotherapy (n=80)
Arthroscopic capsular release	7 (4%)	0	5 (6%)
Manipulation under anaesthesia	1 (1%)	1 (1%)	3 (4%)
Further non-surgical treatment			
Steroid injection	3 (2%)	3 (2%)	3 (4%)
Glenohumeral joint injection	2 (1%)	0	0
Ultrasound guided injection	0	1 (1%)	1 (1%)
Other or further physiotherapy	2 (1%)	3 (2%)	6 (8%)
Rheumatology clinic	0	0	1 (1%)
Total number of further treatments	15	8	19
Total number of patients having one or more further treatments (% of randomised)	14/201 (7%)	8/203 (4%)	15/99 (15%)

Data are n (%).

Table 2: **Further treatments for patients who completed treatment and as per randomised groups**

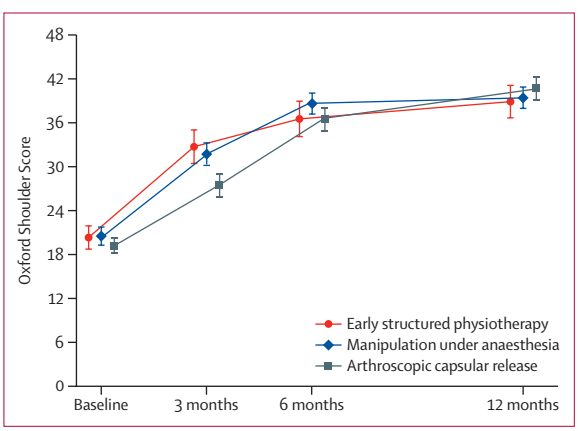


Figure 2: **Primary outcome: Oxford Shoulder Score**
Data points show means and error bars represent 95% CIs.

See Online for appendix

Role of the funding source

The funders monitored the trial progress but had no role in the study design, data collection, data analysis, data interpretation, writing and approving the report, or the decision to submit for publication. The corresponding author had full access to all the data in the study and had final responsibility for the decision to submit for publication.

Results

Between April 1, 2015, and Dec 31, 2017, we screened 914 patients with a frozen shoulder, from whom we randomly assigned 503 (55%) patients, including 201 to manipulation, 203 to capsular release, and 99 to early structured physiotherapy (figure 1). Follow-up was completed on Jan 31, 2019. The baseline characteristics, distribution of patients across sites, and number of treating surgeons and physiotherapists per patient are shown in table 1.

Within the allocated treatment groups, 164 (82%) of 201 participants completed manipulation, 162 (80%) of 203 participants completed capsular release, and 80 (81%) of 99 participants completed physiotherapy (figure 1). In addition, 164 (82%) participants had a steroid injection in the manipulation group, 45 (22%) in the capsular release group, and 79 (80%) in the physiotherapy group. Further details about the delivery, type, and dose of the steroid are provided in the appendix (p 2). 16 (3%) of 503 participants crossed over to a different trial treatment, and 17 (3%) received an alternative treatment. Overall, 64 (13%) participants did not receive any treatment. Waiting times to the start of each randomised

treatment varied considerably. Participants waited a median of 14 days (IQR 7–22) for physiotherapy, 57 days (IQR 35–89) for manipulation, and 72 days (IQR 42–116) for capsular release (appendix p 1). Following completion of their randomised treatment, some participants received further treatment (table 2). The most further treatments were received by participants in the physiotherapy group (n=15 [15%]), followed by the manipulation group (n=14 [7%]), and the capsular release group (n=8 [4%]; table 2).

At the primary endpoint of 12 months, many participants had improved to nearly full shoulder functioning, with a median overall OSS of 43 (out of 48) points, compared with an initial median overall OSS of 20 points. Excluding the participants for whom no OSS data were available at any follow-up point, we analysed the primary outcome in 189 (94%) of 201 participants who were randomly assigned to receive manipulation, 191 (94%) of 203 participants randomly assigned to receive capsular release, and 93 (94%) of 99 participants randomly assigned to receive early structured physiotherapy. Participants randomly assigned to arthroscopic capsular release had statistically significantly higher (ie, better) OSS scores than those assigned to manipulation under anaesthesia (40·3 *vs* 38·3 points; difference 2·01 points, 95% CI 0·10 to 3·91) or to early structured physiotherapy (40·3 *vs* 37·2 points; difference 3·06 points, 0·71 to 5·41). The manipulation group had higher mean OSS scores than the physiotherapy group (38·3 *vs* 37·2 points; difference 1·05 points, –1·28 to 3·39; figure 2). Mean estimates were less than the minimal clinically important effect size of 4–5 OSS points (table 3). For the short-term follow-up at 3 months after randomisation, capsular release had lower (ie, worse) outcomes than the other two interventions. Differences of clinically important magnitude were included in the 95% CIs for the benefit of

	Mean estimates			MUA *vs* ESP		ACR *vs* ESP		ACR *vs* MUA	
	MUA	ACR	ESP	Mean difference (95% CI)	p value	Mean difference (95% CI)	p value	Mean difference (95% CI)	p value
OSS*									
3 months	30·2	26·9	31·6	–1·36 (–3·70 to 0·98)	0·25	–4·72 (–7·06 to –2·39)	<0·0001	–3·36 (–5·27 to –1·45)	0·0006
6 months	37·1	35·9	34·9	2·15 (–0·12 to 4·42)	0·064	0·98 (–1·31 to 3·26)	0·40	–1·17 (–3·02 to 0·67)	0·21
12 months	38·3	40·3	37·2	1·05 (–1·28 to 3·39)	0·38	3·06 (0·71 to 5·41)	0·011	2·01 (0·10 to 3·91)	0·039
Average effect over 12 months	35·2	34·4	34·6	0·61 (–1·31 to 2·53)	0·53	–0·23 (–2·15 to 1·70)	0·82	–0·84 (–2·41 to 0·72)	0·29
OSS time-adjusted†									
3 months	28·2	26·0	29·4	–1·18 (–3·10 to 0·73)	0·23	–3·33 (–5·25 to –1·40)	0·0007	–2·14 (–3·71 to –0·57)	0·0076
6 months	32·5	31·5	32·7	–0·15 (–1·90 to 1·60)	0·87	–1·13 (–2·88 to 0·62)	0·21	–0·98 (–2·40 to 0·44)	0·18
12 months	41·1	42·5	39·2	1·92 (–0·16 to 4·00)	0·071	3·26 (1·18 to 5·35)	0·0022	1·35 (–0·33 to 3·02)	0·12
EQ-5D-5L‡									
Baseline	0·46	0·43	0·40	0·05 (–0·01 to 0·12)	0·10	0·03 (–0·04 to 0·09)	0·42	–0·03 (–0·08 to 0·02)	0·28
3 months	0·63	0·57	0·61	0·03 (–0·03 to 0·08)	0·38	–0·04 (–0·10 to 0·02)	0·18	–0·06 (–0·11 to –0·02)	0·0056
6 months	0·73	0·68	0·68	0·05 (–0·01 to 0·10)	0·10	–0·004 (–0·06 to 0·05)	0·88	–0·05 (–0·10 to –0·01)	0·019
12 months	0·73	0·74	0·69	0·04 (–0·02 to 0·10)	0·20	0·05 (–0·02 to 0·10)	0·15	0·005 (–0·04 to 0·05)	0·85
QuickDASH§									
3 months	38·8	44·4	37·1	1·77 (–3·41 to 6·96)	0·50	7·33 (2·16 to 12·49)	0·0054	5·55 (1·32 to 9·78)	0·010
6 months	27·7	27·4	29·2	–3·55 (–8·68 to 1·58)	0·18	–1·82 (–6·94 to 3·31)	0·49	1·73 (–2·39 to 5·86)	0·41
12 months	29·9	18·2	23·4	–0·50 (–5·70 to 4·70)	0·85	–5·20 (–10·42 to 0·02)	0·051	–4·71 (–8·91 to –0·50)	0·028
Pain NRS§									
3 months	4·1	4·7	3·7	0·43 (–0·17 to 1·03)	0·16	1·02 (0·42 to 1·61)	0·0008	0·59 (0·10 to 1·07)	0·018
6 months	2·8	2·8	3·0	–0·19 (–0·78 to 0·40)	0·53	–0·14 (–0·74 to 0·45)	0·63	0·05 (–0·43 to 0·52)	0·85
12 months	2·4	1·7	2·5	–0·08 (–0·66 to 0·50)	0·78	–0·81 (–1·39 to –0·23)	0·0066	–0·73 (–1·20 to –0·25)	0·0026
Extent of recovery¶									
3 months	51·4	54·0	53·9	–2·55 (–11·68 to 6·58)	0·58	0·11 (–9·02 to 9·23)	0·98	2·66 (–4·84 to 10·15)	0·49
6 months	31·9	34·7	38·6	–6·71 (–15·83 to 2·42)	0·15	–3·93 (–13·06 to 5·21)	0·40	2·78 (–4·50 to 10·06)	0·45
12 months	27·3	21·2	26·9	0·46 (–7·79 to 8·70)	0·91	–5·65 (–13·91 to 2·61)	0·18	–6·11 (–12·86 to 0·64)	0·076

MUA=manipulation under anaesthesia. ESP=early structured physiotherapy. ACR=arthroscopic capsular release. OSS=Oxford Shoulder Score. EQ-5D-5L=EuroQOL 5-Dimension questionnaire, 5-level version. QuickDASH=Quick Disabilities of the Arm, Shoulder, and Hand score. NRS=Numeric Rating Scale. *Linear mixed covariance pattern model adjusted for age, gender, diabetes, OSS at baseline (fixed effects), and site (random effect). †Linear mixed random intercept model adjusted for age, gender, diabetes, OSS at baseline (fixed effects), and site (random effect). ‡Univariate generalised linear model, including group as a fixed effect factor and baseline EQ-5D-5L score as a covariate. §Linear mixed covariance pattern model adjusted for age, gender, diabetes, QuickDASH at baseline (fixed effects), and site (random effect). ¶Based on 0–100 Visual Analogue Scale of perceived need for further treatment. Linear mixed covariance pattern model adjusted for age, gender, diabetes, extent of recovery at baseline (fixed effects), and site (random effect).

Table 3: **Estimated mean outcome differences**

manipulation and physiotherapy compared with capsular release at 3 months, and for the benefit of capsular release compared with physiotherapy at 12 months (table 3).

Compared with the primary analysis, group differences in the model adjusted for waiting times tended to be of smaller magnitude, with the exception of the difference between capsular release and physiotherapy at 12 months (3·26 points [95% CI 1·18 to 5·35] in favour of capsular release; appendix p 3). From the CACE analysis, the outcomes for participants who adhered to physiotherapy treatment remained lower than for participants in the surgery groups (–1·84 OSS points, –4·41 to 0·74), although the difference was not statistically significant (data not shown). Predictors of missingness were age and OSS outcome before being missing. These variables are already incorporated in the primary analysis. Sensitivity analyses regarding the timing of questionnaire return and adjustment for employment status did not show marked differences from the primary results. There were no significant subgroup interactions.

Of the secondary outcomes, QuickDASH and shoulder pain followed a similar pattern to that of OSS, with significantly poorer outcomes for the capsular release group at 3 months but better outcomes at 12 months after randomisation compared with manipulation or physiotherapy (table 3). There were no clear group differences in the extent of recovery based on the treatment-seeking VAS.

In total, ten serious adverse events were reported for nine (2%) of 503 participants, including eight (4%) of 203 in the capsular release group and two (1%) of 201 in the manipulation group (table 4). One (<0·5%) participant in the capsular release group had a serious adverse event from non-trial physiotherapy (table 4). The numbers were insufficient for formal analysis. 33 non-serious adverse events were reported for 31 (6%) of 503 participants, with similar rates in the three groups (table 4). There was no evidence for statistical differences in the proportion of non-serious adverse events (p=0·19).

The base-case economic analysis with multiple imputation showed that manipulation was £276·51 (95% CI 65·67 to £487·35) more expensive per participant than was early structured physiotherapy. Capsular release was substantially more costly than physiotherapy (on average £1733·78 [1529·48 to 1938·06] more per participant) and manipulation (on average £1457·26 [1282·73 to 1631·79] more per participant). Overall, capsular release had worse QALYs than did manipulation under anaesthesia (mean difference –0·0293, –0·0616 to 0·0030) and manipulation had better QALYs than did physiotherapy (mean difference 0·0396, –0·0008 to 0·0800). Manipulation was the intervention most likely to be cost-effective at a threshold of £20 000 per QALY (manipulation 86%; physiotherapy 14%; capsular release 0%; appendix pp 1–2).

	Manipulation under anaesthesia (n=201)	Arthroscopic capsular release (n=203)	Early structured physiotherapy (n=99)
Serious adverse events			
Attended accident and emergency for visual disturbance, headache, heaviness, and numbness of arm	1 (<0·5%)*	0	0
Chest infection	0	1 (<0·5%)	0
Decreased oxygen saturation	0	1 (<0·5%)	0
Deep vein thrombosis	0	1 (<0·5%)†	0
Elevated blood sugars (prolonging hospitalisation)	0	1 (<0·5%)	0
Hypoglycaemic seizure while under anaesthetic	0	1 (<0·5%)	0
Probable anterior dislocation	0	1 (<0·5%)‡	0
Patient noticed facial drooping or weakness after surgery	0	1 (<0·5%)	0
Septic joint arthritis	1 (<0·5%)	0	0
Stroke (3 months after treatment)	0	1 (<0·5%)	0
Total	2 (1%)	8 (4%)	0
Non-serious adverse events			
Additional diagnosis requiring further treatment	1 (<0·5%)	0	0
Adverse reaction to concurrent medication	0	1 (<0·5%)	0
Allergic reaction to dressing	0	1 (<0·5%)	0
Chest infection	1 (<0·5%)	0	0
Episode of inflammation	1 (<0·5%)	0	0
Infection	0	1 (<0·5%)	0
Injury to adjacent structures such as nerve, tendon, bone, or joint	1 (<0·5%)	1 (<0·5%)‡	0
Ipsilateral face swelling, face flushed, and neck and face hot	1 (<0·5%)	0	0
Long head biceps tendon pain and rupture	0	0	1 (1%)
Neuropathic symptoms	1 (<0·5%)	2 (1%)§	0
Patient investigated for neck problems	0	1 (<0·5%)	0
Persistent pain	0	1 (<0·5%)	1
Persistent pain requiring further treatment	1 (<0·5%)	1 (<0·5%)	0
Persistent stiffness and pain requiring treatment	1 (<0·5%)	0	0
Pins and needles to hand	1 (<0·5%)	0	0
Postprocedural worsening of shoulder pain	3 (1%)	3 (1%)	1 (1%)¶
Recurrent stiffness requiring further treatment	0	0	1 (1%)¶
Supraspinatus tendinopathy	0	0	1 (1%)
Surgical site infection	0	1 (<0·5%)‖	0
Transient hyperglycaemia, steroid flare, or joint sepsis following corticosteroid injection	3 (1%)**	0	0
Total	15 (7%)	13 (6%)	5 (5%)

Footnotes indicate when the treatment received was different from that of randomisation. *Recorded as receiving "no trial treatment". †Recorded as receiving "non-trial physiotherapy". ‡Received manipulation under anaesthesia. §One patient recorded as receiving "other" treatment (subacromial decompression). ¶Received arthroscopic capsular release. ‖One patient recorded as receiving "other" treatment (capsular release without manipulation). **Received early structured physiotherapy.

Table 4: **Adverse events by treatment arm as randomised**

Discussion

To our knowledge, UK FROST is the largest randomised clinical trial to date that has evaluated common surgical interventions and a specifically designed physiotherapy pathway with a steroid injection for the treatment of adults with a frozen shoulder in the UK NHS. Patient-reported shoulder pain and function improved substantially from

baseline with all three trial treatments. At the primary endpoint of 12 months, the magnitude of difference of capsular release over manipulation and physiotherapy was statistically significant but unlikely to be clinically important. This finding was consistent for all patient-reported clinical outcomes. Arthroscopic capsular release was associated with higher risks, and manipulation under anaesthesia was the most cost-effective option. A detailed economic evaluation of relative cost-effectiveness of the three treatment options will be published separately, but the key results have been included because they are integral to interpreting the main clinical effectiveness findings.

The differences in patient-reported outcomes between the treatment groups at 3 months were influenced by longer waiting times for the surgical interventions (26 [13%] manipulation participants and 46 [23%] capsular participants commenced treatment after the 3-month follow-up). The planned analysis of our primary outcome, OSS, adjusted for variable waiting times between the three interventions using additional data that was collected on the day of treatment and 6 months after treatment. In this analysis, the difference in benefit of capsular release over physiotherapy at 12 months included a confidence interval that marginally overlapped with the minimal clinically important difference of 5 points. Therefore, clinically meaningful group differences might potentially exist between capsular release and early structured physiotherapy in the wider population. We observed no meaningful differences in OSS between the two surgical interventions at any timepoint. Although patients with diabetes had poorer outcomes than patients without diabetes at all timepoints, we found no evidence of an effect on the primary outcome of participants' diabetes status, receipt of previous physiotherapy, baseline treatment preferences, or length of frozen shoulder symptoms at baseline.

Serious complications were rare, although the arthroscopic capsular release group was relatively less safe. Only two participants allocated to manipulation under anaesthesia had a serious complication. One of the participants in the capsular release group who was diagnosed with deep vein thrombosis received non-trial physiotherapy. There was, therefore, only a marginal difference in the safety profile between manipulation and physiotherapy. Although no participants allocated to physiotherapy had a serious complication, these participants were more likely to need further treatment. Participants in the capsular release group received fewest further treatments.

It is notable that the difference in OSS scores and the difference in health-related quality of life are similar, with only a small difference in OSS and QALYs across the groups. A possible trend of the capsular release group improving over time, which might continue with longer-term follow-up, could be explained by the timing of the delivery of the interventions. This timing has been examined and does not alter the interpretation of the findings of the primary analysis. We are confident that important costs, including the costs of complications, were captured during the trial follow-up.

The strengths of this study were the pragmatic design, recruiting from 35 hospitals across a range of rural and urban areas, involving 90 surgeons and 285 physiotherapists with minimal exclusions. This design makes the results generalisable and applicable to clinical practice in the UK. There were low levels of attrition within and between groups in the completion of the extensively validated patient-reported primary outcome, which measures pain and the effect of any stiffness on shoulder function.[22] The rate of crossovers was also low. The statistical model meant that only 30 (6%) of 503 trial participants were not included in the primary analyses and consequently ensured that we achieved the planned statistical power of 90%. The results were robust to the sensitivity and subgroup analyses. Diagnosis of frozen shoulder can be challenging, and there is no reference standard for comparison.[6] Because the visual estimation of external rotation has fair to good reliability,[13] restrictions (typically with pain) in both passive and active external rotation have been used as diagnostic criteria in clinical studies.[7] This approach helped to ensure correct diagnoses in our study population. We also focused on delivering good standards of care, with surgeons using techniques with which they were familiar and most operations being conducted by consultant surgeons. Physiotherapy was delivered by qualified physiotherapists. Crucially, we standardised the physiotherapy pathway in all groups of the trial to reduce variations in care between participants and trial groups. All participants were provided with written advice detailing the home exercises that they needed to do.[20]

The main limitation of the study was that participants who had capsular release or manipulation had to wait longer to receive their treatment. However, our additional analysis incorporating different waiting times confirmed that this factor did not influence the main trial results. For participants who started treatment, it was reassuring that their OSS was stable between baseline and start of treatment, but it is possible that only participants with a more resistant frozen shoulder had surgery. This analysis is also limited, because it reflects treatment effects at pragmatic follow-up times, accounting for the different outcome trajectories, rather than observing what would have happened if all three trial treatments were delivered at similar times. Given the nature of the trial treatments, masking participants and clinicians to treatment allocation was not possible or desirable in this pragmatic trial. However, the absence of any subgroup effect of participant baseline treatment preferences on OSS might in part mitigate concerns about the lack of masking. A further potential threat to study validity was non-compliance with the treatments. However, the trial findings were consistent when analysed both as randomised (intention-to-treat)

and with CACE analysis. Finally, only 6% of UK practitioners were using hydrodilatation when we surveyed practice to inform the design of UK FROST and consequently, this was not identified as a priority intervention for evaluation.[10] Its popularity has increased since then, and although recent small trials have compared hydrodilatation with manipulation, capsular release, and intra-articular steroid injections,[33,34] evidence of its effectiveness is inconclusive.

In conclusion, all three treatments in our study led to substantial improvements in patient-reported shoulder pain and function. None of the treatments were clearly superior. Arthroscopic capsular release resulted in the least number of further treatments but carried higher risks and costs. The early structured physiotherapy pathway with steroid injection could be accessed quickly in the NHS, but more patients who had physiotherapy needed further treatment. Manipulation under anaesthesia was the most cost-effective option but with a longer waiting time to access than physiotherapy. These findings should help clinicians to discuss treatment options with patients during shared decision making and encourage surgeons to use capsular release more selectively when less costly and less invasive interventions fail.

Contributors

AR was the Chief Investigator and lead applicant. SDB, MN, LK, LG, CC, ID, SR, and ES contributed to trial conduct and data collection. AK and CH provided the statistical expertise, and BC and GR provided the health economics expertise. CS and FT led on the qualitative aspects of the study. SDB, LK, SR, and CMcD did the focused systematic review. AR, SDB, NH, SEL, SS, and DT provided expert trial methodological input. AR, CPC, AA, AB, AC, and JJD provided expertise as orthopaedic surgeons, LG, NH, and SEL provided expertise as physiotherapists, and SS provided expertise on patient-reported outcome measures. AR, SDB, AK, and BC led on writing the manuscript. All authors read, commented on, and approved the final manuscript.

UK FROST trial collaborators

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Declaration of interests

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Data sharing

All data requests should be submitted to the corresponding author (AR) for consideration as agreed in our publication plan. Access to anonymised data may be granted following review with the Trial Management Group and agreement of the chief investigator (AR). Related documents including the statistical analyses plan will be available on request.

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