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Corbacho Martín, Belén orcid.org/0000-0002-2359-0379, Brealey, Stephen Derek orcid.org/0000-0001-9749-7014, Keding, Ada orcid.org/0000-0002-1182-887X et al. (5 more authors) (Accepted: 2021) Cost-effectiveness of surgical treatments compared with early structured physiotherapy in secondary care for adults with primary frozen shoulder: economic evaluation of UK FROST trial. Bone & Joint Open. ISSN 2633-1462 (In Press)

Cost-effectiveness of surgical treatments compared with early structured physiotherapy in secondary care for adults with primary frozen shoulder: economic evaluation of UK FROST trial.

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APPENDIX

Table A Missing data: number and proportions of patients with complete data by treatment arm [18].

Complete at	ESP (N=99)	MUA (N=201)	ACR (N=203)
COMPLETE- HEALTH RELATED QUALITY OF LIFE			
Baseline	95 (95.96%)	199 (99.00%)	200 (98.52%)
3 months	88 (88.89%)	173 (86.07%)	175 (86.21%)
6 months	75 (75.76%)	172 (85.57%)	165 (81.28%)
12 months	86 (86.87%)	178 (88.56%)	175 (86.21%)
Overall	64 (64.65%)	156 (77.61%)	149 (73.40%)
COMPLETE - COSTS			
3 months	78 (78.79%)	164 (81.59%)	158 (77.83%)
6 months	71 (71.72%)	155 (77.11%)	150 (73.89%)
12 months	77 (77.78%)	161 (80.10%)	158 (77.83%)
Overall	55 (55.56%)	123 (61.19%)	121 (59.61%)
COMPLETE – BOTH HEALTH RELATED QUALITY OF LIFE AND COSTS			
3 months	76 (76.77%)	161 (80.10%)	154 (75.86%)
6 months	68 (68.69%)	152 (75.62%)	144 (70.94%)
12 months	75 (75.76%)	159 (79.10%)	157 (77.34%)
Overall	46 (46.46%)	117 (58.21%)	116 (57.14%)

Table B Missing data: description of economic variables in UKFROST [18].

		Missing values (%)						
		Total	ESP	MUA	ACR	Range	Mean	SD
BASELINE VARIABLES								
age	Age at trial entry	0	0	0	0	30 to 70	54.25	7.72
gender	Male or female	0	0	0	0	1,2	63% Female	
eq5d_B	EQ-5D-5L at baseline	1.79	4.04	0.99	1.48	-0.37 to 1.00	0.43	0.26
OSS_B	OSS score at baseline	0.40	0	0.50	0.49	1 to 48	19.89	8.25
Diabetes	Diabetic yes/no at baseline	0	0	0	0	1,3	70% No Dia.	
alloc	Treatment allocation	0	0	0	0	1,3		
OUTCOME VARIABLES FOR HEALTH RELATED QUALITY OF LIFE								
eq5d_3m	EQ-5D-5L at 3 months	13.32	11.1	13.9	13.8	-0.245 to 1.00	0.60	0.26
eq5d_6m	EQ-5D-5L at 6 months	18.09	24.2	14.4	18.7	-0.257 to 1.00	0.70	0.23
eq5d_12m	EQ-5D-5L at 12 months	12.72	13.1	11.4	13.8	-0.328 to 1.00	0.73	0.26
OUTCOME VARIABLES FOR COSTS								
Cost_ESP	Costs of ESP ^	0	0	0	0	59.8 to 768.4	279.46	148.8
Cost_MUA	Costs of MUA ^	0	0	0	0	259.2 to 972.0	424.81	115.5
Cost_ACR	Costs of ACR ^	0	0	0	0	877.3 to 3,082.3	2,170.46	431.1
Cost_PPP	Costs of physiotherapy ~	0	0	0	0	0 to 975.2	209.65	152.9
Cost_add	Additional treatments [a]	0	0	0	0	0 to 167.97	2.83	21.0
Cost_further	Further treatments [b]	0	0	0	0	0 to 1,521.87	41.41	204.2
Cost_other	Other treatments [c]	0	0	0	0	0 to 668	7.18	49.42
Cost_crossovers	Treat. after crossover [d]	0	0	0	0	0 to 125.01	0.50	7.87
Cost_Hosp_INP	Inp costs re complications[e]	0	0	0	0	0 to 4,926.24	32.85	312.1
Cost_Hosp_OUP	Out costs re complications[f]	0	0	0	0	0 to 875.07	19.37	82.71
Cost_GP_pr	Costs of GP visits (surgery)	33.0	37.4	31.8	32.0	0 to 822.8	57.26	110.6
Cost GP_phone	Costs of GP visits (phone)	34.2	38.3	32.3	34.0	0 to 197.6	6.33	23.01
Cost Nurse_pr	Costs of Practice Nurse	36.4	40.4	34.3	36.4	0 to 75.95	2.10	6.54
Cost_Nure_dis	Costs of District Nurse	33.8	37.4	32.8	33.0	0 to 380	1.94	21.69
Cost_Physio_c	Costs of District Physio	33.4	35.3	32.8	33.0	0 to 1,214.4	56.27	183.1
Cost_OT_c	Costs Occupational Therapist	16.9	16.2	16.4	17.7	0 to 282	0.67	13.79
OUTCOMES FOR COSTS EFFECTIVENESS								
Total_QALYs	Total QALYs over 1 year	26.6	35.3	22.4	26.6	-0.225 to 0.979	0.66	0.207
Total Costs	Total Costs over 1 year	40.5	44.4	38.8	40.4	0 to 5,732.54	1,372.36	1,095.99

^For those who had ESP/surgery (MUA/ARCR).

~ Costs of Post Procedure Physiotherapy for those who had surgery (MUA/ARCR).

a Any treatments received before/during receiving randomised treatment.
b Any treatments received after completing randomised treatment.
c Any non-trial treatments the patient had if they did not start/complete their randomised treatment.
d Cost of further treatments following crossover.
e Hospital inpatient stay costs related to complications.
f Outpatient hospital costs related to complications.
g Costs of Adverse event

Figure A. Post imputation distributions
A1. Total Costs post imnputation
A2. Total QALYs post imputation

Table C. Logistic regression for (i) missingness of costs and QALYs on baseline variables; and (ii) for missingness between missing costs and QALYs and observed outcomes [18].

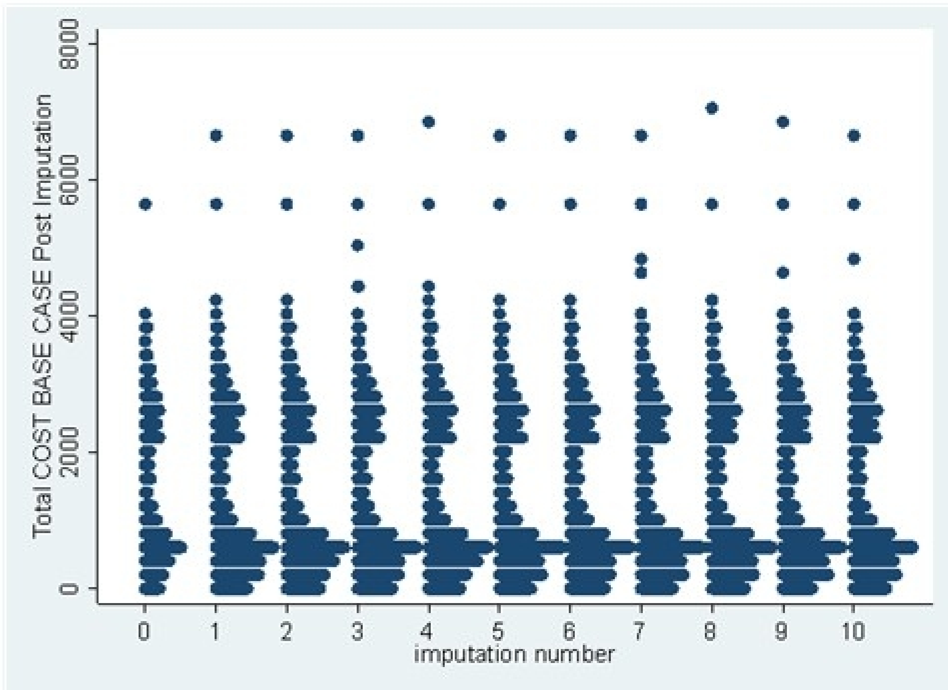
	Odds ratio in logistic regression for missing data (95% CI)	
	Missing data on costs	Missing data on QALYs
Treatment allocation ~ (MUA vs ESP)	0.80 (0.48 – 1.32)	0.60 (0.34 – 1.05)
Treatment allocation ~ (ACR vs ESP)	0.85 (0.52 – 1.41)	0.71 (0.41 – 1.23)
Gender	1.26 (0.85 - 1.88)	0.87 (0.55 – 1.37)
Age	0.99 (0.97- 1.01)	0.95 (0.93 – 0.98)**
Diabetes	1.11 (0.89 – 1.38)	1.06 (0.82 – 1.35)
EQ-5D at baseline	0.28 (0.14 – 0.57)**	0.31 (0.14 – 0.67)**
QALYs at 3 months	0.003 (0.00 to 0.09)**	0.00 (0.00 to 0.50)**
QALYs at 6 months	0.007 (0.00 to 0.306)**	0.15 (0.0001 to 1.15)
Costs at 3 months	1.00 (0.99 to 1.00)	0.99 (0.99 to 1.00)
Costs at 6 months	1.00 (0.99 to 1.00)	1.00 (0.99 to 1.00)

** statistically insignificant results (p>0.05)

Table D: Sensitivity analysis (Scenario 6): summary for incremental analysis (ITT), cost-effectiveness results and uncertainty of different methods to handle missing data (MUA vs ESP) [18].

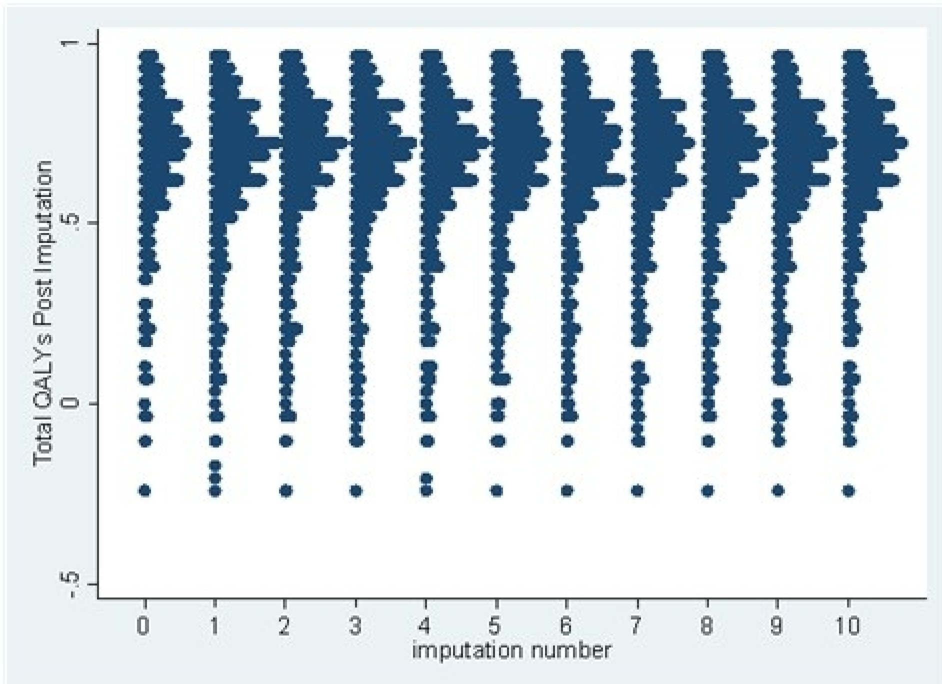
	Incremental cost (£) [95% CI]	Incremental QALYs [95% CI]	ICER (£ per QALY)	Probability Cost-effective at £20,000/QALY
MAR	276.507 ^ (65.67 to 487.35) 228.605 ~ (0.94 to 456.27)	0.0396 (-0.0008 to 0.0800) 0.0339 (-0.0138 to 0.0816)	6,984 6,750	88% 81%
Same MNAR parameters in MUA and ESP ~				
M1: -10% QoL in both arms	228.605 (0.94 to 456.27)	0.0414 (-0.0041 to 0.0868)	5,227	89%
M2: +10% cost in both arms	234.7271 (-6.91 to 476.36)	0.0339 (-0.0138 to 0.0816)	6,935	80%
M3: -50% QoL in both arms	228.605 (0.94 to 456.27)	0.0713 (0.0221 to 0.1206)	3,204	99%
M4: +50% cost in both arms	259.2152 (-52.66 to 571.09)	0.0339 (-0.0138 to 0.0816)	7,665	78%
M5: -10% QoL and +10% costs in both arms	234.7271 (-6.91 to 476.36)	.0413277 (-0.004 to 0.087)	5,680	88%

M6: -50% QoL and +50% costs in both arms	259.2152 (-52.66 to 571.09)	0.0710225 (0.0217 to 0.1203)	3,650	98%
Different MNAR parameters in MUA and ESP				
M7: -10% QoL in ESP	228.605 (0.94 to 456.27)	0.0559849 (0.010 to 0.102)	4,083	96%
M8: -10% QoL in MUA	228.605 (0.94 to 456.27)	0.0192851 (-0.0281 to 0.0667)	11,854	62%
M9: +10% cost in ESP	199.748 (-32.80 to 432.29)	0.0338503 (-0.0139 to 0.0816)	5,901	82%
M10: +10% cost in MUA	261.540 (28.02 to 495.06)	0.0338673 (-0.0138 to 0.0816)	7,722	79%
M11: -50% QoL in ESP	228.605 (0.94 to 456.27)	0.144459 (0.101 to 0.188)	1,582	99%
M12: -50% QoL in MUA	228.605 (0.94 to 456.27)	-0.0390401 (-0.0895 to 0.0114)	-5,856	3%
M13: +50% cost in ESP	84.318 (-171.7 to 340.42)	0.0337907 (-0.0139 to 0.0815)	2,495	87%
M14: +50% cost in MUA	393.28 (130.9 to 655.60)	0.0338787 (-0.014 to 0.082)	11,608	71%



Appendix Fig A1: Total Costs post imputation

82x60mm (150 x 150 DPI)



Appendix Fig A2:Total QALYs post imputation

82x60mm (150 x 150 DPI)

Cost-effectiveness of surgical treatments compared with early structured physiotherapy in secondary care for adults with primary frozen shoulder: economic evaluation of UK FROST trial.

Abstract

Background

A pragmatic multicentre randomised controlled trial (UK FROST) was conducted in the UK National Health Service (NHS) comparing the cost-effectiveness of commonly used treatments for adults with primary frozen shoulder in secondary care.

Methods

A cost utility analysis from the NHS perspective was performed. Differences between manipulation under anaesthesia (MUA), arthroscopic capsular release (ACR) and early structured physiotherapy plus steroid injection (ESP) in costs (2018 GBP) and quality adjusted life years (QALYs) at one year were used to estimate the cost effectiveness of the treatments using regression methods.

Results

ACR was £1,734 more costly than ESP [(95% confidence intervals (CI) £1,529 to £1,938)] and £1,457 more costly than MUA (95% CI £1,283 to £1,632). MUA was £276 (95% CI £66 to £487) more expensive than ESP. Overall, ACR had worse QALYs compared with MUA (-0·0293; 95% CI -0·0616 to 0·0030) and MUA had better QALYs compared with ESP (0·0396; 95% CI -·0008 to 0·0800). At a £20,000 per QALY willingness-to-pay threshold, MUA had the highest probability of being cost-effective (0·8632) then ESP (0·1366) and ACR (0·0002). The results were robust to sensitivity analyses.

Conclusions

While ESP was less costly, MUA was the most cost-effective option. ACR was not cost-effective.

INTRODUCTION

Adhesive capsulitis or frozen shoulder is a common disorder affecting 8.2% of men and 10.1% of women of working age [1], with an estimated cumulative incidence of 2.4 per 1000 population per year [2]. The capsule of the shoulder joint becomes inflamed, then scarred and contracted causing pain, stiffness and loss of function [3].

A range of treatment options of varying effectiveness and costs are available for the management of frozen shoulder in secondary care [4]. A survey of specialist health professionals conducted in the United Kingdom (UK) in 2009 identified three interventions as being most commonly used: physiotherapy; manipulation under anaesthesia; and arthroscopic capsular release [5]. The UK national physiotherapy guidelines for frozen shoulder recommends exercise and manual therapy either in isolation or to supplement with an intra-articular steroid injection [6]. Both manipulation under anaesthesia and capsular release are expected to facilitate quicker recovery but are costly and invasive and there is a lack of rigorous evidence [7-9].

The UK FROzen Shoulder Trial (UK FROST) was conducted to provide evidence of clinical effectiveness and cost-effectiveness of manipulation under anaesthesia, arthroscopic capsular release and a specific non-surgical pathway designed for the trial to include intra-articular steroid injection and structured physiotherapy using the best available evidence and consensus from expert shoulder physiotherapists [6,7,10]. We have called this 'Early' Structured Physiotherapy as it is more quickly accessible than the surgery interventions and the similarly developed pathway of post-procedural physiotherapy that followed surgery. Therefore, specifically for the purposes of the trial, participants underwent standardised physiotherapy programmes in all three groups as described in detail elsewhere, early structured physiotherapy in the non-surgical group and post-procedural physiotherapy in the tow surgical groups [11].

The clinical effectiveness results of UKFROST have been reported [12]. In summary, we sought a target difference of 5 points on the Oxford Shoulder Score (OSS) between early structured physiotherapy and either surgical treatment, or a difference of 4 points between the two surgical treatments. Mean group differences on the OSS at one year were 2·01 points between participants randomised to capsular release and manipulation under anaesthesia (95% confidence interval (CI) 0·10 to 3·91), 3·06 points between capsular release and early structured physiotherapy (95% CI 0·71 to 5·41), and 1·05 points between manipulation under anaesthesia and early structured physiotherapy (95% CI -1·28 to 3·39). All of the mean differences on the assessment of shoulder pain and function (OSS) at the primary endpoint of one year were less than the target differences. Therefore, none of the three interventions were considered to be clinically superior.

To inform decision-making, it is important to identify the cost-effective intervention for the treatment of frozen shoulder in secondary care. This paper reports on the economic evaluation conducted alongside the UK FROST trial, which aimed to assess the health-related quality of life, costs and cost-effectiveness of surgical treatments (manipulation under anaesthesia and capsular release followed by post-procedural physiotherapy) versus non-surgical treatment (early structured physiotherapy) for the management of adults with frozen shoulder within the NHS.

METHODS

Overview

Individual patient data (IPD) collected alongside the UK FROST trial were used to perform a cost utility analysis. Costs and health benefits were compared for the three groups over one year, and hence discounting was not required. Costs (2018 price base) were evaluated from the UK NHS and Personal Social Services perspective. Health benefits were expressed in terms of quality-adjusted life-years (QALYs), based on patient's health related quality of life using the EuroQol-5 Dimensions (EQ-5D-5L) [13,14]. Adjusted differences in mean costs and mean QALYs at one year were used to estimate the cost-effectiveness of the three treatment options. The base-case analysis was conducted on the multiple imputed dataset and followed an intention-to-treat (ITT) approach; thus the treatment groups were compared based on their initial random allocation irrespective of protocol deviations or withdrawal. The National Institute for Health and Clinical Excellence (NICE) guidelines were applied to all methods used for this economic analysis [15]. All analyses and modelling were conducted in StataTM 16 (StataCorp LP, College Station, Texas, USA).

Trial design, interventions, and economic data collection

UK FROST recruited 503 adults with a clinical diagnosis of frozen shoulder from 35 hospital sites in the UK between April 2015 and December 2017. Detailed inclusion and exclusion criteria are published elsewhere [16]. Patients were randomised on a 2:2:1 basis to manipulation under anaesthesia with steroid injection (n=201), arthroscopic capsular release (n=203) or early structured physiotherapy with steroid injection (n=99).

For the purposes of the trial, physiotherapy programmes were standardised in all three groups using the best available evidence and consensus of expert shoulder physiotherapists [6,7,10,11]. Physiotherapy in all three groups was to be up to 12 sessions unless exceptionally, the physiotherapist decided that more than 12 sessions were needed. Patients were also offered an intra-articular steroid (glucocorticoid) injection at the earliest opportunity in the early structured physiotherapy pathway. The injection was administered with or without imaging guidance depending on usual practice of the hospital site, as current evidence did not support superiority of either approach [17]. We did not anticipate that a steroid injection was normally given as part of post-procedural physiotherapy that followed the two surgical interventions. All participants were provided with instructions on a graduated home exercise programme progressing from gentle pendular exercises to firm stretching exercises according to stage, as is accepted good practice [6, 11]. The development of the standardised physiotherapy programmes for UK FROST are described in detail elsewhere [11].

Manipulation under anaesthesia and capsular release were performed as day case surgical procedures. With manipulation under anaesthesia, the surgeon manipulated the affected shoulder in a controlled fashion to stretch and tear the tight capsule when the patient was under general anaesthesia; and that was supplemented by an intra-articular steroid injection. If the manipulation was judged to be incomplete, the surgeons were asked not to cross-over intra-operatively to do capsular release in order to allow assessment of the outcome of the manipulation. Arthroscopic capsular release was performed under general anaesthesia to surgically divide the contracted anterior capsule in the rotator interval; and that was supplemented with manipulation to complete and confirm optimal capsular release. Procedures like posterior capsular release were permitted at the discretion of the operating surgeon and were recorded.

All interventions were delivered either by participating surgeons who were familiar with the surgical procedures or by qualified physiotherapists (i.e. not students or assistants). There was no minimum number of surgical procedures that the surgeon had to have performed and no grades of surgeon were excluded. No additional training was required for either programme of physiotherapy. However, a standardised booklet was used to record the physiotherapy that participants received in all three trial arms which provided instructions for delivering the early structured physiotherapy or post-procedural physiotherapy pathways.

NHS ethical approval was obtained on 18 November 2014 from the National Research Ethics Service (NRES Committee North East – Newcastle & North Tyneside 2; Research Ethics Committee Reference 14/NE/1176). 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). Written informed consent was obtained from all trial participants by suitably qualified local study personnel at each participating site.

As detailed in the trial protocol [16], cost and health outcome data were collected prospectively via patient questionnaires at three months, six months and one year; and via hospital forms (baseline characteristics, details of surgery, physiotherapy, complications, and hospital care due to additional and further treatments received before/during/after completing randomised treatment). Copies of these forms will be included in Supplementary Material published alongside the NIHR Health Technology Assessment report [18].

Health outcomes and quality adjusted life-years

The main outcome measure for the economic analysis was QALYs based on the EQ-5D-5L questionnaire. The EQ-5D has been validated for a range of shoulder conditions [19, 20]. The EQ-5D-5L was completed by trial participants at baseline, three and six months and one year. The EQ-5D-5L defines health related quality of life in terms of five dimensions: ‘mobility’, ‘self-care’, ‘usual activities’, ‘pain/discomfort’ and ‘anxiety/depression’. Responses in each dimension are divided into five ordinal levels coded (1) no problems, (2) slight problems, (3) moderate problems, (4) severe problems and (5) extreme problems/unable to perform. We used the Van Hout et al. 2012 mapping function to derive utilities [21]. QALYs were calculated by combining the utility estimates by the duration of time in each health state using the area under the curve (AUC) method [22]. The difference in mean QALYs between treatments groups was adjusted for baseline utility [23].

Resource use and costs

The cost for each trial participant was calculated by multiplying health care resource use by the associated unit costs. Total cost comprises the cost of the initial intervention; hospital stays and outpatient appointments after initial intervention, including physiotherapy; and visits to primary and community health care professionals over one year. Costs relating to the surgical interventions was based on operation times, staff, consumables, and length of stay. The hospital-based staff cost per minute was estimated using PSSRU 2018 (Personal Social Services Research Unit) data [24]. These unit cost estimates included staff salaries, salary on-costs, overheads, and capital overheads. Drug tariff per milligram for medications (i.e. anaesthesia, antibiotics, and steroid injections) were obtained from the British National Formulary [25]. To cost length of stay we used NHS Reference costs [26] taking the weighted average inpatient bed-day for all major and intermediate shoulder procedures. Physiotherapy data (i.e. session duration and staff delivering the session) was collected using physiotherapy forms designed for the trial. Physiotherapists cost per hour was estimated using PSSRU 2018 (Bands 5 to 8). The cost of other hospital-based care and for the primary care and community-based services were estimated by applying unit costs from national tariffs to resource volumes. Other costs included lost productivity measured as number of days off work. The costs of time taken off work were estimated by applying costs from the Office National Statistics (ONS) [27] to occupational information derived from self-reported work status information. Table 1 presents the unit costs used to calculate the total cost per patient in the trial. The base-case analysis included only shoulder related resource use, except for hospital stay, which included both shoulder and general medical complications that could apply to the affected shoulder.

Table 1 Unit costs used for the analysis (£, 2018 prices) [18].

Item	Unit cost (£)	Source
PRIMARY AND COMMUNITY CARE		
GP visit at GP practice	37	PSSRU 2018 [23]
GP visit at home	94	PSSRU 2018 [23]
GP by phone [a]	15	PSSRU 2018 [23]
Nurse visit at GP practice	11	PSSRU 2018 [23]
District/ community nurse	38	PSSRU 2018 [23]
Occupational therapist visit	47	PSSRU 2018 [23]
Physiotherapist visit [b]	57	PSSRU 2018 [25]
HOSPITAL CARE		
Inpatient stay (shoulder) [c]	258 (MUA) 449 (ACR)	NHS Reference Costs 2017-2018 [25]
Inpatient stay (non-shoulder)	384	NHS Reference Costs 2017-2018 [25]
Day case visit (shoulder) [c]	420 (MUA) 2,512 (ACR)	NHS Reference Costs 2017-2018 [25]
Outpatient visits (shoulder)	125	NHS Reference Costs 2017-2018 [25]
Outpatient visits (non-shoulder)	124	NHS Reference Costs 2017-2018 [25]
Hospital physiotherapy visit	55	NHS Reference Costs 2017-2018 [25]
Other health service visit	74	NHS Reference Costs 2017-2018 [25]
Consultant surgical	108	PSSRU 2018 [23]
Associate specialist	105	PSSRU 2018 [23]
Speciality Registrar	43	PSSRU 2018 [23]
Foundation doctor FY1	32	PSSRU 2018 [23]
Foundation doctor FY2	28	PSSRU 2018 [23]
Physiotherapist B5	35	PSSRU 2018 [23]
Physiotherapist B6	46	PSSRU 2018 [23]
Physiotherapist B7	55	PSSRU 2018 [23]
Physiotherapist above B8 [d]	72	PSSRU 2018 [23]
Nurse B5	37	PSSRU 2018 [23]
Nurse B6	45	PSSRU 2018 [23]
Nurse B7	54	PSSRU 2018 [23]
MEDICATIONS		
Depomedrone 40mg	3	BNF [24]
Depomedrone 80mg	7	BNF [24]
Triamcinolone 40mg	18	BNF [24]
Triamcinolone 80mg	36	BNF [24]

Bupivacaine 0.5% (10ml)	1	BNF [24]
General anaesthesia	31	BNF [24]
Antibiotics	6	BNF [24]
PRIVATE CARE		
Private Non-NHS physiotherapy	50	https://www.capitalphysio.com
Private osteopath	42	https://www.nhs.uk/conditions/osteopathy
Private chiropractitioner	55	https://www.nhs.uk/conditions/chiropractic
Community care service	49	Averaged of three above
Private hospital - night	337	PSSRU 2018 [23]

[a] Durations sourced from Personal Social Research Unit (PSSRU) 2015. [b] Community Health Services, Physiotherapist, adult, one to one (currency code A08A1). [c] Sum of total expenditure on excess bed days (elective and non-elective) divided by total activity for HRG codes relating to shoulder: MUA (HD24E; non inflammatory, bone or joint disorders, with CC score 8-11)); ACR (HN53A, HN53B, HN53C, HN54A, HN54B, HN54C; major and intermediate procedures for non-trauma with CC score 4+, 2-3 and 0-1). [d] PPP form is featured to record staff at or above Band 8. Hence unit cost for physio at or above Band is estimated as averaged Band 8a (£66) and Band 8b (£78).

Handling missing data

We have previously reported details of the approach applied to handle missing data [18, 28] and we have used the same methods in this study, as described below. Complete case analysis (CCA) excludes all participants with any missing or incomplete data. Excluding patients with missing data leads to loss of statistical power and can bias the results [29]. Multiple imputation (MI) has been recommended as the appropriate method to reflect the uncertainty in the results of an economic evaluation attributable to missing data [30]. Multiple imputation assumes that data are missing at random (MAR), i.e. that the probability that data is unobserved is dependent only on observed variables [31]. We conducted a comprehensive investigation following missing data guidelines [29, 32, 33] to prove that MAR was a plausible assumption fitting UK FROST dataset. Thus, incomplete data on costs and QALYs were imputed using MI with chain equations and predictive mean matching over 60 imputations. Age, sex, baseline OSS score, diabetes (yes/no) at baseline, baseline utility and all predictors of missingness were included as an explanatory variable in the imputation models. Mean estimates of costs and QALYs, variances and CI were obtained using Rubin's rules [34]. The MI model was validated using graphical plots to visualise whether the distribution of imputed data resembles the distribution of original data. We explored possible departures from the MAR assumption by means of sensitivity analyses, including complete case analysis. this Additionally, a mixed model, which does not require an imputation process, is also presented as per the sensitivity analysis.

Base Case analysis

The base case analysis was conducted on the imputed dataset on an ITT basis. Cost-effectiveness was estimated as the difference in mean costs divided by the difference in mean QALYs between the trial comparators at twelve months follow-up, using conventional decision rules and estimating incremental cost-effectiveness ratios (ICERs) as appropriate [35]. The mean difference estimates and their 95% CI were generated by means of seemingly unrelated regression (SUREG) adjusted for age, sex, baseline EQ-5D-5L score, baseline OSS score and diabetes (yes/no). In order to compute the probability of each intervention being cost-effective at a given cost-effective threshold, the SUREG was conducted with a bootstrapping approach on five imputed datasets to generate 10,000 replicates of incremental costs and benefits. These replicates were represented graphically as cost-effectiveness acceptability curves (CEACs). The probability that each intervention is cost-effective is reported at the cost-effectiveness thresholds applied by NICE of £20,000 to £30,000/QALY [14], and a threshold of £13,000/QALY as suggested by recent research [36,37]. The ICER was re-expressed in terms of net monetary benefit (NMB) as an estimate of the gain (or loss) in resources of investing in the intervention when those resources might be used somewhere else.

Analyses of uncertainty

The uncertainty around the cost effectiveness results was explored using sensitivity analyses all of which controlled for the same covariates: (Scenario1) recalculating costs including non-shoulder costs (ITT approach); (Scenario 2) adopting a broader perspective that includes productivity and private care costs; (Scenario 3) restricting the analyses to complete cases (ITT approach); (Scenario 4) imputing QALY data at aggregated level rather than at the index-score level; (Scenario 5) mix model approach; and (Scenario 6) missing not at random scenario, which allocated higher costs or worse health outcomes to patients with missing data.

RESULTS

Study population and missing data

The baseline study population for the economic analysis was 503 patients: early structured physiotherapy (n=99), manipulation under anaesthesia (n=201) and capsular release (n=203). A total of 19 participants fully withdrew from the trial for whom we used multiple imputation techniques to impute missing economic data. There were 16 participants who crossed over from their initial randomisation i.e. from early structured physiotherapy to capsular release (n=7), from manipulation under anaesthesia to early structured physiotherapy (n=4), from capsular release to early structured physiotherapy (n=2) and from capsular release to manipulation under anaesthesia (n=3). A total of 369 (73%) participants [156 (78%) in manipulation, 149 (73%) in capsular release, and 64 (65%) in early structured physiotherapy] comprised the complete case for utilities i.e. data for all five EQ-5D-5L dimensions were available for all four assessment time points. Overall, the proportion of participants with complete economic data (i.e. both costs and QALYs) were similar between treatment groups:

early structured physiotherapy (46.46%), manipulation under anaesthesia (58.21%) and capsular release (57.14%) (see Appendix, Table A).

A description of economic variables in UK FROST and figures representing the distribution of economic data before and after the imputation can be found in the Appendix (Table B, Figure A). Missing data was non-monotonic, since in all groups, individuals with missing data at one follow-up point may provide data subsequently (i.e. more individuals are observed at year one than in month 6). The results of logistic regression analysis (see Appendix, Table C) showed that participants with lower EQ-5D-5L at baseline were significantly more likely to have missing data on costs (OR 0.28; 95% CI 0.14 to 0.57) and QALYs (OR 0.31; 95% CI 0.14 to 0.67). Baseline age predicted missing data on quality of life (OR 0.95; 95% CI 0.93 to 0.98); sex and diabetes were associated with missingness but not statistically significant (p> 0.05). Regarding the association between missingness and the observed outcomes, missing QALYs at one year were significantly associated with QALYs at three months (OR 0.00; 95% CI 0.00 to 0.50); whilst missing costs at one year were significantly associated with QALYS at three months (OR 0.003; 95% CI 0.00 to 0.09) and QALYs at six months (OR 0.007; 95% CI 0.00 to 0.306).

Health care resource use and costs

The mean cost of manipulation under anaesthesia was £425 (SD=£115). For 97% of the cases manipulation was delivered as a day case, only 3% of the cases required hospitalization (only one night); the average duration of the manipulation was 25.11 minutes (SD=14.20). The mean cost of arthroscopic capsular release was £2,170 (SD=£431). For 90% of the cases it was delivered as a day case; 10% of the cases required hospitalization for on average 2.8 nights (median=1; min=1; max=31) in hospital; and the average duration of the intervention was 76.61 min (SD=24.22). A total of 160 (80%) participants allocated to manipulation under anaesthesia and 159 (78%) allocated to capsular release received post procedural physiotherapy. The mean (SD/max) number of sessions was similar for both groups [manipulation under anaesthesia: 6.42 (4.95/18) vs capsular release: 6.65 (4.81/18)]. The mean (SD) cost of post procedural physiotherapy was £214 (£157) for manipulation under anaesthesia compared with £209 (£153) for capsular release. A total of 162 (97%) patients who had manipulation under anaesthesia received an injection compared with 46 (27%) who received capsular release. The mean cost of early structured physiotherapy was £260 (SD=£155) [i.e. mean cost of physiotherapy was £217 (SD=£147); mean cost of a steroid injection was £43 (SD=£32)]. A total of 85 (86%) patients who had early structured physiotherapy received an injection as part of their treatment. The mean (SD) number of sessions received in the early structured physiotherapy pathway was 8.28 (3.45), with a maximum of 15 sessions and a minimum of two.

Resource use related to primary and community care was slightly higher for the capsular release group, although differences between the groups appeared small (Table 2). Over the entire follow up period, a higher proportion of participants in the capsular release group had more days lost off work. Inpatient hospital costs related to complications after initial treatment up to one year was greater for the manipulation group. However, participants who received early structured physiotherapy were more likely to need further treatment following their index intervention and accumulated greater outpatient costs after discharge. Participants in the capsular release group received fewest further treatments, however, they accumulated greater total costs over the trial follow-up; as expected, costs of the surgery were the major cost driver for this group (Table 3). Participants waited a median of 14 days for early structured physiotherapy, median of 56·5 days for manipulation under anaesthesia, and a median of 71·5 days for capsular release [11]. The longer waiting times were reflected in the actual days off work and increased productivity costs which were greater for the capsular release arm. Private costs were similar among the three arms. To note that total costs estimates shown in Table 3 are unadjusted means, and relates to complete cases, therefore there is limited value in interpreting differences between treatments. Mean differences for each surgical treatment versus early structured physiotherapy and corresponding 95% CIs, adjusted for patient covariates, and taking into consideration the correlation between costs and QALYs are shown in Table 4 (i.e. cost-effectiveness results).

Table 2 – Average primary and community resource use (shoulder related) and lost days off work per treatment group [18].

Resource Type	MUA (n=201)				ACR (n=203)				ESP (n=99)			
	N	Mean (SD)	Median	Missing (%)	N	Mean (SD)	Median	Missing (%)	N	Mean (SD)	Median	Missing (%)
GP surgery Total	**137**	**1.61 (3.04)**	**0**	**64 (31.8)**	**138**	**1.73 (3.23)**	**0**	**65 (32.0)**	**62**	**0.90 (1.89)**	**0**	**37 (37.4)**
3 months	168	0.82 (1.64)	0	33 (16.42)	171	1.05 (1.97)	0	32 (15.76)	84	0.58 (1.44)	0	15 (15.15)
6 months	162	0.30 (1.25)	0	39 (19.40)	163	0.49 (1.60)	0	40 (19.70)	76	0.35 (0.89)	0	23 (23.23)
12 months	169	0.34 (1.20)	0	64. (31.84)	162	0.24 (0.76)	0	65 (32.02)	80	0.25 (0.88)	0	37 (37.37)
GP telephone Total	**136**	**0.54 (2.05)**	**0**	**65 (32.3)**	**134**	**0.44 (1.1)**	**0**	**69 (33.9)**	**61**	**0.10 (0.47)**	**0**	**38 (38.4)**
3 months	168	0.28 (1.24)	0	3 (16.42)	165	0.32 (0.99)	0	28 (18.72)	82	0.06 (0.33)	0	17 (17.17)
6 months	162	0.16 (1.13)	0	39 (19.40)	161	0.09 (0.41)	0	42 (20.69)	74	0.03 (0.16)	0	25 (25.25)
12 months	168	0.05 (0.17)	0	33 (16.42)	162	0.03 (0.22)	0	41 (20.20)	83	0.01 (0.011)	0	16 (16.16)
Physiotherapist	**135**	**0.83 (2.8)**	**0**	**66 (32.8)**	**136**	**1.25 (3.8)**	**0**	**67 (33.0)**	**64**	**1.17 (4.0)**	**0**	**35 (35.3)**
3 months	167	0.66 (2.26)	0	34 (16.92)	167	0.64 (2.95)	0	36 (17.73)	83	0.42 (1.72)	0	16 (16.16)
6 months	161	0.14 (0.79)	0	40 (19.90)	161	0.31 (1.24)	0	42 (20.69)	77	0.49 (2.25)	0	22 (22.22)
12 months	170	0.71 (0.92)	0	31 (15.42)	162	0.31 (1.32)	0	41 (20.20)	83	0.24 (0.22)	0	16 (16.16)
Nurse surgery	**132**	**0.07 (0.3)**	**0**	**69 (34.3)**	**129**	**0.39 (0.8)**	**0**	**74 (36.4)**	**59**	**0.05 (0.3)**	**0**	**40 (40.4)**
3 months	166	0.2 (0.15)	0	35 (17.41)	165	0.34 (1.09)	0	38 (18.72)	79	0.05 (0.32)	0	20 (20.20)
6 months	160	0.01 (0.08)	0	41 (20.40)	156	0.08 (0.30)	0	47 (23.15)	75	0.04 (0.26)	0	24 (24.24)
12 months	165	0.05 (0.29)	0	36 (17.91)	160	0.02 (0.14)	0	43 (21.18)	79	0 (0)	0	20 (20.20)
Community nurse	**135**	**0 (0)**	**0**	**66 (32.8)**	**136**	**0.12 (0.9)**	**0**	**67 (33.0)**	**62**	**0 (0)**	**0**	**37 (37.4)**
3 months	168	0 (0)	0	33 (16.42)	168	0.07 (0.51)	0	35 (17.24)	83	0 (0)	0	16 (16.16)
6 months	160	0 (0)	0	41 (20.40)	161	0.07 (0.79)	0	42 (20.69)	75	0 (0)	0	24 (24.24)
12 months	170	0.01 (0.15)	0	31 (15.42)	161	0 (0)0		42 (20.69)	82	0 (0)	0	17 (17.17)
Occupational Therapy	**137**	**0.09 (0.7)**	**0**	**64 (31.8)**	**137**	**0.06 (0.7)**	**0**	**66 (32.5)**	**63**	**0 (0)**	**0**	**36 (36.4)**
3 months	168	0.03 (0.46)	0	33 (16.42)	167	0 (0)	0	36 (17.73)	83	0 (0)	0	16 (16.16)
6 months	161	0 (0)	0	40 (19.90)	162	0.01 (0.08)	0	41 (20.20)	76	0 (0)	0	23 (23.23)
12 months	171	0.05 (0.48)	0	32 (15.92)	162	0.05 (0.63)	0	41 (20.20)	82	0 (0)	0	19 (19.19)
Lost days off work	**105**	**17.5 (26.4)**	**6**	**96 (47.8)**	**92**	**32.8 (44.2)**	**14**	**111 (54.)**	**34**	**11.5 (27.8)**	**0**	**65 (65.6)**
3 months	138	12.5 (22.0)	2	63 (31.34)	125	13.3 (23.6)	0	78 (38.42)	61	7.2 (20.6)	0	38 (38.38)
6 months	132	3.5 (10.5)	0	69 (34.32)	125	10.9 (23.2)	0	78 (38.42)	50	5.2 (18.8)	0	49 (49.49)
12 months	138	2.8 (13.3)	0	63 (31.34)	129	3.1 (13.1)	0	74 (36.45)	57	3.9 (13.1)	0	42 (42.42)

Table 3 Costs for cases with complete data by trial allocation and cost category (£, 2018-19 prices) related to the shoulder [18].

Costs	**MUA Mean (SE) (£)**	**ACR Mean (SE) (£)**	**ESP Mean (SE) (£)**
MUA surgical procedure	349 (192)	5 (56)	0
ACR surgical procedure	0	1,762 (935)	113 (496)
ESP	7 (59)	1 (13)	260 (155)
Physiotherapy Hospital setting (i.e. PPP)	176 (164)	175 (162)	7 (36)
Physiotherapy Community setting	44 (146)	66 (202)	62 (211)
Further treatments	60 (248	18 (67)	104 (290)
Hospital Inpatient care	43 (361)	34 (334)	9 (48)
Hospital outpatient care	19 (84)	12 (61)	34 (113)
GP at surgery	60 (114)	65 (121)	34 (71)
GP on the phone	8 (31)	7 (17)	1 (7)
Nurse at surgery	1 (3)	4 (9)	0.5 (3)
Community nurse	0 (0)	5 (34)	0 (0)
Occupational therapist	4 (34)	3 (32)	0 (0)
Total NHS shoulder costs (a)	**834 (753)**	**2,271 (902)**	**599 (359)**
Total NHS non- shoulder costs – (b)	182 (229)	196 (304)	242 (366)
Productivity costs – (c)	1,995 (2,999)	3,736 (5,031)	1,309 (3,165)
Private care costs – (d)	31 (118)	21 (111)	40 (144)
Total broader costs (a+b+c+d)	3,201 (3,824)	5,377 (4,240)	1,475 (2,368)

Health outcomes and quality adjusted life-years

The overall distribution of the EQ-5D scores (utilities) for the different follow-up assessments is illustrated in Figure 1. Patients allocated to manipulation under anesthesia started from a higher utility value compared to the other groups [manipulation (mean 0.456) vs capsular release (mean 0.428) vs early structured physiotherapy (mean 0.402)]. Patients allocated to the surgical groups had similar utility values (adjusted for baseline utility) at 12 months follow up [capsular release (mean 0.739) vs manipulation under anaesthesia (mean 0.734)]; both manipulation under anaesthesia and capsular release had better utility values compared to early structured physiotherapy at 12 months (mean 0.693). QALYs estimates at one year, when controlling for baseline utility (for available cases), shows that patients allocated to manipulation under anaesthesia accrued more QALYs than the other two groups: manipulation under anaesthesia (0.6765) > early structured physiotherapy (0.6492) > capsular release (0.6475).

Figure 1

Cost-effectiveness analysis

The incremental analysis for the base-case is summarised in Table 4. Compared to early structured physiotherapy, manipulation under anaesthesia cost a mean of £276 more per patient (95% CI £66 to £487) and marginally improved health outcomes over the 12 months [on average 0.0396 more QALYs per participant than structured physiotherapy (95% CI -

0.0008 to 0.0800)]. The resulting ICER for manipulation under anaesthesia was £6,984 per additional QALY when compared to early structured physiotherapy. Arthroscopic capsular release is considerably more costly than early structured physiotherapy [on average £1,734 more expensive per participant (95% CI (£1,529 to £1,938)]; and despite the QALY gained by capsular release participants [on average 0.0396 more QALYs per participant than physiotherapy (95% CI -0.0008 to 0.0800)] this was not sufficient to support capsular release as being a cost-effective use of NHS resources when compared with early structured physiotherapy. Similarly, capsular release is dominated by manipulation under anaesthesia, with higher mean costs and lower QALYs. As illustrated by the CEAC in Figure 2, at a £20,000 per QALY threshold the probability of manipulation under anaesthesia being cost-effective was high (86%) compared with early structured physiotherapy (13%) and capsular release (0%)

Table 4. Adjusted mean differences in costs and QALYs between interventions (base case) [18].

	Adjusted difference in means with SUREG[a]	**95% confidence limits (CI)**		
Difference in costs (£)				
MUA vs ESP	276.51	(65.67 to 487.35)		
ACR vs ESP	1,733.78	(1,529.48 to 1,938.06)		
ACR vs MUA	1,457.26	(1,282.73 to 1,631.79)		
Difference in QALYs				
MUA vs ESP	0.0396	(-0.0008 to 0.0800)		
ACR vs ESP	0.0103	(-0.0304 to 0.0510)		
ACR vs MUA	-0.0293	(-0.0616 to 0.0030)		
	ICER [b] (£ per QALY)	**Probability cost-effective at £13,000/QALY**	**Probability cost-effective at £20,000/QALY**	**Probability cost-effective at £30,000/QALY**
MUA	6,984	0.7942	0.8632	0.8978
ACR	> 100,000	0.0000	0.0002	0.002
ESP	-	0.2058	0.1366	0.1002

[a] Seemingly unrelated regression. [b]Compared with ESP, as it is the alternative with lower costs and health outcomes

Figure 2

Sensitivity analysis

Table 5 shows that the base case analysis results were robust to including non-shoulder costs with manipulation under anaesthesia continuing to be a cost-effective use of NHS resources. In contrast, cost-effectiveness results were sensitive to a broader perspective scenario, suggesting the ICER from a wider perspective was higher than the thresholds that NICE normally consider for reimbursement decisions. Capsular release continued to be dominated by manipulation under anaesthesia in both costs' scenarios. Given that capsular release was dominated in all scenarios, sensitivity analyses around missing data were restricted to the comparison of manipulation under anaesthesia compared with early structured physiotherapy (Table 6). Both multiple imputation and the mixed model agree that manipulation under anaesthesia is the cost-effective alternative, although mean difference in costs and QALYs changed according to the method. The mixed model has slightly larger standard errors than MI in both the incremental costs and QALYs, possibly because of the large number of parameters to estimate compared with the analysis model post-imputation. Finally, increasing costs or decreasing QALYs (scenario 6) in both patient groups make little difference to results (see Appendix, table D). Manipulation under anaesthesia remains the intervention most likely to be cost-effective even if their imputed QALYS are reduced by 10% or its cost is increased by 50%.

Table 5 Sensitivity analysis (Scenario 1 and Scenario 2): Summary for incremental analysis (ITT), cost-effectiveness results and uncertainty under different costs scenarios [18].

		MI of costs (shoulder – NHS perspective) and QALYs analysis with SUREG^ Base-Case analysis	MI of costs (shoulder and non-shoulder – NHS perspective) and QALYS analysis with SUREG SA (Scenario 1)	MI of costs (broader perspective) and QALYS analysis with SUREG SA (Scenario 2)
MUA vs ESP				
Difference in costs (£)	**Mean**	276	163	1,032
	SE	107	113	595
	95% CI	66 to 487	-58 to 384	-137 to 2,201
Difference in QALYs	**Mean**	0.039	0.0375	0.0375
	SE	0.0206	0.0207	0.0207
	95% CI	-0.001 to 0.080	-0.0032 to 0.0782	-0.0032 to 0.0781
	ICER	6,984	4,336	27,522
ACR vs ESP				
Difference in costs (£)	**Mean**	1,734	1,555	4,110
	SE	104	112	648
	95% CI	1,529 to 1,938	1,335 to 1,775	2,836.20 to 5,383.73
Difference in QALYs	**Mean**	0.0103	0.0080	0.0081
	SE	0.0207555	0.0208	0.0208
	95% CI	-0.0304 to 0.0510	-0.0328 to 0.0488	-0.0327 to 0.0488
	ICER	168,613	194,895	507,707
ACR vs MUA				
Difference in costs (£)	**Mean**	1,457	1,393	3,078
	SE	89	91	548
	95% CI	1,282.73 to 1,631.79	1,213 to 1,572	1,999 to 4,157
Difference in QALYs	**Mean**	-0.0293	-0.0296	-0.0294
	SE	0.0164678	0.0165	0.0165
	95% CI	-0.0616 to 0.0030	-0.0619 to 0.0028	-0.0618 to 0.0030
	ICER	ACR dominated by MUA	ACR dominated by MUA	ACR dominated by MUA

^ Seemingly unrelated regression.

Table 6: Sensitivity analysis (Scenario 3, Scenario 4 and Scenario 5): Summary for incremental analysis (ITT), cost-effectiveness results and uncertainty under different missing data assumptions [18].

		Complete case analysis with SUREG^ (Scenario 3)	MI of costs and utilities followed by SUREG (Scenario 4)	Mixed model with adjustment for covariates (Scenario 5)
Difference in costs (£)	**Mean**	339	193	256
	SE	136	107	129
	95% CI	72 to 606	-14 to 399	2 to 509
Difference in QALYs	**Mean**	0.016	0.0357	0.030
	SE	0.026	0.020	0.022
	95% CI	-0.034 to 0.066	(-0.004 to 0.076)	-0.014 to 0.073
	ICER	21,443	5,395	8,562
Probability that MUA is cost-effective		0.48	0.89	0.76

^ Seemgly unrelated regression.

DISCUSSION

Main findings

UK FROST is the largest randomised clinical trial to our knowledge to date that provides robust evidence on the cost-effectiveness of common surgical interventions followed by post-procedural physiotherapy compared with a non-surgical pathway of early structured physiotherapy and steroid injection for the treatment of patients with a frozen shoulder. Participants' health related quality of life improved with all three treatments during the trial follow-up. Overall, participants who had manipulation under anaesthesia accrued more QALYs compared to those who had capsular release and early structured physiotherapy. The greater costs of capsular release make this intervention difficult to justify. In particular, capsular release was dominated by manipulation, with higher mean costs and lower QALYs. Compared to early structured physiotherapy, participants who had capsular release accrued on average more QALYs, but this was not sufficient to support capsular release as a cost-effective alternative to early structured physiotherapy. At a £20,000 per QALY threshold the probability of manipulation under anaesthesia being cost-effective was high (86%) compared with early structured physiotherapy (13%) and capsular release (0%). Therefore, from an NHS perspective, this is clear evidence that manipulation under anaesthesia is the most cost-effective option and would represent good value for money.

Strengths and weaknesses

This analysis presents an up to date estimate of the cost-effectiveness of three common treatment pathways for the management of frozen shoulder in the NHS setting. The strengths of this study were the pragmatic design and the recruitment of patients from 35 hospitals across a range of rural and urban areas, involving 90 surgeons and 285 physiotherapists. There were minimal exclusion of patients and the rate of crossovers were low. We also used very detailed hospital forms designed for the trial, together with multiple sources of cost data available for the analyses, to permit an exhaustive micro-costing to optimise the accuracy of the estimation of the treatment costs. The UK FROST trial, therefore, provides timely and direct evidence of clinical and resource implications for the NHS that may also be generalisable to other healthcare systems that offer these treatment options.

The EQ-5D instrument has been well validated in patients with a frozen shoulder [18,19]. However, a systematic review identified a lack of use of generic preference-based measures in existing frozen shoulder clinical studies [7]. The elicitation of the EQ-5D-5L from patients with frozen shoulder is another strength of our study, providing further evidence on the impact of this condition on patient's overall health related quality of life.

There are two potential limitations with the analysis. The first relates to the problem of missing data, which is a common issue in economic evaluations nested within clinical trials. We conducted a comprehensive analysis of missing data and a number of sensitivity analyses to test the assumptions we used to impute missing data in our economic models. Sensitivity analyses showed that results were robust to alternative assumptions on missing data, indicating that manipulation under anaesthesia continued to be a cost-effective use of NHS resources. It is therefore highly unlikely that such assumptions regarding missing data will change the conclusions of our analysis.

The second limitation relates to the length of follow-up, as one year could be argued to be too short to capture the full effects of all the treatments. Clinical effectiveness results showed 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), compared with an initial median overall OSS of 20 points [11]. It is notable that the difference in OSS scores and the difference in quality of life are found in the same direction, with only a small difference in QALYS observed across groups. It could be argued that there is a possible trend of the capsular release group improving over time, which might continue with longer time follow up. This could be explained by the timing of the delivery of the interventions. However, additional analysis adjusting for delivery times of interventions confirmed this did not alter the interpretation of the primary findings, which in turn, also suggests that it is unlikely that any important difference in QALYs would emerge beyond the trial follow-up [12]. Regarding costs, we are confident that important costs, including costs of complications, have been captured during the trial follow-up.

It is important to consider that all three treatment groups received standardised physiotherapy specifically designed for the purposes of the trial. This is likely to have resulted in patients receiving more physiotherapy and possibly steroid injections in the early structured physiotherapy pathway than would be received routinely in the NHS and consequently increased its costs. More physiotherapy, however, was also likely to have been received in both the surgical pathways than that provided in the NHS. Furthermore, the rationale for the number of physiotherapy sessions that patients were encouraged to receive in the early structured physiotherapy intervention was to give every opportunity for the physiotherapy to be effective. Despite this, early structured physiotherapy was not found to be clinically superior compared with the surgical treatments or to be the most cost-effective option to the NHS.

Finally, it should be noted that this study did not take into consideration the economic impact of hydrodilatation. This is because when we undertook a survey of practice to inform the design of UK FROST, only 6% of UK practitioners were using hydrodilatation. Consequently, this was not identified as a priority intervention for evaluation [38]. Its popularity has increased since then, and although hydrodilatation has been compared with manipulation, capsular release, and intra-articular steroid injections [39,40] evidence of its effectiveness and cost-effectiveness is inconclusive.

Conclusions

To the best of our knowledge there is very limited evidence regarding the cost-effectiveness of the three commonly used treatments for the frozen shoulder that were compared in UK FROST. We found that while our specifically designed non-surgical pathway of early structured physiotherapy and steroid injection was the least costly intervention, manipulation under anaesthesia was the most cost-effective management pathway for the NHS as the extra cost was good value for money for the benefits gained by patients. Evidence presented from this economic evaluation should help clinicians 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.

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Figure 1 EQ-5D-5L scores distribution at the different time points over the 12 months

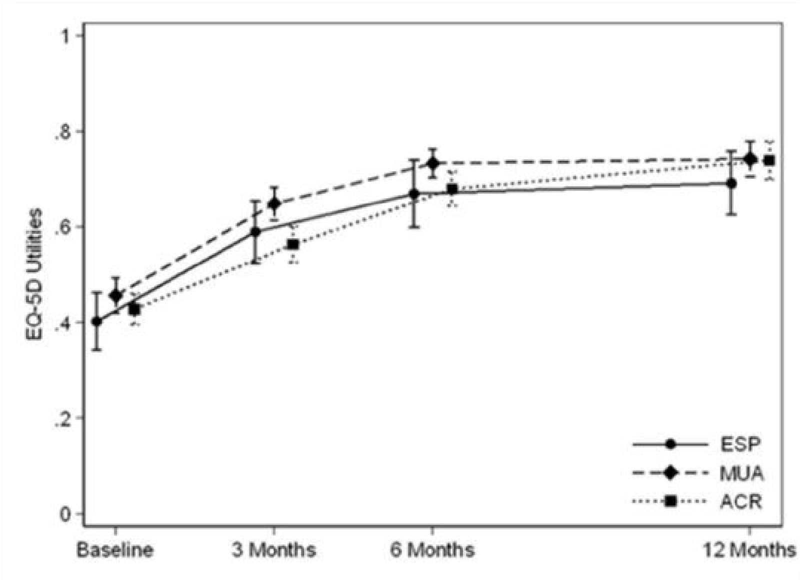

Figure 2 - Base case cost-effectiveness acceptability curves