Article:
Rombach, I. orcid.org/0000-0003-3464-3867, Merritt, N., Shirkey, B.A. et al. (6 more authors) (2019) Cost-effectiveness analysis of a placebo-controlled randomized trial evaluating the effectiveness of arthroscopic subacromial decompression in patients with subacromial shoulder pain. Bone and Joint Journal, 101-B (1). pp. 55-62. ISSN 2049-4394

https://doi.org/10.1302/0301-620x.101b1.bjj-2018-0555.r1

■ SHOULDER & ELBOW

Cost-effectiveness analysis of a placebo-controlled randomized trial evaluating the effectiveness of arthroscopic subacromial decompression in patients with subacromial shoulder pain

I. Rombach,
N. Merritt,
B. A. Shirkey,
J. L. Rees,
J. A. Cook,
C. Cooper,
A. J. Carr,
D. J. Beard,
A. M. Gray

From University of Oxford, Oxford, United Kingdom

■ I. Rombach, DPhil, Researcher in Health Economics; Senior Statistician, University of Oxford, Health Economics Research Centre, Nuffield Department of Population Health; Nuffield Department of Orthopaedics, Rheumatology and Musculoskeletal Sciences, Oxford, UK.

■ N. Merritt, BSc, Study Coordinator
■ B. A. Shirkey, PhD, Medical Statistician
■ J. L. Rees, FRCS (Tr&Orth), Professor of Orthopaedic Surgery and Musculoskeletal Science
■ J. A. Cook, PhD, Associate Professor
■ C. Cooper, MSc, Senior Trial Manager
■ A. J. Carr, FRCS, Head of Nuffield Department of Orthopaedics and Nuffield Professor of Orthopaedics
■ D. J. Beard, DPhil, Professor of Musculoskeletal Sciences and Co-Director of the Surgical Intervention Trials Unit (SITU) University of Oxford, Nuffield Department of Orthopaedics, Rheumatology and Musculoskeletal Sciences, Oxford, UK.

■ A. M. Gray, PhD, Professor of Health Economics and Director of the Health Economics Research Centre (HERC), University of Oxford, Health Economics Research Centre, Nuffield Department of Population Health, Oxford, UK.

Correspondence should be sent to I. Rombach; email: ines.rombach@ndorms.ox.ac.uk

doi:10.1302/0301-620X.101B1.BJJ-2018-0555.R1 $2.00

Bone Joint J 2019;101-B:55–62.

Aims

The aims of this study were to compare the use of resources, costs, and quality of life outcomes associated with subacromial decompression, arthroscopy only (placebo surgery), and no treatment for subacromial pain in the United Kingdom National Health Service (NHS), and to estimate their cost-effectiveness.

Patients and Methods

The use of resources, costs, and quality-adjusted life-years (QALYs) were assessed in the trial at six months and one year. Results were extrapolated to two years after randomization. Differences between treatment arms, based on the intention-to-treat principle, were adjusted for covariates and missing data were handled using multiple imputation. Incremental cost-effectiveness ratios were calculated, with uncertainty around the values estimated using bootstrapping.

Results

Cumulative mean QALYs/mean costs of health care service use and surgery per patient from baseline to 12 months were estimated as 0.640 (standard error (SE) 0.024)/£3147 (SE 166) in the decompression arm, 0.656 (SE 0.020)/£2830 (SE 183) in the arthroscopy only arm and 0.522 (SE 0.029)/£1451 (SE 151) in the no treatment arm. Statistically significant differences in cumulative QALYs and costs were found at six and 12 months for the decompression *versus* no treatment comparison only. The probabilities of decompression being cost-effective compared with no treatment at a willingness-to-pay threshold of £20 000 per QALY were close to 0% at six months and approximately 50% at one year, with this probability potentially increasing for the extrapolation to two years.

Discussion

The evidence for cost-effectiveness at 12 months was inconclusive. Decompression could be cost-effective in the longer-term, but results of this analysis are sensitive to the assumptions made about how costs and QALYs are extrapolated beyond the follow-up of the trial.

Cite this article: *Bone Joint J* 2019;101-B:55–62.

The clinical results of the CSAW Trial[1,2] (Can Shoulder Arthroscopy Work?; ISRCTN 33864128) were recently published. This randomized controlled trial (RCT) aimed to address uncertainties about the most appropriate treatment for patients with subacromial pain in the shoulder. This common condition[3] is associated with significant impairment of quality of life and a substantial socioeconomic burden.[4] The trial investigated the mechanism by which surgical decompression[5] might benefit patients, and the effectiveness of this treatment. The aims were addressed by comparing the clinical and cost-effectiveness of arthroscopic subacromial decompression (referred to henceforth as decompression), arthroscopy only (diagnostic investigative arthroscopy and thus the surgery without removal of the tissue and bone spur), and no treatment. Crucially, the arthroscopy only arm was included to investigate the mechanisms of decompression by comparing

decompression with arthroscopy only. Arthroscopy only has never been suggested as a routine curative treatment for subacromial pain.

The patients were followed-up for 12 months after randomization, with the primary endpoint of clinical effectiveness being assessed at six months. Full details of the study are reported elsewhere,[1] and the patient-reported outcome measures (PROMs) and clinical results have been published.[2] The primary analysis used the patients as they were randomized, regardless of compliance using the intention to treat (ITT) principle, and failed to show a clinically or statistically significant difference between the decompression and arthroscopy only arms, as measured by the Oxford Shoulder Score (OSS),[6] which was the primary outcome measure of this RCT. The clinically meaningful difference was defined as 4.5 points, and the mean difference for decompression *versus* arthroscopy only was -1.3 (95% CI -3.9 to 1.3). A small statistically, but not clinically, significant improvement was found for both surgical groups compared with the no treatment group, with differences still evident at the one-year follow-up. A recent study from Finland[7] had a similar design but included exercise therapy instead of a no treatment arm. Their primary endpoint was pain in the shoulder measured on a visual analogue scale at 24 months, and the results were consistent with the CSAW trial, in that no benefit of decompression over arthroscopy was found. No cost-effectiveness analysis has been reported for this trial.

The aim of this further study was to compare health-related quality of life (QoL), the use of resources, and costs associated with decompression, arthroscopy only, and no treatment for the 313 patients in the CSAW trial. To our knowledge, this is the first trial to assess the cost-effectiveness of subacromial decompression compared with arthroscopy only and with no treatment.

Patients and Methods

The CSAW trial randomized patients from 30 centres in the United Kingdom between 2012 and 2015, allocating them to one of three options for the management of subacromial pain: subacromial decompression, arthroscopy only, and no treatment. Randomization was minimized by site, age (< 40, 40 to 55, 56+ years), gender, and baseline OSS (< 19, 19 to 26, 27 to 33, 34+ points). The target sample size was 300 patients (100 per arm), based on the primary clinical endpoint, the OSS. Inclusion criteria involved subacromial pain for at least three months, no evidence of rotator cuff tears, patients who had completed a nonoperative management programme, had at least one steroid injection, and were eligible for surgery. Additional details on the inclusion and exclusion criteria and sample size calculation can be found in the protocol.[1]

The primary outcome of the health economics analysis was the incremental cost per quality-adjusted life-year (QALY) gained, based on EuroQol (EQ)-5D-3L responses during the 12-month follow-up. QALYs combine information about QoL and time. One QALY signifies one year of life in perfect health, and lower values indicate a lower QoL and/or death during that year. We focused on decompression *versus* no treatment and decompression *versus* arthroscopy only. The arthroscopy *versus* no treatment comparison is reported for completeness as Supplementary Material, but is omitted from the main analysis, as arthroscopy was offered only in the context of a randomized experiment to control for any surgical placebo effect. Furthermore, it is not considered a valid routine form of treatment for these patients. The analysis was undertaken in the United Kingdom's National Health Service (NHS) healthcare system. The time horizon was the duration of the CSAW trial, thus to one year after randomization, with data collection at six months and one year, with additional longer-term extrapolation of data to two years post-randomization.

Data collection and attribution of costs. The costs of the initial surgical procedures were calculated as a sum of equipment costs, which were obtained from manufacturer's list prices, using a 15% discount, costs per minute for the time each patient spent in the operating theatre, and a minimal surgical procedure cost for shoulder procedures (day cases), intended to cover other items related to a surgical admission such as administrative processing, work-up, and recovery. The small number of subsequent operations (two) and adverse events (nine) were not costed separately, but treated as included in the resources which were used during follow-up. Unit costs for the use of resources for the year 2015/16 were obtained from national unit costs (Supplementary Table i) and applied to all components.

The following details on the use of resources were collected for each patient: the type of initial procedure (decompression, arthroscopy only, rotator cuff repair (RCR), and 'other', including a mixture of intermediate and major procedures) was collected from the theatre form for all patients who underwent a surgical procedure within the trial, and the total time in the operating theatre for each patient. Details of the main equipment required for each procedure were identified in discussion with the trial team. The use of resources during follow-up, including the number of GP and nurse visits, attendance to A&E departments, orthopaedic and other outpatient clinics and day hospitals, NHS physiotherapy appointments, and overnight inpatient stays, were collected at six and 12 months after randomization.

Health-related QoL was measured at baseline, and at six and 12 months after randomization using the EQ-5D-3L. Utility scores were calculated from responses using Stata's 'eq5d' command,[8] using the United Kingdom population tariff;[9] index scores of 1 indicate full health, 0 represents states equal to death, and negative values indicate states considered worse than death. QALYs for each patient were calculated using an area under the curve (AUC) approach after linear interpolation between timepoints.

Cost-effectiveness analyses. All analyses were conducted in Stata/SE 14 (StataCorp. LP, College Station, Texas). In the primary analysis, outcomes were analyzed as randomized, regardless of compliance with the randomized procedure (intention to treat (ITT) approach). Imputation of missing data allowed for the inclusion of all randomized patients. Supplementary analyses included a per-protocol analysis, restricted to those who had received only their allocated intervention at 12 months, a complete cases analysis (including only those who had no missing observations for any utility or health resource use), and sensitivity analyses for unit costs.

Descriptive statistics (mean and standard errors (SE)) for the use of resources and related costs were calculated by treatment

Table I. Overview of the randomized patients, initial procedures, and the numbers included in the analyses

	Randomized arm		
	Decompression, n (%)	**Arthroscopy only, n (%)**	**No treatment, n (%)**
Total number randomized	106	103	104
Initial procedures			
Decompression	80 (*75*)*	3 (*3*)†	18 (*17*)
Arthroscopy only	0 (*0*)	69 (*67*)*†	0 (*0*)
Rotator cuff repairs‡	5 (*5*)	4 (*4*)	1 (*1*)
Other shoulder surgery	4 (*4*)	4 (*4*)	6 (*6*)
No surgery	17 (*16*)	23 (*22*)	79 (*76*)*§
Populations analyzed			
Included in the intention-to-treat population¶	106 (*100*)	103 (*100*)	104 (*100*)
Included in per-protocol population**	80 (*75*)	68 (*66*)†	78 (*75*)§
Included in complete cases analysis††	81 (*76*)	86 (*83*)	79 (*76*)

*Patients who received their randomized procedures

†There are two differences between this information and the details provided in the Can Shoulder Arthroscopy Work? (CSAW) Consolidated Standards of Reporting Trials (CONSORT) flow diagram shown in the main clinical paper. One participant allocated to 'arthroscopy only' was listed as having received 'decompression' in the main clinical paper at 12 months. However, the decompression was their second operation; arthroscopy only was initially performed as categorized here. This participant is not included in the per-protocol population

‡Most rotator cuff repairs included decompression

§One participant allocated to the 'no treatment' group was listed as withdrawn in the main clinical paper. They did not have surgery until the point of withdrawal and they are listed as 'no surgery' in this summary for ease of presentation. They are not included in the per-protocol population

¶All randomized participants were included in the intention-to-treat population. Missing data were imputed

**The per-protocol population includes all participants who received their allocation intervention, and none of the other trial interventions by 12 months post-randomization. Numbers included in this per-protocol population differ from those in the main clinical paper, as this analysis does not exclude additional participants due to missing outcome data. Missing data were imputed

††The complete cases analysis includes all participants who had no missing observations for any utility or health resource use over the 12 months' follow-up. The numbers included in this complete case analysis are different from those in the main clinical paper, which focused on participants with available Oxford Shoulder Score data

arm. Differences between treatment arms were adjusted for the minimization factors, i.e. linear regression models were adjusted for gender, age, and baseline OSS (used as continuous variables), while also adjusting for clustering within trial site using the 'cluster' option within Stata's regression command. Differences in health-related QoL and QALYs were adjusted for baseline EQ-5D-3L values instead of OSS baseline values. 95% confidence intervals (CIs) and 5% significance levels were used throughout.

A cost-utility analysis was performed for three different time horizons. An analysis covering the six months following randomization was conducted to align with the primary analysis of the trial.[2] A one-year analysis covered the entire follow-up period, and an analysis to 24 months after randomization was undertaken to explore cost-effectiveness using some minimal assumptions concerning longer-term effects beyond the period of follow-up. Incremental cost-effectiveness ratios (ICERs) were calculated as the incremental cost per QALY gained for each treatment comparison. Uncertainty around the ICERs was represented by 1000 non-parametric bootstrapped replicates of the differences in mean total cost and QALY between the groups, which were then used to plot cost-effectiveness planes and to calculate the probability of one treatment arm being cost-effective at £20 000 per QALY against its comparator.

The following assumptions were made for the extrapolation to two years after randomization: differences in QoL between the treatment arms were assumed to remain constant after 12 months, while no differences were assumed in mean costs between different treatment arms after the one-year follow-up point. Further analyses considered a scenario in which costs incurred over the six- to 12-month period continued to be incurred at the same rate during the following year by each patient. Both cost and QoL outcomes beyond one year of follow-up were discounted at an annual rate of 3.5%, in line with current recommendations.[10]

Analyses of sensitivity examined the effect of different discounts in price being applied to the manufacturers' list prices (i.e. 0% and 30% instead of 15%).

Missing data were handled as follows: where patients had partly completed information about the use of resources, but had left some items unanswered, it was assumed that these health care resources were not used within the relevant follow-up period. Where patients had not answered any questions about the use of resources or given any EQ-5D-3L data, or the follow-up form was missing, multiple imputation by chained equations (MICE) was used.[11] Missing data for health-related QoL and use of resources at baseline (EQ-5D-3L only), six months, and 12 months after randomization were imputed simultaneously using linear regression models and a predicted mean matching approach, imputing observed values from the pool of the five data points with the most similar predictive values.[11] Additional independent variables included in the imputation model included baseline OSS and EQ-5D-3L index, baseline use of

Table II. Overview of the use of resources and costs by randomization allocation

	Decompression, mean cost in £ (SE), n = 106	Arthroscopy only, mean cost in £ (SE), n = 103	No treatment, mean cost in £ (SE), n = 104	Decompression *vs* arthroscopy only, mean cost difference in £* (95% CI; p-value)	Decompression *vs* no treatment, mean cost difference in £* (95% CI; p-value)
Total surgery cost	1767 (83)	1299 (81)	536 (95)	461 (274 to 649; < 0.001)†	1231 (955 to 1508; < 0.001)†
Costs of health service use from baseline to 6 mths (including initial trial procedure where relevant)	2571 (113)	2287 (144)	1008 (120)	266 (-135 to 666; 0.184)	1563 (1169 to 1956; < 0.001)†
Costs of health service use from 6 to 12 mths	577 (130)	543 (84)	443 (58)	15 (-256 to 286; 0.911)	129 (-148 to 406; 0.346)
Costs of health service use and surgery from baseline to 12 mths	3147 (166)	2830 (183)	1451 (151)	281 (-142 to 703; 0.183)	1691 (1216 to 2167; < 0.001)†

*Differences are adjusted for baseline Oxford Shoulder Score, age at randomization, gender, and randomizing site (i.e. adjusted for clustering within trial site using the 'cluster' option within Stata's regression command

†Statistically significant

SE, standard error; CI, confidence interval

resources, gender, age at randomization, and the initial surgery that was undertaken. Imputations were run separately by treatment arm. A total of 20 sets of imputed values were obtained using Stata's 'mi impute' command, and combined with the 'mi estimate' command to account for uncertainty around the imputations. Information about employment and change in employment during the study, the number of sick days, and out-of-pocket expenses were summarized descriptively and are reported in the Supplementary Material.

Results

A total of 313 patients were randomized, 106 allocated to decompression, 103 to arthroscopy only, and 104 to no treatment. The baseline characteristics of the groups were well balanced. The mean age of the patients at the time of entering the trial was 53.3 years (SD 10.3), 158 were female (50.5%), and the mean OSS was 25.8 (SD 8.5).

The randomized intervention was received by 75%, 67%, and 76% of patients in the decompression, arthroscopy only, and no treatment arms, respectively. Additional details about the initial procedures received in each treatment arm (used to generate average total surgery costs) and the numbers included in the per-protocol and complete cases analyses are shown in Table I.

The rates of returns of the questionnaire were high: 100% of baseline questionnaires, 88% at six months, and 85% at 12 months were received. For a small number of additional patients (up to 4% overall), information on the use of resources and EQ-5D-3L was missing completely. The type of procedure was available for all patients who underwent surgery within the period of follow-up. Total times in the operating theatre were missing for three patients (one randomized to decompression, two to no treatment), who all underwent a decompression. The mean time recorded for decompression was used for these patients.

Costs and resource use for the initial trial procedures and follow-up. The volume and cost of resources for the initial procedures and during follow-up are summarized in Table II, with full details in Supplementary Table ii.

The mean time in the operating theatre per patient, and hence costs for this time, and basic costs of the procedure differed significantly between all three treatment arms. The total mean costs of surgery per patient were highest in the decompression arm (£1767, SE 83), followed by the arthroscopy only arm (£1299, SE 81), and lowest in the no treatment arm (£536, SE 95). These differences were statistically significant.

During the follow-up from baseline to six months, differences in the use of resources and costs between treatment arms were seen for NHS physiotherapy appointments, day hospital admissions, and inpatient nights. Costs for health services use during this time, including the cost of the initial procedure, were: decompression (£2571, SE 113), arthroscopy only (£2287, SE 144), and no treatment (£1008, SE 120). Costs in the decompression arm were significantly higher than for no treatment ($p < 0.001$), but no significant differences were seen between the decompression and arthroscopy only arms ($p = 0.184$).

The use of health services and costs between six and 12 months' follow-up were similar across treatment arms. The combined costs of surgery and health service use during the follow-up to 12 months were £3147 (SE 166) in the decompression arm, £2830 (SE 183) in the arthroscopy only arm, and £1451 (SE 151) in the no treatment arm. Decompression had significantly higher costs than no treatment ($p < 0.001$); costs in the decompression arm were not significantly different from those in the arthroscopy only arm ($p = 0.183$).

Quality of life outcomes. Information on QoL is presented in Table III. Improvements from baseline to six months and 12 months were seen in all groups. Adjusted mean differences between the decompression and no treatment group were statistically significant at six months ($p = 0.007$). There were no statistically significant differences between decompression and arthroscopy only at six or 12 months (six months, $p = 0.954$; 12 months, $p = 0.397$).

Information about the QALYs are shown in Table III. The adjusted difference in QALYs during one year follow-up between the decompression and arthroscopy only arms was not significant. The mean QALYs in the no treatment arm over the 12-month follow-up was significantly lower compared with the decompression arm ($p = 0.002$). The QALYs from baseline to six months, six to 12 months, and baseline to two years were also significantly higher in the decompression arm compared with the no treatment arm, but no significant differences were found between the decompression and arthroscopy only arms.

Table III. Quality of life (QoL) and quality-adjusted life-years (QALYs)

	Decompression, mean (SE), n = 106	Arthroscopy only, mean (SE), n = 103	No treatment, mean (SE), n = 104	Decompression *vs* arthroscopy only,* mean (95% CI; p-value)	Decompression *vs* no treatment,* mean (95% CI; p-value)
QoL (EQ-5D-3L)					
Baseline	0.517 (0.029)	0.553 (0.028)	0.499 (0.032)		
6 mths	0.654 (0.030)	0.672 (0.027)	0.526 (0.036)	-0.002 (-0.086 to 0.081; p = 0.954)	0.120 (0.040 to 0.210; p = 0.007)†
12 mths	0.735 (0.030)	0.728 (0.027)	0.658 (0.034)	0.027 (-0.038 to 0.093; p = 0.397)	0.080 (-0.010 to 0.160; p = 0.065)
QALYs					
Baseline to 6 mths	0.293 (0.012)	0.306 (0.011)	0.256 (0.015)	-0.001 (-0.022 to 0.020; p = 0.954)	0.030 (0.010 to 0.050; p = 0.007)†
6 to 12 mths	0.347 (0.013)	0.350 (0.011)	0.296 (0.015)	0.006 (-0.025 to 0.038; p = 0.683)	0.050 (0.020 to 0.080; p = 0.003)†
Baseline to 12 mths	0.640 (0.024)	0.656 (0.020)	0.552 (0.029)	0.006 (-0.045 to 0.056; p = 0.819)	0.080 (0.030 to 0.130; p = 0.002)†
Baseline to 2 yrs‡	1.349 (0.050)	1.359 (0.043)	1.188 (0.056)	0.032 (-0.072 to 0.136; p = 0.528)	0.160 (0.040 to 0.270; p = 0.008)†

*Differences are adjusted for baseline EQ-5D-3L index, age at randomization, gender, and randomizing site (i.e. adjusted for clustering within trial site using the 'cluster' option within Stata's regression command)

†Statistically significant

‡Assumptions made in the extrapolation: Carry forward quality of life from 12 months; also carry over cost observed from six to 12 months for each additional six-month period (extrapolation scenario 1)

SE, standard error; EQ-5D-3L, Euro-Qol 5D-3L; CI, confidence interval

Table IV. Incremental cost-effectiveness

	Analysis and comparison	Difference in costs (£),* mean (95% CI; p-value)	Difference in QALYs,* mean (95% CI; p-value)	Mean incremental cost per QALY gained	More effective, %	Less costly, %	Cost-effective at £20 000 per QALY gained, %
Baseline to 6 mths	Decompression *vs* no treatment	1563 (1169 to 1956; < 0.001)	0.030 (0.010 to 0.050; 0.007)	52 100 (NE quadrant)	*100*	*0*	*0*
	Decompression *vs* arthroscopy only	266 (-135 to 666; 0.184)	-0.001 (-0.022 to 0.020; 0.954)	-266 000 (NW quadrant)	*53*	*16*	*23*
Baseline to 12 mths	Decompression *vs* no treatment	1691 (1216 to 2167; < 0.001)	0.080 (0.030 to 0.130; 0.002)	21 138 (NE quadrant)	*100*	*0*	*50*
	Decompression *vs* arthroscopy only	281 (-142 to 703; 0.183)	0.006 (-0.045 to 0.056; 0.819)	46 833 (NE quadrant)	*63*	*17*	*46*
Baseline to 2 yrs (extrapolation scenario 1)†	Decompression *vs* no treatment	1691 (1216 to 2167; < 0.001)	0.160 (0.040 to 0.270; 0.008)	10 569 (NE quadrant)	*100*	*0*	*89*
	Decompression *vs* arthroscopy only	281 (-142 to 703; 0.183)	0.032 (-0.072 to 0.136; 0.528)	8 781 (NE quadrant)	*76*	*17*	*70*
Baseline to 2 yrs (extrapolation scenario 2)‡	Decompression *vs* no treatment	1940 (1046 to 2834; < 0.001)	0.160 (0.040 to 0.270; 0.008)	12 125 (NE quadrant)	*100*	*0*	*84*
	Decompression *vs* arthroscopy only	309 (-484 to 1103; 0.428)	0.032 (-0.072 to 0.136; 0.528)	9656 (NE quadrant)	*76*	*24*	*67*

*Differences are adjusted for baseline Oxford Shoulder Score (costs)/baseline EQ-5D-3L index, age at randomization, gender, and randomizing site (i.e. adjusted for clustering within trial site using the 'cluster' option within Stata's regression command)

†Extrapolation scenario 1: carry forward quality of life from 12 months; assume no differential costs between the treatment arms

‡Extrapolation scenario 2: carry forward quality of life from 12 months; also carry over cost observed from six to 12 months for each additional six-month period

CI, confidence interval; QALY, quality-adjusted life year; NE, north-east quadrant of the cost-effectiveness plane; NW, north-west quadrant of the cost-effectiveness plane

Incremental cost-effectiveness. The results from the incremental cost-effectiveness are shown in Table IV (Supplementary Table iv also shows the cost-effectiveness for the arthroscopy only arm). Significantly larger mean costs were associated with the decompression arm compared with the no treatment group, while differences in QALYs are small at the six-month follow-up and moderate at 12 months. A cost-effectiveness plane (Fig. 1, also Supplementary Fig. a) shows the uncertainty around the estimates at 12 months. On the cost-effectiveness plane, higher values on the vertical axis indicate higher differences in cost and points further to the right on the horizontal axis indicate a larger difference in QALYs for decompression compared with its comparators. Points that fall below the dashed line are cost-effective at a £20 000 per QALY willingness-to-pay threshold. The probability of decompression being cost-effective at a £20 000 per QALY compared with no treatment is close to 0% at six months and 50% at 12 months. Extrapolating to two years after randomization, the probability of decompression being cost-effective compared with no treatment at £20 000 per QALY increases to between 84% and 89% for decompression, depending on the assumptions made in the extrapolation.

Decompression had similar QoL outcomes to arthroscopy only at six months, but slightly higher outcomes at 12 months (adjusted differences), while being a mean of £266 and £281 more expensive at six and 12 months, respectively. The

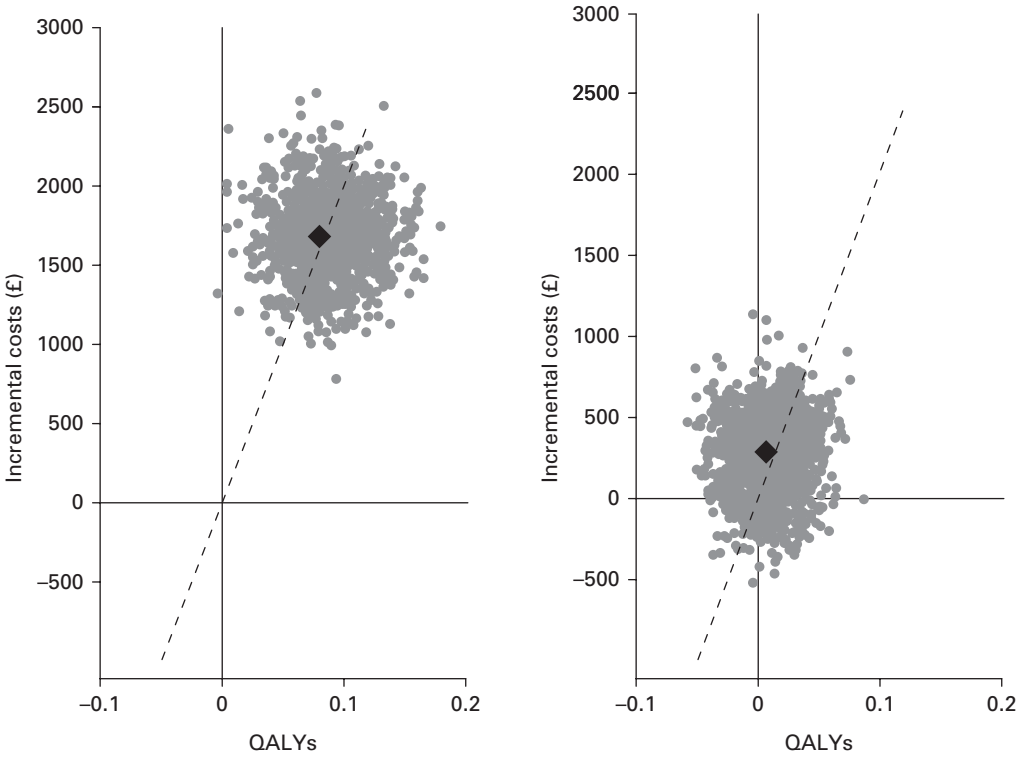

Fig. 1a

Fig. 1b

Cost-effectiveness planes, baseline to 12 months, for a) decompression *versus* no treatment and b) decompression *versus* arthroscopy only. Points that fall below the dashed line are cost-effective at a £20 000 per quality-adjusted life-year (QALY) willingness-to-pay threshold.

probability of decompression being cost-effective compared with arthroscopy only at £20 000 per QALY at six and 12 months was 23% and 46%, respectively. At two years post randomization, the probability of decompression being cost-effective at £20 000 compared with arthroscopy only is between 67% and 70%, depending on the assumptions made in the extrapolation.

The results from the per-protocol analysis, the complete cases analyses, and scenarios considering 0% and 30% price discounts are consistent with these findings with little evidence of cost-effectiveness at a £20 000 per QALY gain threshold (Supplementary Tables v and vi). The probability of decompression being cost-effective at £20 000 per QALY compared with no treatment or arthroscopy only using the per-protocol population is 0% and 8%, respectively, at six months after randomization, and 12% and 49%, respectively, at 12 months after randomization. By excluding patients who did not receive their allocated procedure in the per-protocol analysis, the differences in mean costs are more pronounced between the decompression and no treatment arms. The changes in these differences are driven by the costs of the procedures. Using the complete cases analysis, the probability of decompression being cost-effective at £20 000 per QALY compared with no treatment or arthroscopy only is 0% and 7%, respectively, at six months after randomization, and 44% and 31%, respectively, at 12 months after randomization.

Sensitivity analyses examining the effect of other discounts applied to surgical equipment (0% and 30% instead of a 15% discount as used in the primary analysis) had little effect on the differences in cost between treatment arms, as well as the ICERs generated, and produced similar results to the primary analysis. The effects of the change in discounts were diluted by non-compliance to the randomized intervention. Thus, the mean cost per patient changed by approximately £80, £44, and £23 in the decompression, arthroscopy only, and no treatment arms at 12 months, respectively, with increases of this amount seen for a decrease in discount to 0%, and a decrease of this amount observed for an increase in discount to 30%. These differences were small compared with the overall costs per patient in each treatment arm, and thus decompression remained significantly more expensive than no treatment. The difference in costs between decompression and arthroscopy only remained non-significant. The probability of decompression being cost-effective compared with no treatment at one year remained similar to that reported for the primary analysis.

Employment and out-of-pocket expenses. There was no evidence of significant differences in employment, change in employment, number of sick days (Supplementary Tables vii, viii, and ix), use of additional over-the-counter medication, private practitioners, and exercise equipment or activities (Supplementary Table x), or costs incurred by the patient, including money spent on additional over the counter medication, private practitioners and exercise equipment or activities (Supplementary Table xi) between the treatment arms.

Discussion

We found that randomization to decompression was associated with significantly higher costs during a one-year follow-up than

randomization to no treatment (mean difference £1691, 95% CI £1216 to £2167). These differences were mainly due to the operation, and to a lesser extent to an increased health service use, particularly the use of physiotherapists, admissions to day hospitals, and inpatient nights during the first six months of follow-up. We found no significant differences in costs between the decompression and arthroscopy arms during the 12 months' follow-up. At six months after randomization, self-reported QoL was significantly higher in both surgery arms compared with no treatment, but not significantly different between those randomized to decompression and arthroscopy only. There were no significant differences in QoL at the end of the 12-month follow-up period, although those in the decompression arm had a marginally higher mean EQ-5D-3L value than those in the arthroscopy only arm. Similar trends were observed for other PROMs recorded in the CSAW trial.[2]

For both decompression *versus* no treatment and decompression *versus* arthroscopy only, there is an approximately 50% chance of being cost-effective at £20 000 per QALY gained at the end of the one-year follow-up. Extrapolating the outcomes to two years after randomization, in particular assuming that small differences in QoL at 12 months persist to 24 months, had a large effect on the results, increasing the probability of decompression *versus* no treatment and decompression *versus* arthroscopy only being cost-effective. However, no long-term data are available on these patients, and it is not known how realistic these assumptions are.

This cost-effectiveness analysis was conducted alongside a RCT that recruited patients from 30 hospitals in the United Kingdom, and so is broadly based and had low levels of loss to follow-up and missing data. However, it has limitations. First, information on actual discounts offered to hospitals for surgical equipment is hard to obtain, and so the same level of discount was assumed across all sites. However, analyses of sensitivity examining different levels of discounts did not greatly alter the results. Second, not all patients received their randomized procedure. Between 24% and 33% of patients were treated with other or additional procedures. The costs therefore incorporate a mixture of procedures and the results should be interpreted as an ITT analysis. Third, the analysis was performed from the perspective of the healthcare system alone, and information about wider societal costs such as time off work, and out-of-pocket expenses that were incurred by patients was only summarized descriptively, and is reported as Supplementary Material. Finally, the maximum duration of follow-up was 12 months, which may not have been long enough to capture longer-term effects of the procedures with respect to costs and particularly QoL. A simple extrapolation over a short period of an additional 12 months and using highly restrictive assumptions nevertheless had a large effect on the estimates of cost-effectiveness.

In the CSAW trial, arthroscopy only was offered as part of the randomized experiment to control for any surgical placebo effect. The results from a cost-effectiveness analysis of a comparison between arthroscopy only *versus* no treatment are not easily interpretable, since, even if shown to be cost-effective, the arthroscopy only procedure could not be used in these patients. We have not discussed these results in this paper, although they are shown in the Supplementary Material.

In conclusion, this study shows no evidence that decompression is cost-effective during the one-year follow-up period. It could be cost-effective in the long-term, but results of this analysis are sensitive to the assumptions made about how costs and QALYs are extrapolated beyond the follow-up of the trial. Studies with longer-term follow-up are needed.

Take home message

- Arthroscopic subacromial decompression is a commonly performed surgery in patients with subacromial pain, but recent research demonstrated no clinical benefit of decompression surgery compared with arthroscopy only or no treatment.
- This study is the first to assess the cost-effectiveness of subacromial decompression compared to arthroscopy only and to no treatment.
- This research adds comparative evidence on the costs and quality of life of these procedures. It shows that decompression is significantly more costly than no treatment over 12 months, with no clear evidence that it is cost-effective.
- Further evidence on longer-term outcomes and costs is still required, as in some projected scenarios decompression could be cost-effective depending on how costs and QALYs are extrapolated beyond the trial follow-up.

Twitter

Follow the authors @SITU_Oxford
Follow N. Merritt @Naomi_R_Merritt

Supplementary material (available online)

Tables and figures showing unit costs, as well as detailed information on resource use, costs, and quality of life, are provided in the Supplementary Material. Incremental cost-effectiveness for the sensitivity analyses at six months and 12 months post-randomization (per-protocol and complete case analysis, variation in price discounts), as well as adjusted differences between the arthroscopy only and no treatment arm, are also presented. Cost-effectiveness planes for all comparisons covering time from randomization to 12 months and for the extrapolation to 24 months are included. Tables summarizing employment and change of employment information, sick days, use of additional over-the-counter medication, use of private practitioners, and money spent on exercise equipment or activities are presented.

References

1. **Beard D, Rees J, Rombach I, et al.** The CSAW Study (Can Shoulder Arthroscopy Work?) - a placebo-controlled surgical intervention trial assessing the clinical and cost effectiveness of arthroscopic subacromial decompression for shoulder pain: study protocol for a randomised controlled trial. *Trials* 2015;16:210.
2. **Beard DJ, Rees JL, Cook JA, et al.** Arthroscopic subacromial decompression for subacromial shoulder pain (CSAW): a multicentre, pragmatic, parallel group, placebo-controlled, three-group, randomised surgical trial. *Lancet* 2018;391:329–338.
3. **Mitchell C, Adebajo A, Hay E, Carr A.** Shoulder pain: diagnosis and management in primary care. *BMJ* 2005;331:1124–1128.
4. **Virta L, Joranger P, Brox JI, Eriksson R.** Costs of shoulder pain and resource use in primary health care: a cost-of-illness study in Sweden. *BMC Musculoskelet Disord* 2012;13:17.
5. **Judge A, Murphy RJ, Maxwell R, Arden NK, Carr AJ.** Temporal trends and geographical variation in the use of subacromial decompression and rotator cuff repair of the shoulder in England. *Bone Joint J* 2014;96-B:70–74.
6. **Dawson J, Rogers K, Fitzpatrick R, Carr A.** The Oxford shoulder score revisited. *Arch Orthop Trauma Surg* 2009;129:119–123.
7. **Paavola M, Malmivaara A, Taimela S, et al.** Subacromial decompression versus diagnostic arthroscopy for shoulder impingement: randomised, placebo surgery controlled clinical trial. *BMJ* 2018;362:k2860.

8. **Ramos-Goñi JM, Rivero-Arias O.** eq5d: A command to calculate index values for the EQ-5D quality-of-life instrument. *Stata J* 2011;11:120–125.
9. **Dolan P, Gudex C, Kind P, Williams A.** A Social Tariff for EuroQol: Results from a UK General Population Survey. (Discussion paper 138): Centre for Health Economics, University of York, 1995. https://www.york.ac.uk/che/pdf/DP138.pdf (date last accessed 17 October 2018).
10. **No authors listed.** Guide to the methods of technology appraisal 2013. National Institute for Health and Care Excellence (NICE). https://www.nice.org.uk/process/pmg9/resources/guide-to-the-methods-of-technology-appraisal-2013-pdf-2007975843781 (date last accessed 17 October 2018).
11. **White IR, Royston P, Wood AM.** Multiple imputation using chained equations: issues and guidance for practice. *Stat Med* 2011;30:377–399.

Author contributions:
I. Rombach: Designed and implemented the study, Performed the statistical analysis for the clinical paper, Performed the cost-effectiveness analysis, Wrote the manuscript.
N. Merritt: Coordinated the study.
B. A. Shirkey: Performed the statistical analysis for the clinical paper.
J. L. Rees: Co-applicant on the grant application to Arthritis Research UK.
J. A. Cook: Co-applicant on the grant application to Arthritis Research UK, Contributed to the statistical analysis for the clinical paper.
C. Cooper: Co-applicant on the grant application to Arthritis Research UK.
A. J. Carr: Co-Chief Investigator.
D. J. Beard: Co-Chief Investigator.
A. M. Gray: Designed and implemented the study, Performing the analysis, Wrote the manuscript.
D. J. Beard and A. M. Gray contributed equally to this paper.

Funding statement:
This study was funded by Arthritis Research UK (Clinical Studies Grant 19707), the National Institute for Health Research (NIHR) Oxford Biomedical Research Centre (BRC; previously the Biomedical Research Unit), and the Royal College of Surgeons (England). The NIHR Oxford BRC is based at the Oxford University Hospitals NHS Foundation Trust and run in partnership with the University of Oxford, funded by the NIHR. The University of Oxford sponsored the study.

J. Cook held a Medical Research Council Methodology Fellowship (G1002292) for part of the duration of the study. The Nuffield Department of Orthopaedics, Rheumatology and Musculoskeletal Sciences coordinated the study via the Surgical Intervention Trials Unit from the Royal College of Surgeons (England) Surgical Trials Initiative.

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

The views expressed in this report are those of the authors and do not necessarily reflect the views of the funders.

No benefits in any form have been received or will be received from a commercial party related directly or indirectly to the subject of this article.

Data sharing:
Due to the confidential nature of some of the research materials supporting this publication, not all of the data can be made accessible to other researchers. Please contact the corresponding author for more information.

Acknowledgements:
We would like to thank the British Elbow and Shoulder Society for supporting and promoting this trial in the UK, all participants for their involvement in the study, and the Principal Investigators and their teams at each of the Can Shoulder Arthroscopy Work? (CSAW) sites. We acknowledge The Oxford Clinical Trials Research Unit, the National Institute of Health Research Clinical Research Network, and The Nuffield Department of Orthopaedics, Rheumatology and Musculoskeletal Sciences (NDORMS) for their support.

This article was primary edited by J. Scott.