Cost-effectiveness of surgical versus non-surgical treatment of adults with displaced fractures of the proximal humerus: economic evaluation alongside the PROFHER trial

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Abstract

A pragmatic, multicentre randomised controlled trial (PROFHER) was conducted in United Kingdom (UK) National Health Service (NHS) hospitals to evaluate the clinical effectiveness and cost-effectiveness of surgery compared with non-surgical treatment for displaced fractures of the proximal humerus involving the surgical neck in adults.

A cost utility analysis from the NHS perspective was performed. Differences between surgical and non-surgical treatment groups in costs and quality adjusted life years (QALYs) at two years were used to derive an estimate of the cost-effectiveness of surgery using regression methods.

Patients randomised to receive surgical intervention accumulated on average greater costs and marginally lower QALYs than patients randomised to non-surgery. The surgical intervention cost on average £1758 more per patient (95% CI £1126 to £2389). Total QALYs for the surgical group were smaller than those for non-surgery -0.0101 (95% CI -0.13 to 0.11). The probability of surgery being cost-effective was less than 10% given the current NICE willingness to pay threshold of £20 000 for an additional QALY. The results were robust to sensitivity analyses.

The results suggest that current surgical treatment is not cost-effective for the majority of displaced fractures of the proximal humerus involving the surgical neck in the UK NHS.

Introduction

Proximal humeral fractures account for 5% to 6% of all adult fractures, with the majority occurring in people aged over 65 years[1]. Around half of these fractures are displaced (51%), with the majority involving the surgical neck[2]. Surgical treatment, either internal fixation or humeral head replacement, is being increasingly used[3, 4]. This has substantially contributed to the increased treatment costs for upper limb fractures[4]. The outcome following both surgical and non-surgical treatment of these fractures is frequently unsatisfactory[5], with subsequent costs including those of revision and secondary surgery.

Given the established lack of evidence to conclude whether surgical intervention produces consistently better outcomes than non-surgical treatment for these fractures[5], the Proximal Fracture of the Humerus Evaluation by Randomisation (PROFHER) trial was conducted to evaluate the clinical effectiveness and cost-effectiveness of surgery compared with non-surgical treatment of the majority of displaced fractures of the proximal humerus involving the surgical neck in adults[6].

Full details of the trial design and the clinical effectiveness results have been reported[7, 8]. PROFHER recruited 250 adults with acute displaced fractures of the proximal humerus involving the surgical neck from the orthopaedic departments (fracture clinics or wards) of 32 acute care NHS hospitals between September 2008 and April 2011. The study inclusion and exclusion criteria are summarised in Table 1. There was no statistically or clinically significant difference between surgical and non-surgical treatment in the primary outcome, the Oxford Shoulder Score (OSS) averaged over 2 years (0·75 points in favour of surgery, 95% CI -1·33 to 2·84; P = 0·48). There were no significant between group differences in secondary outcomes, including surgical or fracture related complications (30 of 125 in the surgical group versus 23 of 125 in the non-surgical group; P = 0·28); secondary surgery to shoulder (11 versus 11); increased or new shoulder related therapy (7 versus 4; P = 0·58); and mortality (9 versus 5; P = 0·27)[7].

Despite the finding of a lack of clinical superiority of surgical treatment, it remains important to assess the relative healthcare costs of the two treatments over the two year period that also takes into account subsequent treatment and health-related quality of life. This study aimed to assess the cost-effectiveness of surgical versus non-surgical treatment for treating displaced fractures of the proximal humerus involving the surgical neck in adults, using individual patient data (IPD) from PROFHER.

Patients and methods

We performed a cost utility analysis where health related quality of life (HRQoL) was measured in terms of quality adjusted life years (QALYs), which represent years lived in perfect health. Costs and QALYs were evaluated on the basis of the NHS and Personal Social Services (NHS perspective) and expressed in UK pound sterling (GBP) at a 2012 price base. Costs and QALYs were discounted from year one at a rate of 3.5% in accordance to the current guidance[9]. The analysis was conducted on an intention-to-treat basis (ITT); thus the treatment groups were compared based on their initial random allocation irrespective of protocol deviations or withdrawal. The base-case analysis was conducted on a dataset generated by multiple imputation by chained equations[10-12]. Sensitivity analyses included complete case (CC) analysis to test the impact of excluding patients with missing data on the final results. All analyses and modelling were conducted in Stata™ 12 (StataCorp LP, College Station, Texas, USA).

The mean age of the 250 trial participants was 66 years, range 24 to 92 years, and 192 (77%) were women. Patients were randomised on an equal basis to surgical or non-surgical treatment. The choice of surgical intervention was left to the treating surgeons, typically consultants, who used surgical interventions with which they were fully experienced. Non-surgical treatment was initial sling-use. The measures taken to ensure comparability of good standard rehabilitation, are detailed elsewhere[13]. Trial participants were followed up for two years.

The PROFHER protocol[6] and all amendments were reviewed and approved by the York or Leeds (West) Research Ethics Committee (08/H1311/12). As detailed in the trial protocol[6], cost and health outcome data were collected prospectively in parallel with the clinical outcomes. Data collection for cost outcomes was via hospital forms (baseline characteristics, details of surgery, inpatient stay, treatment confirmation at one month, physiotherapy and end of physiotherapy, one and two year follow-up) and patient questionnaires at 3, 6, 12 and 24 months; copies of these forms are available elsewhere[8].

The main outcome for the economic analysis was QALYs based on the EQ-5D-3L™ (EuroQol Group, Rotterdam, The Netherlands) questionnaire reported by trial participants at baseline and subsequently. A prospective study assessing the validity of the EQ-5D for patients with proximal humeral fractures found the EQ-5D displayed good internal and external responsiveness and recommended its use as a quality of life measure in these

patients[14]. In order to estimate utilities (HRQoL weights), and to reflect the preferences of the general UK population, the EQ-5D health states were valued using a UK-based social tariff[15]. QALYs were calculated by combining the utility estimates by the duration of time in each health state using the area under the curve method (AUC)[16]. Despite the randomisation process, which ensures that baseline variables are balanced between the arms of the trial, in practice (regardless of sample size) it is normal to find an imbalance in mean baseline utility. As baseline utility is likely to be correlated with QALYs gained over time, there are robust reasons to control for baseline utility when estimating QALYs. Therefore the difference in mean QALYs between treatments groups was adjusted for baseline utility[17].

Resource use related to the primary surgical intervention was collected using surgical forms completed by healthcare professionals present at each operation. These forms collected information on operation times, staff involved, the type of implant used, disposables required and whether there were any unexpected procedures during the intervention. Resource use after discharge was assessed using (i) patient questionnaires at 3, 6, 12 and 24 months to estimate visits to primary care professionals; and (ii) hospital forms at 1 and 2 years to estimate hospital visits, physiotherapy sessions and subsequent hospital treatment. The unit costs are presented in Table 2. These were sourced from the Personal Social Services Research Unit[18], Department of Health (NHS reference costs)[19], hospitals (implant costs) and the British National Formulary[20].

Complete case assessment excludes all patients with any missing or incomplete data. Additional to the resulting sample usually being much reduced, complete case analysis might be biased if the data are not missing completely at random[21]. Thus incomplete data on costs and QALYs were imputed using multiple imputation (MI) with chain equations and predictive mean matching; which assumes that data are missing at random[22]. The same covariates applied in the primary effectiveness analysis were selected with stepwise regressions: EQ-5D^{TM}, costs, treatment allocation, sex, age and tuberosity (involvement or not of either or both tuberosities). Rubin's rules were used to combine point and variance estimates across imputed datasets, allowing the estimation of difference in costs and QALYs between treatment groups[22].

The base case analysis included only shoulder-related resource use. The cost-effectiveness of surgery was estimated by comparing mean adjusted incremental costs and QALYs between the two treatments groups in the trial at two years. The differences were estimated using seemingly unrelated regression (SUR)[23]. The incremental cost-effectiveness ratio (ICER) was estimated according to standard decision rules as the difference in mean total

costs divided by the difference in mean total QALYs from baseline to two years. According to the National Institute for Health and Clinical Excellence (NICE) the current recommended threshold ranges between £20 000 - £30 000 per QALY[9]. Therefore if the estimated cost per QALY is below this threshold range, surgery would be considered to be cost-effective and its use in the NHS recommended. 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 this surgical intervention when those resources might be used elsewhere.

The uncertainty around the cost effectiveness results was explored by means of sensitivity analyses, all of which were controlled for covariates: (i) complete–case (CC) analysis ITT; (ii) MI and (iii) CC with inclusion of both shoulder and non-shoulder related resource use; and (iv) MI and (v) CC using patient questionnaires as the main source for estimating hospital visits and overnight stay. Non-parametric bootstrapping[24] was used to derive the cost effectiveness acceptability curves (CEAC) to express the probability that surgery is cost-effective for the range of thresholds used by NICE.

RESULTS

Although a relatively high proportion (87% in each group) of patients returned their questionnaires at two years, the number of patients with complete follow-up assessments for all periods was much lower. A total of 173 (69%) patients – 95 (76%) allocated surgery and 78 (62%) not surgery – comprised the complete case for utilities; i.e. data for all five EQ-5Ds dimensions were available for all five assessment time points. Complete data (both costs and utilities) were available for 54 (43%) patients allocated to surgery and 46 (37%) to non-surgery. Fourteen patients died during the trial period, nine (7.2%) in the surgical arm and five (4.0%) in the non-surgical arm.

Patients in the surgery group had on average more outpatient appointments but fewer inpatient admissions (after their initial stay) than non-surgery group patients. The greater number of inpatient admissions in the non-surgery group reflected, in part, the finding that twice as many patients in this group were treated for newly diagnosed medical complications, such as cardiac or peripheral vascular events, compared with the surgical group (31 versus 15). The number of physiotherapy sessions received did not differ between treatment groups (Table 3).

The resource use required for the surgical intervention was estimated in terms of the staff involved in the operation, the type of implant and disposables used and the length of stay. Of the 109 patients allocated surgery who received primary surgery, locking plates were used in 90 (82%) cases, hemiarthroplasty in 10 (9%) cases, intramedullary nails in 4 (4%) cases and other surgery in 5 (5%) cases. The mean operation time in theatre was 144 minutes. The mean average cost of surgery in the trial was £3053 per patient for an average length of stay of 3.8 nights in hospital. This is in accordance with NHS 2011-12 reference costs, which estimate a unit cost of £3550 (weighted by activity levels and adjusted using the elective to non-elective ratio) and an average length of stay of 3.8 nights for the selected Healthcare Resource Groups (HRGs) codes (Table 1).

A large portion of the cost associated with patients in the surgical group was attributable to the first three months of follow-up, inclusive of the costs of surgery (Table 3). Thus, as expected, costs of surgery were the major cost driver for the surgery group. Conversely, hospital admissions were the main cost driver for the non-surgical group.

Patients in the surgery group started from a higher baseline utility on average (surgery 0·43 versus not surgery 0·38). However, at the end of the second year there was little difference in EQ-5D scores between treatment groups: surgery 0.67 versus not surgery 0.69 (Figure 1). Patients allocated to non-surgery obtained on average a higher QALY gain than patients allocated to surgery. The difference in QALYs at two years (surgery – not surgery) when controlling for baseline utility (for available cases: 95 surgery versus 78 not surgery) was -0.066 (95% CI -0.186 to 0.054).

The incremental analysis (Table 4) shows that the surgical intervention cost on average £1758 more per patient when compared with non-surgical treatment (95% CI: £1126 to £2389). Patients in the surgical group accrued less QALYs than those for non-surgery both adjusting for covariates (-0·0101, 95% CI -0·13 to 0·11) or adjusting exclusively for baseline utility (-0·0158, 95% CI -0·13 to 0·10). Therefore the results indicate surgery was dominated by non-surgical intervention. Mean differences in both costs and QALYs were estimated with sampling uncertainty. As illustrated by the CEAC in Figure 2, the probability of surgery being cost-effective was less than 10% given the NICE currently accepted threshold range of £20 000 to £30 000 per additional QALY.

The results of the five sensitivity analyses are presented in Table 4. The base case analysis results were robust to the inclusion of all resource use (both shoulder and non-shoulder

related) in the assessment: surgery remained a non-cost-effective intervention (MI dataset). Although surgery did not represent a dominated option for the CC when including both shoulder and non-shoulder resource use, the ICER was higher than the thresholds that NICE normally consider for reimbursement decisions (£20 000 to £30 000 per QALY gained). The results were similar when we investigated the impact of using patient questionnaires (rather than hospital forms) as main source for resource use data.

DISCUSSION

The results of the study provide robust evidence that surgery was more costly from the NHS perspective and provided less health benefits compared with non-surgical treatment for the majority of patients with displaced proximal humeral fractures involving the surgical neck. Given the uncertainty of the cost-effectiveness estimates it is unlikely that surgery represents an efficient intervention for the NHS, as the probability of surgery being cost-effective was 6% for the base case analysis. These results were robust to sensitivity analyses.

A key strength of our study is its pragmatic multicentre design, which has the advantage of reflecting actual practice in the UK hospitals thus providing timely and direct evidence of clinical and resource implications for the NHS. It should be highlighted that because of the pragmatic nature of the trial and the significant drawbacks of per protocol (PP) type analyses[25], the base case used the ITT approach. Furthermore, PP analysis would not have been justified given the small number of cross-overs in the trial. A further strength is that the very detailed hospital forms designed for the trial, together with the multiple sources of cost data available for the analysis, allowed us to conduct an exhaustive micro costing exercise. This is core as it improved the accuracy of estimation of the cost associated to the treatment of proximal humeral fractures in an UK specific setting. Finally the use of QALYs, rather than any other clinical end point, provides evidence about the impact of this type of fracture on quality of life. The long-term consequences of proximal humeral fractures are reflected not only in shoulder function but in other domains of health as well. Using QALYs allows us to reflect the impact of fractures on whether individuals carry on with their usual activities or on their anxiety or depression levels, which are key to reflecting the benefits of any intervention related to its treatment. There is growing evidence that the EQ-5D is sensitive to changes in health status in older people with serious fractures[26]. Moreover, the internal and external responsiveness of the EQ-5D instrument has been positively validated in patients with proximal humeral fractures[14]; therefore we can be confident that this instrument can capture small yet clinically important changes.

However, there are three potential limitations with the analysis of note. The first relates to the problem of missing data, which is a common issue in economic evaluations nested within clinical trials. Although the use of hospital forms rather than patient questionnaires helped to minimise the problem of incomplete data, missing data was a key determinant in our decisions of the best approach for our analysis. Despite the magnitude of missingness the results were robust to alternative assumptions on the pattern of missing data as illustrated by the complete case scenarios. Equally this did not change the outcome for cost-effectiveness. It is therefore very unlikely that such assumptions regarding missing data will change the conclusions of our analysis. The second limitation relates to the duration of the study, as two years might still be considered too short in view of potential functional deterioration, with associated reduction in quality of life, and requirement for subsequent operations resulting from complications, such as avascular necrosis, that can occur or become symptomatic later on. It is notable, however, that the majority of complications occurred in the first year. Furthermore the HRQoL observed over the study, which shows little difference between the two groups in overall mean QALYs (Figure 1), also suggests that it is unlikely that any important difference in QALYs would emerge beyond the trial follow-up. These results are supported by the lack of clinically or statistically differences between surgical and non-surgical treatment, either overall or at individual time points (at 6, 12 and 24 months) for the Oxford Shoulder Score (primary outcome of the trial) or any other secondary outcome[7]. Finally, as per the cost-effectiveness analysis plan, we did not undertake pre-specified subgroup analysis by age or fracture type because no clinically important subgroup effect emerged from the trial. Nonetheless, given age and fracture type were included as covariates in the model, the results already capture the impact they might have on the cost-effectiveness of surgical treatment.

To the best of our knowledge there is very little evidence regarding the cost-effectiveness of surgery for the treatment of proximal humeral fractures. Fjalestad et al[27] conducted an economic evaluation based on a single centre randomised controlled trial comparing surgical versus conservative treatment for severely displaced proximal humeral fractures in 50 elderly patients. The follow-up period was only one year and QALYs were measured using the 15D instrument (a generic 15-dimensional, standardised and self-administered measure of HRQoL). Although there are essential differences in the design and populations of this trial compared with the PROFHER trial that limit the scope for comparison, it is noteworthy that Fjalestad et al found there was no significant difference in QALYs or costs between surgical and conservative care.

From this analysis we conclude that surgery is not cost-effective compared with providing non-surgical treatment. The NMB associated with surgery was negative, indicating that the resources to be displaced would be greater than the benefit to be gained if surgery was implemented in the NHS. However, there is a trend of increased surgery among patients with displaced proximal humeral fractures involving the surgical neck. In terms of policy implications disinvesting in existing non cost-effective interventions will give the opportunity to invest NHS resources elsewhere. In England there were 3,519 first listed consultant episodes for people with proximal humeral fractures involving an operation during 2011/12. If we assume, based approximately on fracture epidemiology[2], that around 80% of these were displaced fractures involving the surgical neck then the annual cost saving to NHS England from not operating on half of the people with the trial fractures would be around £2.5 million.

The evidence presented here relates to surgery conducted in the UK. Inevitably different economic parameters will apply in other countries, which limits the generalisability of our results [28]. However, given the similarities in the choice of implants and surgical procedures in many other countries, we suggest these results are more generally applicable.

Future research on costs and outcomes would strengthen the results of the current economic evaluation. To this end, a long term follow-up of the PROFHER trial is already ongoing, with 80% of the trial participants giving their consent to be followed up at 3, 4 and 5 years. This will allow us to explore how the cost-effectiveness of surgery compared with non-surgical treatment evolves over time. In case any potential benefit is found, the extrapolation of economic outcomes over a lifetime period will be considered.

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Table 1 Inclusion and exclusion criteria

Inclusion criteria
1. Adults (aged 16 or above) presenting within 3 weeks of their injury with a radiologically confirmed displaced fracture of the humerus involving the surgical neck. This should include all 2 part surgical neck fractures; 3 part (including surgical neck) and 4 part fractures of proximal humerus (Neer Classification). It may also include displaced surgical neck fractures that do not meet the exact displacement criteria of the Neer classification (1 cm or/and 45° angulation of displaced parts) where this reflects an individual surgeon's equipoise (e.g., whether or not the surgical neck fracture should be treated surgically).
Exclusion criteria
1. Associated dislocation of the injured shoulder joint
2. Open fracture
3. Mentally incompetent patient: unable to understand trial procedure or instructions for rehabilitation; significant mental impairment that would preclude compliance with rehabilitation and treatment advice
4. Co-morbidities precluding surgery/anaesthesia
5. A clear indication for surgery such as severe soft-tissue compromise requiring surgery/emergency treatment (nerve injury/dysfunction)
6. Multiple injuries: same limb fractures; other upper limb fractures
7. Pathological fractures (other than osteoporotic) & terminal illness
8. Participant not resident in trauma-centre catchment area

Table 2. Unit costs (and sources) used to estimate total cost for each individual patient

Primary Surgery	**Unit Cost £**	**Source**
Surgeon/Anaesthetist Registrar	1.43	PPSRU 2012[21] (Unit cost *per minute*)
Hospital Radiographer	0.60	
Nurse Band 7	1.00	
Nurse Band 6	0.80	
Nurse Band 5	0.70	
Nurse Band 4	0.22	
Nurse Band 3	0.20	
Nurse Band 2	0.17	
Senior House Officer	0.43	
Associate Specialist	0.94	
Staff Grade	0.74	
Surgical assistant B5	0.50	
Surgical assistant B6	0.64	
Plates and Screws 3 hole	444.28	Manufacturer price (2012)(*) (Unit cost *per item*)
Plates and Screws 5 hole	455.50	
Lock screws	59.80	
Cortical screws	17.14	
Hemiarthroplasties	904.23	
Nail	482.43	
Propofol 200 mg	4.18	BNF 2013[23]
Fentanyl 100 µmg	0.60	
Morphine 10 mg	15.00	
Ondansetron 4 mg	1.00	
Dexamethasone 8 mg	2.80	
Atracurium 50 mg	6.00	
Neostigmine 2.5 mg	0.50	
Glycopyrolate 2.5 mg	0.91	
Cefuroxime 1.5 g	5.05	
Co-amoxiclav 1 g	1.06	
Hospital Care	**Unit Cost £**	**Source**
Surgical ward per night(**)	369.95	NHS Costs 2011-12[22]
General ward per night	320.79	
Shoulder hospital stay(+)	4363.19	
Non-shoulder hospital stay(++)	3347.98	
Non-shoulder excess hospital stay(^)	320.79	
Outpatient visit(~)	130.28	
Day case(~)	836.99	
Physiotherapy	**Unit Cost £**	**Source**
Physiotherapy session(¬)	41.79	PPSRU 2012[21]
Primary Care	**Unit Cost £**	**Source**
Visit to GP	49.16	P PPSRU 2012[21]
Visit to GP nurse	13.52	
Visit to Community nurse	15.98	
Occupational therapist	54.08	

(*) All manufacturer prices were provided by hospitals. Five different types of plates and screws provided by different manufacturers were used in the trial: PHILOS (Synthes), AXSOS (Stryker), S3 Plate (DePuy), Polarus PHP (Acumed) and NCB plate (Zimmer). Costs

were obtained from hospitals for three of the four hemiarthroplasties used: Epoca (Synthes), Anatomical (Zimmer) and Global FX/Advantage (DePuy); and for the two nailing systems which were used in just four patients: Polarus (Acumed) and Expert (Synthes); **(**)** Excess Bed day averaged (elective and non elective) per activity across all trusts using the relevant shoulder HRG codes selected for the analysis; **(+)** Averaged (elective and non-elective), weighted by activity levels across all trusts, using the relevant shoulder HRG codes selected for the analysis: HA61B, HA61C, HA62Z, HA63Z, HB61B, HB61C, HB62B, HB62C, HB63Z **++)** Averaged (elective and non-elective), weighted by activity levels across all trusts and specialities **(^)** Excess bed day averaged (elective and non elective) per activity across all trusts and specialities **(~)** Outpatient visits and day cases averaged per activity across all trusts **(¬)** Average duration for a physiotherapy session was half an hour.

Table 3. Average resource use over the 2 years for available data^

	N	Mean (sd)	Min	Max	Median	Missing
GP visits						
Surgery	76	0.85 (1.33)	0	6	0	39%
Non-surgery	71	1.18 (1.98)	0	12	1	43%
Practice nurse visits						
Surgery	74	0.78 (2.04)	0	15	0	41%
Non-surgery	75	0.28 (0.72)	0	4	0	40%
Community nurse visits						
Surgery	87	0.56 (2.31)	0	16	0	30%
Non-surgery	82	0.17 (1.33)	0	12	0	34%
Occupational therapist visits						
Surgery	86	0.66 (1.93)	0	10	0	31%
Non-surgery	81	0.59 (2.03)	0	12	0	35%
Hospital inpatient nights~						
Surgery	110	0.25 (1.23)	0	16	0	12%
Non-surgery	116	1.05 (3.15)	0	10	0	7%
Outpatient appointments						
Surgery	106	0.41 (1.02)	0	5	0	10%
Non-surgery	112	0.34 (0.92)	0	5	0	15%
Day case admissions						
Surgery	114	0.10 (0.32)	0	2	0	9%
Non-surgery	114	0.10 (0.32)	0	6	0	9%
Physiotherapist sessions						
Surgery	118	9.57 (6.22)	1	36	8	5%
Non-surgery	117	9.60 (6.59)	1	43	8	6%

^ Imputation was conducted at cost level (rather than resource use level). Therefore this table refers to available data and not MI.

~ The average number of inpatient days in the surgery group excludes the number of nights that surgery patients spent in hospital as a result of their initial surgery

Table 4. Break down of total cost over 2 years and per cost category for the average patient based on all available cases and according to treatment allocation

	Mean Costs £ (sd)		Difference^
	Surgery	Not surgery	(Surgery - Not surgery)
Month 3	2767 (1469)	694 (1869)	2073 (1596; 2550)
Month 6~	12 (33)	30 (141)	-18 (-47; 10)
Month 12	183 (751)	231 (848)	-48 (-294; 198)
Month 24	58 (367)	180 (708)	-122 (-289; 45)
Physiotherapy	326 (287)	327 (224)	-1 (-57; 55)
Surgery	2566 (1634)	235 (1224)	2331 (1971; 2690)
GP	34 (53)	47 (79)	-13 (-35; 9)
GP nurse	9 (22)	3 (8)	6 (0; 11)
Community nurse	7 (25)	2 (17)	5 (-2; 13)
Occup. therapist	25 (102)	8 (58)	17 (-8; 43)
Hospital inpatient	341 (1198)	922 (2222)	-581 (-1052; -109)
Hospital outpatient	43 (108)	36 (96)	7 (-20; 35)
Hospital day case	65 (20)	65 (20)	0 (-55; 55)
Physiotherapy	326 (287)	327 (224)	-1 (-57; 55)

^ Difference between groups and 95 per cent confidence intervals were estimated by ordinary least squares regression

~ Resource use data at six months were collected only in the patient questionnaires and thus are exclusively related to primary care in the base case analysis

Table 5. Summary of incremental analysis (ITT), cost-effectiveness results and uncertainty for the base case (highlighted) and sensitivity analyses

Analysis	Difference in costs*	Difference in QALYs*	ICER for surgery (£ per QALY)	Probability Cost-effective† £20 000/QALY
Base case (MI)	**1758 (1126; 2389)**	**-0.0101 (-0.13; 0.11)**	**Surgery dominated**	**6%**
Sensitivity i (CC)	1517 (615; 2419)	-0.0066 (-0.16; 0.15)	Surgery dominated	16%
Sensitivity ii	1739 (909; 2569)	-0.0110 (-0.13; 0.11)	Surgery dominated	6%
Sensitivity iii	1312 (-606; 3231)	0.0338 (-0.14; 0.21)	38 783	37%
Sensitivity iv	1563 (497; 2629)	-0.0103 (-0.13; 0.11)	Surgery dominated	10%
Sensitivity v	1793 (701; 2884)	-0.0120 (-0.15; 0.12)	Surgery dominated	9%

Sensitivity analysis i: Complete case (CC)
Sensitivity analysis ii: Including all resource use (shoulder and non-shoulder related), MI
Sensitivity analysis iii: Including all resource use (shoulder and non-shoulder related), CC
Sensitivity analysis iv: Source patient's questionnaires, MI
Sensitivity analysis v: Source patient's questionnaires, CC
* Difference between groups (surgery – not-surgery) and 95 per cent confidence intervals were estimated from bivariate model using seemingly unrelated regression. The covariates used to adjust for in the model were age, gender, treatment group, baseline utility and tuberosity involvement (yes/no) at baseline
† Probability of surgery being cost-effective estimated by non-parametric bootstrapping.