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# Cost-effectiveness of group-based outpatient physical therapy after total knee replacement: results from the economic evaluation alongside the ARENA multicentre randomised controlled trial

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**Abstract**

*Objective:* To assess the cost-utility and cost-effectiveness of a group-based outpatient physical therapy intervention delivered six-weeks after primary total knee replacement (TKR) compared with usual care, alongside the Activity-orientated REhabilitation following kNee Arthroplasty (ARENA) multi-centre randomised controlled trial.

*Methods:* The economic analyses were performed from the perspective of the health and social care payer. We collected resource use for health and social care and productivity losses, and patient outcomes for 12 months after surgery to derive costs and quality-adjusted life-years (QALYs). Results were expressed in incremental cost-effectiveness ratios (ICERs), and incremental net monetary benefit statistics (INMBs) for a society willing-to-pay £20,000 per QALY gained, with sensitivity analyses to model specification and perspective.

*Results:* ARENA physical therapy classes cost, on average, £179 (SD=£39) per patient. Treatment in the year following surgery cost, on average, £1,739 (95%CI -£742, £4,221) per patient in the intervention group (n=89), an additional £346 (95%CI £38, £653) compared with usual care (n=91, £1,393;95%CI -£780, £3568). QALY benefits were 0.0506 higher (95%CI 0.009, 0.09) in the intervention group, corresponding to an additional 19 days in perfect health. The ICER for the intervention was £6,842 per QALY gained and the INMB was £665 (, 95%CI £139, £1,191) with a 92% probability of being cost-effective, and no less than 73% in all sensitivity analysis scenarios.

*Conclusion:* The addition of group-based outpatient physical therapy classes to usual care improves quality-of-life and is a cost-effective treatment option following TKR for a society willing-to-pay £20,000 per QALY gained.

*Trial Registration:* ISRCTN:32087234.

**Significance and Innovations**

- We found that supplementing usual care with a novel 6-week group-based outpatient physical therapy intervention is a cost-effective treatment option for the health and social care payer to offer all patients after primary total knee replacement for a society willing-to-pay £20,000 per QALY gained.

- Patients in the intervention arm had better quality of life in the year following surgery, spending, on average, an additional 19 days in "perfect health" compared with patients in the usual care group.

- Delivering the physical therapy intervention was relatively cheap (£179 per patient, on average). A year of care in the intervention group cost, on average, £346 more compared with usual care.

## Introduction

Each year, around 110,000 people receive knee replacements in the UK (1, 2), and a further 10,000 in Sweden (3), 11,000 in Norway (4) and 790,000 in the USA (5). Primary total knee replacements account for around 87% of all knee replacement surgeries in the UK. On average patients are 70 years of age (interquartile range 64-77) (1). A small proportion of patients experience reduced mobility and persistent pain after knee replacement (6), which is associated with worse health-related quality of life (7). Physical therapy (PT) can improve short-term outcomes after knee replacement (8), but provision is variable across the UK, and often only when needed (9).

The Activity-orientated REhabilitation following kNee Arthroplasty (ARENA) randomised controlled trial aimed to investigate whether providing a novel group-based outpatient physical therapy intervention to all patients would be an effective and cost-effective treatment option to optimize function in the longer term (10). The ARENA intervention led to a small improvement in function at 3 and 12 months after surgery, albeit below the minimum clinically important difference (10). The aim of this paper is to report the results of the cost-utility and cost-effectiveness analyses performed alongside the ARENA trial.

## Methods

### *Overview of economic evaluation*

We have conducted a 12-month cost–utility analysis and a cost-effectiveness analysis alongside the ARENA trial. The trial compared a group-based outpatient physical activity intervention, offered to all patients after primary total knee replacement, with usual care which may or may not offer physical therapy to some (10). The primary analysis took an NHS plus Personal Social Services (PSS) (NHS+PSS) perspective, in accordance with NICE guidelines.(11) The secondary analysis took a societal perspective on costs, which included private expenses and productivity losses. All analyses followed the pre-specified health economics analysis plan (12) and study protocol (13).

### *Trial design*

The ARENA study was a multicentre, pragmatic, unblinded, superiority randomised controlled trial aiming to investigate whether providing a novel group-based outpatient physical therapy intervention to all patients would be effective and cost-effective. The trial design was informed by a systematic review (8), a survey of current practice (14) and a feasibility study (15). Clinical results of the ARENA trial are reported elsewhere (10).

*Patients*

The ARENA trial recruited 180 patients waiting for total knee replacement for osteoarthritis from two large orthopaedic centres in Bristol, UK: Southmead Hospital, a National Health System (NHS) funded hospital at North Bristol NHS trust, and Emersons Green, a private Independent Treatment Centre. To relieve pressure in NHS hospitals, the NHS often contracts elective TKR surgeries to the private sector. All patients in the ARENA trial were NHS patients treated in these two different hospitals. All physical therapy received in the intervention and control arms was also funded by the NHS regardless of hospital providing the surgery. The patients were randomised (n=89 in the intervention group and n=91 in the usual care group) and followed up at 3, 6, and 12 months by postal questionnaires. Patients completed a baseline questionnaire prior to surgery.

*Intervention and usual care*

The ARENA intervention is an outpatient physical therapy intervention, consisting of six weekly 1-hour group-based physical therapy classes, starting six weeks after surgery. Classes were delivered in an NHS outpatient gymnasium by two physical therapists, or one physical therapist and a technician, on a weekly rolling basis. Classes could accommodate a maximum of 12 patients per class. Patients could join and leave the group freely so that at any one time the group would include patients who had undertaken differing numbers of sessions to each other. Patients completed an exercise circuit, consisting of 10 task-related exercise stations and two individualised exercise stations. Physical therapists individualised exercises for each patient within a task-oriented exercise circuit.

Usual care consisted of knee-specific and functional advice and referral to outpatient physical therapy on a need-specific basis, depending on the range of motion post-surgery or muscle weakness. Further details of the intervention and usual care are described in the protocol and clinical effectiveness papers (10, 13).

*Resource use for the economic evaluation*

NHS costs included: (a) additional physical therapy received in hospital or in the community; (b) other therapies (such as hydrotherapy, chiropraxis or acupuncture); (c) hospital readmissions; (d) additional outpatient appointments or A&E attendances; and (e) medications. Personal Social Services costs included: (f) food at home services; (g) home care help services and (h) special orthopaedic equipment or house adaptations. In our societal perspective, we further included: (i) patient out-of-pocket healthcare and therapy expenses (if any), (j) lost income, and (k) productivity losses in terms of time off paid and unpaid work, time off usual activities, and time spent on informal care by a friend or relative.

*Outcome measures for the economic evaluation*

We used the EQ-5D-5L questionnaire (16), a standardised and validated patient-reported outcome instrument, for collecting health-related quality of life data and derive quality-adjusted life years (QALYs). The EQ-5D-5L consists of one question for each of five dimensions: mobility, self-care, usual activities, pain/discomfort, and anxiety/depression. It allows outcomes for different clinical interventions to be directly comparable.

The Lower Extremity Functional Scale (LEFS) was the primary clinical outcome for the ARENA trial. The LEFS is a 20-item patient-reported outcome measure that produces a total score includes questions on four different groups of activities: (a) hardest activities, (b) moderately difficult activities, (c) moderately easy activities and (d) easy activities. Each item ranges from 0 (extremely difficult) to 4 (no difficulty) and the total score ranges from 0 (high disability) to 80 (no disability). A minimum clinically important difference in LEFS is defined as a 9-point difference or more (17).

*Data collection*

Resources used in relation to the delivery of the intervention were recorded on study report forms. Physical therapist and physical therapy-technicians also recorded time to prepare class, set up the gym, and clear-up after class, as well as writing patient notes, the time spent preparing and delivering sessions, and the number of patients attending each session. These data enabled the estimation of the cost of the intervention.

Data on resource use were collected from patients at 3, 6 and 12 months, using postal resource-use questionnaires (RUQs). Bespoke RUQs were designed by the research team (including orthopaedic surgeons and physical therapists) in collaboration with a musculoskeletal patient and public involvement and engagement group. We further designed resource use logs for patients to tick use of resources prospectively and advised patients to refer to their logs when completing the RUQs. Data on outcomes (EQ-5D-5L scores (18) and LEFS) were collected prior to surgery (baseline) and at 3, 6 and 12 months post-operative. Resources used within 2 weeks of surgery were not collected as randomisation took place 2 weeks after surgery and no difference in resource use between groups within 2 weeks was expected.

*Patient and Public Involvement*

The trial design and management was informed by a group of 9 patients in a patient and public involvement (PPI) group (19). Patients in the PPI group informed the design of the resource-use questionnaires.

*Dealing with missing data*

We explored the patterns of missingness in the data and assumed data were not missing completely at random (MNAR). We used multiple imputation methods (20), using chained equations, with 60 sets and predictive mean matching. Missing cost variables, utility scores, and LEFS scores were imputed at each time point (3, 6, and 12 months) and later aggregated. It was computationally not feasible to impute EQ-5D scores by domain. Our imputation model included age, sex, hospital site, and baseline utility and LEFS scores.

*Valuing resource use to derive costs*

In a micro-costing approach, we used the Unit Costs of Health and Social Care (PSSRU) to value staffing costs, using staff grades and time spent delivering the intervention (21). Other cost components were valued in a macro-costing approach based on UK NHS reference costs (22) for community care and secondary care and the British National Formulary for medications (23). The costs associated with productivity losses and informal care were valued using a human capital approach and ONS averaged gross weekly wages per age group. The cost associated with each resource-use item was calculated by multiplying the units of resource used in the 12-month period by its unit cost, creating a measure of cost per year. All resources were valued in 2017-18 Great British pounds (£).

*Valuing health states in the EQ-5D-5L to derive QALYs*

We attached published UK societal utility tariffs for the EQ-5D-3L to the EQ-5D-5L response profiles using Van Hout's crosswalk,(18) as per the NICE position statement on valuation of the EQ-5D-5L.(24) This produced a composite health-related quality-of-life (QoL) score at each time point (2 weeks, and 3, 6, and 12 months post-operative) for each patient. These quality-of-life or utility scores were treated as continuous variables, bound at a maximum of 1 (corresponding to perfect health), where 0 corresponds to death, and negative values were permitted for health states worse than death. We calculated accumulated QALYs gained per patient using the area-under-the-curve approach, assuming a linear change between utility scores at each time point (2 weeks and 3, 6 and 12 months).

*Cost-utility and cost-effectiveness analysis*

We adjusted costs and QALYs for hospital site (trial stratification variable) and pre-specified need-predicting variables (age, sex, and comorbidities) as controls. The index for comorbidities was based on the count of simultaneous comorbidities per patient, in line with the literature (25). QALYs were further adjusted for utility at baseline and LEFS score at baseline (26). Costs and QALYs were not discounted due to the 12-month time frame of the analysis.

We used Seemingly Unrelated Regressions (SUR) to jointly estimate the differences in costs and outcomes between arms from baseline. The SUR methodology has the advantage of also calculating the correlation of residuals between costs and QALYs, and testing if the two are independent or related. We then calculated the Incremental Cost-Effectiveness Ratio (ICER) and the Incremental Net Monetary Benefit (INMB), using a willingness-to-pay (WTP) threshold of £20,000 per QALY, in accordance with NICE guidelines (27, 28). We plotted cost-effectiveness acceptability curves (CEAC) for primary and secondary analyses to illustrate the uncertainty surrounding the decision to adopt the intervention by indicating the probability that our group physical therapy intervention is cost-effective over usual care, for a range of societal WTP values.

All analyses were intention-to-treat. Randomised participants were included in the economic analysis based on the group to which they were originally assigned, regardless of whether they received the allocated treatment or not.

*Uncertainty and sensitivity analyses*

We addressed the uncertainties around our analysis methods and findings by conducting one-way deterministic sensitivity analyses. We recognise the cost of the intervention may vary in different settings and patient groups within the NHS. We created an optimistic scenario, where all physical therapy classes were attended by 12 patients; and a pessimistic scenario, where only 2 patients attended each physical therapy class, to understand the impact of class size on costs and cost-effectiveness. We conducted a complete case analysis to deal with the uncertainty arising from imputing missing data and examined patterns of missingness in the data. To address model uncertainty in the estimation of our costs and QALYs, we adjusted these using a second set of models. Models of type 2 included all variables in the first model plus ethnicity, employment status, alone living status, marital status, education and Index of Multiple Deprivation (IMD) deciles, as for the statistical analysis of clinical results (published elsewhere (29)).

## Results

*Descriptive statistics*

Table 1 describes patient demographic and socio-economic characteristics by arm and overall. One hundred and eighty patients were randomised between March 2015 and March 2017. No major differences were observed between trial arms for all variables except marital status.

*Resource use, costs, and QALYs*

In total, 98 physical therapy classes were carried out as part of the trial. The average length of time of each class was 100 minutes; no class was shorter than 90 minutes, and included physical therapists' time to set up, clear up, and write patients' notes. Sixty nine of the 89 patients (78%) randomised to receive the intervention attended four or more classes and 42 patients (47%) attended all six classes. All 89 patients randomised to receive the intervention attended at least one class. No patients assigned to the control arm received any of the intervention classes. On average, 5.46 patients attended each class. The intervention cost on average £178.97 (95% CI £108.12, £249.81) per patient offered the physical therapy intervention.

Table 2 presents adjusted cost components and outcomes by trial arm including imputed data for the 12 months after primary TKR surgery. Code for the imputation model can be found in supplementary materials. The cost drivers for this trial are the costs of additional physical therapy, which are larger for the intervention group. This reflects the fact that more patients in the intervention arm sought additional physical therapy, as reported in Table 2 of the clinical results paper (10). The mean NHS+PSS costs for the year post surgery per patient were £1,739 (95% CI -£742, £4,221) in the intervention group, compared with £1,393 (95% CI -£780, £3,568) in the usual care group, representing an additional £346 (95% CI £38, £653) in the intervention arm.

The QALY benefits were also 0.0506 higher (95% CI 0.009, 0.09) in the intervention group (mean QALY gain over 12-months 0.7156; 95% CI 0.244, 1.18) compared with the usual care group (mean QALY gain 0.6650; 95% CI 0.235, 1.09). This equates to approximately 18.5 additional days in full health for patients in the intervention arm.

*Cost-utility and cost-effectiveness base case results*

The mean INMB statistic is £665 (95% CI £139, £1,191), for a willingness-to-pay threshold of £20,000 per QALY (Table 3). This means that the physical therapy group intervention costs, on average, an additional £6,842 per QALY gained compared with usual care, from an NHS+PSS perspective. From a societal perspective, the costs accruing from both intervention and usual care arms were higher, and the mean INMB statistic was £407 (95% CI £56, £758). The ICER was £8,002 per QALY gained which, although higher than in our primary analysis, still sits comfortably under the £20,000 threshold used by NICE.

The mean difference in LEFS score between arms was below the minimal clinically important difference. The intervention costs an additional £74 per unit LEFS score gained from an NHS+PSS perspective, and £87 per unit LEFS score gained from a societal perspective.

The correlation coefficients in the SUR models were negative for both the relationship between costs and QALYs (-0.0123 for the NHS+PSS perspective; -0.109 for the societal perspective); costs and LEFs scores (-0.328 and -0.336 respectively). This means that patients with high health care or societal costs were those with worse health outcomes.

Figures 1(a) and (b) depict the probability of the intervention being cost-effective for WTP thresholds varying from £0 to £50,000 per QALY gained in cost-effectiveness acceptability curves. At £20,000 per QALY gained, the intervention is 91.74% likely to be cost-effective from an NHS+PSS perspective and 89.41% likely to be cost-effective from the societal perspective.

*Sensitivity analysis results*

The sensitivity analysis to our statistical models yielded slightly higher costs and more conservative results. From an NHS+PSS perspective, the costs associated with the intervention and usual care arms were £2,181 and £1,866 on average, respectively, and from a societal perspective, these were £4,013 and £3,671 on average, respectively. However, the mean difference in outcomes (QALYs and LEFS) between arms was also greater, resulting in higher mean INMBs (£769 from an NHS+PSS perspective; £745 from a societal perspective) and smaller ICERs (Table 4).

The differences in costs from the NHS+PSS and societal perspectives are, on average, smaller (£248 and £309) when classes run at capacity, with 12 participants per session in the optimistic scenario, compared with the base case. The differences are greater (£655 and £716) with only two participants per class in the pessimistic scenario, for both perspectives on costs. Even in the pessimistic scenario, the probability that the intervention is cost-effective is above 70% when willing-to-pay £20,000 per QALY.

Our complete case analysis included 108 patients with complete information prior to imputation. Our findings are more conservative but the probability that the intervention is cost-effective at £20,000 WTP is still higher than 75%, for both perspectives.

**Discussion**

The novel group-based outpatient physical therapy six weeks after total knee replacement costs an incremental £6,842 per QALY gained from an NHS+PSS perspective and incremental £8,002 per QALY gained from a societal perspective. The additional physical therapy delivered in the ARENA intervention costs, on average, £179 per patient. In the year following surgery, care in the intervention group cost, on average, £346 more than usual care, as patients in the intervention group sought additional physiotherapy to the intervention, which is already more than usually offered in standard care. The QALY gains associated with the intervention are on average 0.0506 (95%CI 0.009, 0.09) higher, corresponding to 18.5 additional days of full health over the year for patients in the intervention group. This group-based intervention is likely to be a cost-effective treatment from both an NHS+PSS perspective and a societal perspective when compared with usual care alone for a society willing-to-pay £20,000 per QALY gained, and our findings were robust to model specification and different scenarios of patient uptake across the wider NHS.

The ARENA study was a large randomised controlled trial in the clinical rehabilitation literature, and included an economic evaluation, which allowed us to estimate whether spending additional resources to provide this intervention would be an efficient use of resources. By including a societal perspective on costs, we are also considering the burden of the intervention on patients, their carers, and society.

The ARENA intervention is a novel intervention developed by the study's physiotherapy team. It is a short intervention, delivered to all patients "early" at 6 weeks post-surgery, which is an improvement on current practice of delivering therapy on an "as needed" basis. It is delivered in a group setting, where physical therapists can run a weekly group class and patients can enter and leave the group at will. This setting makes the logistics of delivery easy to organise and cost-effective for hospitals to provide. The exercises in the class are tailored to each patient and thus patients can undertake a tailored intervention within a group setting. We found that even when the class size is only two patients per class, the intervention's incremental cost-effectiveness ratio is still less than £20,000 per QALY gained and is over 70% likely to be cost-effective. We observed that patients in the intervention arm received more additional physical therapy. We expected that offering physical therapy to all patients in the ARENA intervention would substitute prescribed additional therapy on a "need-to" basis; instead, we found it induced demand for additional prescribed therapy in the intervention group. We expected patients in the usual care group to seek further treatment to supplement their usual care, due to participating in trial. Although this may have happened, it was surpassed by the additional therapy sought by patients in the intervention group. The improvement of 0.051 QALY gains (SD 0.21) observed at one year is higher than QALY gains observed in some other trials in TKR, (30-32) but evidence is lacking on what constitutes a meaningful difference for QALY gains measured by the EQ-5D-5L tool and valued using a crosswalk from the 3L values. The ARENA intervention is therefore cost-effective in relation to this observed QALY gain and for a society willing-to-pay £20,000 per QALY gained. The improvement in LEFS score was too small to determine the cost-effectiveness in relation to the primary clinical outcome.

All outcome and resource-use data were collected from patient-completed questionnaires at follow-up periods, which allow for a wider perspective on costs to be taken but are prone to recall bias and missing data. However, our complete case analysis results were consistent with the imputed data findings. Our findings may not be generalisable in settings where there is no availability of gym space and or staff time to deliver the intervention. Despite the relatively large sample size of this trial, we did not compute a sample size for the economic results, and they may be underpowered.

In October 2019, NICE started a consultation for further evidence on postoperative rehabilitation of joint replacement, including knee. (33) Our results suggest that group-based physical therapy classes are cost-effective for a society willing-to-pay £20,000 per QALY gained and increase health-related quality of life by approximately 18.5 additional days in full health, and therefore have the potential to contribute to future clinical guidelines. Other studies have already demonstrated the cost-effectiveness of group-based physical therapy for treatment of knee arthritis (34-36), but these studies were for interventions prior to knee replacement surgery, and the findings were based mostly on lower costs of the intervention, with very small increments in quality-of-life. More recently a study compared a home-based rehabilitation programme with traditional one-to-one physiotherapy after partial and total knee replacement and found no evidence that the home-based programme led to great improvements in function or quality-of-life. (30) Our study provides new evidence that short-term group-based physical therapy classes may be cost-effective alternatives to rehabilitation following total knee replacement, largely due to improvements in quality-of-life. We present evidence on potentially efficient intervention available to all patients after

TKR, which, if implemented, may reduce inequalities in access to care for underserved populations in TKR.

## Conclusion

We found that group-based outpatient physical therapy classes delivered six weeks after surgery in addition to usual NHS care is a cost-effective clinical rehabilitation option for patients following primary total knee replacement for a society willing-to-pay £20,000 per QALY gained. It costs an additional £346 per patient to the health care provider in the year following surgery and leads to increases in quality-adjusted life years and small, non-meaningful, improvements in function. Our findings were robust in a range of sensitivity analyses and when taking a societal perspective on costs.

## List of Abbreviations

ARENA - Activity-orientated REhabilitation following kNee Arthroplasty
CEAC – Cost-effectiveness Acceptability Curve
CEA – Cost-Effectiveness Analysis
CUA – Cost Utility Analysis
ICER – Incremental Cost-Effectiveness Ratio
IMD – Index of Multiple Deprivation
INMB – Incremental Net Monetary Benefit
LEFS - Lower Extremity Functional Scale
NHS – National Health System
NICE - National Institute for Health Care and Excellence
PSS – Personal Social Services
QALY – Quality-Adjusted Life Year
RUQ – Resource Use Questionnaire
SUR - Seemingly Unrelated Regressions
UK – United Kingdom
WTP – Willingness to Pay

**Declarations**

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*Availability of data and material*

The datasets generated during the current study will be available in the University of Bristol Research Data Repository (https://data.bris.ac.uk/data/). Access to the data will be restricted to ensure that data are only made available to bona fide researchers for ethically approved research projects, on the understanding that confidentiality will be maintained and after a Data Access Agreement has been signed by an institutional signatory.

*Contributions*

EL, NA, VW, AB, and EM designed the study. EM designed the economic evaluation. ES prepared the data. EB carried out the analysis of data with support from EM and JT. EB produced the initial draft and EM revised it. All authors have critically revised the manuscript for intellectual content and approved the final version for publication.

*Ethics approval and consent to participate*

The trial received ethics approval from the National Research Ethics Committee Southwest-Central Bristol (reference 14/SW/1144). All participants provided informed, written consent.

*Competing interests*

The authors declare that they have no competing interests.



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**List of Tables and Figures**

Table 1 – Participants' baseline characteristics

| Sample characteristics | Usual Care (N=91) | | Intervention group (N=89) | |
|---|---|---|---|---|
| | *mean* | *sd* | *mean* | *sd* |
| Age | 69.87 | 8.68 | 69.50 | 9.17 |
| Comorbidities | 1.65 | 0.85 | 1.77 | 0.97 |
| IMD | 6.43 | 2.80 | 6.68 | 2.64 |
| | *count* | *%* | *count* | *%* |
| Female | 49 | 54% | 50 | 56% |
| White | 88 | 99% | 84 | 95% |
| Lives alone | 23 | 26% | 28 | 32% |
| Married | 60 | 67% | 54 | 61% |
| Retired | 64 | 72% | 59 | 67% |
| Education: left before or at school leaving age | 65 | 71% | 57 | 64% |

IMD = Index of Multiple Deprivation

Table 2 – Costs and outcomes by trial arm for 12 months after TKR by perspective

| **Costs and Outcomes** | **Usual Care (N=91)** | | | **Intervention group (N=89)** | | | **Difference** | |
|---|---|---|---|---|---|---|---|---|
| **COSTS** | number of patients using resource | mean cost per patient | sd | number of patients using resource | mean cost per patient | sd | mean | sd |
| ***NHS+PSS costs*** | | **£1,394** | **£1,109** | | **£1,740** | **£1,266** | **£346** | **£157** |
| PT intervention classes | 0 | - | - | 89 | £179 | £36 | £179 | - |
| Additional physiotherapy | 66 | £139 | £293 | 83 | £277 | £323 | -£138 | £30 |
| Other therapies | 37 | £80 | £199 | 35 | £75 | £156 | £5 | -£43 |
| Hospital readmission | 19 | £192 | £874 | 11 | £125 | £570 | £66 | -£305 |
| Outpatient or AE visit | 59 | £127 | £191 | 54 | £129 | £239 | -£2 | £48 |
| Special orthopedic equipment | 77 | £62 | £62 | 79 | £109 | £488 | -£47 | £426 |
| Medication | 80 | £22 | £33 | 66 | £41 | £143 | -£19 | £110 |
| Additional health and social services use | 76 | £77 | £117 | 76 | £91 | £152 | -£14 | £35 |
| ***SOCIETAL Costs*** | | **£3,418** | **£1,266** | | **£3,826** | **£1,445** | **£407** | **£179** |
| Time-off paid work | 27 | £146 | £492 | 23 | £193 | £532 | -£47 | £40 |
| Time-off unpaid work | 56 | £38 | £85 | 52 | £35 | £87 | £3 | £3 |
| Informal care | 57 | £26 | £44 | 52 | £18 | £29 | £8 | -£14 |
| **OUTCOMES** | | mean benefit | sd | | mean benefit | sd | mean | sd |
| QALYs | | 0.665 | 0.219 | | 0.716 | 0.240 | 0.051 | 0.021 |
| Utility at baseline | | 0.466 | 0.248 | | 0.411 | 0.269 | - 0.055 | 0.021 |
| Utility at 12 months | | 0.730 | 0.232 | | 0.749 | 0.241 | 0.019 | 0.009 |
| LEFS score | | 48.22 | 17.58 | | 52.85 | 20.03 | 4.64 | 2.45 |
| LEFS score at baseline | | 28.59 | 14.74 | | 25.39 | 14.58 | -3.20 | -0.16 |
| LEFS score at 12 months | | 53.29 | 17.53 | | 55.79 | 18.48 | 2.50 | 0.95 |

Note: costs and outcomes were estimated adjusting for sex, age, hospital site, comorbidities and baseline outcomes in SUR baseline models complete data using 60 imputed datasets.

Table 3 – Base Case results - Cost Utility Analysis (CUA) and Cost Effectiveness (CEA)

| **Results** | **NHS+PSS Perspective** | **Societal Perspective** |
|---|---|---|
| **CUA** | | |
| ICER (£/QALY) | £ 6,842 | £ 8,003 |
| Prob. cost-effectiveness | 91.74% | 89.41% |
| INMB* [95%CI] | £665 [£139, £1191] | £407 [£56, £758] |
| **CEA** | | |
| ICER (£/LEFS score) | £ 61.89 | £ 66.88 |

Note: 1) Base case models adjust for age, gender, comorbidities and hospital site; 2) ICER = incremental cost-effectiveness ratio, INMB = incremental net monetary benefit. QALY = quality-adjusted life year; 3) *Measured at a willingness to pay for a QALY of £20,000.

Table 4 – Sensitivity Analyses: using models type 2 specification, optimistic and pessimistic scenarios, complete case analyses

| Results | NHS+PSS Perspective | Societal Perspective |
|---|---|---|
| **MODELS TYPE 2** | | |
| ICER (£/QALY) | £ 5,819 | £ 8,003 |
| Prob. cost-effectiveness | 95.22% | 94.14% |
| INMB* [95%CI] | £769 [£291, £1,247] | £745 [£308, £1,183] |
| **OPTIMISTIC SCENARIO** | | |
| ICER (£/QALY) | £ 4,914 | £ 6,086 |
| Prob. cost-effectiveness | 94.42% | 92.62% |
| INMB* [95%CI] | £763 [£237, £1,289] | £708 [£225, £1,191] |
| **PESSIMISIC SCENARIO** | | |
| ICER (£/QALY) | £ 12,960 | £ 14,084 |
| Prob. cost-effectiveness | 77.11% | 73.10% |
| INMB* [95%CI] | £365 [-£169, £882] | £301 [-£181, £783] |
| **COMPLETE CASE ANALYSIS** | | |
| ICER (£/QALY) | £ 9,282 | £ 9,410 |
| Prob. cost-effectiveness | 76.01% | 75.95% |
| INMB* [95%CI] | £419 [-£195, £1,034] | £428 [-£149, £1,007] |

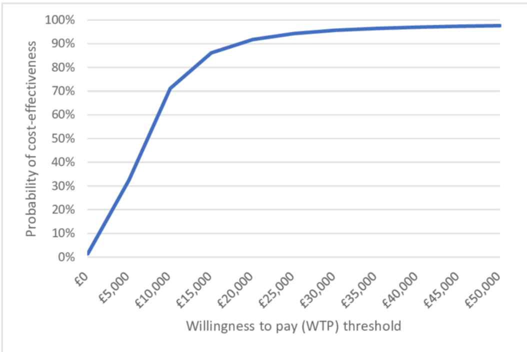
* Measured at willing-to-pay £20,000 for a QALY.

Figure 1 - Cost-effectiveness acceptability curve (CEAC) showing the probability that the intervention is cost-effective vs. usual care at different values of the societal willingness to pay for a QALY

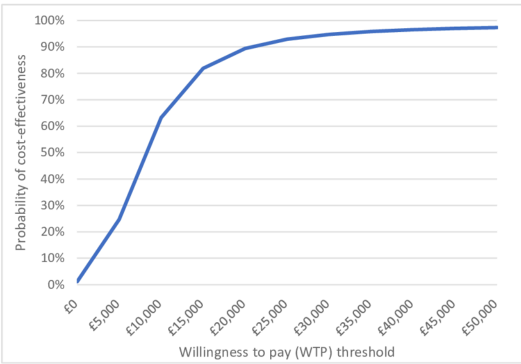
(a) NHS + PSS perspective

(b) Societal perspective

NHS + PSS perspective




Societal perspective

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