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Original article

Cost–utility analysis of interventions to improve effectiveness of exercise therapy for adults with knee osteoarthritis: the BEEP trial

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Abstract

Objectives. Evidence regarding the cost-effectiveness of enhancing physical therapy exercise programmes in order to improve outcomes for patients with knee OA remains unclear. This study investigates the cost-effectiveness of two enhanced physical therapy interventions compared with usual physical therapy care (UC) for adults with knee OA.

Methods. A trial-based cost–utility analysis of individually tailored exercise (ITE) or targeted exercise adherence (TEA) compared with UC was undertaken over a period of 18 months. Patient-level costs were obtained, and effectiveness was measured in terms of quality-adjusted life years (QALYs), allowing the calculation of cost per QALY gained from a base-case UK health-care perspective.

Results. The UC group was associated with lower National Health Service (NHS) costs [ITE-UC: £273.30, 95% CI: £−62.10 to £562.60; TEA-UC: £141.80, 95% CI: £−135.60 to £408.10)] and slightly higher QALY gains (ITE-UC: −0.015, 95% CI: −0.057 to 0.026; TEA-UC: −0.003, 95% CI: −0.045 to 0.038). In the base case, UC was the most likely cost-effective option (probability <40% of ITE or TEA cost-effective at £20 000/QALY). Differences in total costs were attributable to intervention costs, number of visits to NHS consultants and knee surgery, which were higher in both ITE and TEA groups.

Conclusion. This is the first economic evaluation comparing usual physical therapy care *vs* enhanced exercise interventions for knee OA that involves greater exercise individualization, supervision and progression or that focuses on exercise and physical activity adherence over the longer term. Our findings show that UC is likely to be the most cost-effective option.

Trial registration. Current Controlled Trials ISRCTN 93634563.

Trial protocol. Full details of the trial protocol can be found in the Supplementary Appendix, available with the full text of this article at http://www.biomedcentral.com/1471-2474/15/254 doi: 10.1186/1471-2474-15-254

Key words: economic evaluation, cost-effectiveness, cost–utility, osteoarthritis, knee pain, exercise

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Introduction

OA-related hip and knee pain are common and one of the leading causes of disability and poor quality of life among the elderly [1–3]. It is estimated that ∼23% of adults aged ≥50 years report symptoms of severe pain and disability [4]. Hip and knee OA are often significant contributors to the economic burden on society, estimated to account for between 1 and 2.5% of the gross national product in countries including the USA,

ORIGINAL ARTICLE

Key messages

- Usual physical therapy care is likely to be the most cost-effective option for the management of knee OA.
- The cost-effectiveness of exercise interventions for knee OA beyond the 18-month follow-up in this analysis remains unclear.
- Further research on long-term cost-effective exercise interventions among knee OA patients is needed.

Canada, the UK, France and Australia [5–9]. Most of the direct costs of knee OA are attributable to hospital stays, specifically orthopaedic surgery, with ~76 000 total knee replacement (TKR) procedures undertaken per year in the UK [10]. Knee OA-related morbidity also results in substantial indirect costs, estimated at £3.2 billion in the UK (1999–2000 prices), attributable to work absenteeism and early retirement [11].

Given the socioeconomic impact of OA, there is a strong rationale to test ways to improve patient outcomes of pain and function and to ensure that healthcare systems make decisions about the use of resources based on high-quality evidence. Clinical trials and systematic reviews consistently show the benefit of exercise therapy, in a variety of forms, for this patient group [12–15]. Exercise is a low-cost treatment option, which makes it accessible to many sufferers [16], and different forms of exercise have been found to be cost-effective in the USA [17], New Zealand [18] and Finland [19]. In the UK, previous studies have demonstrated that physical therapist-led exercise is cost-effective in the short and long term [20–24]. However, the optimal exercise regimen remains unclear, and there is currently limited evidence that patient outcomes can be improved by offering enhanced physical therapist-led exercise programmes by greater focus on individualization, supervision and progression of lower-limb exercise or a greater focus on long-term exercise and physical activity adherence.

This study reports the economic evaluation conducted alongside the Benefits of Effective Exercise for knee Pain (BEEP) trial, to determine the cost-effectiveness of two enhanced physical therapist-led exercise interventions: (i) individually tailored exercise (ITE), and (ii) targeted exercise adherence (TEA), in patients with knee OA in primary care, compared with usual physical therapy care (UC) [25–27].

Methods

Overview

The trial-based economic evaluation took the form of a cost–utility analysis alongside a three parallel-group, pragmatic, randomized controlled trial using quality-adjusted life years (QALYs) as the benefit measure, over an 18-month follow-up period. QALYs take into account survival and quality of life, and the focus here was on the potential for quality-of-life gains from a reduction in pain and improvements in physical function from three physical therapy-led exercise interventions. The primary outcomes of the trial were lower-limb pain and function measured using the WOMAC OA Index [28], and the primary time point was 6 months after randomization. Participants in the trial were recruited from 65 general practices and five physical therapy services in the West Midlands and Cheshire regions of the UK. Adults aged ≥45 years with current knee pain and/or stiffness in one or both knees who met the criteria recommended by the National Institute for Health and Care Excellence guidelines for a clinical diagnosis of knee OA [2] were invited to take part. Full details of the trial methods are provided in the published trial protocol [25]. The trial was approved by the North West 1 Research Ethics Committee, Cheshire UK (REC reference: 10/H1017/45), and all participants gave informed consent to participate.

Interventions

All participants in the BEEP trial received an information booklet providing information about benefits of exercise and physical activity and a home exercise programme. Usual physical therapy care (UC) included advice and lower-limb exercise provided in up to four individual, one-to-one treatment sessions over 12 weeks, in line with usual physical therapy practice in the National Health Service (NHS). The usual care arm of the BEEP trial was developed following a national survey of current physical therapy practice in the UK for knee OA [27]. The other two groups received substantially enhanced care compared with UC. ITE involved a supervised, individually tailored and progressed lower-limb exercise programme provided in six to eight one-to-one treatment sessions over 12 weeks. Participants received a print-out of a specific exercise prescription individualized for them based on their progress on the programme. TEA started with a focus on lower-limb exercise (as in the ITE protocol), with an aim to support progress to increasing general physical activity adherence over 6 months. It consisted of four individual face-to-face treatments up to week 12, and a further 4–6 follow-up contacts (face-to-face or over the telephone) from week 12 through to 6 months (a total of 8–10 treatment contacts). More comprehensive details are reported elsewhere [25–26].

Health outcomes

A questionnaire was administered to participants at baseline, 3, 6, 9 and 18 months after randomization. The questionnaire contained the EQ-5D 3L, a generic instrument measuring and valuing health-related quality of life [29]. At each time point, the individual responses to the EQ-5D questionnaire were converted to utility values [ranging from −0.594 (the worst health state) to 1.000 (full health), with 0 equivalent to death] obtained using the UK value set, derived from a UK general population survey [30]. QALYs were then generated for each individual using the area-under-the-curve approach that links the participant utility scores at different time points [31]. In order to avoid bias, adjustment for differences between the groups in baseline EQ-5D scores was also undertaken using a regression-based adjustment [32].

Resource use and cost analysis

In the base-case analysis, costs were measured from the UK NHS perspective, with non-NHS health-care costs incurred by the patient considered in sensitivity analysis. Knee OA-related resource use data were collected from self-report postal questionnaires administered at 6 and 18 months. NHS resource use data included primary care consultations [general practitioners (GPs), practice nurses and community physical therapists], consultations with other health-care professionals (e.g. hospital consultants, hospital physical therapists and acupuncturists), hospital-based investigations (e.g. X-rays and MRI scans) and procedures (knee joint-related injections, knee joint-related surgery such as partial or total knee replacement or arthroscopy), and prescribed medications. Additional information on any knee surgery that had occurred or was scheduled to occur within the 18-month follow-up period was also occasionally provided separately by participants via telephone, during a consultation with BEEP trial physical therapists (and therefore noted on a treatment case report form) or written elsewhere on one of their returned questionnaires, and this was also retrieved and included in the cost analysis. Non-NHS (health-care) costs were obtained by asking patients about their use of private health care and purchase of over-the-counter medicines, appliances and devices, treatments and use of local exercise facilities. In order to assess broader economic consequences of the interventions beyond health-care resources, self-reported data on occupation and time taken off work owing to their knee pain over the 18-month period were also collected.

Information on resource use was also collected within the trial to estimate participant-specific costs for the intervention they received. Details of the number of trial-related physical therapy sessions attended by each participant were collected through treatment case report forms (CRFs). Patients randomized to UC received advice and a lower-limb exercise programme in up to four treatment sessions within a period of 12 weeks. The costs required to deliver the ITE and TEA interventions included additional physical therapy sessions (in both the ITE and TEA interventions), telephone contacts and pedometers (in the TEA intervention). Intervention costs included an average 47-min initial physical therapy assessment and treatment session, followed by 28-min face-to-face treatment sessions and 11-min telephone call contacts in the TEA intervention (based on data from CRFs for trial participants). Participants in all three arms of the trial received an advice and information booklet about knee OA; the cost of the advice and information booklet was not included in the analysis because it would not contribute to the incremental cost analysis between the groups.

Unit costs were obtained from various sources, including the British National Formulary [33] for the cost of drugs, and the NHS Reference costs [34] and Unit Costs of Health and Social Care [35] were applied to other resource use items. All unit costs used in this analysis are reported in Table 1, using a common 2012–13 price year. We calculated indirect costs for time off paid work using the human capital approach, based on respondent job-specific wage estimates identified from annual earnings data and UK Standard Occupational Classification coding [36–38].

Statistical analysis

An incremental cost–utility analysis was conducted, according to the intention-to-treat principle, to determine the difference in costs and QALYs between the ITE and TEA groups compared with UC [39]. The unit of outcome was the cost per additional QALY gained (incremental costs divided by incremental QALYs). Multiple imputation was used to impute all missing values for the EQ-5D and total cost estimates for non-responders to the 6- and 18-month follow-up questionnaires [40]. In the base-case analysis, only NHS costs excluding surgery were imputed. This was owing to some patients providing information on knee surgery but not returning a resource use questionnaire, resulting in missing resource use data. This additional knee surgery information was used as part of a secondary analysis. Confidence intervals for the mean differences in costs were obtained by bias-corrected and accelerated non-parametric bootstrapping, using 1000 replications [41]. Although costs were collected over an 18-month period, discounting was not applied to the 18-month questionnaire data, as this contained resource use data from both the last 6 months of year 1 and the first 6 months of year 2 and could not be disaggregated. In order to account for uncertainty, bootstrapping techniques were used to derive 5000 paired estimates of mean differential cost and QALY scores. The bootstrapped cost-effect pairs were then graphically presented on a cost-effectiveness plane [42,43]. Cost-effectiveness acceptability curves were then calculated showing the probability that an intervention was cost-effective at a specific threshold of cost per QALY gained [44]. All statistical analyses were performed using Stata version 12.0 [45]. The base-case analysis was from a UK NHS perspective, using the imputed dataset and adjusting for baseline EQ-5D scores. Two sensitivity analyses were performed to assess robustness of the findings. Firstly, a complete-case analysis was undertaken to assess the impact of missing cost and EQ-5D data. Secondly, the

Table 1 Health-care resource use unit costs

Health care resource	Unit cost (£)	Unit course (reference)
Primary care contacts		
GP consultation per 11.7 min	34	[35]
Practice nurse consultation per hour	44	[35]
Nurse home visit per hour	60	[35]
Community physical therapist per hour[a]	30	
Hospital-based care		
Orthopaedic surgeon: first attendance	128	[34]
Orthopaedic surgeon: follow-up	102	[34]
Rheumatologist: first attendance	202	[34]
Rheumatologist: follow-up	133	[34]
Acupuncturist: first attendance	49	[34]
Acupuncturist: follow-up	44	[34]
Hospital physical therapist: first attendance[b]	49	[34]
Hospital physical therapist: follow-ups[b]	44	[34]
Occupational therapist: first attendance	75	[34]
Occupational therapist: follow-up	68	[34]
Podiatrist: first attendance	74	[34]
Podiatrist: follow-up	68	[34]
Diagnostic tests: X-ray	35	[34]
Diagnostic test: MRI	169	[34]
Diagnostic test: CT scan	98	[34]
Surgery: knee replacement major	5,676	[34]
Surgery: knee replacement minor	2,221	[34]
Surgery: arthroscopy	2,942	[34]
Intervention cost[c]		[34]
First physical therapist session: 47 min	23.5	
Follow-up physical therapist sessions: 28 min	14	
Telephone physical therapy consultation: 11 min	5.3	
Pedometer	5	
Prescribed medication	Patient specific	[33]
Medical investigations/ interventions	Patient specific	[34]

[a]Relates to additional physical therapy visits via primary care services.
[b]Relates to additional physical therapy visits accessed via hospital-based care services.
[c]Relates to the unit cost used in costing the interventions as part of the BEEP trial intervention. GP: general practitioner.

imputed analysis was performed excluding the additional knee surgery-related costs. This was to assess the impact of excluding costs calculated from additional resource use information on knee replacement surgery provided outside the health-care utilization section on the follow-up questionnaires. Results were also presented from a health-care perspective, taking into account non-NHS health-care utilization. Finally, a complete-case analysis of the impact of knee pain on time off work was also reported, including calculation of the monetary value of productivity losses.

Results

A total of 514 participants (UC: $n = 175$; ITE: $n = 176$; and TEA: $n = 163$) with knee pain attributable to OA formed the dataset for the analysis. All base-case analysis reflects the imputed dataset unless stated otherwise. Complete EQ-5D 3L outcome data at all time points were available for 325 patients (64% of the total sample), and this sample was used as part of the sensitivity analysis. At each of the time points, complete data were available for 97% (baseline), 80% (3 months), 87% (6 months), 76% (9 months) and 78% (18 months) of participants. The mean age of participants in the groups was 63 years, with slightly more women (51%); and slightly >42% were in paid employment. On average, participants in the groups had moderate pain and disability, and there were no important differences between groups at baseline.

Health outcomes

Mean EQ-5D scores at baseline and follow-up time points and mean QALYs are shown in Table 2. Health-related quality of life increased in all three intervention groups from baseline to 3 months, and remained higher than baseline scores at the 18-month follow-up. The adjusted and imputed mean QALYs over 18 months were higher for the UC group than for the ITE or TEA groups, but differences between intervention arms were very small. This result did not change with the unadjusted or complete-case analyses.

Resource use and costs

Table 3 shows the disaggregated details of mean resource use for participants with complete resource use data. Over 18 months, only small differences in the uptake of primary care and secondary care NHS services were found between the three groups, with the exception of the number of visits to NHS consultants and knee joint-related surgeries. The numbers of NHS consultant visits were higher in both the ITE and TEA groups, and the number of participants reporting TKR was highest in the ITE group [10 TKR (7%) within 18 months] compared with the UC group [3 TKR (2%)] and the TEA group [5 TKR (4%)]. In total, 50 (10%) BEEP trial participants proceeded to visit NHS consultants for their knee and 33 (6%) had knee joint-related surgery over the 18-month follow-up period.

Less than half the patients in the trial were in paid employment at the 18-month follow-up; 43% in the UC group and 34% in both the ITE and TEA groups. Data

TABLE 2 Outcomes by treatment group over 18 months

Variable	UC	ITE	TEA
Primary imputed analysis	$n = 175$	$n = 176$	$n = 163$
EQ-5D scores, mean (S.D.)			
Baseline	0.636 (0.230)	0.644 (0.229)	0.629 (0.229)
3 months	0.686 (0.201)	0.708 (0.188)	0.669 (0.227)
6 months	0.690 (0.225)	0.692 (0.215)	0.692 (0.217)
9 months	0.698 (0.217)	0.665 (0.249)	0.702 (0.199)
18 months	0.700 (0.219)	0.700 (0.206)	0.682 (0.232)
QALYs			
Unadjusted, mean (S.D.)	1.035 (0.268)	1.026 (0.273)	1.026 (0.271)
Incremental QALYs[b] (95% CI)		−0.009 (−0.061 to 0.048)	−0.009 (−0.067 to 0.045)
Adjusted[a]	1.035	1.019	1.032
Incremental QALYs[b] (95% CI)		−0.015 (−0.057 to 0.026)	−0.003 (−0.045 to 0.038)
Complete-case analysis	$n = 109$	$n = 113$	$n = 103$
QALYs			
Unadjusted, mean (S.D.)	1.058 (0.2687)	1.048 (0.206)	1.028 (0.2961)
Incremental QALYs[b] (95% CI)		−0.010 (−0.083 to 0.059)	−0.029 (−0.105 to 0.046)
Adjusted[a]	1.061	1.033	1.041
Incremental QALYs[b] (95% CI)		−0.027 (−0.084 to 0.029)	−0.020 (−0.078 to 0.037)

[a]Predicted scores after adjusting for outcome at baseline.
[b]ITE-UC and TEA-UC. EQ-5D: EuroQol; ITE: individually tailored exercise; QALYs: quality-adjusted life years; TEA: targeted exercise adherence; UC: usual physical therapy care.

on employment and time off work are reported in supplementary Table S1, available at *Rheumatology Advances in Practice* online. Of those who reported being in employment, only 2 (3%) patients in the UC group reported time off paid work because of knee pain, compared with 11 (24%) in the ITE group and 6 (15%) in the TEA group. During the 18-month follow-up period, the mean number of days off work was higher in the ITE group (13.5 days) and the TEA group (6.9 days) than in UC (1.8 days). This translated into higher productivity costs in the ITE (£1313.60) and TEA groups (£691.00) compared with UC (£127.80), and this difference was significant. Overall, the ITE group was associated with more days off work related to knee-related surgeries than the TEA and UC groups (supplementary Table S1, available at *Rheumatology Advances in Practice* online).

Table 4 shows the disaggregated mean (S.D.) health-care costs per patient for each intervention and total cost estimates for the imputed data analysis. The mean costs per patient were £86 for TEA and £71 for ITE, compared with £44 for UC. These costs reflect the higher resource use in these categories in both the ITE and TEA groups attributable to additional physical therapy treatment sessions in the BEEP trial. Total mean NHS costs over 18 months of follow-up were lower in the UC group (£383) than in the ITE (£656) and TEA (£524) groups (Table 4). The direction of this result did not change when total health-care costs were considered or when a complete-case analysis was undertaken (supplementary Table S2, available at *Rheumatology Advances in Practice* online). The results from multiple imputation of total NHS costs (rather than the base-case imputation of all NHS costs excluding surgery) were also in line with the base-case findings (supplementary Table S2, available at *Rheumatology Advances in Practice* online).

Cost–utility analysis

The base-case analysis showed that UC was slightly more effective and less costly than ITE or TEA, resulting in a position of dominance (Table 5). The cost-effectiveness planes in Figs 1A and 1B confirm this finding. In Fig. 1 (ITE *vs* UC), most cost–QALY difference pairs (68%) are located in the north-west quadrant, suggesting that UC is dominant over ITE. The cost-effectiveness plane for TEA *vs* UC has 45% of cost–QALY difference pairs in the north-west quadrant (Fig. 1B). The corresponding cost-effectiveness acceptability curves (Fig. 1C) showed a low probability (<40%) of either the ITE or TEA interventions being cost-effective compared with UC if society was willing to pay up to £20 000 per additional QALY.

Discussion

Our results demonstrate that usual NHS physical therapy-led advice and exercise delivered in up to four treatment sessions is likely to be the most cost-effective use of health-care resources compared with either of the enhanced physical therapy interventions (ITE or TEA). Usual physical therapy care incurred lower costs and was slightly more effective in terms of health-related quality of life than the other interventions, with

TABLE 3 Health-care resource use per patient by treatment group over 18 months

Resource category	UC n = 141, mean (S.D.)	ITE n = 134, mean (S.D.)	TEA n = 120, mean (S.D.)
Primary care: GP	1.42 (2.3)	1.50 (3.2)	1.33 (2.7)
Primary care: practice nurse	0.19 (0.7)	0.37 (1.7)	0.45 (2.3)
Primary care: other professionals	0.32 (1.3)	0.28 (1.4)	0.35 (1.6)
NHS consultant	0.93 (2.3)	1.68 (3.6)*	1.64 (4.2)**
NHS other health-care professionals	0.12 (0.6)	0.17 (0.9)	0.04 (0.2)
Private consultant	0.50 (2.8)	0.43 (2.1)	0.11 (0.8)
Private other health-care professionals	0.45 (0.5)	0.32 (3.1)	0.00 (–)
	n (%)	*n* (%)	*n* (%)
Knee-related investigations and treatment[a]	29 (21)	36 (27)	29 (24)
Total knee replacement[b]	3 (2)	10 (7)	5 (4)
Knee arthroscopy[b]	6 (4)	4 (3)	4 (3)
Partial knee replacement[b]	0 (–)	0 (–)	1 (1)
Prescribed medication[b]	*n* (%)	*n* (%)	*n* (%)
Simple analgesics	36 (26)	30 (22)	21 (18)
Moderate combination opioids	1 (1)	2 (1)	2 (2)
NSAIDs and COX-2 inhibitors	23 (16)	11 (8)	12 (10)
Strong combination opioids + opioids	17 (12)	23 (17)	19 (16)
Very strong single opioids	0 (–)	1 (1)	1 (1)
Weak combination opioids	16 (11)	13 (10)	13 (11)
Over-the-counter[b] treatments	*n* (%)	*n* (%)	*n* (%)
Simple analgesics	67 (48)	73 (54)	63 (53)
NSAIDs and COX-2 inhibitors[c]	2 (1)	3 (2)	1 (1)
Weak combination opioids[d]	4 (3)	8 (6)	5 (4)

[a]Knee-related investigations and treatments are investigations or treatments such as injections or X-rays, excluding knee-related surgery.
[b]The numbers (percentages) of participants reporting usage within the procedures, investigations, procedures, out-of-pocket and prescribed medication categories are reported instead of mean (S.D.) because of multiple usage, purchases and/or prescriptions.
[c]Values reported include selected NSAIDs that are available over the counter.
[d]Values reported include weak opioids available at low doses over the counter.
**$P < 0.1$, *$P < 0.05$ for UC *vs* ITE and UC *vs* TEA. GP: general practitioner; ITE: individually tailored exercise; NHS: National Health Service; TEA: targeted exercise adherence; UC: usual physical therapy care; NSAIDs: Non-Steroidal Anti-Inflammatory Drugs; COX-2 inhibitors: Cyclo-oxygenase-2 inhibitors.

higher total QALYs at 18 months. As expected, the ITE and TEA interventions were associated with higher treatment costs resulting from more physical therapy sessions. The results regarding outcomes are in line with those found in the analysis of participants' clinical outcomes of pain and function. A further finding was a higher rate of NHS consultant outpatient appointments in both the ITE and TEA groups, and a greater number of participants in the ITE group who had TKR surgery within the 18-month follow-up period. This resulted in more days off work in this patient group. This might be attributable to patients having increased opportunities through a greater number of physical therapy sessions to discuss the appropriateness of other treatment options and, in particular, the role of surgery. It might also be explained by the greater number of treatment sessions in the ITE group, through which there was greater individualization and progression of exercise. It is possible that for some patients this more intensive exercise programme highlighted their physical limitations more clearly, prompting them to seek other health-care advice and treatment as a result.

A review focused on cost-effectiveness of conservative management of hip and/or knee OA highlighted that there was only limited cost-effectiveness evidence and that more high-quality economic evaluations are needed [46]. No previous trials had assessed the cost-effectiveness of an enhanced programme of physical therapy-led exercise that extends the number of treatment sessions to allow greater exercise individualization, supervision and progression or that focuses on exercise and physical activity adherence over the longer term. This is the first economic evaluation comparing these enhanced interventions with usual physical therapy care for knee OA. Two previous studies assessed the cost-effectiveness of a package of up to 12 physical therapist-led exercise sessions and found this to be more cost-effective than usual GP-led care in the short term (6 months), with some long-term benefits (12 months) [23,24]. In comparison, our analyses show that

Table 4 Mean (s.d.) costs per participant by treatment group over 18 months, unless otherwise stated

	UC	ITE	TEA
	$n = 175$	$n = 176$	$n = 163$
Complete-case analysis	$n = 141$ (£)	$n = 134$ (£)	$n = 120$ (£)
Intervention cost (£)	43.9 (20.8)	70.8 (32.9)*	85.9 (41.7)*
Primary care			
GP consultations	34.5 (55.3)	36.7 (73.8)	34.7 (71.7)
Practice nurse consultations	2.5 (8.7)	5.2 (27.1)	6.3 (33.9)
Consultations with other professionals	5.9 (34.9)	4.7 (32.4)	7.0 (35.6)
Prescriptions	7.6 (17.4)	7.6 (21.7)	4.8 (9.6)
Secondary care			
NHS consultant	67.1 (191.1)	106.3 (231.4)	103.9 (250.4)
Consultation with other NHS professional	0.00 (–)	3.3 (19.3)**	1.4 (12.4)
Knee surgery[a]	213.8 (1194.5)	389.4 (1501.5)	259.9 (1118.6)
NHS investigations and treatments[b]	15.4 (51.6)	16.31 (48.9)	16.7 (64.3)
Private consultant	26.8 (149.2)	30.9 (166.8)	8.2 (46.1)
Consultation with other private health-care professional	0.0 (–)	13.8 (138.1)	0.0 (–)
Over-the-counter purchases[c]	17.6 (72.3)	16.8 (44.5)	28.9 (133.3)
Base-case analysis (imputed)	$n = 175$	$n = 176$	$n = 163$
Total NHS cost, £	382.6 (1351.3)	656.0 (1617.1)	524.4 (1258.2)
Adjusted mean difference (95% CI)	–	273.3 (−62.1 to 562.6)	141.8 (−135.6 to 408.1)
Total health-care costs, £	427.2 (1457.8)	711.1 (1683.7)	560.4 (1307.1)
Adjusted mean difference (95% CI)	–	283.9 (−73.4 to 591.6)	133.2 (−178.3 to 410.7)

[a]Knee surgery includes all full knee replacement, partial knee replacement and arthroscopic surgical procedures.
[b]NHS investigations and treatments are investigations or treatments such as injections or X-rays, excluding knee-related surgery.
[c]Includes treatments or appliances bought over the counter.
**$P < 0.1$, *$P < 0.05$ for UC *vs* ITE and UC *vs* TEA. GP: general practitioner; ITE: individually tailored exercise; NHS: National Health Service; TEA: targeted exercise adherence; UC: usual physical therapy care.

Table 5 Cost–utility analysis for 18 months of follow-up

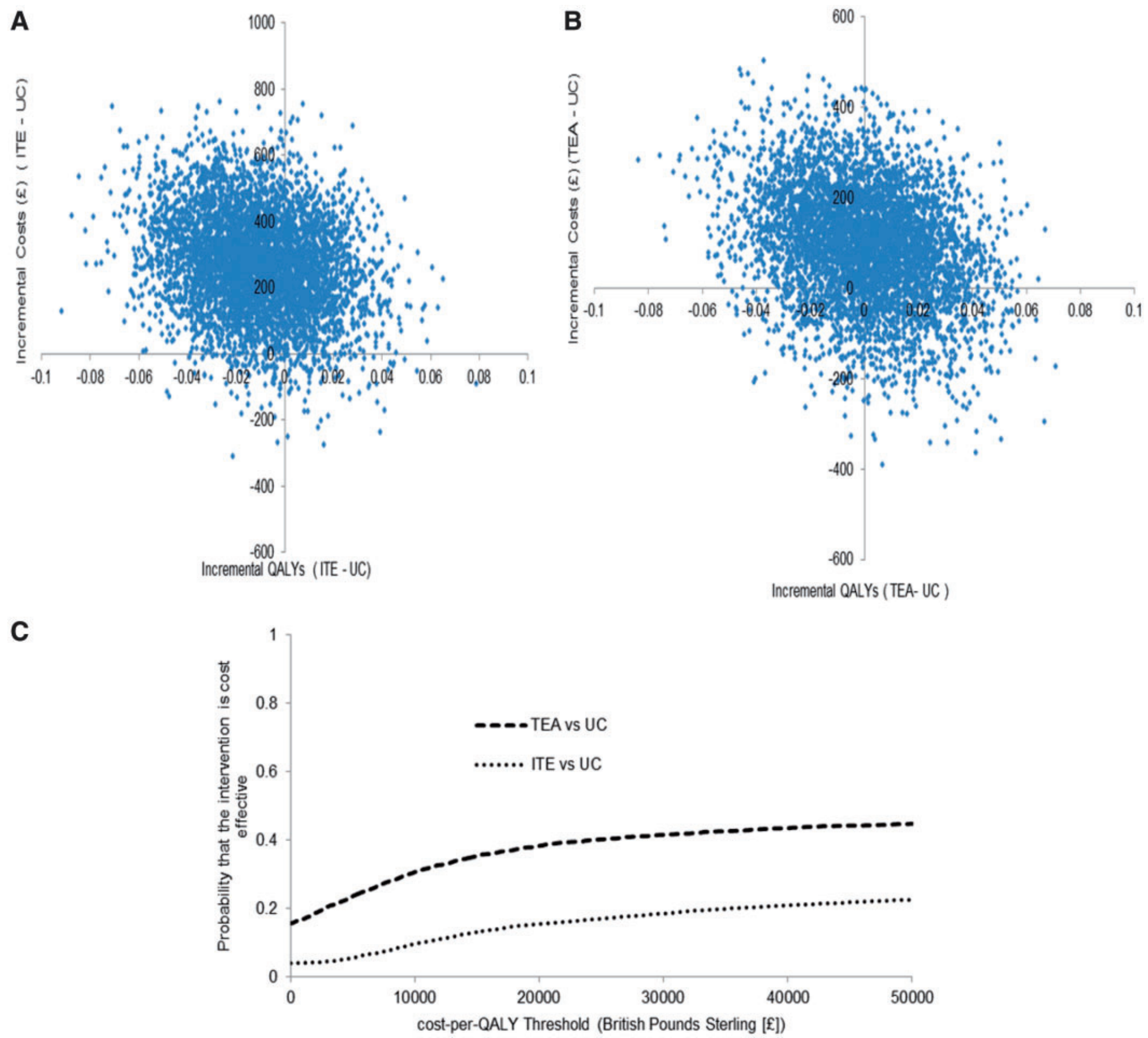
Intervention	Costs [mean (s.d.); (£)]	Mean QALYs	ICER (£/QALY gained)
UC	382.6 (1351.3)	1.035	–
ITE	656.0 (1617.1)	1.032	Dominated by usual care
TEA	524.4 (1258.2)	1.019	Dominated by usual care

[–]A value for an ICER is not relevant here. ICER: incremental cost-effectiveness ratio; ITE: individually tailored exercise; QALY: quality-adjusted life year; TEA: targeted exercise adherence; UC: usual physical therapy care.

greater exercise tailoring and targeting of physical activity adherence by physical therapists have additional cost implications but are likely to generate only similar effectiveness (based on QALYs) to up to four sessions of usual physical therapy care.

This study has estimated that 6% of 514 patients in primary care proceed to TKR within 18 months, and this compares with 3% over 6 years and 10% over 10 years in other comparable studies [47,48]. However there are some limitations to our analysis. The amount of missing data requiring imputation may be of concern, particularly for the cost outcomes; only 64% of participants provided complete data at 18 months of follow-up. However, imputation was done at all data collection time points and a sensitivity analysis performed, which showed that the results did not differ when a complete-case analysis was undertaken. One reason for missing data might be withdrawal from the trial or non-completion of questionnaires owing to knee surgery in the 18-month follow-up period, a procedure associated with high costs to the NHS. This might be attributable to patients being less willing to complete a questionnaire if they feel that surgery has resolved their problem. However, this was unlikely to influence the results, as cost analyses with and without the additional information we gathered on any knee surgery both resulted in a greater number of participants in the ITE group having TKR. Resource use data were requested from patients in their 18-month

Fig. 1 Uncertainty around cost-utility analysis results presented using cost-utility planes and cost-utility acceptability curves.



(A) Cost–utility plane comparing individual tailored exercise (ITE) with usual physical therapy care (UC). **(B)** Cost–utility plane comparing targeted exercise adherence (TEA) with UC. **(C)** Cost–utility acceptability curves comparing targeted exercise adherence (TEA) and individually tailored exercise (ITE) with usual physical therapy care (UC). QALY: quality-adjusted life year. Data were based on 5000 bootstrapped cost–effect pairs.

questionnaire, requiring recall of resource use over the previous 12 months, and this length of time might have resulted in inaccurate estimates. However, this was the case for patients in all three trial groups, so it is likely any inaccuracies are balanced. The trial included participants from many primary care general practices; therefore the findings are generalizable to the wider population of primary care patients with knee OA in the UK. However, the interventions in this trial were compared with usual physical therapy practice in the UK [25–27], and the findings may not be generalizable to other countries or health systems with different usual care programmes.

This economic evaluation demonstrated that neither increasing the individual tailoring of, nor targeting the adherence to exercise and physical activity in older adults with knee OA is likely to be cost-effective compared with usual physical therapy care. The clinical results showed that ~50% of patients could be classified as treatment responders in the BEEP trial; therefore, further health economics research is needed that investigates how best to use health-care resources for adults with knee OA. Our findings show that usual physical therapy care is likely to be the most cost-effective option.

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Supplementary data

Supplementary data are available at *Rheumatology Advances in Practice* online.

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