Systematic review of cost-effectiveness of enhanced recovery following hip and knee arthroplasty

Table S6.1. Full search terms for Ovid MEDLINE

	Ovid MEDLINE
1	arthroplasty, replacement, hip/ or arthroplasty, replacement, knee/
2	((knee? or hip) adj (replace$ or arthroplast*)).ti,ab.
3	1 or 2
4	simulation model$.ti,ab.
5	markov.ti,ab.
6	monte carlo.ti,ab.
7	decision tree$.ti,ab.
8	decision analy$.ti,ab.
9	qaly$.ti,ab.
10	(valu$ adj2 quality).ti,ab.
11	utility value$.ti,ab.
12	((disability or quality) adj adjusted).ti,ab.
13	((life adj2 year$) or health year equivalent$).ti,ab.
14	(health adj utilit$).ti,ab.
15	hui$1.ti,ab.
16	(quality adj3 well$).ti,ab.
17	qwb.ti,ab.
18	(qald$ or qale$ or qtime$).ti,ab.
19	(well being or wellbeing).tw.
20	(health adj2 stat$).tw.
21	((adjusted adj2 life) or qaly$).ti,ab.
22	(daly or qol or hql or hqol or hrqol or hr ql or hrql).tw.
23	cost-utility.ti,ab.
24	cost-effectiveness.ti,ab.
25	cost-benefit.ti,ab.
26	cost-minimisation.ti,ab.
27	cost-minimization.ti,ab.
28	modelling.ti,ab.
29	modeling.ti,ab.
30	decision model.ti,ab.
31	QALY.ti,ab.
32	quality adjusted life year$.ti,ab.
33	cost.ti,ab.
34	life year$.ti,ab.
35	incremental cost-effectiveness ratio.ti,ab.
36	(quality adj2 life).ti,ab.
37	Technology Assessment, Biomedical/
38	"Costs and Cost Analysis"/
39	technology assessment$.ti,ab.
40	economic evaluation$.ti,ab.
41	economic model$.ti,ab.
42	discrete event simulat$.ti,ab.
43	cost utility.ti,ab.
44	cost effectiv$.ti,ab.
45	cost benefit.ti,ab.
46	cost minimisation.ti,ab.
47	cost minimization.ti,ab.
48	ICER$.ti,ab.
49	EQ-5D$.ti,ab.
50	(SF-12 or SF12 or Short Form 12).ti,ab.
51	(SF-36 or SF36 or Short Form 36).ti,ab.

Ovid MEDLINE	
52	(SF-6D or SF6D or Short Form 6D).ti,ab.
53	rosser index.ti,ab.
54	person trade off.ti,ab.
55	standard gamble.ti,ab,kw.
56	time trade off.ti,ab,kw.
57	Hye.ti,ab,kw.
58	Hyes.ti,ab,kw.
59	Euroquol.ti,ab,kw.
60	4 or 5 or 6 or 7 or 8 or 9 or 10 or 11 or 12 or 13 or 14 or 15 or 16 or 17 or 18 or 19 or 20 or 21 or 22 or 23 or 24 or 25 or 26 or 27 or 28 or 29 or 30 or 31 or 32 or 33 or 34 or 35 or 36 or 37 or 38 or 39 or 40 or 41 or 42 or 43 or 44 or 45 or 46 or 47 or 48 or 49 or 50 or 51 or 52 or 53 or 54 or 55 or 56 or 57 or 58 or 59
61	3 and 60

Table S6.2. Full search terms for Ovid EMBASE

EMBASE	
1	hip replacement/ or hip arthroplasty/
2	total knee replacement/ or knee replacement/ or knee arthroplasty/
3	((knee? or hip) adj (replace$ or arthroplast$)).ti,ab.
4	1 or 2 or 3
5	simulation model$.ti,ab.
6	markov.ti,ab.
7	monte carlo.ti,ab.
8	decision tree$.ti,ab.
9	decision analy$.ti,ab.
10	qaly$.ti,ab.
11	(valu$ adj2 quality).ti,ab.
12	utility value$.ti,ab.
13	((disability or quality) adj adjusted).ti,ab.
14	((life adj2 year$) or health year equivalent$).ti,ab.
15	hui$1.ti,ab.
16	(quality adj3 well$).ti,ab.
17	qwb.ti,ab.
18	(qald$ or qale$ or qtime$).ti,ab.
19	(well being or wellbeing).tw.
20	(health adj2 stat$).tw.
21	((adjusted adj2 life) or qaly$).ti,ab.
22	(daly or qol or hql or hqol or hrqol or hr ql or hrql).tw.
23	cost-utility.ti,ab.
24	cost-benefit.ti,ab.
25	cost-minimisation.ti,ab.
26	cost-minimization.ti,ab.
27	modelling.ti,ab.
28	modeling.ti,ab.
29	QALY.ti,ab.
30	quality adjusted life year$.ti,ab.
31	cost.ti,ab.
32	life year$.ti,ab.
33	incremental cost-effectiveness ratio.ti,ab.
34	(quality adj2 life).ti,ab.
35	decision model$.ti,ab.
36	cost-effectiv$.ti,ab.
37	"cost benefit analysis"/
38	biomedical technology assessment/
39	technology assessment$.ti,ab.

EMBASE	
40	economic evaluation$.ti,ab.
41	economic model$.ti,ab.
42	discrete event simulat$.ti,ab.
43	cost utility.ti,ab.
44	cost effectiv$.ti,ab.
45	cost benefit.ti,ab.
46	cost minimisation.ti,ab.
47	cost minimization.ti,ab.
48	ICER$.ti,ab.
49	(health adj utilit$).ti,ab.
50	EQ-5D$.ti,ab.
51	(SF-12 or SF12 or Short Form 12).ti,ab.
52	(SF-36 or SF36 or Short Form 36).ti,ab.
53	(SF-6D or SF6D or Short Form 6D).ti,ab.
54	rosser index.ti,ab.
55	person trade off.ti,ab.
56	standard gamble.ti,ab,kw.
57	time trade off.ti,ab,kw.
58	Hye.ti,ab,kw.
59	Hyes.ti,ab,kw.
60	Euroquol.ti,ab,kw.
61	5 or 6 or 7 or 8 or 9 or 10 or 11 or 12 or 13 or 14 or 15 or 16 or 17 or 18 or 19 or 20 or 21 or 22 or 23 or 24 or 25 or 26 or 27 or 28 or 29 or 30 or 31 or 32 or 33 or 34 or 35 or 36 or 37 or 38 or 39 or 40 or 41 or 42 or 43 or 44 or 45 or 46 or 47 or 48 or 49 or 50 or 51 or 52 or 53 or 54 or 55 or 56 or 57 or 58 or 59 or 60
62	4 and 61

Table S6.3. Full search terms for NHS EED

National Health Service Economic Evaluations Database, via the Cochrane Library	
Hip	Title, Abstract, Keywords: “Hip arthroplasty” OR
	Title, Abstract, Keywords: “Hip arthroplasties” OR
	Title, Abstract, Keywords: “Hip replacement”
Knee	Title, Abstract, Keywords: “Knee arthroplasty” OR
	Title, Abstract, Keywords: “Knee arthroplasties” OR
	Title, Abstract, Keywords: “Knee replacement”

Table S6.4. Full search terms for Econlit

EconLit, via ProQuest
TI,AB(hip) OR TI,AB(knee) AND TI,AB(Replace*) OR TI,AB(arthroplasty*) OR TI,AB(Replacement) OR TI,AB(arthroplasties)

Table S6.5. Overview of studies included in the review.

Author year	Population	Perspective	Time horizon	Discounting	Currency, cost year
Enhanced recovery pathway					
Brunenberg 2005	Patients on the waiting list for either a THA (48 patients recruited to Joint Recovery Programme (JRP), 50 to usual care) or TKA (30 patients to JRP, 32 to usual care), mean age 64.4 years, one-third male	Societal	1 year	None	USD, 2002
Larsen 2009	Patients in trial[100] having THA, THA or UKA, mean age having accelerated intervention 64, 26 women, 30 men	Societal	1 year	None	DKK, 2006
Preoperative: *Assessment and optimization of comorbidities*					
McLawhorn 2016	50-year-old morbidly obese patient with end-stage unilateral knee osteoarthritis	Societal	40 years	3%	USD, 2012
Preoperative: Staphylococcus aureus *prophylaxis*					
Courville 2012	65-year-olds with end stage hip or knee osteoarthritis for whom medical management has failed and TJA recommended.	Societal	1 year	None	USD, 2005
Intraoperative: *Avoid unnecessary blood transfusion*					
Jackson 2000	Patients undergoing TJA, average age 65 years, range 20 to 80 years	Not stated	Lifetime	3% and 5%	USD, not reported
Sonnenberg 2002	65-year-old of composite sex and race undergoing THA	Not stated	Lifetime	3%	USD, 2000
Intraoperative: *Local infiltration of analgesia*					
Marques 2015	Patients in trial[98] having THA or TKA, mean ages 66–69.5 years, 52%–65% female	Health and social care payer	1 year	None	GBP, not reported
Intraoperative: *Infection prevention*					
Cummins 2009	68-year-olds of average health for their age undergoing THA due to degenerative arthritis	Hospital	Lifetime	3%	USD, 2002
Graves 2016	Simulated cohort of patients who had THA in 2012	UK NHS	Lifetime	3%	GBP, 2012
Merollini 2013	Not described	Health service	30 years	3%	AUD, 2011
Postoperative: *Physical therapy*					
Fusco 2016	Average age of 60 years, 44% males, 19% experienced complications during or after surgery	Societal, and Italian health service	Lifetime	3%	Euro, 2013
Kauppila 2011	Patients in trial aged 60–80 years having unilateral TKR for knee osteoarthritis	Healthcare system	1 year	None	Euro, 2006
Postoperative: *Scheduling of follow-up*					
Bolz 2010	THA patients, mean age 69.9 years	Health services	7 years	3%	AUD, not reported

NHS: National Health Service; THA: total hip arthroplasty; TJA: total joint arthroplasty; TKA: total knee arthroplasty; UKA: unicompartmental knee arthroplasty; AUD: Australian dollar; DKK: Danish krone; GBP: British pound; USD: US dollar

Table S6.6. Populations and tools used for eliciting utilities.

Author year	EQ-5D	15 D	QWB	SG	VAS / rating scale	TTO	AQoL
Studies eliciting utilities							
Brunenberg 2005	Patients in trial (UK tariff)						
Larsen 2009	Patients in trial (Danish tariff)	—	—	—	—	—	—
Marques 2015	Patients in trial (UK tariff)	—	—	—	—	—	—
Kauppila 2011	—	Patients in trial (Finnish tariff)	—	—	—	—	—
Fusco 2016	TKR patients in trial (UK tariff)	—	—	—	—	—	—
Studies using published utilities[*]							
McLawhorn 2016	TKR patients in a trial; patients having bariatric surgery	—	—	—	Patients having bariatric surgery	—	—
Courville 2012	—	—	Population reporting arthritis	—	—	—	—
Jackson 2000	—	—	People with HIV infection	People with HIV infection	People with HIV infection	People with HIV infection	—
Sonnenberg 2002	—	—	People with HIV infection	—	—	—	—
Cummins 2009	—	—	—	—	—	THA patients	—
Graves 2016	THA patients	THA patients	—	—	—	—	THA patients with prosthesis infection
Merollini 2013	—	THA patients	—	—	—	—	THA patients with prosthesis infection
Bolz 2010	—	THA patients	—	—	—	—	—

* Details of utilities obtained from expert opinion are not included in this table

15-D, 15-dimension instrument; AQoL, Assessment of Quality of Life; EQ-5D, EuroQoL five-dimension instrument; HIV, human immunodeficiency virus; SG, standard gamble; THA, total hip arthroplasty; TKA, total knee arthroplasty; TTO, time trade-off; QWB, Quality of Well-being scale; VAS, visual analogue scale

Table S6.7. Summary of findings from studies included in this analysis

Author year, country	Population	Strategy	Cost	Outcome in QALYs	ICER in cost per QALY*	Probability of cost-effectiveness (threshold in cost per QALY)
Enhanced care pathway						
Brunenberg 2005, Netherlands	THA	Conventional care	USD 11 312	0.65		
		Joint Recovery Programme (pre- assessment and intensive rehabilitation)	USD 10 051	0.70		
		Increment	USD −1261	0.07†	Dominates	0.94 (USD 45 000)
	TKA	Conventional care	USD 12 877	0.61		
		Joint Recovery Programme (pre-operative assessment and intensive rehabilitation)	USD 8541	0.65		
		Increment	USD −3336	0.04†	Dominates	0.99 (USD 45 000)
Larsen 2009, Denmark	THA + TKA	Conventional care	DKK 90 227	0.78		
		Accelerated perioperative care and rehabilitation	DKK 71 344	0.83		
		Increment	DKK −18 880	0.05	Dominates	0.97‡ (DKK 160 000)
	THA	Conventional care	DKK 87 657	0.75		
		Accelerated perioperative care and rehabilitation	DKK 71 768	0.84		
		Increment	DKK −15 889	0.09	Dominates	0.98‡ (DKK 160 000)
	TKA	Accelerated perioperative care and rehabilitation	DKK 70 644	0.81		
		Conventional care	DKK 95 367	0.85		
		Increment	DKK 24 723	0.04	DKK 618 075	NR
Preoperative						
Assessment and optimization of comorbidities						
McLawhorn 2016, US	Morbidly obese with unilateral end-stage knee osteoarthritis					
		Immediate TKA	USD 60 453	10.83		
		Bariatric surgery, followed by TKA 2 years later	USD 84 099	12.53		
		Increment	USD 23 646	1.70	USD 13 910	0.988 (USD 100 000)

Author year, country	Population	Strategy	Cost	Outcome in QALYs	ICER in cost per QALY*	Probability of cost-effectiveness (threshold in cost per QALY)
Staphylococcus aureus *prophylaxis*						
Courville 2012, US	THA	Standard infection prevention measures without *S. aureus* screening or mupirocin decolonization	USD 24 506	0.7980		
		Preoperative nasal screening for *S. aureus* followed by mupirocin treatment for patients with positive cultures	USD 24 471	0.7983	D	
		Empirical treatment of all preoperative patients with mupirocin	USD 24 258	0.7985		
		Increment (compared to standard measures)	USD −248	0.0005	Dominates	NR
	TKA	Standard infection prevention measures without *S. aureus* screening or mupirocin decolonization	USD 24 667	0.6783		
		Preoperative nasal screening for *S. aureus* followed by mupirocin treatment for patients with positive cultures	USD 24 611	0.6785	D	
		Empirical treatment of all preoperative patients with mupirocin	USD 24 378	0.6787		
		Increment (compared to standard measures)	USD −289	0.0004	Dominates	NR
Intraoperative						
Avoid unnecessary blood transfusion						
Jackson 2000, US	THA + TKA	Usual transfusion practice	NR	NR		
		Postoperative erythrocyte recovery and transfusion	NR	NR		
		Increment	USD 53	0.00001	USD 5 700 000	NR (USD 50 000)
Sonnenberg 2002, US	THA	Usual practice without autologous donation	USD 1395	NR		
		Autologous blood donation and transfusion	USD 1539	NR		
		Increment	USD 144	0.0523	USD 2750	NR (USD 50 000)
Local infiltration of analgesia						
Marques 2015, UK	THA	Standard anaesthesia	NR	NR		
		Intraoperative local anaesthetic wound infiltration administered before wound closure in addition to standard anaesthesia	NR	NR		
		Increment	GBP −86	0.052	Dominates	0.98 (GBP 20 000)
	TKA	Standard anaesthesia	NR	NR		

Author year, country	Population	Strategy	Cost	Outcome in QALYs	ICER in cost per QALY*	Probability of cost-effectiveness (threshold in cost per QALY)
		Intraoperative local anaesthetic wound infiltration administered before wound closure in addition to standard anaesthesia	NR	NR		
		Increment	GBP −77	0.009	Dominates	0.60 (GBP 20 000)
Infection prevention						
Cummins 2009, US	THA	Conventional cement	USD 24 100	9.439		
		Antibiotic-impregnated bone cement	USD 23 900	9.454		
		Increment	USD −200	0.015	Dominates	NR
Graves 2016, UK[§]	THA	No systemic antibiotics, plain cement and conventional ventilation	GBP 0[§]	0[§]		
		Systemic antibiotics, antibiotic-impregnated cement, laminar ventilation and body exhaust suit	GBP 781 075	62	D	0.01[‖] (GBP 18 000)
		No systemic antibiotics, antibiotic-impregnated cement and conventional ventilation	GBP −4 634 647	89	D	0.07[‖] (GBP 18 000)
		Systemic antibiotics, plain cement and conventional ventilation	GBP −7 226 732	101	D	0.15[‖] (GBP 18 000)
		Systemic antibiotics, antibiotic-impregnated cement, conventional ventilation and body exhaust suit	GBP −3 960 897	106	D	0.11[‖] (GBP 18 000)
		Systemic antibiotics, plain cement and laminar airflow	GBP −5 271 040	118	D	0.10[‖] (GBP 18 000)
		Systemic antibiotics, antibiotic-impregnated cement and laminar airflow	GBP −6 152 877	124	D	0.06[‖] (GBP 18 000)
		No systemic antibiotics, plain cement and laminar airflow	GBP −3 271 749	124	D	0.18[‖] (GBP 18 000)
		Systemic antibiotics, antibiotic-impregnated cement and conventional ventilation	GBP −8 325 277	147		
		Increment (compared to systemic antibiotics, plain cement and conventional ventilation)	GBP −1 098 545	46	Dominates	0.32[e] (GBP 18 000)
Merollini 2013, Australia[¶]	THA	No antibiotic prophylaxis	AUD 1 517 954	−163.1		
		Antibiotic prophylaxis and laminar airflow	AUD 4 592 200	−126.9	D	
		Antibiotic prophylaxis	AUD 0[¶]	0[¶]	D	
		Antibiotic prophylaxis and antibiotic-impregnated cement	AUD −126 375	32.3		

Author year, country	Population	Strategy	Cost	Outcome in QALYs	ICER in cost per QALY*	Probability of cost-effectiveness (threshold in cost per QALY)
		Increment	AUD −126 375	32.3	Dominates	0.986 (AUD 40 000)**
Postoperative						
Physical therapy						
Fusco 2016, Italy	TKA, societal perspective	20 face-to-face rehabilitation sessions	EUR 1315	13.02		
		10 face-to-face rehabilitation sessions plus 10 telesessions	EUR 977	13.02		
		Increment	EUR −338	0	Dominates	NR (EUR 30 000)
	TKA, Italian NHS perspective	20 face-to-face rehabilitation sessions	EUR 1124	13.02		
		10 face-to-face rehabilitation sessions plus 10 telesessions	EUR 862	13.02		
		Increment	EUR −262	0	Dominates	NR (EUR 30 000)
Kauppila 2011, Finland	TKA	Multidisciplinary biopsychosocial outpatient rehabilitation programme	EUR 12 950	NR		
		Conventional orthopaedic care	EUR 11 120	NR		
		Increment	EUR −1830	0.0192	Dominates	NR
Scheduling of follow-up						
Bolz 2010, Australia††	THA, assuming 5% revisions delayed under no follow-up‡‡					
		2-yearly routine follow-up	AUD 26 426 908	147 940		
		Follow-up at 3 months and 1 or 2 years	AUD 21 331 518	147 940	D	
		No follow-up	AUD 14 867 616	147 949		
		Increment	AUD −6 463 902	9	Dominates	NR

* Strategies listed in order of increasing effectiveness; ICER presented compared to next most effective strategy that is not extended-dominated; no ICER presented for dominated or extended-dominated strategies; ICERs have been calculated where not explicitly presented in the reference, where ICERs have been presented they may differ slightly from what would be calculated from the presented figures due to rounding.
† Adjusted for baseline quality of life using regression analysis
‡ Probability of being the dominant strategy
§ Total costs and outcomes for a cohort of 77 321 patients, relative to the cost of the strategy of no systemic antibiotics, plain cement and conventional ventilation
‖ Probability of being most cost-effective strategy in the model
¶ Total costs and outcomes per 30 000 primary THRs, relative to the cost of the strategy of antibiotic prophylaxis
** Cost-effectiveness ≥98.6% at typical willingness-to-pay values of AUD 40 000 to AUD 64 000
†† Total costs and outcomes for a cohort of 30 440 patients
‡‡ Four different probabilities were modelled (1%, 5%, 10%, 50%), but the direction of the results did not change between them

Author year, country	Population	Strategy	Cost	Outcome in QALYs	ICER in cost per QALY*	Probability of cost-effectiveness (threshold in cost per QALY)

AUD, Australian dollar; D, dominated; DKK, Danish krone; EUR, euro; GBP, British pound; ICER, incremental cost-effectiveness ratio; NHS, National Health Service; NR, not reported; QALY, quality-adjusted life year; THA, total hip arthroplasty; TKA, total knee arthroplasty; UK, United Kingdom; US, United States; USD, United States dollar

Table S6.8. Costs included in each study

Author year	Direct medical	Direct treatment	In-patient	Out-patient	Day care	Community healthcare	Medication	Side effect costs	Staff	Labs/diagnostic	Capital equipment	Social care	Travel costs	Productivity losses	Income forgone due to illness
Brunenberg 2005	+	+	+	+		+	+		+			+		+	+
Larsen 2009	+	+	+	+		+	+		+					+	+
McLawhorn 2016	+	+	+					+							
Courville 2012	+	+	+				+			+					
Jackson 2000	+	+	+	+			+		+	+					
Sonnenberg 2002	+	+	+	+			+								
Marques 2015	+	+	+	+	+	+	+		+			+			
Cummins 2009	+	+	+												
Graves 2016	+	+	+				+				+				
Merollini 2013	+	+	+				+		+		+				
Fusco 2016	+	+	+	+					+		+		+	+	+
Kauppila 2011	+	+	+	+	+	+						+			
Bolz 2010	+		+	+						+					

Table S6.9. Components of enhanced recovery pathway in the trials of an entire pathway

	Larsen 2009		Brunenberg 2005	
Intervention type	**Standard protocol**	**Accelerated protocol**	**Usual care**	**Joint recovery programme**
Pre-operative assessment	NA	NA	No standardized screening	History, examination & blood testing 6 weeks prior to surgery
Pre-operative education	Information given to patients on admission	Information provided in groups at outpatient clinic prior to hospitalization	No information session	Information session 1–2 weeks prior to surgery
Day of admission	Day before surgery	Day of surgery	NA	NA
Bed allocation in hospital	Amongst other patients	Patients having joint replacement placed together in separate part of ward	NA	NA
Staff involved	Various	One nurse in charge of multidisciplinary team of nurses, OT & PT	NA	Supervised by PT & nurses throughout admission
Nutrition	Screening	Screening plus daily intake 1.5 L fluid & 2 protein drinks	NA	NA
Start of mobilization	1 day after surgery	Day of surgery	NA	NA
Description of mobilization	Individual & gradual mobilization according to patient tolerance	Intensive mobilization in teams with pre-set goals	Conventional physiotherapy	Rehabilitation in groups in a room resembling the home situation
Duration of mobilization	4 hours daily	8 hours daily	1 hour daily	Duration not specified
Discharge planning	NA	NA	During admission	6 weeks prior to surgery
Other details	NA	NA		Patients could involve a family member or friend to give emotional support

NA, not applicable; OT, occupational therapists; PT, physiotherapists