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Enhanced recovery of hip and knee replacement

Cost-effectiveness of enhanced recovery in hip and knee replacement: a systematic review protocol

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Enhanced recovery of hip and knee replacement

ABSTRACT

Introduction

Hip and knee replacement represents a significant burden to the UK healthcare system. A new "enhanced recovery" pathway has been introduced in the NHS for patients undergoing hip and knee replacement, with the aim of improving outcomes and timely recovery after surgery. To support policy-making there is a need to evaluate the cost-effectiveness of enhanced recovery pathways across jurisdictions. Our aim is to systematically summarise the published cost-effectiveness evidence on enhanced recovery as whole, and on each component of the pathway, in hip and knee replacement.

Methods and analysis

A systematic review will be conducted in MEDLINE, EMBASE, Econlit and NHS EED. Separate search strategies were developed for the different databases including terms relating to hip and knee replacement/arthroplasty, economic evaluations, decision modelling, and quality of life measures.

We will extract peer-reviewed studies published between 2000 and 2017 reporting economic evaluations of pre-, peri- or post-operative enhanced recovery interventions within hip or knee replacement. Economic evaluations alongside cohort studies or based on decision models will be included. Only studies with patients undergoing elective replacement surgery of the hip or knee will be included. Data will be extracted using a pre-defined pro-forma following best practice guidelines for economic evaluation, decision modelling and model validation.

Our primary outcome will be the cost-effectiveness of enhanced recovery (entire pathway and individual components) in terms of incremental cost per quality-adjusted life year. A narrative synthesis of all studies will be presented, focussing on cost-effectiveness results, study design, quality and validation status.

Ethics and dissemination

This systematic review is exempt from ethics approval because the work is carried out on published documents. The results of the review will be disseminated in a peer-reviewed academic journal and at conferences.

Registration number

PROSPERO: CRD42017059473.

Keywords

Systematic review, hip replacement, hip arthroplasty, knee replacement, knee arthroplasty, osteoarthritis, economic evaluation, cost-effectiveness

Enhanced recovery of hip and knee replacement

Strengths of the study

- This systematic review protocol of enhanced recovery pathway for hip/knee replacement was based on a detailed search strategy that will be complemented with a comprehensive data extraction and analysis of the studies.
- The review will followed the latest guidelines and assessed the quality and validity of the cost-effectiveness evidence using published modelling checklists.

Limitations of the study

- The quality and validity of the studies identified may depend on the reporting quality and transparency.

Enhanced recovery of hip and knee replacement

Introduction

Hip and knee replacement represents a significant burden to the UK healthcare system. In 2015, over 88,000 primary total hip replacements (THRs) and primary total knee replacements (TKRs) were registered in the National Joint Registry, covering procedures performed in NHS and independent hospitals in England, Wales, Northern Ireland and the Isle of Man [1 2].

Following the establishment of the Department of Health Enhanced Recovery Partnership Programme in April 2009 [3] a new "enhanced recovery" pathway has been introduced in many NHS hospitals for patients undergoing hip and knee replacement [4]. According to a Department of Health report [3], the principles of enhanced recovery are to ensure: "the patient is in the best possible condition for surgery; the patient has the best possible management during and after his/her operation; the patient experiences the best post-operative rehabilitation." Therefore, enhanced recovery considers the pre-, peri-, and post-operative management of patient care, to enable improved and faster recovery and discharge from hospital.

To inform national policy and local decisions across many jurisdictions, evidence on both the effectiveness and cost-effectiveness of interventions is needed. Economic evaluations of enhanced recovery interventions in hip and knee replacement patients provide such evidence. Estimates of the impact of the interventions in terms of quality of life and costs relative to current practice enable providers to base decisions not only on clinical effectiveness, but also on their value for money.

Previous systematic reviews of economic evaluations in patients having hip or knee replacement have not looked at enhanced recovery or its components but rather focussed on the surgical procedure and its cost-effectiveness.[5 6] [7-9] Here, recent evidence suggests that total joint replacement is cost-effective compared to conservative management [5 7], and unicompartmental knee replacement is less costly then TKR and for some age groups is more effective.[6] We therefore identified a need for a more comprehensive summary of the published economic evidence on enhanced recovery in hip and knee replacement, including each component of the pathway from pre-operative to post-discharge.

Our aim is to systematically summarise and assess the quality of cost-effectiveness evidence of enhanced recovery in hip and knee replacement, for patients of any age with common indications for surgery. Our objectives are to:

- Summarise peer-reviewed published economic evaluations of enhanced recovery interventions in populations of individuals undergoing elective hip or knee replacement
- Report the cost-effectiveness findings in terms of cost per quality-adjusted life year (QALY) for the overall pathway and individual components of enhanced recovery (pre-, peri- and post-operative interventions).
- Assess study quality and risk of bias.
- Identify and discuss research gaps for future economic evaluations

Enhanced recovery of hip and knee replacement

Methods and analysis

Review registration and timelines

This systematic review protocol was developed with reference to the Preferred Reporting Items for Systematic Reviews and Meta-Analysis for Protocols 2015 (PRISMA-P) guidelines [10] (completed checklist provided in the Supplementary Information), and published recommendations for performing systematic reviews of economic evaluations [11-13]. The systematic review is registered in the International Prospective Register of Systematic Reviews (PROSPERO), registration number CRD42017059473 [14]. Important amendments to this protocol will be reported and published with the results of the review.

Search strategy

We defined the search strategies and database selection with assistance from an information specialist and by comparing our search terms with those from previous reviews and review protocols of economic evaluations in hip/knee replacement [5-9].

The following electronic databases were searched up to 1st March 2017: Ovid MEDLINE, Embase, the National Health Service Economic Evaluations Database (NHS EED) (via the Cochrane Library) and EconLit (via ProQuest). NHS EED contains records of economic evaluations published up until the end of December 2014, with bibliographic records being added to the database up to March 2015 [15]. We anticipate that economic studies published after December 2014 will be identified using the other databases in the review.

Articles were restricted to English-language literature but no geographical restrictions were applied to the search. Abstracts or conference presentations were not included as sufficient data were not presented to allow critical appraisal of the economic evaluations. Date restrictions limiting the review to studies published after the year 2000 were applied during the study selection process.

The search strategy and inclusion/exclusion criteria were piloted by two reviewers using 10% of the initial study results. The search strategies include terms relating to hip and knee replacement, economic evaluations, decision modelling, and quality of life measures. The full search strategies are provided in the Supplementary Information. Additional articles will be identified by searching the reference list of the studies included in this review as well as those of previous literature reviews on economic evaluations of hip or knee replacement populations.

Study selection

ENDNOTE X7, Thomson Reuters, was used to manage the references. Duplicates were removed after the initial searches and two reviewers independently assessed all abstracts to determine whether a full text review is needed. Discrepancies were resolved between reviewers or referred to a third study team member. Following PRISMA guidelines, we will present a flow diagram reporting the selection process.

Enhanced recovery of hip and knee replacement

Study eligibility criteria

Population

We will include studies with participants undergoing THR and TKR surgery for common indications. In the UK, osteoarthritis was the surgical indication in 90% of primary hip replacement procedures [16] and 96.1% of primary knee replacements [17]. Studies exclusively concerning populations with other indications such as avascular necrosis, inflammatory arthropathy, previous/failed surgery, cancer, congenital conditions or infection will be excluded, as will studies looking at emergency procedures (for example due to trauma).

Intervention

Economic evaluations of any pre-, peri- or post-operative intervention within the hip/knee replacement enhanced recovery pathway will be included, in addition to studies considering enhanced recovery pathways as a whole. Interventions must be those that form part of the usual pathway of care (with or without enhanced recovery) for hip/knee replacement.

Comparators

The comparator in each study must be an intervention within the clinical pathway of hip or knee replacement, respectively, or no intervention/placebo. Studies with comparators consisting only of interventions not within the hip or knee replacement pathway (for example, comparing to non-surgical interventions) will be excluded.

Types of studies

Both model-based and randomized controlled trials/cohort-based economic evaluations will be included. We will restrict the analysis to cost-utility analyses (i.e. reporting costs per QALY) but will report number of cost-effectiveness studies reporting incremental costs per other units of health gain (e.g. life years). As cost-utility analysis is the preferred approach to inform decisions on healthcare resource allocation [18 19] we will also exclude cost-benefit analysis and cost-minimisation analysis, as well as cost-consequence analysis if incremental costs per QALYs cannot be estimated.

Outcomes

In order to inform policy and achieve comparable results between studies, the primary outcome of interest is cost-effectiveness findings in terms of the incremental cost per QALY gained..

The secondary outcomes of interest are the probability of being the most cost-effective intervention (to reflect uncertainty), study design and quality, model type, structure and validation status (for model-based studies), and the source and quality of the data used for the analysis.

Data extraction

Data extraction will be divided between two reviewers using a standardised form and referred to a third reviewer where necessary to resolve discrepancies. Data extraction items are based on published checklists [20-24] and will include: study question and comparators, patient population, study type

(model or trial-based economic evaluation), model type and design (where applicable), data sources and hierarchy of evidence (quality assessment), currency and cost year, cost-effectiveness results (point estimate, and probability of being cost-effective), study conclusions, and a risk of bias assessment. The pro-forma for data extraction is given in the Supplementary Information. The data will be entered into a spreadsheet in Microsoft Excel and the completed data extraction form for each study will be retained. The data extraction forms were piloted by two reviewers using selected examples of included studies.

Risk of bias

In line with published recommendations [13], the quality of reporting and risk of bias of the economic evaluations will be assessed using published checklists from the Consensus on Health Economic Criteria project [25] for economic evaluations and the International Society for Pharmacoeconomics and Outcomes Research taskforce for decision models [26]. Items in the checklists will be marked as Yes, No, Unknown or Not Applicable for each study, and a final assessment of the risk of bias will be made by the reviewer.

Data synthesis

Data for synthesis will be managed using Microsoft Excel. A narrative synthesis will be presented outlining the overall cost-effectiveness findings from the included studies. Hip and knee replacement findings will be reported separately. We will also discuss the quality and risk of bias of the individual studies, and the generalisability of the findings to settings other than those reported, in order to assess the overall strength of the body of economic evidence. Finally, we will identify intelligence gaps and challenges that need to be addressed for future evaluations of recovery pathway interventions in populations of hip or knee replacement patients.

Discussion

Cost-utility data are relevant to understand the value of health care interventions and to support decisions concerning which interventions to implement in jurisdictions where healthcare resources are limited. Given the high volume of hip and knee replacement and the associated costs, there is significant interest in identifying cost-effective strategies to reduce and improve the recovery time of these patients. We anticipate that the review will influence practice by providing a comprehensive summary of the cost-effectiveness of enhanced recovery components according to measures that are comparable between interventions. This will enable healthcare providers to tailor their approach according to the most cost-effective interventions. Our findings will inform the challenges and research gaps concerning future economic evaluations of enhanced recovery interventions. We anticipate that this review may also inform future guidelines around enhanced recovery by providing robust cost-effectiveness evidence from international studies.

Enhanced recovery of hip and knee replacement

Dissemination

The results of the review will be disseminated in a peer-reviewed academic journal and at conferences.

Enhanced recovery of hip and knee replacement

Supplementary information

Full details of the search strategy, data extraction forms, assessment of quality and bias checklists, and a completed PRISMA-P systematic review protocol checklist [10] for this review are given in the Supplementary Information.

Ethics

This systematic review is exempt from ethics approval because the work is carried out on published documents.

Declarations

Funding

This work was supported as part of a research grant from the National Institute for Health Research, Health Services and Delivery Research Programme [HS&DR – 14/46/02]. The funder was not involved in developing the protocol.

Competing interests

None declared.

Authors' contributions

JM, JL and LYC developed the search strategies. JM, JL, MGP, LYC and RJ defined the inclusion criteria. JM and LYC piloted the search strategy and inclusion criteria. JM and JL developed the data extraction pro-forma. JM, MGP, LYC and RJ piloted the data extraction pro-forma. All authors approved the final manuscript. Jose Leal is the guarantor of the review.

Acknowledgments

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Enhanced recovery of hip and knee replacement

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Enhanced recovery of hip and knee replacement

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Enhanced recovery of hip and knee replacement

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SUPPLEMENTARY INFORMATION 1: Search strategy

Table 1.1: MEDLINE

	Search terms
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.

SUPPLEMENTARY INFORMATION 1: Search strategy

51	(SF-36 or SF36 or Short Form 36).ti,ab.
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 1.2: EMBASE

	Search terms
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.

SUPPLEMENTARY INFORMATION 1: Search strategy

35	decision model$.ti,ab.
36	cost-effectiv$.ti,ab.
37	"cost benefit analysis"/
38	biomedical technology assessment/
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	(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 1.3: Cochrane library (hip)

	Search terms
	Title, Abstract, Keywords: “Hip arthroplasty”
OR	Title, Abstract, Keywords: “Hip arthroplasties”
OR	Title, Abstract, Keywords: “Hip replacement”

Table 1.4: Cochrane library (knee)

	Search terms
	Title, Abstract, Keywords: “Knee arthroplasty”
OR	Title, Abstract, Keywords: “Knee arthroplasties”
OR	Title, Abstract, Keywords: “Knee replacement”

SUPPLEMENTARY INFORMATION 1: Search strategy

Table 1.5: EconLit

	Search terms
AND	TI,AB(hip) OR TI,AB(knee) TI,AB(Replace*) OR TI,AB(arthroplasty*) OR TI,AB(Replacement) OR TI,AB(arthroplasties)

SUPPLEMENTARY INFORMATION 2: Data extraction pro-forma

Reviewer:			
Date form completed:			
Title:			
Author(s):			
Year Published:			
Citation (incl. doi):			
Type of study:	Trial-based EE ☐	Model-based EE ☐	Non-EE modelling study ☐

Economic evaluation details (if applicable) N/A ☐				**Location in text** (page/figure/ table/other)
Objective/decision problem:				
Patient population characteristics *(describe)*:				
Location *(country/city)*:				
Setting *(describe):*				
Economic study design:	CEA ☐	CBA ☐		
	CUA ☐	CMA ☐		
	CCA ☐	Cost(s) only ☐		
	Health outcomes(s) only ☐			
Perspective of analysis:	Societal ☐	Individual clinician ☐		
	Patient and patient family ☐	Insurer/third party payer ☐		
	Healthcare system ☐	Other: ☐		
	Healthcare provider ☐			
Primary costs/consequences/outcome measure(s) *(please list):*				
Strategies/comparators:				
Time horizon of analysis:				
Was discounting used? *(state annual or otherwise)*	Discount rate for costs: ……			
	Discount rate for health outcomes: …….			
	No Discounting ☐			
	N/A (no information/not relevant) ☐			

SUPPLEMENTARY INFORMATION 2: Data extraction pro-forma

Modelling details (if applicable) N/A ☐ [Adapted from Philips 2006 and Vemer 2016 (AdViSHE) checklists]				**Location in text** *(page/figure /table/other)*
Model type	Cohort-based decision tree (DT)	☐		
	Cohort-based State Transition model (MM)	☐		
	Individual patient-level DT	☐		
	Individual patient-level MM	☐		
	Discrete event simulation	☐		
	Agent-based model	☐		
	System dynamics model	☐		
	Other:			
Rationale for model type:	Yes No	☐ ☐	If Yes please specify:	
Model structure *(paste structure):*				
Rationale for model structure:	Yes No	☐ ☐	If Yes please specify:	
Structural assumptions, *incl. cycle length (describe):*				
Have experts been asked to judge the appropriateness of the model?	Yes No	☐ ☐	If Yes please specify: 1. Who: 2. Why they are experts: 3. Level of agreement:	
Has the model been compared with other models found in the literature?	Yes No	☐ ☐	If Yes please provide reference/citation:	
Was patient heterogeneity modelled?	Yes No	☐ ☐	If Yes please specify:	
Source of data for clinical effect sizes, adverse events & complications:	**1** Meta-analysis of RCTs with direct comparison between comparator therapies, measuring final outcomes.	☐		
	2 Single RCT with direct comparison between comparator therapies, measuring final outcomes	☐		
	3 Meta-analysis of RCTs with direct comparison between comparator therapies, measuring surrogate outcomes	☐		
	Meta-analysis of placebo-controlled RCTs with similar trial populations, measuring final outcomes for each individual therapy	☐		
	4 Single RCT with direct comparison between comparator therapies, measuring surrogate outcomes	☐		

SUPPLEMENTARY INFORMATION 2: Data extraction pro-forma

Modelling details (if applicable) N/A ☐ [Adapted from Philips 2006 and Vemer 2016 (AdViSHE) checklists]			**Location in text** *(page/figure /table/other)*
	Single placebo-controlled RCTs with similar trial populations, measuring final outcomes for each individual therapy	☐	
	5 Meta-analysis of placebo-controlled RCTs with similar trial populations, measuring surrogate outcomes	☐	
	6 Single placebo-controlled RCTs with similar trial populations, measuring surrogate outcomes for each individual therapy	☐	
	7 Case-control or cohort studies	☐	
	8 Non-analytic studies, for example, case reports, case series	☐	
	9 Expert opinion	☐	
	0 Not stated	☐	
	Other: Specify relevant data sources: More than 1 data source per parameter? Reasons for excluding data sources? Evidence synthesis performed? Calibration?	☐	
Source of baseline clinical data:	**1** Case series or analysis of reliable administrative databases specifically conducted for the study covering patients solely from the jurisdiction of interest.	☐	
	2 Recent case series or analysis of reliable administrative databases covering patients solely from the jurisdiction of interest.	☐	
	3 Recent case series or analysis of reliable administrative databases covering patients solely from another jurisdiction.	☐	
	4 Old case series or analysis of reliable administrative databases. Estimates from RCTs	☐	
	5 Estimates from previously published economic analyses: unsourced	☐	
	6 Expert opinion	☐	
	0 Not stated	☐	
	Other: Specify relevant data sources: More than 1 data source per parameter?	☐	

SUPPLEMENTARY INFORMATION 2: Data extraction pro-forma

Modelling details (if applicable) N/A ☐ [Adapted from Philips 2006 and Vemer 2016 (AdViSHE) checklists]			**Location in text** *(page/figure /table/other)*
	Reasons for excluding data sources? Evidence synthesis performed? Calibration?		
Source of data for duration of primary effect (i.e. after end of follow-up of source of primary effect size)	**1** Analysis of reliable administrative databases specifically conducted for the study covering patients solely from the jurisdiction of interest	☐	
	2 Recent analysis of reliable administrative databases covering patients solely from the jurisdiction of interest	☐	
	3 Recent analysis of reliable administrative databases covering patients solely from another jurisdiction	☐	
	4 Old analysis of reliable administrative databases.	☐	
	5 Estimates from previously published economic analyses: unsourced	☐	
	6 Expert opinion	☐	
	0 Not stated	☐	
	Other: Specify relevant data sources: More than 1 data source per parameter? Reasons for excluding data sources? Evidence synthesis performed? Calibration?	☐	
Source of data for resource use:	**1** Prospective data collection or analysis of reliable administrative data from same jurisdiction for specific study	☐	
	2 Recently published results of prospective data collection or recent analysis of reliable administrative data – same jurisdiction	☐	
	3 Unsourced data from previous economic evaluations – same jurisdiction	☐	
	4 Recently published results of prospective data collection or recent analysis of reliable administrative data – different jurisdiction	☐	
	5 Unsourced data from previous economic evaluation – different jurisdiction	☐	
	6 Expert opinion	☐	
	0 Not stated	☐	
	Other: Specify relevant data sources:	☐	

SUPPLEMENTARY INFORMATION 2: Data extraction pro-forma

Modelling details (if applicable) N/A ☐ [Adapted from Philips 2006 and Vemer 2016 (AdViSHE) checklists]		**Location in text** *(page/figure /table/other)*
	More than 1 data source per parameter? Reasons for excluding data sources? Evidence synthesis performed? Calibration?	
Are methods for identifying and synthesising input data reported?	Yes ☐ No ☐ If Yes please specify:	
Were all data sources described and reported?	Yes ☐ No ☐	
Were mutually inconsistent data reported in the model?	Yes ☐ If Yes were the choices justified? No ☐	
Model uncertainty	Methodological uncertainty ☐ If yes, describe: Structural uncertainty ☐ If yes, describe: Heterogeneity ☐ If yes, list subgroups: Parameter uncertainty ☐ If yes, list method:	
Have experts been asked to judge the appropriateness of the input data?	Yes ☐ If Yes please specify: No ☐ 1. Who: 2. Why they are experts: 3. Level of agreement:	
When input parameters are based on regression models, have statistical tests been performed?	Yes ☐ If Yes please specify tests: No ☐	
Model internal validation (mathematical logic and accuracy of coding)	Computerised model examined by modelling experts ☐ Model run for specific, extreme sets of parameter values to detect coding errors ☐ Patients tracked through model to determine if its logic is correct ☐ Tested individual sub-modules of the computerised model ☐ Internal validation not reported ☐	
Model external validation	Model outcomes assessed by experts ☐ Model outcomes compared with the outcomes of other models that address similar problems ☐ Model outcomes compared with the outcomes obtained when using alternative input data ☐ Model outcomes compared with empirical data ☐ Model calibrated against independent data with differences explained and justified ☐ Counterintuitive results from model explained and justified ☐ External validation not reported ☐	
Other model validation *(describe)*:		

SUPPLEMENTARY INFORMATION 2: Data extraction pro-forma

Data details (all analyses) [Adapted from Coyle & Lee 2002, and with additional items]							**Location in text** *(page/figure /table/other)*
Costs included:	Direct medical	☐	Direct non-medical	☐	Productivity losses	☐	
	Direct treatment	☐	Social care	☐	Income forgone due to illness	☐	
	In-patient	☐	Social benefits	☐			
	Out-patient	☐	Travel costs	☐	Income forgone due to death	☐	
	Day care	☐	Caregiver out-of-pocket	☐			
	Community healthcare	☐	Criminal Justice	☐	Income forgone due to death	☐	
	Medication	☐	Training of staff	☐			
	Side effect costs or	☐					
	Staff	☐					
	Medication	☐					
	Labs/diagnostic	☐					
	Overhead	☐					
	Capital equipment	☐					
	Real estate	☐					
	Other:	☐					
Source of data for costs:	**1** Cost calculations based on reliable databases or data sources conducted for specific study – same jurisdiction					☐	
	2 Recently published cost calculations based on reliable databases or data sources – same jurisdiction					☐	
	3 Unsourced data from previous economic evaluation – same jurisdiction					☐	
	4 Recently published cost calculations based on reliable databases or data sources – different jurisdiction					☐	
	5 Unsourced data from previous economic evaluation – different jurisdiction					☐	
	6 Expert opinion					☐	
	0 Not stated					☐	
	Other:					☐	
	Specify relevant data sources:						
	More than 1 data source per parameter?						
	Reasons for excluding data sources?						
	Evidence synthesis performed?						

SUPPLEMENTARY INFORMATION 2: Data extraction pro-forma

	Calibration?	
Source of data for utilities:	**1** Direct utility assessment for the specific study from a sample either: (a) of the general population, or (b) with knowledge of the disease(s) of interest, or (c) of patients with the disease(s) of interest	☐
	Indirect utility assessment for the specific study from patient sample with disease(s) of interest, using a tool validated for the patient population	☐
	2 Direct utility assessment from a previous study from a sample either: (a) of the general population, or (b) with knowledge of the disease(s) of interest, or (c) of patients with the disease(s) of interest	☐
	Indirect utility assessment from a previous study from patient sample with disease(s) of interest, using a tool validated for the patient population	☐
	3 Indirect utility assessment from a patient sample with disease(s) of interest, using a tool **not** validated for the patient population	☐
	Patient preference values obtained from a visual analogue scale	☐
	4 Delphi panels, expert opinion	☐
	0 Not clearly stated	☐
	Other:	☐
	Specify relevant data sources:	
	More than 1 data source per parameter?	
	Reasons for excluding data sources?	
	Evidence synthesis performed?	
	Calibration?	
Were QOL estimates derived:	Yes ☐ No ☐	
If validated tools were used, which instrument(s):	Rosser Index ☐	Health Utilities Index (HUI) ☐
	EQ-5D ☐	Quality of Well Being (QWB) ☐
	15D ☐	SF-36 ☐
	SF-12 ☐	SF-6 ☐
Converted into utilities?	Yes ☐ No ☐ If Yes report value set:	
If direct elicitation was used, which approach(s):	Standard Gamble ☐ VAS/rating scale ☐ Time trade-off ☐ Person trade-off ☐	

SUPPLEMENTARY INFORMATION 2: Data extraction pro-forma

Utility values combined with survival to form QALYs?	Yes No	☐ ☐

Study results		**Location in text** (page/figure/ table/other)
Currency and cost year		
Cost-effectiveness results (e.g. ICER)	Point estimate: Probabilistic results (probability of being cost-effective):	
Study conclusions		

Quality and risk of bias for economic evaluations (if applicable)				**N/A ☐**
Checklists completed:	CHEC (all EE) ☐	ISPOR (models only) ☐		
Risk of bias [CHEC, ISPOR]:	High ☐	Medium ☐	Low ☐	Unknown ☐
Comments on study quality and limitations:				

SUPPLEMENTARY INFORMATION 3: Risk of bias checklists

Table 3.1: Risk of bias checklist, adapted from Evers et al {Evers, 2005 #30}

Is the study population clearly described?
Are competing alternatives clearly described?
Is a well-defined research question posed in answerable form?
Is the economic study design appropriate to the stated objective?
Is the chosen time horizon appropriate in order to include relevant costs and consequences?
Is the actual perspective chosen appropriate?
Are all important and relevant costs for each alternative identified?
Are all costs measured appropriately in physical units?
Are costs valued appropriately?
Are all important and relevant outcomes for each alternative identified?
Are all outcomes measured appropriately?
Are outcomes valued appropriately?
Is an incremental analysis of costs and outcomes of alternatives performed?
Are all future costs and outcomes discounted appropriately?
Are all important variables, whose values are uncertain, appropriately subjected to sensitivity analysis?
Do the conclusions follow from the data reported?
Does the study discuss the generalizability of the results to other settings and patient/client groups?
Does the article indicate that there is no potential conflict of interest of study researcher(s) and funder(s)?
Are ethical and distributional issues discussed appropriately?

SUPPLEMENTARY INFORMATION 3: Risk of bias checklists

Table 3.2: Risk of bias checklist, adapted from Caro et al {Caro, 2014 #33}

Relevance
Is the population relevant?
Are any critical interventions missing?
Are any relevant outcomes missing?
Is the context (settings and circumstances) applicable?
Credibility
Validation
Is external validation of the model sufficient to make its results credible for your decision?
Is internal verification of the model sufficient to make its results credible for your decision?
Does the model have sufficient face validity to make its results credible for your decision?
Design
Is the design of the model adequate for your decision problem?
Data
Are the data used in populating the model suitable for your decision problem?
Analysis
Were the analyses performed using the model adequate to inform your decision problem?
Was there an adequate assessment of the effects of uncertainty?
Reporting
Was the reporting of the model adequate to inform your decision problem?
Interpretation
Was the interpretation of results fair and balanced?
Conflict of Interest
Were there any potential conflicts of interest?
If there were potential conflicts of interest, were steps taken to address these?

Enhanced recovery of hip and knee replacement

PRISMA 2015 checklist for systematic review protocols

Section and topic	Item No.	Checklist Item	Reported in section
Administrative Information			
Identification	1a	Identify the report as a protocol of a systematic review	Abstract, Introduction, Methods
Update	1b	Identify protocol as an update of a previous systematic review if applicable	n/a
Registration	2	Name of registry and registration number	Abstract, Methods
Authors			
Contact		Provide name, institutional affiliation, e-mail address of all protocol authors; provide physical mailing address of corresponding author	Title page
Contributions		Describe contributions of protocol authors and identify the guarantor of the review	Declarations
Amendments		If the protocol represents an amendment of a previously completed or published protocol, identify as such and list changes; otherwise, state plan for documenting important protocol amendments	n/a
Support			
Sources	5a	Indicate Sources of financial or other support for the review	Declarations
Sponsor	5b	Provide name for the review funder and/or sponsor	Declarations
Role of sponsor or funder	5c	Describe roles of funder(s), sponsor(s) and/or institution(s), if any, in developing the protocol	Declarations
Introduction			
Rationale	6	Describe the rationale for the review in the context of what is already known	Introduction
Objectives	7	Provide an explicit statement of the question(s) the review will address with reference to participants, interventions, comparators, and outcomes (PICO)	Introduction, Search strategy
Methods			
Eligibility Criteria	8	Specify the study characteristics (such as PICO, study design, setting, time frame) and report characteristics (such as years considered, language, publication status) to be used as criteria for eligibility for the review	Search strategy
Information Sources	9	Describe all intended information sources (such as electronic databases, contact with study authors, trial registers or other grey literature sources) with planned dates of coverage	Search strategy
Search Strategy	10	Present draft of search strategy to be used for at least one electronic database, including planned limits, such that it could be repeated	Supplementary Information
Study Records			
Data Management	11a	Describe the mechanism(s) that will be used to manage records and data throughout the review	Study selection, Data extraction, Data synthesis
Selection Process	11b	State the process that will be used for selecting studies (such as two independent reviewers) through each phase of the review (that is, screening, eligibility and inclusion in meta-analysis)	Search strategy
Data Collection Process	11c	Describe planned method of extracting data from reports (such as piloting forms, done independently, in duplicate), any processes for obtaining and confirming data from investigators	Data extraction
Data Items	12	List and define all variables for which data will be sought (such as PICO items, funding sources), any pre-planned data assumptions and simplifications	Methods
Outcomes and prioritization	13	List and define all outcomes for which data will be sought, including prioritization of main and additional outcomes, with rationale	Methods – Outcomes, Data extraction

Enhanced recovery of hip and knee replacement

Risk of bias in individual studies	14	Describe anticipated methods for assessing risk of bias of individual studies, including whether this will be done at the outcome or study level, or both; state how this information will be used in data synthesis	Methods – risk of bias
Data Synthesis	15a	Describe criteria under which study data will be quantitatively synthesised	N/A
	15b	If data are appropriate for quantitative synthesis, describe planned summary measures, methods of handling data and methods of combining data from studies, including any planned exploration of consistency	N/A
	15c	Describe any proposed additional analyses (such as sensitivity or subgroup analyses, meta-regression)	N/A
	15d	If quantitative synthesis is not appropriate, describe the type of summary planned	Methods - data synthesis
Meta-bias(es)	16	Specify any planned assessment of meta-bias(es) (such as publication bias across studies, selective reporting within studies)	N/A
Confidence in cumulative evidence	17	Describe how the strength of the body of evidence will be assessed	Methods – risk of bias and quality assessment

BMJ Open

Cost-effectiveness of enhanced recovery in hip and knee replacement: a systematic review protocol

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Date Submitted by the Author:	10-Nov-2017
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Primary Subject Heading:	Health economics
Secondary Subject Heading:	Surgery
Keywords:	systematic review, hip replacement, knee replacement, osteoarthritis, cost-effectiveness, Health economics < HEALTH SERVICES ADMINISTRATION & MANAGEMENT

Enhanced recovery of hip and knee replacement

Cost-effectiveness of enhanced recovery in hip and knee replacement: a systematic review protocol

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Enhanced recovery of hip and knee replacement

ABSTRACT

Introduction

Hip and knee replacement represents a significant burden to the UK healthcare system. "Enhanced recovery" pathways have been introduced in the NHS for patients undergoing hip and knee replacement, with the aim of improving outcomes and timely recovery after surgery. To support policy-making there is a need to evaluate the cost-effectiveness of enhanced recovery pathways across jurisdictions. Our aim is to systematically summarise the published cost-effectiveness evidence on enhanced recovery in hip and knee replacement, both as a whole and for each of the various components of enhanced recovery pathways.

Methods and analysis

A systematic review will be conducted in MEDLINE, EMBASE, Econlit and NHS EED. Separate search strategies were developed for the different databases including terms relating to hip and knee replacement/arthroplasty, economic evaluations, decision modelling, and quality of life measures.

We will extract peer-reviewed studies published between 2000 and 2017 reporting economic evaluations of pre-, peri- or post-operative enhanced recovery interventions within hip or knee replacement. Economic evaluations alongside cohort studies or based on decision models will be included. Only studies with patients undergoing elective replacement surgery of the hip or knee will be included. Data will be extracted using a pre-defined pro-forma following best practice guidelines for economic evaluation, decision modelling and model validation.

Our primary outcome will be the cost-effectiveness of enhanced recovery (entire pathway and individual components) in terms of incremental cost per quality-adjusted life year. A narrative synthesis of all studies will be presented, focussing on cost-effectiveness results, study design, quality and validation status.

Ethics and dissemination

This systematic review is exempt from ethics approval because the work is carried out on published documents. The results of the review will be disseminated in a peer-reviewed academic journal and at conferences.

Registration number

PROSPERO: CRD42017059473.

Keywords

Systematic review, hip replacement, hip arthroplasty, knee replacement, knee arthroplasty, osteoarthritis, economic evaluation, cost-effectiveness

Enhanced recovery of hip and knee replacement

Strengths of the study

- This systematic review protocol of enhanced recovery pathway for hip/knee replacement will be based on a detailed search strategy that will be complemented with a comprehensive data extraction and analysis of the studies.
- The review will followed the latest guidelines and assessed the quality and validity of the cost-effectiveness evidence using published modelling checklists (modelling-specific or general economic evaluation checklists as appropriate).

Limitations of the study

- The quality and validity of the studies identified may depend on the reporting quality and transparency.

Enhanced recovery of hip and knee replacement

Introduction

Hip and knee replacement represents a significant burden to the UK healthcare system. In 2015, over 88,000 primary total hip replacements (THRs) and primary total knee replacements (TKRs) were registered in the National Joint Registry, covering procedures performed in NHS and independent hospitals in England, Wales, Northern Ireland and the Isle of Man [1 2].

Following the establishment of the Department of Health Enhanced Recovery Partnership Programme in April 2009 [3] a new "enhanced recovery" pathway has been introduced in many NHS hospitals for patients undergoing hip and knee replacement [4]. According to a Department of Health report [3], the principles of enhanced recovery are to ensure: "the patient is in the best possible condition for surgery; the patient has the best possible management during and after his/her operation; the patient experiences the best post-operative rehabilitation." Therefore, enhanced recovery considers the pre-, peri-, and post-operative management of patient care, to enable improved and faster recovery and discharge from hospital. Enhanced recovery programmes vary between hospitals, but generally include a combination of best practice initiatives and medical interventions. Examples of such interventions include: (pre-operative) patient education and setting of expectations around surgery and rehabilitation, nutrition, physiotherapy; (peri-operative) optimised anaesthesia, shortened surgical times, minimal use of drains and tubes; (post-operative) same day mobilisation and discharge, engagement of multidisciplinary teams in provision of physiotherapy and occupational therapy, clear rehabilitation instructions; and/or other interventions as agreed in each hospital.

To inform national policy and local decisions across many jurisdictions, evidence on both the effectiveness and cost-effectiveness of interventions is needed. Economic evaluations of enhanced recovery interventions in hip and knee replacement patients provide such evidence. Estimates of the impact of the interventions in terms of quality of life and costs relative to current practice enable providers to base decisions not only on clinical effectiveness, but also on their value for money.

Previous systematic reviews of economic evaluations in patients having hip or knee replacement have not looked at enhanced recovery or its components but rather focussed on the surgical procedure and its cost-effectiveness.[5 6] [7-9] This recent evidence suggests that total joint replacement is cost-effective compared to conservative management [5 7], and unicompartmental knee replacement is less costly then TKR and for some age groups is more effective.[6] We therefore identified a need for a more comprehensive summary of the published economic evidence on enhanced recovery in hip and knee replacement, including each component of the pathway from pre-operative to post-discharge.

Our aim is to systematically summarise and assess the quality of cost-effectiveness evidence of enhanced recovery in hip and knee replacement, for patients of any age with common indications for surgery. Our objectives are to:

Enhanced recovery of hip and knee replacement

- Summarise peer-reviewed published economic evaluations of enhanced recovery interventions in populations of individuals undergoing elective hip or knee replacement
- Report the cost-effectiveness findings in terms of cost per quality-adjusted life year (QALY) for the overall pathway and individual components of enhanced recovery (pre-, peri- and post-operative interventions).
- Assess study quality and risk of bias.
- Identify and discuss research gaps for future economic evaluations

Methods and analysis

Review registration and timelines

This systematic review protocol has been developed with reference to the Preferred Reporting Items for Systematic Reviews and Meta-Analysis for Protocols 2015 (PRISMA-P) guidelines [10], and published recommendations for performing systematic reviews of economic evaluations [11-13]. The systematic review is registered in the International Prospective Register of Systematic Reviews (PROSPERO), registration number CRD42017059473 [14]. Important amendments to this protocol will be reported and published with the results of the review.

Search strategy

We have defined the search strategies and database selection with assistance from an information specialist and by comparing our search terms with those from previous reviews and review protocols of economic evaluations in hip/knee replacement [5-9].

The following electronic databases will be searched up to 1st March 2017 (with no start date specified): Ovid MEDLINE, Embase, the National Health Service Economic Evaluations Database (NHS EED) (via the Cochrane Library) and EconLit (via ProQuest). NHS EED contains records of economic evaluations published up until the end of December 2014, with bibliographic records being added to the database up to March 2015 [15]. We anticipate that economic studies published after December 2014 will be identified using the other databases in the review.

Articles will be restricted to English-language literature but no geographical restrictions will be applied to the search. Abstracts or conference presentations will not be included as results are not presented in sufficient detail to allow critical appraisal of the economic evaluations. Date restrictions limiting the review to studies published after the year 2000 will be applied during the study selection process.

The search strategy and inclusion/exclusion criteria were piloted by two reviewers. For the latter, the search was run and inclusion/exclusion criteria were applied to 10% of the search results to check consistency between reviewers.. The search strategies include terms relating to hip and knee replacement, economic evaluations, decision modelling, and quality of life measures. The full search strategies are provided in the Supplementary File 1. Additional articles will be identified by searching

the reference list of the studies included in this review as well as those of previous literature reviews on economic evaluations of hip or knee replacement populations.

Study selection

ENDNOTE X7, Thomson Reuters, will be used to manage the references. Duplicates will be removed after the initial searches and two reviewers will independently assess all abstracts to determine whether a full text review is needed. Discrepancies will be resolved between reviewers or referred to a third study team member. Following PRISMA guidelines, we will present a flow diagram reporting the selection process.

Study eligibility criteria

Population

We will include studies with participants undergoing THR and TKR surgery for common indications. In the UK, osteoarthritis was the surgical indication in 90% of primary hip replacement procedures [16] and 96.1% of primary knee replacements in 2015 [17]. We will therefore include studies with osteoarthritis as an indication for surgery, though we do not intend to pre-specify a minimum required proportion of patients with this indication. Studies exclusively concerning populations with other indications such as avascular necrosis, inflammatory arthropathy, previous/failed surgery, cancer, congenital conditions or infection will be excluded, as will studies looking at emergency procedures (for example due to trauma).

Intervention

Economic evaluations of any pre-, peri- or post-operative intervention within the hip/knee replacement enhanced recovery pathway will be included, in addition to studies considering enhanced recovery pathways as a whole. Interventions must be those that form part of the usual pathway of care (with or without enhanced recovery) for hip/knee replacement.

Comparators

The comparator in each study must be an intervention within the clinical pathway of hip or knee replacement, respectively, or no intervention/placebo. Studies with comparators consisting only of interventions not within the hip or knee replacement pathway (for example, comparing to non-surgical interventions) will be excluded.

Types of studies

Both model-based and randomized controlled trials/cohort-based economic evaluations will be included. We will restrict the analysis to cost-utility analyses (i.e. reporting costs per QALY) but will report number of cost-effectiveness studies reporting incremental costs per other units of health gain (e.g. life years). As cost-utility analysis is the preferred approach to inform decisions on healthcare resource allocation [18 19] we will also exclude cost-benefit analysis and cost-minimisation analysis, as well as cost-consequence analysis if incremental costs per QALYs cannot be estimated.

Outcomes

In order to inform policy and achieve comparable results between studies, the primary outcome of interest is cost-effectiveness findings in terms of the incremental cost per QALY gained. In addition we will report the absolute costs and QALYs per intervention being evaluated as well as the respective incremental values relative to current care. .

The secondary outcomes of interest are the probability of being the most cost-effective intervention (to reflect uncertainty), value of information (VoI) if reported, study design and quality, model type, structure and validation status (for model-based studies), and the source and quality of the data used for the analysis.

Data extraction

Data extraction will be divided between two reviewers using a standardised form and referred to a third reviewer where necessary to resolve discrepancies. Data extraction items are based on published checklists [20-24] and will include: study question and comparators, patient population, study type (model or trial-based economic evaluation), model type and design (where applicable), data sources and hierarchy of evidence (quality assessment), currency and cost year, cost-effectiveness results (point estimate, and probability of being cost-effective), VoI results (if reported), study conclusions, and a risk of bias assessment. The pro-forma for data extraction is given in the Supplementary File 2. Extracted data will be entered into a spreadsheet in Microsoft Excel and the completed data extraction form for each study will be retained. The data extraction forms have been piloted by two reviewers using selected examples of included studies.

Risk of bias

In line with published recommendations [13], the quality of reporting and risk of bias of the economic evaluations will be assessed using published checklists from the Consensus on Health Economic Criteria project [25] for economic evaluations and the International Society for Pharmacoeconomics and Outcomes Research taskforce for decision models [26] (Supplementary File 3). Items in the checklists will be marked as Yes, No, Unknown or Not Applicable for each study, and a final assessment of the risk of bias will be made by the reviewer.

Data synthesis

Data for synthesis will be managed using Microsoft Excel. A narrative synthesis will be presented outlining the overall cost-effectiveness findings from the included studies. Hip and knee replacement findings will be reported separately. We will also discuss the quality and risk of bias of the individual studies, and the generalisability of the findings to settings other than those reported, in order to assess the overall strength of the body of economic evidence. Using the results of sensitivity analyses and VoI methods (if available), we will report recommendations for further research to reduce decision uncertainty. Finally, we will identify intelligence gaps and challenges that need to be addressed for

future evaluations of recovery pathway interventions in populations of hip or knee replacement patients.

Discussion

Cost-utility data are relevant to understand the value of health care interventions and to support decisions concerning which interventions to implement in jurisdictions where healthcare resources are limited. Given the high volume of hip and knee replacement and the associated costs, there is significant interest in identifying cost-effective strategies to reduce and improve the recovery time of these patients. We anticipate that the review will influence practice by providing a comprehensive summary of the cost-effectiveness of enhanced recovery components according to measures that are comparable between interventions. This will enable healthcare providers to tailor their approach according to the most cost-effective interventions. Our findings will inform the challenges and research gaps concerning future economic evaluations of enhanced recovery interventions. We anticipate that this review may also inform future guidelines around enhanced recovery by providing robust cost-effectiveness evidence from international studies.

Ethics and Dissemination

This systematic review is exempt from ethics approval and consent to participate because the work is carried out on published documents. The results of the review will be disseminated in a peer-reviewed academic journal and at conferences.

Enhanced recovery of hip and knee replacement

Supplementary information

Full details of the search strategy, data extraction forms, assessment of quality and bias checklists for this review are given in the Supplementary Files 1, 2 and 3, respectively.

Ethics

This systematic review is exempt from ethics approval because the work is carried out on published documents.

Declarations

Funding

This work is supported as part of a research grant from the National Institute for Health Research, Health Services and Delivery Research Programme [HS&DR – 14/46/02]. The funder was not involved in developing the protocol.

Competing interests

None declared.

Authors' contributions

JM, JL and LYC developed the search strategies. JM, JL, MGP, LYC and RJ defined the inclusion criteria. JM and LYC piloted the search strategy and inclusion criteria. JM and JL developed the data extraction pro-forma. JM, MGP, LYC and RJ piloted the data extraction pro-forma. All authors approved the final manuscript. Jose Leal is the guarantor of the review.

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Enhanced recovery of hip and knee replacement

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Enhanced recovery of hip and knee replacement

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SUPPLEMENTARY FILE 1: Search strategy

Table 1.1: MEDLINE

	Search terms
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.

SUPPLEMENTARY FILE 1: Search strategy

51	(SF-36 or SF36 or Short Form 36).ti,ab.
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 1.2: EMBASE

	Search terms
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.

SUPPLEMENTARY FILE 1: Search strategy

35	decision model$.ti,ab.
36	cost-effectiv$.ti,ab.
37	"cost benefit analysis"/
38	biomedical technology assessment/
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	(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 1.3: Cochrane library (hip)

	Search terms
	Title, Abstract, Keywords: “Hip arthroplasty”
OR	Title, Abstract, Keywords: “Hip arthroplasties”
OR	Title, Abstract, Keywords: “Hip replacement”

Table 1.4: Cochrane library (knee)

	Search terms
	Title, Abstract, Keywords: “Knee arthroplasty”
OR	Title, Abstract, Keywords: “Knee arthroplasties”
OR	Title, Abstract, Keywords: “Knee replacement”

SUPPLEMENTARY FILE 1: Search strategy

Table 1.5: EconLit

	Search terms
AND	TI,AB(hip) OR TI,AB(knee) TI,AB(Replace*) OR TI,AB(arthroplasty*) OR TI,AB(Replacement) OR TI,AB(arthroplasties)

SUPPLEMENTARY FILE 2: Data extraction pro-forma

Reviewer:	
Date form completed:	
Title:	
Author(s):	
Year Published:	
Citation (incl. doi):	
Type of study:	Trial-based EE ☐ Model-based EE ☐ Non-EE modelling study ☐

Economic evaluation details (if applicable)	**N/A ☐**	**Location in text** (page/figure/ table/other)
Objective/decision problem:		
Patient population characteristics *(describe)*:		
Location *(country/city)*:		
Setting *(describe):*		
Economic study design:	CEA ☐ CBA ☐ CUA ☐ CMA ☐ CCA ☐ Cost(s) only ☐ Health outcomes(s) only ☐	
Perspective of analysis:	Societal ☐ Individual clinician ☐ Patient and patient family ☐ Insurer/third party payer ☐ Healthcare system ☐ Other: ☐ Healthcare provider ☐	
Primary costs/consequences/outcome measure(s) *(please list):*		
Strategies/comparators:		
Time horizon of analysis:		
Was discounting used? *(state annual or otherwise)*	Discount rate for costs: …… Discount rate for health outcomes: ……. No Discounting ☐ N/A (no information/not relevant) ☐	

SUPPLEMENTARY FILE 2: Data extraction pro-forma

Modelling details (if applicable) N/A ☐ [Adapted from Philips 2006 and Vemer 2016 (AdViSHE) checklists]				**Location in text** *(page/figure /table/other)*
Model type	Cohort-based decision tree (DT)	☐		
	Cohort-based State Transition model (MM)	☐		
	Individual patient-level DT	☐		
	Individual patient-level MM	☐		
	Discrete event simulation	☐		
	Agent-based model	☐		
	System dynamics model	☐		
	Other:			
Rationale for model type:	Yes No	☐ ☐	If Yes please specify:	
Model structure *(paste structure):*				
Rationale for model structure:	Yes No	☐ ☐	If Yes please specify:	
Structural assumptions, *incl. cycle length (describe):*				
Have experts been asked to judge the appropriateness of the model?	Yes No	☐ ☐	If Yes please specify: 1. Who: 2. Why they are experts: 3. Level of agreement:	
Has the model been compared with other models found in the literature?	Yes No	☐ ☐	If Yes please provide reference/citation:	
Was patient heterogeneity modelled?	Yes No	☐ ☐	If Yes please specify:	
Source of data for clinical effect sizes, adverse events & complications:	**1** Meta-analysis of RCTs with direct comparison between comparator therapies, measuring final outcomes.	☐		
	2 Single RCT with direct comparison between comparator therapies, measuring final outcomes	☐		
	3 Meta-analysis of RCTs with direct comparison between comparator therapies, measuring surrogate outcomes	☐		
	Meta-analysis of placebo-controlled RCTs with similar trial populations, measuring final outcomes for each individual therapy	☐		
	4 Single RCT with direct comparison between comparator therapies, measuring surrogate outcomes	☐		

SUPPLEMENTARY FILE 2: Data extraction pro-forma

Modelling details (if applicable) N/A ☐ [Adapted from Philips 2006 and Vemer 2016 (AdViSHE) checklists]			**Location in text** *(page/figure /table/other)*
	Single placebo-controlled RCTs with similar trial populations, measuring final outcomes for each individual therapy	☐	
	5 Meta-analysis of placebo-controlled RCTs with similar trial populations, measuring surrogate outcomes	☐	
	6 Single placebo-controlled RCTs with similar trial populations, measuring surrogate outcomes for each individual therapy	☐	
	7 Case-control or cohort studies	☐	
	8 Non-analytic studies, for example, case reports, case series	☐	
	9 Expert opinion	☐	
	0 Not stated	☐	
	Other: Specify relevant data sources: More than 1 data source per parameter? Reasons for excluding data sources? Evidence synthesis performed? Calibration?	☐	
Source of baseline clinical data:	**1** Case series or analysis of reliable administrative databases specifically conducted for the study covering patients solely from the jurisdiction of interest.	☐	
	2 Recent case series or analysis of reliable administrative databases covering patients solely from the jurisdiction of interest.	☐	
	3 Recent case series or analysis of reliable administrative databases covering patients solely from another jurisdiction.	☐	
	4 Old case series or analysis of reliable administrative databases. Estimates from RCTs	☐	
	5 Estimates from previously published economic analyses: unsourced	☐	
	6 Expert opinion	☐	
	0 Not stated	☐	
	Other: Specify relevant data sources: More than 1 data source per parameter?	☐	

SUPPLEMENTARY FILE 2: Data extraction pro-forma

Modelling details (if applicable) N/A ☐ [Adapted from Philips 2006 and Vemer 2016 (AdViSHE) checklists]		**Location in text** *(page/figure /table/other)*
	Reasons for excluding data sources? Evidence synthesis performed? Calibration?	
Source of data for duration of primary effect (i.e. after end of follow-up of source of primary effect size)	**1** Analysis of reliable administrative databases specifically conducted for the study covering patients solely from the jurisdiction of interest ☐ **2** Recent analysis of reliable administrative databases covering patients solely from the jurisdiction of interest ☐ **3** Recent analysis of reliable administrative databases covering patients solely from another jurisdiction ☐ **4** Old analysis of reliable administrative databases. ☐ **5** Estimates from previously published economic analyses: unsourced ☐ **6** Expert opinion ☐ **0** Not stated ☐ Other: ☐ Specify relevant data sources: More than 1 data source per parameter? Reasons for excluding data sources? Evidence synthesis performed? Calibration?	
Source of data for resource use:	**1** Prospective data collection or analysis of reliable administrative data from same jurisdiction for specific study ☐ **2** Recently published results of prospective data collection or recent analysis of reliable administrative data – same jurisdiction ☐ **3** Unsourced data from previous economic evaluations – same jurisdiction ☐ **4** Recently published results of prospective data collection or recent analysis of reliable administrative data – different jurisdiction ☐ **5** Unsourced data from previous economic evaluation – different jurisdiction ☐ **6** Expert opinion ☐ **0** Not stated ☐ Other: ☐ Specify relevant data sources:	

SUPPLEMENTARY FILE 2: Data extraction pro-forma

Modelling details (if applicable) N/A ☐ [Adapted from Philips 2006 and Vemer 2016 (AdViSHE) checklists]		**Location in text** *(page/figure /table/other)*
	More than 1 data source per parameter? Reasons for excluding data sources? Evidence synthesis performed? Calibration?	
Are methods for identifying and synthesising input data reported?	Yes ☐ No ☐ If Yes please specify:	
Were all data sources described and reported?	Yes ☐ No ☐	
Were mutually inconsistent data reported in the model?	Yes ☐ If Yes were the choices justified? No ☐	
Model uncertainty	Methodological uncertainty ☐ If yes, describe: Structural uncertainty ☐ If yes, describe: Heterogeneity ☐ If yes, list subgroups: Parameter uncertainty ☐ If yes, list method:	
Have experts been asked to judge the appropriateness of the input data?	Yes ☐ If Yes please specify: No ☐ 1. Who: 2. Why they are experts: 3. Level of agreement:	
When input parameters are based on regression models, have statistical tests been performed?	Yes ☐ If Yes please specify tests: No ☐	
Model internal validation (mathematical logic and accuracy of coding)	Computerised model examined by modelling experts ☐ Model run for specific, extreme sets of parameter values to detect coding errors ☐ Patients tracked through model to determine if its logic is correct ☐ Tested individual sub-modules of the computerised model ☐ Internal validation not reported ☐	
Model external validation	Model outcomes assessed by experts ☐ Model outcomes compared with the outcomes of other models that address similar problems ☐ Model outcomes compared with the outcomes obtained when using alternative input data ☐ Model outcomes compared with empirical data ☐ Model calibrated against independent data with differences explained and justified ☐ Counterintuitive results from model explained and justified ☐ External validation not reported ☐	
Other model validation *(describe)*:		

SUPPLEMENTARY FILE 2: Data extraction pro-forma

Data details (all analyses) [Adapted from Coyle & Lee 2002, and with additional items]							**Location in text** *(page/figure /table/other)*
Costs included:	Direct medical	☐	Direct non-medical	☐	Productivity losses	☐	
	Direct treatment	☐	Social care	☐	Income forgone due to illness	☐	
	In-patient	☐	Social benefits	☐			
	Out-patient	☐	Travel costs	☐	Income forgone due to death	☐	
	Day care	☐	Caregiver out-of-pocket	☐			
	Community healthcare	☐	Criminal Justice	☐	Income forgone due to death	☐	
	Medication	☐	Training of staff	☐			
	Side effect costs	☐					
	or						
	Staff	☐					
	Medication	☐					
	Labs/diagnostic	☐					
	Overhead	☐					
	Capital equipment	☐					
	Real estate	☐					
	Other:	☐					
Source of data for costs:	**1** Cost calculations based on reliable databases or data sources conducted for specific study – same jurisdiction					☐	
	2 Recently published cost calculations based on reliable databases or data sources – same jurisdiction					☐	
	3 Unsourced data from previous economic evaluation – same jurisdiction					☐	
	4 Recently published cost calculations based on reliable databases or data sources – different jurisdiction					☐	
	5 Unsourced data from previous economic evaluation – different jurisdiction					☐	
	6 Expert opinion					☐	
	0 Not stated					☐	
	Other: Specify relevant data sources: More than 1 data source per parameter? Reasons for excluding data sources? Evidence synthesis performed?					☐	

SUPPLEMENTARY FILE 2: Data extraction pro-forma

	Calibration?	
Source of data for utilities:	**1** Direct utility assessment for the specific study from a sample either: (a) of the general population, or (b) with knowledge of the disease(s) of interest, or (c) of patients with the disease(s) of interest	☐
	Indirect utility assessment for the specific study from patient sample with disease(s) of interest, using a tool validated for the patient population	☐
	2 Direct utility assessment from a previous study from a sample either: (a) of the general population, or (b) with knowledge of the disease(s) of interest, or (c) of patients with the disease(s) of interest	☐
	Indirect utility assessment from a previous study from patient sample with disease(s) of interest, using a tool validated for the patient population	☐
	3 Indirect utility assessment from a patient sample with disease(s) of interest, using a tool **not** validated for the patient population	☐
	Patient preference values obtained from a visual analogue scale	☐
	4 Delphi panels, expert opinion	☐
	0 Not clearly stated	☐
	Other:	☐
	Specify relevant data sources:	
	More than 1 data source per parameter?	
	Reasons for excluding data sources?	
	Evidence synthesis performed?	
	Calibration?	
Were QOL estimates derived:	Yes ☐ No ☐	
If validated tools were used, which instrument(s):	Rosser Index ☐	Health Utilities Index (HUI) ☐
	EQ-5D ☐	Quality of Well Being (QWB) ☐
	15D ☐	SF-36 ☐
	SF-12 ☐	SF-6 ☐
Converted into utilities?	Yes ☐ No ☐ If Yes report value set:	
If direct elicitation was used, which approach(s):	Standard Gamble ☐ VAS/rating scale ☐ Time trade-off ☐ Person trade-off ☐	

SUPPLEMENTARY FILE 2: Data extraction pro-forma

Utility values combined with survival to form QALYs?	Yes No	☐ ☐

Study results		**Location in text** (page/figure/ table/other)
Currency and cost year		
Cost-effectiveness results (e.g. ICER)	Point estimate: Probabilistic results (probability of being cost-effective):	
Value of Information	Give details: Not reported: ☐	
Study conclusions		

Quality and risk of bias for economic evaluations (if applicable)				**N/A ☐**
Checklists completed:	CHEC (all EE) ☐	ISPOR (models only) ☐		
Risk of bias [CHEC, ISPOR]:	High ☐	Medium ☐	Low ☐	Unknown ☐
Comments on study quality and limitations:				

SUPPLEMENTARY FILE 3: Risk of bias checklists

Table 3.1: Risk of bias checklist, adapted from Evers et al. 2005

Is the study population clearly described?
Are competing alternatives clearly described?
Is a well-defined research question posed in answerable form?
Is the economic study design appropriate to the stated objective?
Is the chosen time horizon appropriate in order to include relevant costs and consequences?
Is the actual perspective chosen appropriate?
Are all important and relevant costs for each alternative identified?
Are all costs measured appropriately in physical units?
Are costs valued appropriately?
Are all important and relevant outcomes for each alternative identified?
Are all outcomes measured appropriately?
Are outcomes valued appropriately?
Is an incremental analysis of costs and outcomes of alternatives performed?
Are all future costs and outcomes discounted appropriately?
Are all important variables, whose values are uncertain, appropriately subjected to sensitivity analysis?
Do the conclusions follow from the data reported?
Does the study discuss the generalizability of the results to other settings and patient/client groups?
Does the article indicate that there is no potential conflict of interest of study researcher(s) and funder(s)?
Are ethical and distributional issues discussed appropriately?

SUPPLEMENTARY FILE 3: Risk of bias checklists

Table 3.2: Risk of bias checklist, adapted from Caro et al. 2014

Relevance
Is the population relevant?
Are any critical interventions missing?
Are any relevant outcomes missing?
Is the context (settings and circumstances) applicable?
Credibility
Validation
Is external validation of the model sufficient to make its results credible for your decision?
Is internal verification of the model sufficient to make its results credible for your decision?
Does the model have sufficient face validity to make its results credible for your decision?
Design
Is the design of the model adequate for your decision problem?
Data
Are the data used in populating the model suitable for your decision problem?
Analysis
Were the analyses performed using the model adequate to inform your decision problem?
Was there an adequate assessment of the effects of uncertainty?
Reporting
Was the reporting of the model adequate to inform your decision problem?
Interpretation
Was the interpretation of results fair and balanced?
Conflict of Interest
Were there any potential conflicts of interest?
If there were potential conflicts of interest, were steps taken to address these?

Enhanced recovery of hip and knee replacement

PRISMA 2015 checklist for systematic review protocols

Section and topic	Item No.	Checklist Item	Reported in section
Administrative Information			
Identification	1a	Identify the report as a protocol of a systematic review	Abstract, Introduction, Methods
Update	1b	Identify protocol as an update of a previous systematic review if applicable	n/a
Registration	2	Name of registry and registration number	Abstract, Methods
Authors			
Contact		Provide name, institutional affiliation, e-mail address of all protocol authors; provide physical mailing address of corresponding author	Title page
Contributions		Describe contributions of protocol authors and identify the guarantor of the review	Declarations
Amendments		If the protocol represents an amendment of a previously completed or published protocol, identify as such and list changes; otherwise, state plan for documenting important protocol amendments	n/a
Support			
Sources	5a	Indicate Sources of financial or other support for the review	Declarations
Sponsor	5b	Provide name for the review funder and/or sponsor	Declarations
Role of sponsor or funder	5c	Describe roles of funder(s), sponsor(s) and/or institution(s), if any, in developing the protocol	Declarations
Introduction			
Rationale	6	Describe the rationale for the review in the context of what is already known	Introduction
Objectives	7	Provide an explicit statement of the question(s) the review will address with reference to participants, interventions, comparators, and outcomes (PICO)	Introduction, Search strategy
Methods			
Eligibility Criteria	8	Specify the study characteristics (such as PICO, study design, setting, time frame) and report characteristics (such as years considered, language, publication status) to be used as criteria for eligibility for the review	Search strategy
Information Sources	9	Describe all intended information sources (such as electronic databases, contact with study authors, trial registers or other grey literature sources) with planned dates of coverage	Search strategy
Search Strategy	10	Present draft of search strategy to be used for at least one electronic database, including planned limits, such that it could be repeated	Supplementary Information
Study Records			
Data Management	11a	Describe the mechanism(s) that will be used to manage records and data throughout the review	Study selection, Data extraction, Data synthesis
Selection Process	11b	State the process that will be used for selecting studies (such as two independent reviewers) through each phase of the review (that is, screening, eligibility and inclusion in meta-analysis)	Search strategy
Data Collection Process	11c	Describe planned method of extracting data from reports (such as piloting forms, done independently, in duplicate), any processes for obtaining and confirming data from investigators	Data extraction
Data Items	12	List and define all variables for which data will be sought (such as PICO items, funding sources), any pre-planned data assumptions and simplifications	Methods
Outcomes and prioritization	13	List and define all outcomes for which data will be sought, including prioritization of main and additional outcomes, with rationale	Methods – Outcomes, Data extraction

Enhanced recovery of hip and knee replacement

Risk of bias in individual studies	14	Describe anticipated methods for assessing risk of bias of individual studies, including whether this will be done at the outcome or study level, or both; state how this information will be used in data synthesis	Methods – risk of bias
Data Synthesis	15a	Describe criteria under which study data will be quantitatively synthesised	N/A
	15b	If data are appropriate for quantitative synthesis, describe planned summary measures, methods of handling data and methods of combining data from studies, including any planned exploration of consistency	N/A
	15c	Describe any proposed additional analyses (such as sensitivity or subgroup analyses, meta-regression)	N/A
	15d	If quantitative synthesis is not appropriate, describe the type of summary planned	Methods - data synthesis
Meta-bias(es)	16	Specify any planned assessment of meta-bias(es) (such as publication bias across studies, selective reporting within studies)	N/A
Confidence in cumulative evidence	17	Describe how the strength of the body of evidence will be assessed	Methods – risk of bias and quality assessment