Table 19: Review protocol: anaesthesia in knee joint replacement surgery

ID	Field	Content
0.	PROSPERO registration number	Not registered
1.	Review title	Anaesthesia in knee joint replacement surgery
2.	Review question	In adults having primary elective knee joint replacement, what is the clinical and cost effectiveness of regional anaesthesia or general anaesthesia, with or without nerve blocks and local infiltration analgesia, compared with each other or in combination?
3.	Objective	This review seeks to assess the most effective analgesia for total joint replacement. These can include regional or general anaesthetic alone or in combination with each other, nerve blocks or local infiltration.
4.	Searches	The following databases will be searched: Cochrane Central Register of Controlled Trials (CENTRAL) Cochrane Database of Systematic Reviews (CDSR) Embase MEDLINE Epistemonikos Searches will be restricted by: English language Human studies Letters and comments are excluded. Other searches: Inclusion lists of relevant systematic reviews will be checked by the reviewer. The searches may be re-run 6 weeks before final committee meeting and further studies retrieved for inclusion if relevant.

ID	Field	Content
		The full search strategies will be published in the final review.
5.	Condition or domain being studied	Primary elective knee joint replacement surgery
6.	Population	Inclusion: Adults having primary elective knee joint replacement Exclude studies including people meeting any of the following criteria: Adults having joint replacement as immediate treatment following fracture. Adults having revision joint replacement. Adults having joint replacement as treatment for primary or secondary cancer affecting the bones.
7.	Intervention/Exposure/Test	General anaesthesia General anaesthesia with nerve block General anaesthesia with local infiltration analgesia (during or after procedure) General anaesthesia with nerve block and local infiltration analgesia (during or after procedure) Regional anaesthesia Regional anaesthesia with nerve block Regional anaesthesia with local infiltration analgesia (during or after surgery) Regional anaesthesia with nerve block and local infiltration (during or after surgery) General and regional anaesthesia General and regional anaesthesia with nerve block General and regional anaesthesia with local infiltration analgesia (during or after procedure) General and regional anaesthesia with nerve block and local infiltration analgesia (during or after procedure)
8.	Comparator/Reference standard/Confounding factors	Comparison of interventions.
9.	Types of study to be included	Systematic reviews RCTs If no well-conducted RCTs are available, then observational studies with multivariate analysis will be investigated.
10.	Other exclusion criteria	Non-English language studies. Abstracts will be excluded as it is expected there will be sufficient full text published studies available.

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11.	Context	N/A
12.	Primary outcomes (critical outcomes)	Mortality: upto 90 days (dichotomous) Quality of life up to 30 days (continuous) Postoperative pain up to 30 days (continuous) Postoperative neurocognitive decline up to 30 days (dichotomous) Thromboembolic complications up to 90 days (VTE; dichotomous) Hospital readmission up to 30 days (dichotomous)
13.	Secondary outcomes (important outcomes)	Postoperative use of analgesia (dichotomous) Length of stay (continuous) Nausea up to 30 days (dichotomous) Mobilisation within 24 hours after surgery
14.	Data extraction (selection and coding)	EndNote will be used for reference management, sifting, citations and bibliographies. Titles and/or abstracts of studies retrieved using the search strategy and those from additional sources will be screened for inclusion. The full text of potentially eligible studies will be retrieved and will be assessed for eligibility in line with the criteria outlined above. 10% of the abstracts will be reviewed by two reviewers, with any disagreements resolved by discussion or, if necessary, a third independent reviewer. An in-house developed database; EviBase, will be used for data extraction. A standardised form is followed to extract data from studies (see Developing NICE guidelines: the manual section 6.4) and for undertaking assessment of study quality. Summary evidence tables will be produced including information on: study setting; study population and participant demographics and baseline characteristics; details of the intervention and control interventions; study methodology' recruitment and missing data rates; outcomes and times of measurement; critical appraisal ratings. A second reviewer will quality assure the extracted data. Discrepancies will be identified and resolved through discussion (with a third reviewer where necessary).
15.	Risk of bias (quality) assessment	Risk of bias will be assessed using the appropriate checklist as described in Developing NICE guidelines: the manual. For Intervention reviews the following checklist will be used according to study design being assessed: Systematic reviews: Risk of Bias in Systematic Reviews (ROBIS) Randomised Controlled Trial: Cochrane RoB (2.0) Disagreements between the review authors over the risk of bias in particular studies will be resolved by discussion, with

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		involvement of a third review author where necessary.	
16.	Strategy for data synthesis	Where possible, data will be meta-analysed. Pairwise meta-analyses will be performed using Cochrane Review Manager (RevMan5) to combine the data given in all studies for each of the outcomes stated above. A fixed effect meta-analysis, with weighted mean differences for continuous outcomes and risk ratios for binary outcomes will be used, and 95% confidence intervals will be calculated for each outcome. Heterogeneity between the studies in effect measures will be assessed using the I^2 statistic and visually inspected. We will consider an I^2 value greater than 50% indicative of substantial heterogeneity. Sensitivity analyses will be conducted based on pre-specified subgroups using stratified meta-analysis to explore the heterogeneity in effect estimates. If this does not explain the heterogeneity, the results will be presented using random-effects. GRADE pro will be used to assess the quality of each outcome, taking into account individual study quality and the meta-analysis results. The 4 main quality elements (risk of bias, indirectness, inconsistency and imprecision) will be appraised for each outcome. If the population included in an individual study includes children aged under 12, it will be included if the majority of the population is aged over 12, and downgraded for indirectness if the overlap into those aged less than 12 is greater than 20%. Publication bias is tested for when there are more than 5 studies for an outcome. Other bias will only be taken into consideration in the quality assessment if it is apparent. Where meta-analysis is not possible, data will be presented and quality assessed individually per outcome. If sufficient data is available to make a network of treatments, WinBUGS will be used for network meta-analysis.	
17.	Analysis of sub-groups	Age: <60 years old, ≥60 years old Co-morbidities: I-II ASA Grade, III-IV ASA Grade	
18.	Type and method of review	☒	Intervention
		☐	Diagnostic
		☐	Prognostic
		☐	Qualitative
		☐	Epidemiologic
		☐	Service Delivery

ID	Field	Content		
		☐	Other (please specify)	
19.	Language	English		
20.	Country	England		
21.	Anticipated or actual start date	01/02/19		
22.	Anticipated completion date	20/03/20		
23.	Stage of review at time of this submission	Review stage	Started	Completed
		Preliminary searches	☑	☐
		Piloting of the study selection process	☑	☐
		Formal screening of search results against eligibility criteria	☐	☐
		Data extraction	☐	☐
		Risk of bias (quality) assessment	☐	☐
		Data analysis	☐	☐
24.	Named contact	5a. Named contact National Guideline Centre 5b Named contact e-mail Headches@nice.org.uk 5e Organisational affiliation of the review National Institute for Health and Care Excellence (NICE) and the National Guideline Centre		
25.	Review team members	From the National Guideline Centre: Carlos Sharpin [Guideline lead] Alex Allen [Senior Systematic Reviewer] Rafina Yarde [Systematic reviewer] Robert King [Health economist]		

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		Agnès Cuyàs [Information specialist] Eleanor Priestnall [Project Manager]	
26.	Funding sources/sponsor	This systematic review is being completed by the National Guideline Centre which receives funding from NICE.	
27.	Conflicts of interest	All guideline committee members and anyone who has direct input into NICE guidelines (including the evidence review team and expert witnesses) must declare any potential conflicts of interest in line with NICE's code of practice for declaring and dealing with conflicts of interest. Any relevant interests, or changes to interests, will also be declared publicly at the start of each guideline committee meeting. Before each meeting, any potential conflicts of interest will be considered by the guideline committee Chair and a senior member of the development team. Any decisions to exclude a person from all or part of a meeting will be documented. Any changes to a member's declaration of interests will be recorded in the minutes of the meeting. Declarations of interests will be published with the final guideline.	
28.	Collaborators	Development of this systematic review will be overseen by an advisory committee who will use the review to inform the development of evidence-based recommendations in line with section 3 of Developing NICE guidelines: the manual. Members of the guideline committee are available on the NICE website: [NICE guideline webpage].	
29.	Other registration details		
30.	Reference/URL for published protocol		
31.	Dissemination plans	NICE may use a range of different methods to raise awareness of the guideline. These include standard approaches such as: notifying registered stakeholders of publication publicising the guideline through NICE's newsletter and alerts issuing a press release or briefing as appropriate, posting news articles on the NICE website, using social media channels, and publicising the guideline within NICE.	
32.	Keywords	Knee joint replacement surgery, arthroplasty, anaesthesia, analgesia	
33.	Details of existing review of same topic by same authors	N/A	
34.	Current review status	☒	Ongoing
		☐	Completed but not published
		☐	Completed and published
		☐	Completed, published and being updated

ID	Field	Content	
		☐	Discontinued
35..	Additional information	N/A	
36.	Details of final publication	www.nice.org.uk	