National Institute for Health and Care Excellence

Final

Joint replacement (primary): hip, knee and shoulder

[Q] Evidence review for inpatient shoulder postoperative rehabilitation

NICE guideline NG157

Intervention evidence review underpinning recommendation 1.10.1 and the research recommendation in the NICE guideline

June 2020

Final

This evidence review was developed by the National Guideline Centre, hosted by the Royal College of Physicians



Disclaimer

The recommendations in this guideline represent the view of NICE, arrived at after careful consideration of the evidence available. When exercising their judgement, professionals are expected to take this guideline fully into account, alongside the individual needs, preferences and values of their patients or service users. The recommendations in this guideline are not mandatory and the guideline does not override the responsibility of healthcare professionals to make decisions appropriate to the circumstances of the individual patient, in consultation with the patient and, where appropriate, their carer or guardian.

Local commissioners and providers have a responsibility to enable the guideline to be applied when individual health professionals and their patients or service users wish to use it. They should do so in the context of local and national priorities for funding and developing services, and in light of their duties to have due regard to the need to eliminate unlawful discrimination, to advance equality of opportunity and to reduce health inequalities. Nothing in this guideline should be interpreted in a way that would be inconsistent with compliance with those duties.

NICE guidelines cover health and care in England. Decisions on how they apply in other UK countries are made by ministers in the <u>Welsh Government</u>, <u>Scottish Government</u>, and <u>Northern Ireland Executive</u>. All NICE guidance is subject to regular review and may be updated or withdrawn.

Copyright

© NICE 2020. All rights reserved. Subject to Notice of rights.

ISBN 978-1-4731-3722-6

Contents

1	Post	-operat	ive rehabilitation	5
	1.1	replace	v question: In adults who have undergone primary elective shoulder ement, what is the most clinical and cost-effective timing and duration atient rehabilitation?	5
	1.2	Introdu	uction	5
	1.3	table	5	
	1.4	Clinica	Il evidence	6
		1.4.1	Included studies	6
		1.4.2	Excluded studies	6
	1.5	Econo	mic evidence	6
		1.5.1	Included studies	6
		1.5.2	Excluded studies	6
		1.5.3	Unit costs	6
	1.6	Eviden	nce statements	7
		1.6.1	Clinical evidence statements	7
		1.6.2	Health economic evidence statements	7
	1.7	The co	mmittee's discussion of the evidence	7
		1.7.1	Interpreting the evidence	7
		1.7.2	Cost effectiveness and resource use	9
αA	pendi	ces		. 11
•	-		Review protocols	
			Literature search strategies	
			inical search literature search strategy	
			ealth Economics literature search strategy	
	Appe	endix C:	Clinical evidence selection	. 28
	Appe	endix D:	Clinical evidence tables	. 29
	Appe	endix E:	Forest plots	. 29
	Appe	endix F:	GRADE tables	. 29
	Appe	endix G:	Health economic evidence selection	. 30
	Appe	endix H:	Health economic evidence tables	. 32
	Appe	endix I:	Excluded studies	. 33
		I.1 Ex	cluded clinical studies	. 33
		I.2 Ex	cluded health economic studies	. 33
	Appe	endix J:	Research recommendations	. 34
		J.1 Fa	arly shoulder mobilisation	. 34

1 Post-operative rehabilitation

1.1 Review question: In adults who have undergone primary elective shoulder replacement, what is the most clinical and cost-effective timing and duration for inpatient rehabilitation?

1.2 Introduction

Although the number of shoulder replacements are increasing year on year there is still a lack of consensus on the rehabilitation guidance immediately following shoulder replacement surgery. Most people may only be an in-patient for 24 hours following their surgery and priority is therefore focused on safe ambulation and instruction on self-care. People following these operations may experience a number of post-operative complications including nausea, hypotension, pain, delirium and confusion. The role of the multidisciplinary team in this post-operative stage of the inpatient recovery is to minimise these complications to promote early function, with the overall aim on facilitating a safe hospital discharge.

Core interventions in current postoperative inpatient rehabilitation include, advice with regard to sling management, instructions on preventing stiffness in the neck, hand and elbow regions, specific advice on what degree of exercise can be performed at the shoulder (this is dependent on surgeon preference and type of shoulder replacement) and functional-based tasks including washing, dressing and other activities of daily living. These are led by the physiotherapy and occupational therapy team but supported by the whole multidisciplinary team during the individual's hospital stay. Postoperative inpatient rehabilitation also frequently includes an assessment of further, post-discharge rehabilitation needs, which may lead to referral to community physiotherapy or occupational therapy services or to social services or third sector organisations for ongoing support if indicated.

There is inconsistency with the timing and type of postoperative inpatient rehabilitation patients should receive following shoulder replacement surgery. There is uncertainty as to what should be included in the postoperative inpatient rehabilitation programme especially with regards to periods of immobilisation in a sling and degree of movement allowed at the shoulder to help maintain muscle and joint function and periods for these restrictions.

This review seeks to find out what the most clinical and cost effective inpatient rehabilitation intervention is for people who have undergone shoulder replacement, and particularly on when this rehabilitation begins.

1.3 PICO table

For full details, see the review protocol in Appendix A:

Table 1: PICO characteristics of review question

Population	Adults who have undergone primary shoulder joint replacement.			
Intervention	First rehabilitation on the day of surgery			
Comparison	First rehabilitation after the day of surgery			
Outcomes	Critical			
	Quality of life within 6 weeks (continuous) for example EQ-5D, EQ-VAS.			
	Patient Reported Outcome Measures (PROMs) within 6 weeks (continuous)			
	Revision of joint replacement (time to event)			
	Reoperation including dislocation within 6 weeks (dichotomous)			

	 Important Deep surgical site infection within 6 weeks (dichotomous) Superficial surgical site infection within 6 weeks (dichotomous) 				
	Hospital readmissions: within 30 (dichotomous)				
	Length of stay (continuous)				
	To be extracted when not included within a PROM:				
	Function/ADL within 6 weeks (continuous).				
	Pain within 6 weeks (continuous)				
Study design	Randomised controlled trials				
	If no well-conducted RCTs are available, then observational studies with multivariate analysis will be investigated.				

1.4 Clinical evidence

1.4.1 Included studies

After searches for both RCTs and observational studies were conducted, no relevant clinical studies comparing the timing of beginning inpatient rehabilitation after shoulder replacement surgery were identified.

1.4.2 Excluded studies

1.5 Economic evidence

1.5.1 Included studies

No relevant health economic studies were identified for this review. However, evidence from the inpatient rehabilitation for hip and knee replacement review (Evidence review P) was used to support a recommendation.

1.5.2 Excluded studies

No health economic studies that were relevant to this question were excluded due to assessment of limited applicability or methodological limitations.

See also the health economic study selection flow chart in Appendix G:

1.5.3 Unit costs

Some potentially relevant unit costs are provided below to aid consideration of cost effectiveness.

Table 2: Cost per hour of a hospital based physiotherapy or occupational therapy teams by Band

Band 4	Band 5	Band 6	Band 7	Band 8a	Band 8b
£32	£35	£46	£55	£66	£78

⁽a) Source PSSRU 'Unit costs of Health and Social Care 2018¹

(c)

⁽b) Note that the registered workforce starts at Band 5. Staff may also be on Band 3, however the PSSRU does not include unit costs for this Band

The weighted average of the HRG codes for primary elective shoulder replacements in Table 3 are based upon the average length of stay and average cost of an excess bed day

Table 3. Weighted average unit cost for hip and knee HRG codes

Intervention/ Diagnosis	Reference cost HRG	Weighted national average	Weighted average length of stay	Weighted av cost of excess day	_
Very Major Shoulder Procedures for Non-Trauma	Weighted for complications and co morbidities for HRG codes: HN52A, HN52B and HN52C; as recorded for Elective Inpatients	£6,240	2.17	£	455.68

⁽a) Source: NHS Reference Costs 2017/18

1.6 Evidence statements

1.6.1 Clinical evidence statements

No relevant published evidence was identified.

1.6.2 Health economic evidence statements

No relevant economic evaluations were identified.

1.7 The committee's discussion of the evidence

1.7.1 Interpreting the evidence

1.7.1.1 The outcomes that matter most

The critical outcomes were agreed to be quality of life (QOL) within 6 weeks, Patient Reported Outcome Measures (PROMs) within 6 weeks, time until joint replacements were revised and reoperation within 6 weeks. PROMs measure health gain in patients undergoing joint replacement. They vary in terms of content and can cover a range of clinical measures such as QOL, pain, stiffness, and function. Reoperation within 6 weeks was chosen to pick up negative rehabilitation outcomes including dislocation.

Important outcomes were infection, hospital readmissions within 30 days, and length of stay. It was agreed to utilise function or pain as outcomes if they were reported and not included in a PROM.

The follow up timescales for QOL, PROMs, reoperation, infection, pain and function were within 6 weeks to pick up the meaningful benefits of inpatient rehabilitation. The longer-term benefits are explored in the outpatient rehabilitation evidence review. The timing of the hospital readmission timescale was 30 days to match how it is normally reported and this is a short-term timescale that could be influenced by inpatient rehabilitation.

The 30-day mortality after joint arthroplasty is a rare event usually due to pre-existing cardiovascular and/or pulmonary disease and the GC did not consider this to be altered by varying inpatient rehabilitation.

No clinical evidence was found for this question.

1.7.1.2 The quality of the evidence

No clinical evidence was found for this question.

1.7.1.3 Benefits and harms

There is currently great variability between orthopaedic teams in terms of immediate postoperative rehabilitation. Some large centre teams use a sling for 6 weeks and some use a sling for 10 days. There is also variability compared to hip or knee joint replacement because walking is often not limited by shoulder replacement. Walking is often possible and can be enabled through effective pain control. This allows for hospital discharge within 24 hours and there are moves to utilise a day case model.

Increased speed of discharge may promote people to be given early rehabilitation, consisting of advice on self-care, assessment and directions from a physiotherapist. Physiotherapists and/or occupational therapists can advise on how to manage activities of daily living out of hospital with only one usable arm. The physiotherapist interactions include assessment of safe zones as well as mobilisation of the parts of the shoulder and arm that can be done safely. Some physiotherapist intervention could happen before surgery but assessment of safe zones is required after the surgery. A further aspect of this role is to insure people don't get secondary stiffness in the wrist or hand of the affected joint.

The committee stated that ambulation after shoulder replacement surgery is part of the person's progress to hospital discharge and fast discharge was and agreed by all of the committee to be important for a person's wellbeing after joint replacement. However, the committee were clear that a person's specific clinical situation at initial assessment would be considered in care as it currently stands. Signs that the inpatient rehabilitation program, and consequently ambulation, should be slowed or delayed would be made at the initial assessment after surgery by the orthopaedic team. For example, ambulation and discharge within 24 hours would not be actioned if the team finds a detectable limiting factor such as bleeding. The committee agreed that continuing this assessment of each person to ensure they are not contraindicated for rehabilitation within 24 hours after surgery reduces possible adverse effects of an early inpatient rehabilitation program. The committee noted that while it is preferable for rehabilitation to occur on the day of surgery there may be barriers that could prevent this, such as operations at later time-points in the day.

Therefore, the committee decided to make a consensus recommendation with extrapolation from the hip and knee surgery evidence to offer therapy led rehabilitation including mobilisation within 24 hours for people having primary shoulder replacement surgery not due to immediate trauma.

The committee consensus was that there were no harms associated with this recommendation as people's specific clinical situation at initial assessment would be considered and rehabilitation delayed if indicated. The committee did not have evidence or consensus to recommend when the shoulder should be mobilised and were keen that this decision should be taken by the orthopaedic team.

The committee also agreed that two research recommendations were important to fill this gap in the evidence. One research recommendation would directly answer the question posed by this evidence review. Is early inpatient rehabilitation including ambulation within 24 hours of shoulder replacement surgery clinically and cost effective compared to later inpatient rehabilitation including ambulation. The second question not answered by the current evidence base is whether early shoulder mobilisation within 24 hours of shoulder replacement surgery clinically and cost effective compared to later shoulder mobilisation? The committee mentioned that the specifics of the surgery that mean a sling might be used for an extended period. Therefore the surgery technique affects whether it is possible to have early shoulder mobility and then early shoulder mobilisation.

The committee discussed the type of exercises to prescribe. They agreed that these should be tailored to the person's needs and circumstances, taking into account their activities of daily living.

1.7.2 Cost effectiveness and resource use

No economic evaluations were found for early rehabilitation in shoulder replacement. However, two studies included in the inpatient hip and knee rehabilitation review were used to support a recommendation. One study found a cost saving associated with early mobilisation in a total knee replacement. The study also reported improved health outcomes (a reduced length of stay of 0.44 days and greater odds of achieving at least 90 degrees of knee flexion) in the early ambulation group. The other found cost savings associated with 7-day physiotherapy for hip and knee replacement patients compared with weekday-only physiotherapy. The study also reported improved health outcomes (quicker time to mobilise with two sticks for hip and knee, and a trend towards earlier discharge) in the weekend physiotherapy group.

The committee decided to recommend rehabilitation on the day of surgery or within 24 hours of surgery by extrapolating the evidence for hip and knee replacement patients. In the committee's experience, the benefits of inpatient postoperative rehabilitation are similar for shoulder replacements as those seen after hip or knee replacements. All patients who receive a shoulder replacement (5,500 operations in 2017/18 according to Hospital Episode Statistic data) receive some form of physiotherapy and rehabilitation during their inpatient stay as part of current practice. This may be assessing the patient from the bed, assistance in mobilising from the bed and provision of exercises. Inpatient rehabilitation would usually be a 30-45 minute initial session for the majority of patients, from reading the notes to seeing the patient to finishing recording in the notes. For any surgery conducted on Monday, Tuesday, Wednesday or Thursday, the recommendation will not have a substantial resource impact as inpatient rehabilitation within 24 hours of surgery will take place on a weekday when physiotherapists and occupational therapists would be readily available as part of current practice. There was suggestion by the committee that more elective procedures would occur on weekdays, as opposed to weekends, due to greater accident and emergency pressures on the weekend.

All services currently offer a reduced provision of weekend physiotherapists/occupational therapists. However, these staff may not necessarily be seeing this group of patients as part of current practice. This therefore has a resource implication as it means that they would either have to see these patients and not others, or increase services to see these patients. The hourly unit costs for hospital based physiotherapy and occupational therapy team staff is £32-78 (Bands 4-8b), although the weekend costs may be more than those included. Registered physiotherapists and occupational therapists start at Band 5. Staff may also be on Band 3, however costs for this Band are not provided by the Personal Social Services Research Unit (PSSRU). There was discussion that it is important that an appropriately qualified physiotherapist or occupational therapist is available to give the first assessment. However, there are instances where staff on lower Bands who are well supported by members of the rehabilitation team can undertake subsequent inpatient care.

The economic evidence suggests that increasing weekend staff capacity and their associated costs will be at least partially offset by a reduction in length of stay due to faster recovery. The cost of an excess bed day for a primary elective shoulder replacement is £456. The committee believed the recommendation would result in an overall cost saving.

References

- Curtis LA, Burns A. Unit costs of health and social care 2018. Project report. Kent. University of Kent, 2018. Available from: https://kar.kent.ac.uk/70995/1/Unit%20Costs%202018%20-%20FINAL%20with%20bookmarks%20and%20covers%20%282%29.pdf
- 2. Hultenheim Klintberg I, Gunnarsson AC, Styf J, Karlsson J. Early activation or a more protective regime after arthroscopic subacromial decompression--a description of clinical changes with two different physiotherapy treatment protocols--a prospective, randomized pilot study with a two-year follow-up. Clinical Rehabilitation. 2008; 22(10-11):951-65
- 3. Kluczynski MA, Isenburg MM, Marzo JM, Bisson LJ. Does early versus delayed active range of motion affect rotator cuff healing after surgical repair? A systematic review and meta-analysis. American Journal of Sports Medicine. 2016; 44(3):785-91
- National Institute for Health and Care Excellence. Developing NICE guidelines: the manual [updated 2018]. London. National Institute for Health and Care Excellence, 2014. Available from: http://www.nice.org.uk/article/PMG20/chapter/1%20Introduction%20and%20overview
- 5. Saltzman BM, Zuke WA, Go B, Mascarenhas R, Verma NN, Cole BJ et al. Does early motion lead to a higher failure rate or better outcomes after arthroscopic rotator cuff repair? A systematic review of overlapping meta-analyses. Journal of Shoulder and Elbow Surgery. 2017; 26(9):1681-1691

Appendices

Appendix A: Review protocols

Table 4: Review protocol: inpatient rehabilitation after shoulder replacement

ID	Field	Content		
0.	PROSPERO registration number	Not registered		
1.	Review title	Inpatient rehabilitation after shoulder replacement		
2.	Review question	In adults who have undergone primary elective shoulder replacement, what is the most clinical and cost-effective timing and duration for inpatient rehabilitation?		
3.	Objective	Allowing healing of the repaired subscapularis tendon while minimizing stiffness and muscle atrophy are the primary goals of postsurgical rehabilitation. These tend to be 3 or 4 phase regimes with varying timings within these phases and vary when they begin after surgery. This question seeks to address when rehabilitation should begin.		
4.	Searches	The following databases will be searched: Cochrane Central Register of Controlled Trials (CENTRAL) Cochrane Database of Systematic Reviews (CDSR) Embase MEDLINE 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. The full search strategies will be published in the final review.		
_	Condition or domesi-			
5.	Condition or domain	Primary elective shoulder joint replacement surgery		

ID	Field	Content
	being studied	
6.	Population	Inclusion: Adults who have undergone primary shoulder 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/T est	First rehabilitation on the day of surgery
8.	Comparator/Reference standard/Confounding factors	First rehabilitation after the day of surgery
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.
11.	Context	N/A
12.	Primary outcomes (critical outcomes)	Quality of life within 6 to 24 months (continuous) for example EQ-5D, EQ-VAS. Patient Reported Outcome Measures (PROMs) within at 6 to 24 (continuous) Revision of joint replacement (time to event) Reoperation including dislocation within 24 months (dichotomous)
13.	Secondary outcomes (important outcomes)	Deep surgical site infection within 6 weeks (dichotomous) Superficial surgical site infection within 6 weeks (dichotomous) Hospital readmissions: within 30 (dichotomous) Length of stay (continuous)

ID	Field	Content
		To be extracted when not included within an extracted PROM: Function at 6 weeks or earlier (continuous) Pain at 6 weeks or earlier (continuous)
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 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 I² statistic and visually inspected. We will consider an I² 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.

ID	Field	Content		
		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 appraised for each outcome. If the population included in an individual study includes children aged under 12, it will be included if the majority population is aged over 12, and downgraded for indirectness if the overlap into those aged less than 12 is greate 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 qua	ality 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		hroplasty, hemiarthroplasty, reverse total shoulder arthroplasty	
		Intervention type: physiotherapy, occupational therapy, p Cuff (supraspinatus and infraspinatus muscles) integrity:	hysiotherapy and occupational therapy	
18.	Type and method of		Intervention	
	review		Diagnostic	
			Prognostic	
			Qualitative	
			Epidemiologic	
			Service Delivery	
			Other (please specify)	
19.	Language	English		
20.	Country	England		
21.	Anticipated or actual start date	15/08/18		
22.	Anticipated completion date	20/03/20		

ID	Field	Content		
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] 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		

ID	Field	Content		
		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	Joint replacement surgery, arthroplasty, inpatient rehabi	litation	
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	
			Discontinued	
35	Additional information	N/A		
36.	Details of final publication	www.nice.org.uk		

Table F.			
i abie 5:	neaith	economic review	protocoi

	ealth economic review protocol			
Review question	All questions – health economic evidence			
Objectives	To identify health economic studies relevant to any of the review questions.			
Search criteria	 Populations, interventions and comparators must be as specified in the clinical review protocol above. 			
	 Studies must be of a relevant health economic study design (cost-utility analysis, cost-effectiveness analysis, cost-benefit analysis, cost-consequences analysis, comparative cost analysis). 			
	 Studies must not be a letter, editorial or commentary, or a review of health economic evaluations. (Recent reviews will be ordered although not reviewed. The bibliographies will be checked for relevant studies, which will then be ordered.) 			
	 Unpublished reports will not be considered unless submitted as part of a call for evidence. 			
	Studies must be in English.			
Search strategy	A health economic study search will be undertaken using population-specific terms and a health economic study filter – see appendix B below.			
Review strategy	Studies not meeting any of the search criteria above will be excluded. Studies published before 2003, abstract-only studies and studies from low or middle-income countries (e.g. non-OECD countries) or the USA will also be excluded.			
	Each remaining study will be assessed for applicability and methodological limitations using the NICE economic evaluation checklist which can be found in appendix H of Developing NICE guidelines: the manual (2014). ⁴			
	Inclusion and exclusion criteria			
	 If a study is rated as both 'Directly applicable' and with 'Minor limitations' then it will be included in the guideline. A health economic evidence table will be completed and it will be included in the health economic evidence profile. 			
	If a study is rated as either 'Not applicable' or with 'Very serious limitations' then it will usually be excluded from the guideline. If it is excluded then a health economic evidence table will not be completed and it will not be included in the health economic evidence profile. If the description of the serious distribution is the serious distribution of the serious distribution is the serious distribution. If the serious limitations' then it is a serious limitations' then it is a serious limitations' then it is a serious limitations' then it will be serious limitations' then it will usually be excluded then a health economic evidence table will not be completed and it will not be included in the health economic evidence profile.			
	 If a study is rated as 'Partially applicable', with 'Potentially serious limitations' or both then there is discretion over whether it should be included. 			
	Where there is discretion			
	The health economist will make a decision based on the relative applicability and quality of the available evidence for that question, in discussion with the guideline committee if required. The ultimate aim is to include health economic studies that are helpful for decision-making in the context of the guideline and the current NHS setting. If several studies are considered of sufficiently high applicability and methodological quality that they could all be included, then the health economist, in discussion with the committee if required, may decide to include only the most applicable studies and to exclude the remaining studies selectively. All studies excluded based on applicability or methodological limitations will be listed with explanation in the excluded health economic studies appendix below.			
	The health economist will be guided by the following hierarchies. Setting:			
	 UK NHS (most applicable). OECD countries with predominantly public health insurance systems (for example, France, Germany, Sweden). 			
	OECD countries with predominantly private health insurance systems (for example,			

Switzerland).

• Studies set in non-OECD countries or in the USA will be excluded before being assessed for applicability and methodological limitations.

Health economic study type:

- Cost–utility analysis (most applicable).
- Other type of full economic evaluation (cost–benefit analysis, cost-effectiveness analysis, cost–consequences analysis).
- · Comparative cost analysis.
- Non-comparative cost analyses including cost-of-illness studies will be excluded before being assessed for applicability and methodological limitations.

Year of analysis:

- The more recent the study, the more applicable it will be.
- Studies published in 2003 or later but that depend on unit costs and resource data entirely or predominantly from before 2003 will be rated as 'Not applicable'.
- Studies published before 2003 will be excluded before being assessed for applicability and methodological limitations.

Quality and relevance of effectiveness data used in the health economic analysis:

• The more closely the clinical effectiveness data used in the health economic analysis match with the outcomes of the studies included in the clinical review the more useful the analysis will be for decision-making in the guideline.

Appendix B: Literature search strategies

The literature searches for this review are detailed below and complied with the methodology outlined in Developing NICE guidelines: the manual.⁴

For more detailed information, please see the Methodology Review.

B.1 Clinical search literature search strategy

Searches were constructed using a PICO framework where population (P) terms were combined with Intervention (I) and in some cases Comparison (C) terms. Outcomes (O) are rarely used in search strategies for interventions as these concepts may not be well described in title, abstract or indexes and therefore difficult to retrieve. Search filters were applied to the searches where appropriate.

Table 6: Database date parameters and filters used

Database	Dates searched	Search filter used
Medline (OVID)	1946 – 01 May 2019	Exclusions Randomised controlled trials Systematic review studies Observational studies
Embase (OVID)	1974 – 01 May 2019	Exclusions Randomised controlled trials Systematic review studies Observational studies
The Cochrane Library (Wiley)	Cochrane Reviews to 2019 Issue 5 of 12 CENTRAL to 2019 Issue 5 of 12 DARE, and NHSEED to 2015 Issue 2 of 4 HTA to 2016 Issue 4 of 4	None

Medline (Ovid) search terms

1.	arthroplasty/ or arthroplasty, replacement/ or arthroplasty, replacement, hip/ or arthroplasty, replacement, knee/ or arthroplasty, replacement, shoulder/ or hemiarthroplasty/
2.	joint prosthesis/ or hip prosthesis/ or knee prosthesis/ or shoulder prosthesis/
3.	((joint* or knee* or shoulder* or hip*) adj5 (surger* or replace* or prosthe* or endoprosthe* or implant* or artificial or arthroplast* or hemiarthroplast*)).ti,ab.
4.	or/1-3
5.	letter/
6.	editorial/
7.	news/
8.	exp historical article/
9.	Anecdotes as Topic/
10.	comment/
11.	case report/
12.	(letter or comment*).ti.
13.	or/5-12
14.	randomized controlled trial/ or random*.ti,ab.

15.	13 not 14
16.	animals/ not humans/
17.	exp Animals, Laboratory/
18.	exp Animal Experimentation/
19.	exp Models, Animal/
20.	exp Rodentia/
21.	(rat or rats or mouse or mice).ti.
22.	or/15-21
23.	4 not 22
24.	limit 23 to English language
25.	exp Rehabilitation/
26.	Rehabilitation Nursing/
27.	rehab*.ti,ab.
28.	(prehabilitat* or pre habilitat*).ti,ab.
29.	Early Ambulation/
30.	(early adj3 (ambulation or mobili*)).ti,ab.
31.	Physical Therapy Modalities/
32.	exp Exercise Therapy/ or Physical Conditioning, Human/ or Occupational Therapy/ or Recreation Therapy/ or Rehabilitation, Vocational/
33.	Motion Therapy, Continuous Passive/ or Muscle Stretching Exercises/ or Manipulation, Orthopedic/ or Resistance Training/
34.	((physical* or exercise* or motion or movement or occupational or recreation* or vocational) adj3 (therap* or condition*)).ti,ab.
35.	(manipulation or MUA).ti,ab.
36.	((standardi?ed or SE or continuous passive motion or CPM or slider board or SB or range of motion or ROM or resistance or weight bearing or equilibrium or flexibility or stretch*) adj2 (therap* or exercise*)).ti,ab.
37.	physiotherap*.ti,ab.
38.	Hydrotherapy/
39.	(hydrotherap* or aquatic physiotherap*).ti,ab.
40.	Transcutaneous Electric Nerve Stimulation/
41.	(electric* nerve stimulation or TENS).ti,ab.
42.	Patient Education as Topic/
43.	(patient* adj3 (education or information or advice)).ti,ab.
44.	or/25-43
45.	24 and 44
46.	randomized controlled trial.pt.
47.	controlled clinical trial.pt.
48.	randomi#ed.ti,ab.
49.	placebo.ab.
50.	randomly.ti,ab.
51.	Clinical Trials as topic.sh.
52.	trial.ti.
53.	or/46-52
54.	Meta-Analysis/
55.	exp Meta-Analysis as Topic/

56.	(meta analy* or metanaly* or metaanaly* or meta regression).ti,ab.	
57.	((systematic* or evidence*) adj3 (review* or overview*)).ti,ab.	
58.	(reference list* or bibliograph* or hand search* or manual search* or relevant journals).ab.	
59.	(search strategy or search criteria or systematic search or study selection or data extraction).ab.	
60.	(search* adj4 literature).ab.	
61.	(medline or pubmed or cochrane or embase or psychlit or psyclit or psychinfo or psycinfo or cinahl or science citation index or bids or cancerlit).ab.	
62.	cochrane.jw.	
63.	((multiple treatment* or indirect or mixed) adj2 comparison*).ti,ab.	
64.	or/54-63	
65.	Epidemiologic studies/	
66.	Observational study/	
67.	exp Cohort studies/	
68.	(cohort adj (study or studies or analys* or data)).ti,ab.	
69.	((follow up or observational or uncontrolled or non randomi#ed or epidemiologic*) adj (study or studies or data)).ti,ab.	
70.	((longitudinal or retrospective or prospective or cross sectional) and (study or studies or review or analys* or cohort* or data)).ti,ab.	
71.	Controlled Before-After Studies/	
72.	Historically Controlled Study/	
73.	Interrupted Time Series Analysis/	
74.	(before adj2 after adj2 (study or studies or data)).ti,ab.	
75.	or/65-74	
76.	exp case control study/	
77.	case control*.ti,ab.	
78.	or/76-77	
79.	75 or 78	
80.	Cross-sectional studies/	
81.	(cross sectional and (study or studies or review or analys* or cohort* or data)).ti,ab.	
82.	or/80-81	
83.	75 or 82	
84.	75 or 78 or 82	
85.	45 and (53 or 64 or 84)	

Embase (Ovid) search terms

<u> Lilibu</u>	induce (evid) search terms		
1.	*arthroplasty/ or *replacement arthroplasty/ or *hip replacement/ or *knee replacement or *shoulder replacement/ or *hemiarthroplasty/		
2.	*joint prosthesis/ or *hip prosthesis/ or *knee prosthesis/ or *shoulder prosthesis/		
3.	((joint* or knee* or shoulder* or hip*) adj5 (surger* or replace* or prosthe* or endoprosthe* or implant* or artificial or arthroplast* or hemiarthroplast*)).ti,ab.		
4.	or/1-3		
5.	letter.pt. or letter/		
6.	note.pt.		
7.	editorial.pt.		
8.	case report/ or case study/		
9.	(letter or comment*).ti.		

11. randomized controlled trial/ or random*.ti,ab. 12. 10 not 11 13. animal/ not human/ 14. nonhuman/ 15. exp Animal Experiment/ 16. exp Experimental Animal/ 17. animal model/ 18. exp Rodent/ 19. (rat or rats or mouse or mice).ti. 20. or/12-19 21. 4 not 20 22. limit 21 to English language 23. exp rehabilitation/ 24. rehabilitation nursing/ 25. rehab*.ti,ab. 26. (prehabilitat* or pre habilitat*).ti,ab. 27. *mobilization/ 28. (early adj3 (ambulation or mobili*)).ti,ab. 29. *physiotherapy/ or *kinesiotherapy/ or *exercise/ or *occupational therapy/ or *recreational therapy/ or *vocational rehabilitation/ 30. *movement therapy/ or *stretching exercise/ or *orthopedic manipulation/ or *resistat training/ 31. ((physical* or exercise* or motion or movement or occupational or recreation* or vocational) adj3 (therap* or condition*)).ti,ab. 32. (manipulation or MUA).ti,ab. ((standardi?ed or SE or continuous passive motion or CPM or slider board or SB or	10.	or/5-9
12. 10 not 11 13. animal/ not human/ 14. nonhuman/ 15. exp Animal Experiment/ 16. exp Experimental Animal/ 17. animal model/ 18. exp Rodent/ 19. (rat or rats or mouse or mice).ti. 20. or/12-19 21. 4 not 20 22. limit 21 to English language 23. exp rehabilitation/ 24. rehabilitation nursing/ 25. rehab*.ti,ab. 26. (prehabilitation nursing/ 27. *mobilization/ 28. (early adj3 (ambulation or mobili*)).ti,ab. 29. *physiotherapy/ or *kinesiotherapy/ or *exercise/ or *cocupational therapy/ or *recreational therapy/ or *stretching exercise/ or *orthopedic manipulation/ or *resista training/ 31. ((physical* or exercise* or motion or movement or occupational or recreation* or vocational) adj3 (therap* or condition*)).ti,ab. 33. ((standardi?ed or SE or continuous passive motion or CPM or slider board or SB or range of motion or MUA) ti,ab. 34. physiotherap*.ti,ab. 35. hydrotherapy/ 36. ((hydrotherap* or aquatic physiotherap*).ti,ab. 37. transcutaneous electrical nerve stimulation/ 38. (electric* nerve stimulation or TENS).ti,ab. 39. *patient education/ 40. (patient* adj3 (education or information or advice)).ti,ab. 41. or/23-40 42. 22 and 41 43. random*.ti,ab. 44. factorial*.ti,ab. 45. (crossover* or cross over*).ti,ab. 46. ((doubl* or singl*) adj blind*).ti,ab. 47. (assign* or allocat* or volunteer* or placebo*).ti,ab.		
13. animal/ not human/ 14. nonhuman/ 15. exp Animal Experiment/ 16. exp Experimental Animal/ 17. animal model/ 18. exp Rodent/ 19. (rat or rats or mouse or mice),ti. 20. or/12-19 21. 4 not 20 22. limit 21 to English language 23. exp rehabilitation/ 24. rehabilitation nursing/ 25. rehab* ti,ab. 26. (prehabilitat* or pre habilitat*),ti,ab. 27. *mobilization/ 28. (early adj3 (ambulation or mobili*)),ti,ab. 29. *physiotherapy/ or *kinesiotherapy/ or *exercise/ or *occupational therapy/ or *recreational therapy/ or *vectational rehabilitation/ 30. *movement therapy/ or *stretching exercise/ or *orthopedic manipulation/ or *resistat training/ 31. ((physical* or exercise* or motion or movement or occupational or recreation* or vocational) adj3 (therap* or condition*)),ti,ab. 32. ((manipulation or MUA),ti,ab. 33. ((standardi?ed or SE or continuous passive motion or CPM or slider board or SB or arrange of motion or ROM or resistance or weight bearing or equilibrium or flexibility of stretch*) adj2 (therap* or exercise*)),ti,ab. 34. physiotherap*.ti,ab. 35. hydrotherapy.dia (hydrotherap* or aquatic physiotherap*),ti,ab. 36. (hydrotherap* or aquatic physiotherap*),ti,ab. 37. transcutaneous electrical nerve stimulation/ 40. (patient* adj3 (education or information or advice)),ti,ab. 41. or/23-40 42. 22 and 41 43. random*.ti,ab. 44. factorial*.ti,ab. 45. ((doubl* or singl*) adj blind*),ti,ab. 46. ((doubl* or singl*) adj blind*),ti,ab. 47. (assign* or allocat* or volunteer* or placebo*),ti,ab.		
14. nonhuman/ 15. exp Animal Experiment/ 16. exp Experimental Animal/ 17. animal model/ 18. exp Rodent/ 19. (rat or rats or mouse or mice).ti. 20. or/12-19 21. 4 not 20 22. limit 21 to English language 23. exp rehabilitation/ 24. rehabilitation nursing/ 25. rehab*.ti,ab. 26. (prehabilitat* or pre habilitat*),ti,ab. 27. *mobilization/ 28. (early adj3 (ambulation or mobili*)),ti,ab. 29. *physiotherapy/ or *kinesiotherapy/ or *exercise/ or *occupational therapy/ or *recreational therapy/ or *vocational rehabilitation/ 30. *movement therapy/ or *stretching exercise/ or *orthopedic manipulation/ or *resistat training/ 31. ((physical* or exercise* or motion or movement or occupational or recreation* or ovcational) adj3 (therap* or condition*)),ti,ab. 32. (manipulation or MUA),ti,ab. 33. ((standardi?ed or SE or continuous passive motion or CPM or slider board or SB or range of motion or ROM or resistance or weight bearing or equilibrium or flexibility of stretch*) adj2 (therap* or exercise*)),ti,ab. 34. physiotherap/.ti,ab. 35. hydrotherap/.ti,ab. 36. (hydrotherap* or aquatic physiotherap*),ti,ab. 37. transcutaneous electrical nerve stimulation/ 38. (electric* nerve stimulation or TENS),ti,ab. 39. *patient education/ 40. (patient* adj3 (education or information or advice)),ti,ab. 41. or/23-40 42. 22 and 41 43. random*.ti,ab. 44. factorial*.ti,ab. 45. (crossover* or cross over*),ti,ab. 46. ((doubl* or singl*) adj blind*),ti,ab. 47. (assign* or allocat* or volunteer* or placebo*),ti,ab.		
15. exp Animal Experiment/ 16. exp Experimental Animal/ 17. animal model/ 18. exp Rodent/ 19. (rat or rats or mouse or mice) ti. 20. or/12-19 21. 4 not 20 22. limit 21 to English language 23. exp rehabilitation/ 24. rehabilitation nursing/ 25. rehab*.ti, ab. 26. (prehabilitat* or pre habilitat*).ti, ab. 27. "mobilization/ 28. (early adj3 (ambulation or mobili*)), ti, ab. 29. "physiotherapy/ or *kinesiotherapy/ or *exercise/ or *occupational therapy/ or *recreational therapy/ or *trectainal rehabilitation/ 30. "movement therapy/ or *stretching exercise/ or *orthopedic manipulation/ or *resista training/ 31. ((physical* or exercise* or motion or movement or occupational or recreation* or vocational) adj3 (therap* or condition*)).ti, ab. 32. (manipulation or MUA), ti, ab. 33. ((standardi?ed or SE or continuous passive motion or CPM or slider board or SB or range of motion or ROM or resistance or weight bearing or equilibrium or flexibility of stretch*) adj2 (therap* or exercise*)), ti, ab. 34. physiotherap*, ti, ab. 35. hydrotherap* or aquatic physiotherap*), ti, ab. 36. ((hydrotherap* or aquatic physiotherap*), ti, ab. 37. transcutaneous electrical nerve stimulation/ 40. (patient* adj3 (education or information or advice)), ti, ab. 41. or/23-40 42. 22 and 41 43. random*.ti, ab. 44. factorial*.ti, ab. 45. (crossover* or cross over*), ti, ab. 46. ((doubl* or singl*) adj blind*), ti, ab. 47. (assign* or allocat* or volunteer* or placebo*), ti, ab.		
16. exp Experimental Animal/ 17. animal model/ 18. exp Rodent/ 19. (rat or rats or mouse or mice).ti. 20. or/12-19 21. 4 not 20 22. limit 21 to English language 23. exp rehabilitation nursing/ 24. rehabilitation nursing/ 25. rehab* ti,ab. 26. (prehabilitat* or pre habilitat*).ti,ab. 27. *mobilization/ 28. (early adj3 (ambulation or mobili*)).ti,ab. 29. *physiotherapy/ or *kinesiotherapy/ or *exercise/ or *occupational therapy/ or *recreational therapy/ or *recreational therapy/ or *vocational rehabilitation/ 30. *movement therapy/ or *stretching exercise/ or *orthopedic manipulation/ or *resista training/ 31. ((physical* or exercise* or motion or movement or occupational or recreation* or vocational) adj3 (therap* or condition*)).ti,ab. 32. ((manipulation or MUA).ti,ab. 33. ((standardi?ed or SE or continuous passive motion or CPM or slider board or SB or range of motion or ROM or resistance or weight bearing or equilibrium or flexibility or stretch*) adj2 (therap* or exercise*)).ti,ab. 34. physiotherap*.ti,ab. 35. hydrotherap* or aquatic physiotherap*).ti,ab. 36. ((hydrotherap* or aquatic physiotherap*).ti,ab. 37. transcutaneous electrical nerve stimulation/ 48. (electric* nerve stimulation or TENS).ti,ab. 49. *patient education/ 40. (patient* adj3 (education or information or advice)).ti,ab. 41. or/23-40 42. 22 and 41 43. random*.ti,ab. 44. factorial*.ti,ab. 45. (crossover* or cross over*).ti,ab. 46. ((doubl* or singi*) adj blind*).ti,ab. 47. (assign* or allocat* or volunteer* or placebo*).ti,ab.		
17. animal model/ 18. exp Rodent/ 19. (rat or rats or mouse or mice).ti. 20. or/12-19 21. 4 not 20 22. limit 21 to English language 23. exp rehabilitation/ 24. rehab'.ti,ab. 26. (prehabilitat' or pre habilitat').ti,ab. 27. *mobilization/ 28. (early adj3 (ambulation or mobili*)).ti,ab. 29. *physiotherapy/ or *kinesiotherapy/ or *exercise/ or *occupational therapy/ or *recreational therapy/ or *recreational therapy/ or *stretching exercise/ or *orthopedic manipulation/ or *resistal training/ 31. ((physical* or exercise* or motion or movement or occupational or recreation* or vocational) adj3 (therap* or condition*)).ti,ab. 32. ((standard?ed or SE or continuous passive motion or CPM or slider board or SB or range of motion or ROM or resistance or weight bearing or equilibrium or flexibility of stretch*) adj2 (therap* or exercise*)).ti,ab. 34. physiotherapy/ 36. (hydrotherap* or aquatic physiotherap*).ti,ab. 37. transcutaneous electrical nerve stimulation/ 38. (electric* nerve stimulation or TENS).ti,ab. 39. *patient education/ 40. (patient* adj3 (education or information or advice)).ti,ab. 41. or/23-40 42. 22 and 41 43. random*.ti,ab. 44. factorial*.ti,ab. 45. ((crossover* or cross over*).ti,ab. 46. ((doubl* or sing!*) adj blind*).ti,ab. 47. (assign* or allocat* or volunteer* or placebo*).ti,ab.	_	
18. exp Rodent/ 19. (rat or rats or mouse or mice).ti. 20. or/12-19 21. 4 not 20 22. limit 21 to English language 23. exp rehabilitation / rehabilitation nursing/ 24. rehabilitation nursing/ 25. rehab*.ti,ab. 26. (prehabilitat* or pre habilitat*).ti,ab. 27. *mobilization/ 28. (early adj3 (ambulation or mobili*)).ti,ab. 29. *physiotherapy/ or *kinesiotherapy/ or *exercise/ or *occupational therapy/ or *recreational therapy/ or *vocational rehabilitation/ 30. *movement therapy/ or *stretching exercise/ or *orthopedic manipulation/ or *resista training/ 31. ((physical* or exercise* or motion or movement or occupational or recreation* or vocational) adj3 (therap* or condition*)).ti,ab. 32. (manipulation or MUA).ti,ab. 33. ((standardi?ed or SE or continuous passive motion or CPM or slider board or SB or range of motion or ROM or resistance or weight bearing or equilibrium or flexibility of stretch*) adj2 (therap* or exercise*)).ti,ab. 34. physiotherap*.ti,ab. 35. hydrotherapy/ 36. (hydrotherapy or aquatic physiotherap*).ti,ab. 37. transcutaneous electrical nerve stimulation/ 48. (electric* nerve stimulation or TENS).ti,ab. 49. *patient education/ 40. (patient* adj3 (education or information or advice)).ti,ab. 41. or/23-40 42. 22 and 41 43. random*.ti,ab. 44. factorial*.ti,ab. 45. (crossover* or cross over*).ti,ab. 46. ((doubl* or singl*) adj blind*).ti,ab. 47. (assign* or allocat* or volunteer* or placebo*).ti,ab. 48. crossover procedure/		
19. (rat or rats or mouse or mice).ti. 20. or/12-19 21. 4 not 20 22. limit 21 to English language 23. exp rehabilitation/ 24. rehabilitation nursing/ 25. rehab* ti, ab. 26. (prehabilitation or mobili*)).ti, ab. 27. *mobilization/ 28. (early adj3 (ambulation or mobili*)).ti, ab. 29. *physiotherapy/ or *kinesiotherapy/ or *exercise/ or *occupational therapy/ or *recreational therapy/ or *vocational rehabilitation/ 30. *movement therapy/ or *stretching exercise/ or *orthopedic manipulation/ or *resistal training/ 31. ((physical* or exercise* or motion or movement or occupational or recreation* or vocational) adj3 (therap* or condition*)).ti,ab. 32. (manipulation or MUA).ti,ab. 33. ((standard/?ed or SE or continuous passive motion or CPM or slider board or SB or range of motion or ROM or resistance or weight bearing or equilibrium or flexibility of stretch*) adj2 (therap* or exercise*)).ti,ab. 34. physiotherap*.ti,ab. 35. hydrotherapy/ 36. (hydrotherap* or aquatic physiotherap*).ti,ab. 37. transcutaneous electrical nerve stimulation/ 48. (electric* nerve stimulation or TENS).ti,ab. 49. *patient education/ 40. (patient* adj3 (education or information or advice)).ti,ab. 41. or/23-40 42. 22 and 41 43. random*.ti,ab. 44. factorial*.ti,ab. 45. (crossover* or cross over*).ti,ab. 46. ((doubl* or singl*) adj blind*).ti,ab. 47. (assign* or allocat* or volunteer* or placebo*).ti,ab. 48. crossover procedure/		
20. or/12-19 21. 4 not 20 22. limit 21 to English language 23. exp rehabilitation/ 24. rehabilitation nursing/ 25. rehab*, ti,ab. 26. (prehabilitat* or pre habilitat*), ti,ab. 27. *mobilization/ 28. (early adj3 (ambulation or mobili*)), ti,ab. 29. *physiotherapy/ or *kinesiotherapy/ or *exercise/ or *occupational therapy/ or *recreational therapy/ or *vocational rehabilitation/ 30. *movement therapy/ or *stretching exercise/ or *orthopedic manipulation/ or *resista training/ 31. ((physical* or exercise* or motion or movement or occupational or recreation* or vocational) adj3 (therap* or condition*)), ti,ab. 32. ((manipulation or MUA), ti,ab. 33. ((standardî?ed or SE or continuous passive motion or CPM or slider board or SB or range of motion or ROM or resistance or weight bearing or equilibrium or flexibility of stretch*) adj2 (therap* or exercise*)), ti,ab. 34. physiotherap*, ti,ab. 35. hydrotherapy/ 36. (hydrotherap* or aquatic physiotherap*), ti,ab. 37. transcutaneous electrical nerve stimulation/ 38. (electric* nerve stimulation or TENS), ti,ab. 39. *patient education/ 40. (patient* adj3 (education or information or advice)), ti, ab. 41. or/23-40 42. 22 and 41 43. random*, ti,ab. 44. factorial*, ti,ab. 45. (crossover* or cross over*), ti,ab. 46. ((doubl* or singl*) adj blind*), ti,ab. 47. (assign* or allocat* or volunteer* or placebo*), ti,ab. 48. crossover procedure/		•
21. 4 not 20 22. limit 21 to English language 23. exp rehabilitation/ 24. rehabilitation nursing/ 25. rehab*.ti,ab. 26. (prehabilitat* or pre habilitat*).ti,ab. 27. *mobilization/ 28. (early adj3 (ambulation or mobili*)).ti,ab. 29. *physiotherapy/ or *kinesiotherapy/ or *exercise/ or *occupational therapy/ or *recreational therapy/ or *vocational rehabilitation/ 30. *movement therapy/ or *stretching exercise/ or *orthopedic manipulation/ or *resista training/ 31. ((physical* or exercise* or motion or movement or occupational or recreation* or vocational) adj3 (therap* or condition*)).ti,ab. 32. (manipulation or MUA).ti,ab. 33. ((standardi?ed or SE or continuous passive motion or CPM or slider board or SB or range of motion or ROM or resistance or weight bearing or equilibrium or flexibility or stretch*) adj2 (therap* or exercise*)).ti,ab. 34. physiotherap*.ti,ab. 35. hydrotherap*.ti,ab. 36. (hydrotherap* or aquatic physiotherap*).ti,ab. 37. transcutaneous electrical nerve stimulation/ 38. (electric* nerve stimulation or TENS).ti,ab. 39. *patient education/ 40. (patient* adj3 (education or information or advice)).ti,ab. 41. or/23-40 22 and 41 33. random*.ti,ab. 44. factorial*.ti,ab. 45. (crossover* or cross over*).ti,ab. 46. ((doubl* or singl*) adj blind*).ti,ab. 47. (assign* or allocat* or volunteer* or placebo*).ti,ab. 48. crossover procedure/		
22. limit 21 to English language 23. exp rehabilitation/ 24. rehabilitation nursing/ 25. rehab*.ti,ab. 26. (prehabilitat* or pre habilitat*).ti,ab. 27. *mobilization/ 28. (early adj3 (ambulation or mobili*)).ti,ab. 29. *physiotherapy/ or *kinesiotherapy/ or *exercise/ or *occupational therapy/ or *recreational therapy/ or *vocational rehabilitation/ 30. *movement therapy/ or *stretching exercise/ or *orthopedic manipulation/ or *resista training/ 31. ((physical* or exercise* or motion or movement or occupational or recreation* or vocational) adj3 (therap* or condition*)).ti,ab. 32. (manipulation or MUA).ti,ab. 33. ((standardi?ed or SE or continuous passive motion or CPM or slider board or SB or range of motion or ROM or resistance or weight bearing or equilibrium or flexibility of stretch*) adj2 (therap* or exercise*)).ti,ab. 34. physiotherap*.ti,ab. 35. hydrotherap* or aquatic physiotherap*).ti,ab. 36. ((hydrotherap* or aquatic physiotherap*).ti,ab. 37. transcutaneous electrical nerve stimulation/ 38. (electric* nerve stimulation or TENS).ti,ab. 39. *patient education/ 40. (patient* adj3 (education or information or advice)).ti,ab. 41. or/23-40 42. 22 and 41 43. random*.ti,ab. 44. factorial*.ti,ab. 45. (crossover* or cross over*).ti,ab. 46. ((doubl* or singl*) adj blind*).ti,ab. 47. (assign* or allocat* or volunteer* or placebo*).ti,ab. 48. crossover procedure/		
23. exp rehabilitation/ 24. rehabilitation nursing/ 25. rehab*.ti,ab. 26. (prehabilitat* or pre habilitat*).ti,ab. 27. *mobilization/ 28. (early adj3 (ambulation or mobili*)).ti,ab. 29. *physiotherapy/ or *kinesiotherapy/ or *exercise/ or *occupational therapy/ or *recreational therapy/ or *vocational rehabilitation/ 30. *movement therapy/ or *stretching exercise/ or *orthopedic manipulation/ or *resista training/ 31. ((physical* or exercise* or motion or movement or occupational or recreation* or vocational) adj3 (therap* or condition*)).ti,ab. 32. (manipulation or MUA).ti,ab. 33. ((standardi?ed or SE or continuous passive motion or CPM or slider board or SB or range of motion or ROM or resistance or weight bearing or equilibrium or flexibility of stretch*) adj2 (therap* or exercise*)).ti,ab. 34. physiotherap*.ti,ab. 35. hydrotherapy/ 36. (hydrotherap* or aquatic physiotherap*).ti,ab. 37. transcutaneous electrical nerve stimulation/ 38. (electric* nerve stimulation or TENS).ti,ab. 39. *patient education/ 40. (patient* adj3 (education or information or advice)).ti,ab. 41. or/23-40 42. 22 and 41 43. random*.ti,ab. 44. factorial*.ti,ab. 45. (crossover* or cross over*).ti,ab. 46. ((doubl* or singl*) adj blind*).ti,ab. 47. (assign* or allocat* or volunteer* or placebo*).ti,ab. 48. crossover procedure/		
rehabilitation nursing/ rehab*.ti,ab. (prehabilitat* or pre habilitat*).ti,ab. (prehabilitat* or pre habilitat*).ti,ab. (early adj3 (ambulation or mobili*)).ti,ab. (manipulation or mobili*).ti,ab. ((physical* or exercise* or motion or movement or occupational or recreation* or vocational) adj3 (therap* or condition*)).ti,ab. ((standardi?ed or SE or continuous passive motion or CPM or slider board or SB or range of motion or ROM or resistance or weight bearing or equilibrium or flexibility of stretch*) adj2 (therap* or exercise*)).ti,ab. physiotherap*.ti,ab. hydrotherapy/ (hydrotherap* or aquatic physiotherap*).ti,ab. transcutaneous electrical nerve stimulation/ (electric* nerve stimulation or TENS).ti,ab. *patient education/ (patient* adj3 (education or information or advice)).ti,ab. (ror/23-40 22 and 41 3. random*.ti,ab. 44. factorial*.ti,ab. 45. (crossover* or cross over*).ti,ab. 46. ((doubl* or singl*) adj blind*).ti,ab. 47. (assign* or allocat* or volunteer* or placebo*).ti,ab. crossover procedure/		
25. rehab*.ti,ab. 26. (prehabilitat* or pre habilitat*).ti,ab. 27. *mobilization/ 28. (early adj3 (ambulation or mobili*)).ti,ab. 29. *physiotherapy/ or *kinesiotherapy/ or *exercise/ or *occupational therapy/ or *recreational therapy/ or *vocational rehabilitation/ 30. *movement therapy/ or *stretching exercise/ or *orthopedic manipulation/ or *resista training/ 31. ((physical* or exercise* or motion or movement or occupational or recreation* or vocational) adj3 (therap* or condition*)).ti,ab. 32. ((manipulation or MUA).ti,ab. 33. ((standardi?ed or SE or continuous passive motion or CPM or slider board or SB or range of motion or ROM or resistance or weight bearing or equilibrium or flexibility of stretch*) adj2 (therap* or exercise*)).ti,ab. 34. physiotherap*.ti,ab. 35. hydrotherapy/ 36. (hydrotherap* or aquatic physiotherap*).ti,ab. 37. transcutaneous electrical nerve stimulation/ 38. (electric* nerve stimulation or TENS).ti,ab. 39. *patient education/ 40. (patient* adj3 (education or information or advice)).ti,ab. 41. or/23-40 42. 22 and 41 43. random*.ti,ab. 44. factorial*.ti,ab. 45. (crossover* or cross over*).ti,ab. 46. ((doubl* or singl*) adj blind*).ti,ab. 47. (assign* or allocat* or volunteer* or placebo*).ti,ab.		- ·
26. (prehabilitat* or pre habilitat*).ti,ab. 27. *mobilization/ 28. (early adj3 (ambulation or mobili*)).ti,ab. 29. *physiotherapy/ or *kinesiotherapy/ or *exercise/ or *occupational therapy/ or *recreational therapy/ or *vocational rehabilitation/ 30. *movement therapy/ or *stretching exercise/ or *orthopedic manipulation/ or *resistal training/ 31. ((physical* or exercise* or motion or movement or occupational or recreation* or vocational) adj3 (therap* or condition*)).ti,ab. 32. (manipulation or MUA).ti,ab. 33. ((standardi?ed or SE or continuous passive motion or CPM or slider board or SB or range of motion or ROM or resistance or weight bearing or equilibrium or flexibility of stretch*) adj2 (therap* or exercise*)).ti,ab. 34. physiotherap*.ti,ab. 35. hydrotherapy/ 36. (hydrotherapy/ 36. (hydrotherap* or aquatic physiotherap*).ti,ab. 37. transcutaneous electrical nerve stimulation/ 38. (electric* nerve stimulation or TENS).ti,ab. 39. *patient education/ 40. (patient* adj3 (education or information or advice)).ti,ab. 41. or/23-40 42. 22 and 41 43. random*.ti,ab. 44. factorial*.ti,ab. 45. (crossover* or cross over*).ti,ab. 46. ((doubl* or singl*) adj blind*).ti,ab. 47. (assign* or allocat* or volunteer* or placebo*).ti,ab. 48. crossover procedure/		
27. *mobilization/ 28. (early adj3 (ambulation or mobili*)).ti,ab. 29. *physiotherapy/ or *kinesiotherapy/ or *exercise/ or *occupational therapy/ or *recreational therapy/ or *vocational rehabilitation/ 30. *movement therapy/ or *stretching exercise/ or *orthopedic manipulation/ or *resista training/ 31. ((physical* or exercise* or motion or movement or occupational or recreation* or vocational) adj3 (therap* or condition*)).ti,ab. 32. (manipulation or MUA).ti,ab. 33. ((standardi?ed or SE or continuous passive motion or CPM or slider board or SB or range of motion or ROM or resistance or weight bearing or equilibrium or flexibility of stretch*) adj2 (therap* or exercise*)).ti,ab. 34. physiotherap*.ti,ab. 35. hydrotherapy/ 36. ((hydrotherap* or aquatic physiotherap*).ti,ab. 37. transcutaneous electrical nerve stimulation/ 38. (electric* nerve stimulation or TENS).ti,ab. 39. *patient education/ 40. (patient* adj3 (education or information or advice)).ti,ab. 41. or/23-40 42. 22 and 41 43. random*.ti,ab. 44. factorial*.ti,ab. 45. (crossover* or cross over*).ti,ab. 46. ((doubl* or singl*) adj blind*).ti,ab. 47. (assign* or allocat* or volunteer* or placebo*).ti,ab.		
28. (early adj3 (ambulation or mobili*)).ti,ab. 29. *physiotherapy/ or *kinesiotherapy/ or *exercise/ or *occupational therapy/ or *recreational therapy/ or *vocational rehabilitation/ 30. *movement therapy/ or *stretching exercise/ or *orthopedic manipulation/ or *resista training/ 31. ((physical* or exercise* or motion or movement or occupational or recreation* or vocational) adj3 (therap* or condition*)).ti,ab. 32. (manipulation or MUA).ti,ab. 33. ((standardi?ed or SE or continuous passive motion or CPM or slider board or SB or range of motion or ROM or resistance or weight bearing or equilibrium or flexibility of stretch*) adj2 (therap* or exercise*)).ti,ab. 34. physiotherap*.ti,ab. 35. hydrotherapy/ 36. (hydrotherapy/ 37. transcutaneous electrical nerve stimulation/ 38. (electric* nerve stimulation or TENS).ti,ab. 39. *patient education/ 40. (patient* adj3 (education or information or advice)).ti,ab. 41. or/23-40 42. 22 and 41 43. random*.ti,ab. 44. factorial*.ti,ab. 45. (crossover* or cross over*).ti,ab. 46. ((doubl* or singl*) adj blind*).ti,ab. 47. (assign* or allocat* or volunteer* or placebo*).ti,ab. 48. crossover procedure/		
29. *physiotherapy/ or *kinesiotherapy/ or *exercise/ or *occupational therapy/ or *recreational therapy/ or *vocational rehabilitation/ 30. *movement therapy/ or *stretching exercise/ or *orthopedic manipulation/ or *resista training/ 31. ((physical* or exercise* or motion or movement or occupational or recreation* or vocational) adj3 (therap* or condition*)).ti,ab. 32. (manipulation or MUA).ti,ab. 33. ((standardi?ed or SE or continuous passive motion or CPM or slider board or SB or range of motion or ROM or resistance or weight bearing or equilibrium or flexibility of stretch*) adj2 (therap* or exercise*)).ti,ab. 34. physiotherap*.ti,ab. 35. hydrotherapy/ 36. (hydrotherap* or aquatic physiotherap*).ti,ab. 37. transcutaneous electrical nerve stimulation/ 38. (electric* nerve stimulation or TENS).ti,ab. 39. *patient education/ 40. (patient* adj3 (education or information or advice)).ti,ab. 41. or/23-40 42. 22 and 41 43. random*.ti,ab. 44. factorial*.ti,ab. 45. (crossover* or cross over*).ti,ab. 46. ((doubl* or singl*) adj blind*).ti,ab. 47. (assign* or allocat* or volunteer* or placebo*).ti,ab.		
30. *movement therapy/ or *stretching exercise/ or *orthopedic manipulation/ or *resista training/ 31. ((physical* or exercise* or motion or movement or occupational or recreation* or vocational) adj3 (therap* or condition*)).ti,ab. 32. (manipulation or MUA).ti,ab. 33. ((standardi?ed or SE or continuous passive motion or CPM or slider board or SB or range of motion or ROM or resistance or weight bearing or equilibrium or flexibility of stretch*) adj2 (therap* or exercise*)).ti,ab. 34. physiotherap*.ti,ab. 35. hydrotherapy/ 36. (hydrotherap* or aquatic physiotherap*).ti,ab. 37. transcutaneous electrical nerve stimulation/ 38. (electric* nerve stimulation or TENS).ti,ab. 39. *patient education/ 40. (patient* adj3 (education or information or advice)).ti,ab. 41. or/23-40 42. 22 and 41 43. random*.ti,ab. 44. factorial*.ti,ab. 45. (crossover* or cross over*).ti,ab. 46. ((doubl* or singl*) adj blind*).ti,ab. 47. (assign* or allocat* or volunteer* or placebo*).ti,ab.	_	*physiotherapy/ or *kinesiotherapy/ or *exercise/ or *occupational therapy/ or
31. ((physical* or exercise* or motion or movement or occupational or recreation* or vocational) adj3 (therap* or condition*)).ti,ab. 32. (manipulation or MUA).ti,ab. 33. ((standardi?ed or SE or continuous passive motion or CPM or slider board or SB or range of motion or ROM or resistance or weight bearing or equilibrium or flexibility of stretch*) adj2 (therap* or exercise*)).ti,ab. 34. physiotherap*.ti,ab. 35. hydrotherapy/ 36. (hydrotherap* or aquatic physiotherap*).ti,ab. 37. transcutaneous electrical nerve stimulation/ 38. (electric* nerve stimulation or TENS).ti,ab. 39. *patient education/ 40. (patient* adj3 (education or information or advice)).ti,ab. 41. or/23-40 42. 22 and 41 43. random*.ti,ab. 44. factorial*.ti,ab. 45. (crossover* or cross over*).ti,ab. 46. ((doubl* or singl*) adj blind*).ti,ab. 47. (assign* or allocat* or volunteer* or placebo*).ti,ab. 48. crossover procedure/	30.	*movement therapy/ or *stretching exercise/ or *orthopedic manipulation/ or *resistance
32. (manipulation or MUA).ti,ab. 33. ((standardi?ed or SE or continuous passive motion or CPM or slider board or SB or range of motion or ROM or resistance or weight bearing or equilibrium or flexibility of stretch*) adj2 (therap* or exercise*)).ti,ab. 34. physiotherap*.ti,ab. 35. hydrotherapy/ 36. (hydrotherap* or aquatic physiotherap*).ti,ab. 37. transcutaneous electrical nerve stimulation/ 38. (electric* nerve stimulation or TENS).ti,ab. 39. *patient education/ 40. (patient* adj3 (education or information or advice)).ti,ab. 41. or/23-40 42. 22 and 41 43. random*.ti,ab. 44. factorial*.ti,ab. 45. (crossover* or cross over*).ti,ab. 46. ((doubl* or singl*) adj blind*).ti,ab. 47. (assign* or allocat* or volunteer* or placebo*).ti,ab. 48. crossover procedure/	31.	((physical* or exercise* or motion or movement or occupational or recreation* or
range of motion or ROM or resistance or weight bearing or equilibrium or flexibility of stretch*) adj2 (therap* or exercise*)).ti,ab. 34. physiotherap*.ti,ab. 35. hydrotherapy/ 36. (hydrotherap* or aquatic physiotherap*).ti,ab. 37. transcutaneous electrical nerve stimulation/ 38. (electric* nerve stimulation or TENS).ti,ab. 39. *patient education/ 40. (patient* adj3 (education or information or advice)).ti,ab. 41. or/23-40 42. 22 and 41 43. random*.ti,ab. 44. factorial*.ti,ab. 45. (crossover* or cross over*).ti,ab. 46. ((doubl* or singl*) adj blind*).ti,ab. 47. (assign* or allocat* or volunteer* or placebo*).ti,ab. 48. crossover procedure/	32.	
34. physiotherap*.ti,ab. 35. hydrotherapy/ 36. (hydrotherap* or aquatic physiotherap*).ti,ab. 37. transcutaneous electrical nerve stimulation/ 38. (electric* nerve stimulation or TENS).ti,ab. 39. *patient education/ 40. (patient* adj3 (education or information or advice)).ti,ab. 41. or/23-40 42. 22 and 41 43. random*.ti,ab. 44. factorial*.ti,ab. 45. (crossover* or cross over*).ti,ab. 46. ((doubl* or singl*) adj blind*).ti,ab. 47. (assign* or allocat* or volunteer* or placebo*).ti,ab. 48. crossover procedure/	33.	range of motion or ROM or resistance or weight bearing or equilibrium or flexibility or
36. (hydrotherap* or aquatic physiotherap*).ti,ab. 37. transcutaneous electrical nerve stimulation/ 38. (electric* nerve stimulation or TENS).ti,ab. 39. *patient education/ 40. (patient* adj3 (education or information or advice)).ti,ab. 41. or/23-40 42. 22 and 41 43. random*.ti,ab. 44. factorial*.ti,ab. 45. (crossover* or cross over*).ti,ab. 46. ((doubl* or singl*) adj blind*).ti,ab. 47. (assign* or allocat* or volunteer* or placebo*).ti,ab. 48. crossover procedure/	34.	
transcutaneous electrical nerve stimulation/ (electric* nerve stimulation or TENS).ti,ab. *patient education/ (patient* adj3 (education or information or advice)).ti,ab. or/23-40 22 and 41 33. random*.ti,ab. 44. factorial*.ti,ab. 45. (crossover* or cross over*).ti,ab. 46. ((doubl* or singl*) adj blind*).ti,ab. 47. (assign* or allocat* or volunteer* or placebo*).ti,ab. 48. crossover procedure/	35.	hydrotherapy/
38. (electric* nerve stimulation or TENS).ti,ab. 39. *patient education/ 40. (patient* adj3 (education or information or advice)).ti,ab. 41. or/23-40 42. 22 and 41 43. random*.ti,ab. 44. factorial*.ti,ab. 45. (crossover* or cross over*).ti,ab. 46. ((doubl* or singl*) adj blind*).ti,ab. 47. (assign* or allocat* or volunteer* or placebo*).ti,ab. 48. crossover procedure/	36.	(hydrotherap* or aquatic physiotherap*).ti,ab.
39. *patient education/ 40. (patient* adj3 (education or information or advice)).ti,ab. 41. or/23-40 42. 22 and 41 43. random*.ti,ab. 44. factorial*.ti,ab. 45. (crossover* or cross over*).ti,ab. 46. ((doubl* or singl*) adj blind*).ti,ab. 47. (assign* or allocat* or volunteer* or placebo*).ti,ab. 48. crossover procedure/	37.	transcutaneous electrical nerve stimulation/
40. (patient* adj3 (education or information or advice)).ti,ab. 41. or/23-40 42. 22 and 41 43. random*.ti,ab. 44. factorial*.ti,ab. 45. (crossover* or cross over*).ti,ab. 46. ((doubl* or singl*) adj blind*).ti,ab. 47. (assign* or allocat* or volunteer* or placebo*).ti,ab. 48. crossover procedure/	38.	(electric* nerve stimulation or TENS).ti,ab.
41. or/23-40 42. 22 and 41 43. random*.ti,ab. 44. factorial*.ti,ab. 45. (crossover* or cross over*).ti,ab. 46. ((doubl* or singl*) adj blind*).ti,ab. 47. (assign* or allocat* or volunteer* or placebo*).ti,ab. 48. crossover procedure/	39.	*patient education/
42. 22 and 41 43. random*.ti,ab. 44. factorial*.ti,ab. 45. (crossover* or cross over*).ti,ab. 46. ((doubl* or singl*) adj blind*).ti,ab. 47. (assign* or allocat* or volunteer* or placebo*).ti,ab. 48. crossover procedure/	40.	(patient* adj3 (education or information or advice)).ti,ab.
43. random*.ti,ab. 44. factorial*.ti,ab. 45. (crossover* or cross over*).ti,ab. 46. ((doubl* or singl*) adj blind*).ti,ab. 47. (assign* or allocat* or volunteer* or placebo*).ti,ab. 48. crossover procedure/	41.	or/23-40
44. factorial*.ti,ab. 45. (crossover* or cross over*).ti,ab. 46. ((doubl* or singl*) adj blind*).ti,ab. 47. (assign* or allocat* or volunteer* or placebo*).ti,ab. 48. crossover procedure/	42.	22 and 41
45. (crossover* or cross over*).ti,ab. 46. ((doubl* or singl*) adj blind*).ti,ab. 47. (assign* or allocat* or volunteer* or placebo*).ti,ab. 48. crossover procedure/	43.	random*.ti,ab.
46. ((doubl* or singl*) adj blind*).ti,ab. 47. (assign* or allocat* or volunteer* or placebo*).ti,ab. 48. crossover procedure/	44.	factorial*.ti,ab.
47. (assign* or allocat* or volunteer* or placebo*).ti,ab. 48. crossover procedure/	45.	(crossover* or cross over*).ti,ab.
48. crossover procedure/	46.	((doubl* or singl*) adj blind*).ti,ab.
	47.	(assign* or allocat* or volunteer* or placebo*).ti,ab.
49. single blind procedure/	48.	crossover procedure/
-	49.	single blind procedure/
50. randomized controlled trial/	50.	randomized controlled trial/

51.	double blind procedure/
52.	or/43-51
53.	systematic review/
54.	meta-analysis/
55.	(meta analy* or metanaly* or metaanaly* or meta regression).ti,ab.
56.	((systematic* or evidence*) adj3 (review* or overview*)).ti,ab.
57.	(reference list* or bibliograph* or hand search* or manual search* or relevant journals).ab.
58.	(search strategy or search criteria or systematic search or study selection or data extraction).ab.
59.	(search* adj4 literature).ab.
60.	(medline or pubmed or cochrane or embase or psychlit or psyclit or psychinfo or psycinfo or cinahl or science citation index or bids or cancerlit).ab.
61.	cochrane.jw.
62.	((multiple treatment* or indirect or mixed) adj2 comparison*).ti,ab.
63.	or/53-62
64.	Clinical study/
65.	Observational study/
66.	family study/
67.	longitudinal study/
68.	retrospective study/
69.	prospective study/
70.	cohort analysis/
71.	follow-up/
72.	cohort*.ti,ab.
73.	71 and 72
74.	(cohort adj (study or studies or analys* or data)).ti,ab.
75.	((follow up or observational or uncontrolled or non randomi#ed or epidemiologic*) adj (study or studies or data)).ti,ab.
76.	((longitudinal or retrospective or prospective or cross sectional) and (study or studies or review or analys* or cohort* or data)).ti,ab.
77.	(before adj2 after adj2 (study or studies or data)).ti,ab.
78.	or/64-70,73-77
79.	exp case control study/
80.	case control*.ti,ab.
81.	or/79-80
82.	78 or 81
83.	cross-sectional study/
84.	(cross sectional and (study or studies or review or analys* or cohort* or data)).ti,ab.
85.	or/83-84
86.	78 or 85
87.	78 or 81 or 85
88.	42 and (52 or 63 or 87)

Cochrane Library (Wiley) search terms

#1.	MeSH descriptor: [Arthroplasty] this term only
#2.	MeSH descriptor: [Arthroplasty, Replacement] this term only

#3.	MeSH descriptor: [Arthroplasty, Replacement, Hip] this term only		
#4.	MeSH descriptor: [Arthroplasty, Replacement, Knee] this term only		
#5.	MeSH descriptor: [Arthroplasty, Replacement, Shoulder] this term only		
#6.	MeSH descriptor: [Hemiarthroplasty] this term only		
#7.	(or #1-#6)		
#8.	MeSH descriptor: [Joint Prosthesis] this term only		
#9.	MeSH descriptor: [Hip Prosthesis] this term only		
#10.	MeSH descriptor: [Knee Prosthesis] this term only		
#11.	MeSH descriptor: [Shoulder Prosthesis] this term only		
#12.	(or #8-#11)		
#13.	((joint* or knee* or shoulder* or hip*) near/5 (surger* or replace* or prosthe* or endoprosthe* or implant* or artificial or arthroplast* or hemiarthroplast*)):ti,ab		
#14.	(or #7, #12-#13)		
#15.	MeSH descriptor: [Rehabilitation] explode all trees		
#16.	MeSH descriptor: [Rehabilitation Nursing] explode all trees		
#17.	rehab*:ti,ab		
#18.	(prehabilitat* or pre habilitat*):ti,ab		
#19.	MeSH descriptor: [Early Ambulation] this term only		
#20.	(early near/3 (ambulation or mobili*)):ti,ab		
#21.	MeSH descriptor: [Physical Therapy Modalities] this term only		
#22.	MeSH descriptor: [Exercise Therapy] explode all trees		
#23.	MeSH descriptor: [Physical Conditioning, Human] this term only		
#24.	MeSH descriptor: [Occupational Therapy] this term only		
#25.	MeSH descriptor: [Recreation Therapy] this term only		
#26.	MeSH descriptor: [Rehabilitation, Vocational] this term only		
#27.	MeSH descriptor: [Motion Therapy, Continuous Passive] this term only		
#28.	MeSH descriptor: [Muscle Stretching Exercises] this term only		
#29.	MeSH descriptor: [Manipulation, Orthopedic] this term only		
#30.	MeSH descriptor: [Resistance Training] this term only		
#31.	((physical* or exercise* or motion or movement or occupational or recreation* or vocational) near/3 (therap* or condition*)):ti,ab		
#32.	(manipulation or MUA):ti,ab		
#33.	((standardised or standardized or SE or continuous passive motion or CPM or slider board or SB or range of motion or ROM or resistence or weight bearing or equilibrium or flexibility or stretch*) near/2 (therap* or exercise*)):ti,ab		
#34.	physiotherap*:ti,ab		
#35.	MeSH descriptor: [Hydrotherapy] this term only		
#36.	(hydrotherap* or aquatic physiotherap*):ti,ab		
#37.	MeSH descriptor: [Transcutaneous Electric Nerve Stimulation] this term only		
#38.	(electric* nerve stimulation or TENS):ti,ab		
#39.	MeSH descriptor: [Patient Education as Topic] this term only		
#40.	(patient* near/3 (education or information or advice)):ti,ab		
#41.	(or #15-#40)		
#42.	#14 and #41		

B.2 Health Economics literature search strategy

Health economic evidence was identified by conducting a broad search relating to the joint replacement population in NHS Economic Evaluation Database (NHS EED – this ceased to be updated after March 2015) and the Health Technology Assessment database (HTA) with no date restrictions. NHS EED and HTA databases are hosted by the Centre for Research and Dissemination (CRD). Additional health economic searches were run in Medline and Embase.

Table 7: Database date parameters and filters used

Database	Dates searched	Search filter used
Medline	2014 – 01 May 2019	Exclusions Health economics studies
Embase	2014 – 01 May 2019	Exclusions Health economics studies
Centre for Research and Dissemination (CRD)	HTA - Inception – 01 May 2019 NHSEED - Inception to March 2015	None

Medline (Ovid) search terms

1.	arthroplasty/ or arthroplasty, replacement/ or arthroplasty, replacement, hip/ or arthroplasty, replacement, knee/ or arthroplasty, replacement, shoulder/ or hemiarthroplasty/	
2.	joint prosthesis/ or hip prosthesis/ or knee prosthesis/ or shoulder prosthesis/	
3.	((joint* or knee* or shoulder* or hip*) adj5 (surger* or replace* or prosthe* or endoprosthe* or implant* or artificial or arthroplast* or hemiarthroplast*)).ti,ab.	
4.	or/1-3	
5.	letter/	
6.	editorial/	
7.	news/	
8.	exp historical article/	
9.	Anecdotes as Topic/	
10.	comment/	
11.	case report/	
12.	(letter or comment*).ti.	
13.	or/5-12	
14.	randomized controlled trial/ or random*.ti,ab.	
15.	13 not 14	
16.	animals/ not humans/	
17.	exp Animals, Laboratory/	
18.	exp Animal Experimentation/	
19.	exp Models, Animal/	
20.	exp Rodentia/	
21.	(rat or rats or mouse or mice).ti.	
22.	or/15-21	
23.	4 not 22	
24.	limit 23 to English language	

25.	Economics/	
26.	Value of life/	
27.	exp "Costs and Cost Analysis"/	
28.	exp Economics, Hospital/	
29.	exp Economics, Medical/	
30.	Economics, Nursing/	
31.	Economics, Pharmaceutical/	
32.	exp "Fees and Charges"/	
33.	exp Budgets/	
34.	budget*.ti,ab.	
35.	cost*.ti.	
36.	(economic* or pharmaco?economic*).ti.	
37.	(price* or pricing*).ti,ab.	
38.	(cost* adj2 (effective* or utilit* or benefit* or minimi* or unit* or estimat* or variable*)).ab.	
39.	(financ* or fee or fees).ti,ab.	
40.	(value adj2 (money or monetary)).ti,ab.	
41.	or/25-40	
42.	24 and 41	

Embase (Ovid) search terms

1.	*arthroplasty/ or *replacement arthroplasty/ or *hip replacement/ or *knee replacement/ or *shoulder replacement/ or *hemiarthroplasty/
2.	*joint prosthesis/ or *hip prosthesis/ or *knee prosthesis/ or *shoulder prosthesis/
3.	((joint* or knee* or shoulder* or hip*) adj5 (surger* or replace* or prosthe* or endoprosthe* or implant* or artificial or arthroplast* or hemiarthroplast*)).ti,ab.
4.	or/1-3
5.	letter.pt. or letter/
6.	note.pt.
7.	editorial.pt.
8.	case report/ or case study/
9.	(letter or comment*).ti.
10.	or/5-9
11.	randomized controlled trial/ or random*.ti,ab.
12.	10 not 11
13.	animal/ not human/
14.	nonhuman/
15.	exp Animal Experiment/
16.	exp Experimental Animal/
17.	animal model/
18.	exp Rodent/
19.	(rat or rats or mouse or mice).ti.
20.	or/12-19
21.	4 not 20

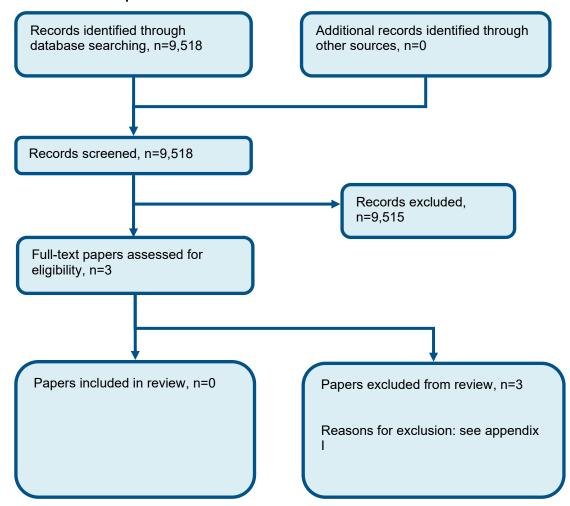
22.	limit 21 to English language	
23.	health economics/	
24.	exp economic evaluation/	
25.	exp health care cost/	
26.	exp fee/	
27.	budget/	
28.	funding/	
29.	budget*.ti,ab.	
30.	cost*.ti.	
31.	(economic* or pharmaco?economic*).ti.	
32.	(price* or pricing*).ti,ab.	
33.	(cost* adj2 (effective* or utilit* or benefit* or minimi* or unit* or estimat* or variable*)).ab.	
34.	(financ* or fee or fees).ti,ab.	
35.	(value adj2 (money or monetary)).ti,ab.	
36.	or/23-35	
37.	22 and 36	

NHS EED and HTA (CRD) search terms

#1.	MeSH DESCRIPTOR arthroplasty
#2.	MeSH DESCRIPTOR arthroplasty, replacement
#3.	MeSH DESCRIPTOR arthroplasty, replacement, hip
#4.	MeSH DESCRIPTOR arthroplasty, replacement, knee
#5.	MeSH DESCRIPTOR arthroplasty, replacement, shoulder
#6.	MeSH DESCRIPTOR hemiarthroplasty
#7.	MeSH DESCRIPTOR joint prosthesis
#8.	MeSH DESCRIPTOR hip prosthesis
#9.	MeSH DESCRIPTOR knee prosthesis
#10.	MeSH DESCRIPTOR shoulder prosthesis
#11.	(((joint* or knee* or shoulder* or hip*) adj5 (surger* or replace* or prosthe* or endoprosthe* or implant* or artificial or arthroplast* or hemiarthroplast*)))
#12.	(#1 OR #2 OR #3 OR #4 OR #5 OR #6 OR #7 OR #8 OR #9 OR #10 OR #11) IN NHSEED
#13.	(#1 OR #2 OR #3 OR #4 OR #5 OR #6 OR #7 OR #8 OR #9 OR #10 OR #11) IN HTA

Appendix C: Clinical evidence selection

Figure 1: Flow chart of clinical study selection for the review of inpatient rehabilitation after shoulder replacement



Appendix D: Clinical evidence tables

No studies were identified.

Appendix E: Forest plots

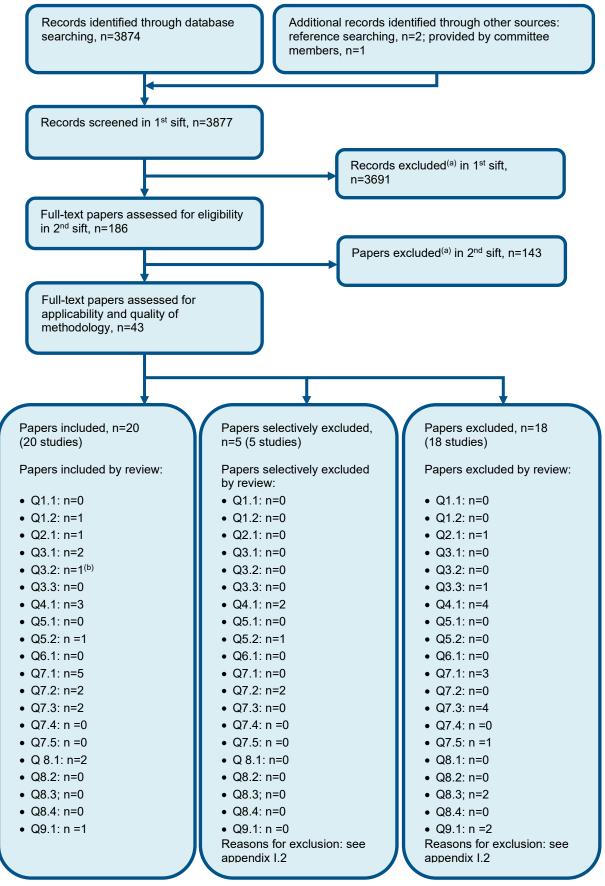
No studies were identified.

Appendix F: GRADE tables

No studies were identified.

Appendix G: Health economic evidence selection

Figure 2: Flow chart of health economic study selection for the guideline



- a) Non-relevant population, intervention, comparison, design or setting; non-English language
- b) One study was applicable to both Q3.1 and Q3.2

Appendix H: Health economic evidence tables

No studies were identified.

Appendix I: Excluded studies

I.1 Excluded clinical studies

Table 8: Studies excluded from the clinical review

Study	Exclusion reason
Hultenheim Klintberg 2008 ²	Not guideline condition
Kluczynski 2016 ³	Not guideline condition
Saltzman 2017 ⁵	Not guideline condition

I.2 Excluded health economic studies

None.

Appendix J: Research recommendations

J.1 Early shoulder mobilisation

Research question: Is early mobilisation of the shoulder after primary elective shoulder replacement surgery more effective than delayed mobilisation in restoring rapid return of function and pain relief?

Why this is important:

Shoulder replacement surgery including both anatomic and reverse replacements is on the increase. Post operative physiotherapy is considered routine practice following this surgery however there is a lack of high quality trials and clinical consensus on when movement of the shoulder should be encouraged following surgery. Restoring range of motion and strength following shoulder replacement is considered important to obtain good outcomes. Given the rise of this procedure there is an urgent need for high quality well powered RCTs to determine effective post operative rehabilitation programmes.

PICO question	Population: People undergoing primary elective shoulder replacement Intervention(s): Mobilisation of the shoulder within 24 hours of surgery Comparison: Delayed mobilisation of the shoulder (up to 3 weeks) Outcome(s): Pain, function, health related quality of life, adverse events, health economic measures (direct and indirect costs), return to work, rate of recovery
Importance to patients or the population	The sooner the shoulder can be mobilised the sooner formal shoulder rehabilitation can begin. Getting back to a more normal functional existence is very important to people who have undergone surgery.
Relevance to NICE guidance	This could lead to a recommendation when this recommendation is updated in the future.
Relevance to the NHS	Earlier return of function may allow people to be discharged from orthopaedic care earlier.
National priorities	Not linked to any national priorities
Current evidence base	There are currently no randomised controlled trials for the timing of mobilisation of the shoulder after shoulder replacement surgery
Equality	There are no equality issues identified for this research recommendation. However the likely effect on people with neurocognitive decline or comorbidities should be considered when the results of the trial are acted upon.
Study design	Randomised controlled trial
Feasibility	It is considered feasible and will either not change or reduce costs associated with rehabilitation.
Other comments	
Importance	 High: the research is essential to inform future updates of key recommendations in the guideline.